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## Friedel-Craft Acylation of Phenols in 1-Ethyl-3-Methylimidazolium Tetrachloroaluminate Ionic Liquid.

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### ABSTRACT

Through this review we would like to introduce clean and efficient method of most conventional Friedel-Craft acylation of phenols using Ionic liquid. This method has best results of acylated phenols in terms of quality and yields are concerned. The Friedel-Craft acylation is an everyday applicable industrial synthesis. Phenols are dihydric, trihydric as well as monohydric hydrocarbons used to undergo acylation. Acetyl chloride is best suitable reagent for aromatic C-acylation. Ionic liquid [EMIM][AlCl<sub>4</sub>] has best solvation and catalytic effect in the reaction.

**Key Word:** Friedel-Craft Acylation, Phenols, Ionic liquid [EMIM][AlCl<sub>4</sub>], Acetyl Chloride

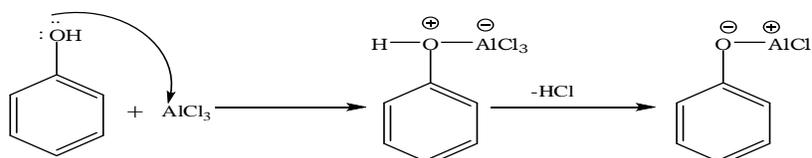
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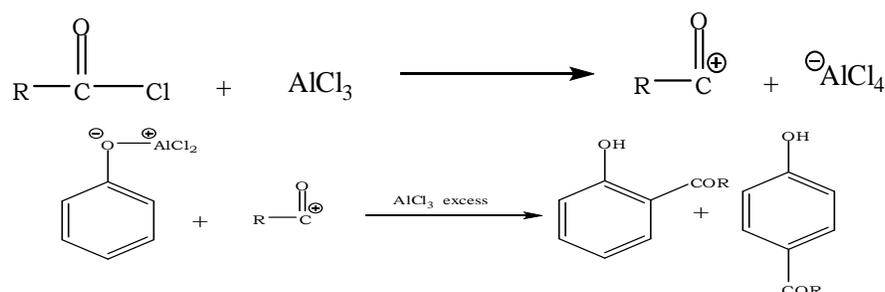
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## INTRODUCTION

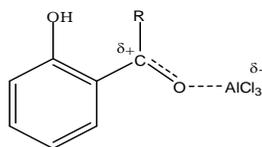
The Friedel-Crafts<sup>1</sup> reaction is one of the most fundamental reactions from synthetic, industrial and pharmacological points of view. In 1877 Friedel and Crafts discovered the catalytic action of aluminium chloride, which is used to synthesis benzene hydrocarbons as well as ketones. Phenols are upon treatment with acid halides, anhydrides in presence of anhydrous aluminium chloride produce *ortho*- and *para*-acylphenols. Phenols react with aluminium chloride to form chloroaluminium salt which is more reactive than phenol.



The chloroaluminium salt reacts with acid halide electrophile yielding mainly *ortho*- and *para*-acyl phenols in presence of the additional amount of aluminium chloride.



Care must be taken to ensure that excess of aluminium chloride is used because phenol reacts with it. One significant point of acylation is that one mole of aluminium chloride is required for the reaction compared with the catalytic quantity, only that is required in the latter. This is because the aluminium chloride complexes with the product ketone as it is formed & is thereby removed from further participation in the reaction.



Electrophilic species that can react with aromatic nucleus are dicationic covers the reaction of several reactive electrophiles. Multiple substitutions are rarely a problem because the deactivated conjugated ketone is much less reactive than benzene. The quantum-chemical calculation of charge-transfer states as possible intermediates in electrophilic aromatic substitution reactions, making allowance for solvation effects. The effective electrophile is the acyl cation as a constituent of an ion pair, or a polarized complex.



Acyl cations have been detected in a number of solid complexes, in the liquid complex between MeCOCl & AlCl<sub>3</sub> in solution in polar solvents. In less polar solvents & under a number of other circumstances, acyl cations are not detectable & it must be the polarized complex that acts as the electrophile. To serve this purpose ionic liquid (IL) is the best solvation media.

