



Short Communication

Preparation of ionic liquids and synthesis of DHPM using ILS

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Available online at: www.isca.in, www.isca.me

Received 29th November 2016, revised 15th January 2017, accepted 10th February 2017

Abstract

Alkylimidazolium and N-alkylbenzimidazolium based ionic liquids having halide and tetrafluoroborate were synthesized and used to study catalytic efficiency for the Biginelli reaction under solvent-free conditions. Among all the ionic liquids, the 1-Butyl-3-Methylimidazolium chloride found as most promising and efficient green solvent for the synthesis of Dihydropyrimidine 4. The process was simple and proceeded in excellent yields.

Keywords: Ionic liquids, Green approach, DHPM synthesis, Biginelli reaction.

Introduction

Ionic liquids are organic salts mostly composed of organic cations and inorganic anions, having boiling point below 100^oC and exhibit in most cases relatively low viscosities¹. The definition allows distinguishing them from a classical molten salt, which is generally a high-melting, highly viscous and very corrosive material.

Conventionally, ionic liquids typically contain bulky asymmetric organic cations, such as imidazolium, pyridinium, pyrrolidinium, quaternary ammonium or tetraalkyl phosphonium, having very low symmetry, weak intermolecular interactions and low charge densities². Therefore, these cations are responsible for steric hindrance in a regular packing of crystal lattice. Thus, solid crystalline state becomes energetically less promising which leads to low melting points³. Furthermore; this effect can be improved by application of anions with a delocalized charge⁴.

The main significance of ionic liquids is negligible volatility, nonflammability, their controlled properties due to arrangement of ions and high compatibility with various organic compounds and other materials. Additionally, they are immiscible with range of solvents so can be easily recycled⁵. Due to fascinating and outstanding properties ionic liquids, they are frequently known as future solvents for catalysis⁶⁻⁷, chemical reactions⁸⁻⁹, extractions¹⁰, electrochemical purposes¹¹, and many other potential applications of particular interest.

Frequently, ILS is termed “green solvents” or “designer solvents”¹²⁻¹⁴. The term of “green solvents” mainly arises from the fact that ILS are non-volatile under normal conditions and therefore do not create atmospheric waste. Using combinations of the various ions their physicochemical properties; solubility, polarity, melting point, viscosity, thermal and electrochemical

stability can be targeted. Therefore, ILS is also known as “designer solvents” or “task-specific ionic liquids”. Ionic liquids were synthesized by applying the green chemistry principles whenever it was possible. Ionic liquids are safer than organic volatile solvents because they do not evaporate or burn easily. In addition, they possess a very key property; they are recyclable. These catalytic and green applications of ILS motivated us to prepare a series of ionic liquids and study their efficiency for the Biginelli reaction.

Material and methods

Preparation of N-methyl Imidazole: 5g (73.4 mmol) of imidazole and 2.93g (73.4 mmol) sodium hydroxide and 3ml of THF as a solvent were placed in RBF and stirred for 10 min. the reaction mixture was heated at 65^oC for 10 minute then cool down at room temperature and 4ml (64.2 mmol) of methyl iodide in 3ml THF was added drop wise using addition funnel and stirred solution for 4 hours. The reaction mixture was poured in to crushed ice. The resulting mixture was extracted with 50ml of chloroform. The organic solvent was evaporated on hot water bath and the product was air dried. B.P. 198-199^oC.

Preparation of benzimidazole: 7ml of formic acid and 10g (90mmol) *o*-Phenylenediamine was added in a 250 ml flask. The reaction was heated at 100-110^oC temp. For 2 hours then cool down at room temperature and added 10% sodium hydroxide solution till reaction mixture becomes alkaline (8 pH). The separated solid was filtered out and dried. Yield: 78.68%, M.P. 170-172^oC.