A number of Lewis acid condensation reactions have been reported in chloroaluminate (III) ionic liquids. These are the Fischer-indol synthesis<sup>2</sup> and the Baeyer condensation<sup>3</sup>, esterifications<sup>4</sup>, Diels-Alder cycloadditions<sup>5</sup>, and the formation of 4-chloropyrans *via* Prins reaction<sup>6</sup>. A number of excellent reviews covering various aspects of ionic liquids applications have been published<sup>7</sup>.

Greener solvent ionic liquid 1-Ethyl-3-methylimidazolium tetrachloroaluminate [EMIM][AlCl<sub>4</sub>]<sup>1</sup> is affording better yields with good quality of products by reducing AlCl<sub>3</sub> in the reaction. [EMIM][AlCl<sub>4</sub>], it has selected to get good regioselectivity<sup>2</sup> during reactions. Cleaner technology is a new dimension that is emerging rapidly at both national and international level. Cleaner production has been identified as a key method for reconciling environment and economic development. The basic idea of cleaner production is to increase product efficiency while at the same time eliminate or at least minimize wastes and emissions at their source. Use of ionic liquid as a Green Chemistry is a science based non regulatory and economically driven approach to achieving the goals of environmental protection and sustainable development. Sustainability, eco-efficiency and green chemistry are new principles that are guiding the development of next generation products and processes.

#### Following are the advantages of ionic liquids

1. Gives highly polarized transition state in reaction media
2. Reduce energy requirements
3. Be atom efficient
4. Avoid use and production of toxic and dangerous chemicals
5. Produce compound which perform better or equal to the existing one and are biodegradable
6. Avoid auxiliary substances
7. Use renewable materials
8. Avoid waste
9. Use catalysts rather than stoichiometric reagents

The first step is a quaternisation of alkyl imidazoles compound typically using haloalkanes as the alkylating agent giving dialkylated imidazolium cation and a halide (typically Cl<sup>-</sup>). This anion can then be exchanged with another anion of interest using appropriate acid or salt form. Furthermore, it was found that increasing the chain length of alkyl substituents on both cations and anions leads to greater lipophilicity of the ionic liquids. They have essentially no vapor pressure, i.e. they do not evaporate and are easy to contain. They generally have reasonable thermal stability. In other words many ionic liquids have liquid ranges of more than 300°C, compared to the 100°C of liquid range of water. They are able to dissolve a wide range of organic, inorganic and organometallic compounds. Organoaluminate Ionic Liquids: a resourceful dual system of solvent and catalyst.

Organoaluminate melts are the most investigated class of molten salts. These compounds are easily prepared by mixing quaternary ammonium salts, especially N-alkylpyridinium and 1,3-dialkylimidazolium halides were among the first ambient-temperature ionic liquids, prepared in 1951. Ionic liquids containing chloroaluminate (AlCl<sub>4</sub><sup>-</sup>, Al<sub>2</sub>Cl<sub>7</sub><sup>-</sup>) anions are strong Lewis acids.

## MATERIALS AND METHOD

1-Ethyl-3-methylimidazolium chloride [EMImCl] has purchased from Sigma–Aldrich trader. AlCl<sub>3</sub> is used as Spectrochem quality. And lab grade phenols purified before experimental trials. LR grade acetyl chloride is consumed for the reactions.

### Method

Anhydrous AlCl<sub>3</sub> and EMImCl (2:1) are mixed in a suitable round bottom flask under moisture free condition allowing liberation of dense HCl fumes. This combination obtained as a ionic liquid (IL) very in molar proportion with respect to phenols.

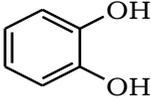
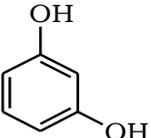
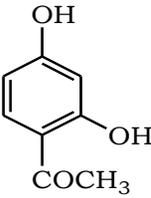
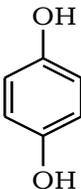
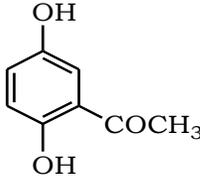
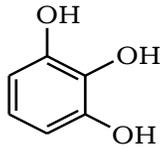
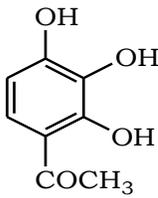
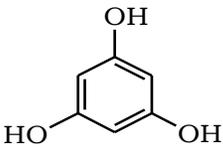
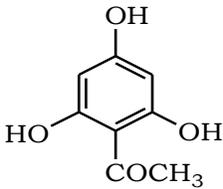
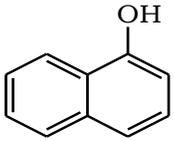
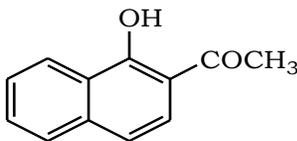
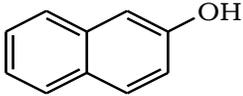
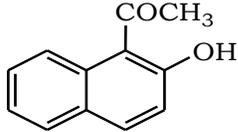
The above homogeneous IL is stirred for 15min and added phenol into it. Then slowly introduce acetyl chloride in 30 to 60min. Heated resulting reaction mass at 100 to 130°C for 1 to 2 hrs. Reaction is monitored on TLC (EtOAc/Hexane: 7/3) to check complete consumption of phenols.

### Isolation

Above resulting semi viscous reaction mass cool to room temperature and dropped slowly 1:1 HCl solution in 60min. Isolated products are dried and checked melting point.

## Experimental Methods

**Scheme 1: Friedel-Craft acylation of phenols in [EMIM][AlCl<sub>4</sub>] using acetyl chloride.**

Entry	Substrate	Ac-Cl (mol eq.)	IL (mol eq.)	Product	Yields (%)
1.		1.4	2.2	No Reaction	--
2.		1.3	2.1		76
3.		1.3	2.1		68
4.		1.42	3.3		83
5.		1.42	3.3		87
6.		1.3	1.9		80
7.		1.3	1.9		71

### Analysis

Scheme-1: **Entry 2**= 2,4 Dihydroxy acetophenone

Melting point= 141-143°C

Crystallization solvent= Water

Scheme -1: **Entry 3**= 2,5 Dihydroxy acetophenone

Melting point= 74-75°C

Crystallization solvent= Aq. ethanol

Scheme -1: **Entry 4**= 2,3,4 Trihydroxy acetophenone

Melting point= 172-173°C

Crystallization solvent= Water

Scheme -1: **Entry 5**= 2,4,6 Trihydroxy acetophenone

Melting point= 217°C

Crystallization solvent= Water

Scheme -1: **Entry 6**= 2-Acetyl, 1-naphthol

Melting point= 182-184°C

Crystallization solvent= Aq. ethanol

Scheme -1: **Entry 7**= 3-Acetyl, 2'-naphthol

Melting point= 112-113°C

Crystallization solvent= Aq. Ethanol

Isolated product quality is checked by TLC.

Structural confirmation has been done by recheck of melting point on double purification, IR spectra and functional group derivatization.

## RESULTS AND DISCUSSION

Ionic liquid using [EMIM][AlCl<sub>4</sub>] was studied with different phenols of mono, di and trihydric using acetyl chloride under solvent free condition at afford acylated ketones. The influence of acylating agents with ionic liquid study reveals that fair to very good yield of acylated phenols. The results on influence of acylating agents promoted us to evaluate the scope of this methodology for different types of phenols using highly reactive acylating agent acetyl chloride. Use of these salts eliminates the need to use volatile and hazardous halogenated solvents and also shortened the reaction times.

## CONCLUSIONS

It has been successfully demonstrated newer methodology using Ionic liquid for phenols acylation. Ionic liquids have been used as solvents for a wide range of synthetic procedures. By using ionic liquid [EMIM][AlCl<sub>4</sub>] reaction regioselectivity are improved and giving better yields of ketones. In conclusion, [EMIM][AlCl<sub>4</sub>] is an efficient, versatile, clean homogeneous and green catalyst for acylation of phenols while using acetyl chloride as acylating reagent. Therefore, it has been shown

that commercially feasible Friedel-Crafts acylation of phenols can be conducted in molten salt [EMIM][AlCl<sub>4</sub>].

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