Preparation of N-Methyl Benzimidazole: 4g (33 mmol) of Benzimidazole and 5.46g (39.6 mmol, 1.1. eq.) of Potassium carbonate was added to a solution of 15ml of DMF in RBF. The reaction mixture was stirred at room temperature for 30 minute. Then 3.2ml (33 mmol, 1 eq.) of DMS was added dropwise.

After completion of the reaction, the resulting reaction mixture was poured in to crushed ice. The separated product was filtered off and dried. M.P. 59-61°C.

Procedure for the synthesis of Ionic Liquid 1-Butylbenzimidazolium Tetrafluoroborate [Bbim] BF₄: A mixture of 3g (0.1 mol) of Benzimidazole, 7ml of 50% NaOH and 2.9ml (0.11 mol) of 1-bromobutane were placed in a three-necked flask. The reaction mixture was stirred for 24 hours at room temperature. The temperature of reaction was raised to 40-50°C at the time of completion, the reaction mixture become liquid. The reaction mixture was extracted with CHCl₃, washed with water and dried over anhydrous sodium sulphate. The solvent was evaporated under vacuum, thus the oil obtained was purified by distillation. 2.3 ml of tetrafluoroboric acid (40% sol. in water) was added drop-wise to a precooled (0-5°C) mixture of 4 ml ethanol solution and 2g Bbim in a two necked flask with stirring. The temperature was maintained for further 1 hr. the solvent was evaporated under *vacuo*. The viscous residue was dehydrated at 80°C in a vacuum oven followed by cooling it gives colorless crystalline solid. White colored; IR : 3500,3003,2130,1448,1214,759; M/Z: 262; ¹H NMR δ ppm 0.75-0.79 (t,3H,-CH₃); 1.16-1.21 (q,2H,-CH₂); 1.73-1.76 (t,2H,-CH₂); 4.25-4.28 (t,2H,-CH₂-N); 7.40-7.59 (dd,4H,-Ar-H); 8.98 (s,1H,-H); ¹³C NMR 139.39, 130.63, 130.23, 126.66, 126.58, 126.36, 126.21, 114.29, 113.87, 113.00, 112.61, 46.69, 30.27, 18.96, 12.56.

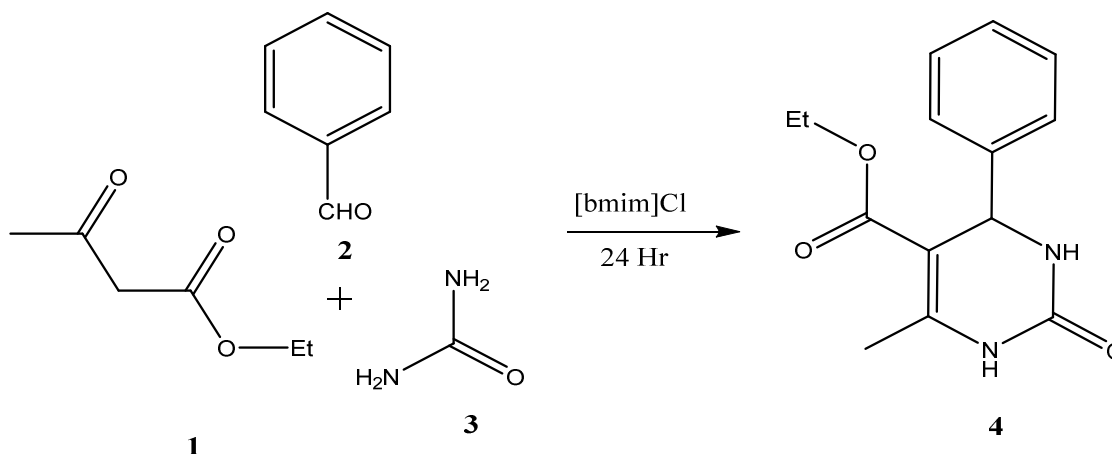
Procedure for the synthesis of Ionic Liquid 1-Butyl-3-Methylimidazolium Bromide [Bbim]Br: 2.06g of 1-Methylimidazole (25 mmol) and 3.62g of 1-bromobutane (26.3 mmol) were added to a round bottomed flask and cooled in an ice-bath under vigorous stirring for 2 hours. After completion of addition the reaction mixture was further stirred for 48 hr. The mixture was separated into two phases. The upper phase containing residual starting materials was decanted and the bottom IL phase was extracted three times, each with 30 ml ethyl acetate. Then the solvent was evaporated under *vacuo* to yield the desired product.

General procedure for the synthesis of Ionic Liquid 1-Butyl-3-Methylimidazolium Chloride: 2.06g (25 mmol, 1 eq.) of freshly distilled *N*-Methyl imidazole and 2.5ml of acetonitrile (CH₃CN) and 3.01 g (32.6 mmol, 1.3 eq.) of 1-chlorobutane were added to RBF and heated to a gentle reflux at 75-80°C. After completion of the reaction the volatile material is removed from the resulting yellow solution under reduced pressure to yield the desired product.

Results and discussion

Initially a series of various alkylated imidazole and benzimidazole compounds have been synthesized to prepare their ionic liquids using reported process. Various ionic liquids have been prepared using optimized reaction conditions. In this context, we have developed four ionic liquids such as; 1-Butylbenzimidazolium tetrafluoroborate, 1-Butyl-3-Methylimidazolium bromide, 1- Butyl-3-methylimidazolium chloride, 1- Propyl-3-methylimidazolium bromide starting from imidazole and Benzimidazole followed by *N*-alkylation using alkyl halide. The ionic liquids have been used as a green solvent for the synthesis of DHPM to study their efficiency. The data are cited in Table-1. Among the various ionic liquids, 1- Butyl-3-Methylimidazolium Chloride [bmim] Cl found as efficient solvent and catalyst for the Biginelli reaction and afford good yield.

A mixture of 0.29g benzaldehyde (2.76 mmol), ethyl acetoacetate 0.16g (2.76 mmol) and urea 0.16g (2.76 mmol) were heated at 80°C using Ionic Liquids (1 ml) in a rbf. The progress of the reaction was monitored by TLC. After 24 hr. the reaction mixture was allowed to cool at room temperature. Thus obtained solid mass was filtered, washed with water and dried. Pale yellow colored; IR: 3342, 3245, 3114, 2978, 1725, 1700, 1648, 1464, 1221, 782cm⁻¹; M/Z: 260; ¹H NMR δ ppm: 1.07-1.10 (t,3H,-CH₃), 2.25 (s,3H,-CH₃), 3.95-3.99 (q,2H,-CH₂), 5.15 (s,1H,Ar-CH), 7.23-7.32 (m,5H,Ar-H), 7.76 (s,1H,-NH), 9.22(s,1H,-NH).



Scheme-1: [Bmim]Cl catalyzed solvent free synthesis of DHPM.

Table-1: Synthesis of DHPM using various ILs.

No.	Ionic liquids	Yield of DHPM
1	1- Butyl-3-Methylimidazolium Chloride [bmim]Cl	88.89%
2	1-Butylbenzimidazolium tetrafluoroborate [bbi]Bf ₄	87.66%
3	1-Butyl-3-Methylimidazolium Bromide [bmim]Br	63.69%

Conclusion

We have prepared various ionic liquids and its employment for the synthesis of DHPM in high yield. We have developed four different ionic liquids based on imidazolium and benzimidazolium moiety. We have demonstrated its application for the synthesis of dihydropyrimidine. Among all the ionic liquids, the 1- Butyl-3-Methylimidazolium chloride found as most promising solvent for the Biginelli reaction. The prepared ionic liquids were characterized by spectral analysis.

Acknowledgement

Authors are thankful for financial assistance given under to UGC-MRP, Sanction No.-47-605/13(WRO), Dated- 20/5/2014. We are also thankful to Shree M. & N. Virani Science College for providing Central Instrumentation Facility and Laboratory Facility.

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