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$ZnBr_2$ functionalized ionic liquid: An efficient solvent and catalyst for the facile synthesis of 1-benzamino-1,4-dihydropyridine †

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Abstract:

Ionic liquids (ILs) are mostly composed of organic cations and organic/inorganic anions. One of the most important class of ILs are imidazolium ILs. The hydrophilicity and hydrophobicity of ILs are regularly influenced by length of alkyl side chain of cation. According to this effect, better hydrophilicity comes from a shorter alkyl side chain and on the contrary, better hydrophobicity comes from a lengthier alkyl side chain of cation. Typical ILs have exceptional properties. Most ILs are stable at about 300 ^{o}C in the liquid state at normal conditions. Due to the exceptional properties of ILs, they have been used in diverse industries including batteries and fuels. As solvents, ILs have been employed in many chemical fields. Solubilities of ILs with organic/inorganic species are completely satisfactory. Here, by N-methyl imidazole (Im), 1,3-dibromopropane, triethanolamine (TEA), and $ZnBr_2$, new ionic liquid (TEA-Im-Zn) was synthesized and used as catalyst and solvent in the synthesis of functionalized 1-benzamino-1,4-dihydropyridine using aromatic aldehydes, malononitrile, triethylamine, arylamine and dialkyl acetylenedicarboxylate.

Keywords: Ionic liquid; Zinc, 1,4-dihydropyridines; Catalyst.

1. Introduction

Since the first report of ionic liquid (IL) by Paul Walden in 1914, thousands of articles were published about ILs until now [1]. Imidazolium-based ILs are the most usable ionic liquids which most researches in this field are on the basis of them. ILs can be used as solvents due to their ability in dissolving wide variety of organic/inorganic solutes [2]. Many applications of ILs were reported till now including: as solvents in bio-transformations, in membrane science as the separation medium, and for the separations in capillary electrophoresis [3-5]. Among wide-ranging applications of ILs, catalysis has been known as a favorable application of ILs. Two models of using ILs as catalysis could be named: Liquid-IL biphasic catalysis, and IL both as solvent and catalyst [6]. Many reports described the catalytic abilities of ILs including: Friedel–Crafts reactions, Beckmann rearrangement, esterification, carbonylation reactions, and benzylation of alcohols [7,8]. In addition, ILs have following applications: as reagents and scavengers, to synthesize energy storage materials, to desulfurize fuel, for energy production, for carbon capture, functional material, and in denitrogenating of fuel oils [9]. According to their applications, many kinds of ILs were synthesized till now: acidic ILS, functionalized ILs, covalently and non-covalently supported ILs, ILs transported into metal-organic frame-works (MOFs), superionic liquids, and magnetic ILs, which each of them have their unique properties [10].

Huisgen’s 1,4-dipoles has attracted much attention in organic synthesis during past decades. These type of compounds can be easily produced from the reaction of alkynes and N-containing nucleophiles. Huisgen’s 1,4-dipoles have also been widely used for the synthesis of heterocyclic compounds by multicomponent reactions [11]. In this contribution, and in continue to our previous researches [12], a new IL using triethanolamine (TEA), N-methyl imidazole (Im), 1,3-dibromopropane and $ZnBr_2$ (Zn), TEA-Im-Zn, was synthesized and by using aromatic aldehydes, arylamine, dimethyl acetylenedicarboxylate, and malononitrile, functionalized 1-benzamino-1,4-dihydropyridine were synthesized.

2. Materials and Methods

2.1. general

All chemicals and solvents were purchased from Merck and Sigma companies and used without any further purification and NMR spectra were recorded by Burker DRX-500 Avance spectrometer (500 MHz/^{1}HNMR and 125 MHz/^{13}CNMR).

2.2. General method for the synthesis of TEA-Im-Zn

A mixture of N-methyl imidazole (3.0 mmol) and 1,3-dibromopropane (3.0 mmol) was added to a 50 mL flask and stirred for 24h h at 90^{o}C under N_2 atmosphere. To this mixture, TEA (1.0 mmol) and 10 mL DMF solvent was added and stirred for 24h at 80^{o}C. After completion the reaction, $ZnBR_2$ (3.0 mmol) was added and stirred at room temperature for 24h. In final step, DMF was separated by rotary and obtained product, TEA-Im-Zn, washed with EtOAc and dried under air atmosphere at r.t for 24h.

2.3. General method for the synthesis of 1-benzamino-1,4-dihydropyridine

2.0 mmol of aromatic aldehyde, 2.0 mmol of malononitrile, catalytic amount of triethylamine and 200 mL of synthesized TEA-Im-Zn IL were added to a 500.0 mL flask and stirred at room temperature for about 30 min. After that, 2.0 mmol of arylamine and 2.0 mmol of dialkyl acetylenedicarboxylate were added to it and stirred at room temperature for 24h. The IL was removed with a separatory funnel and the resulting residue was recrystallized to give the final pure product.

3. Results and Discussion

3.1. characterization of TEA-Im-Zn

Synthesized TEA-Im-Zn was characterized by FT-IR. As can be seen in figure 1, main functional groups of synthesized TEA-Im-Zn were appeared at 1164, 1456, 1564, 1647, 3085 and 3523 cm^{-1}.

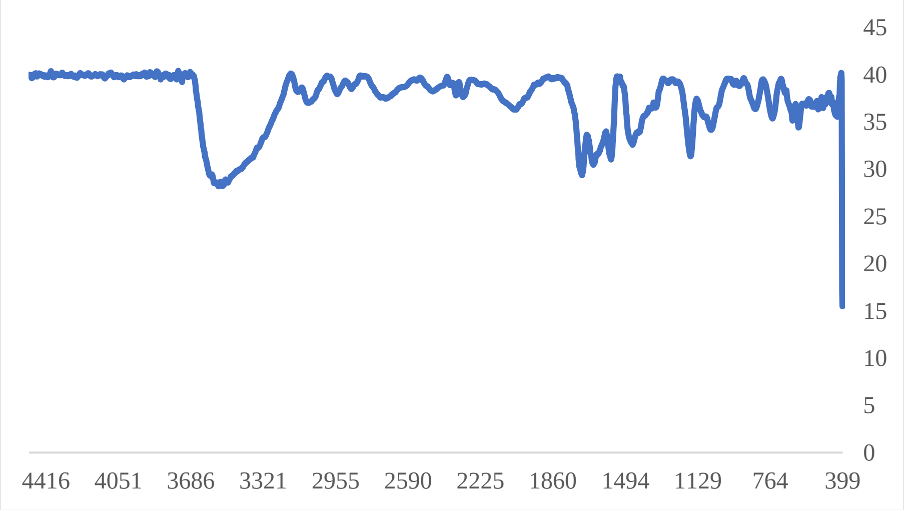
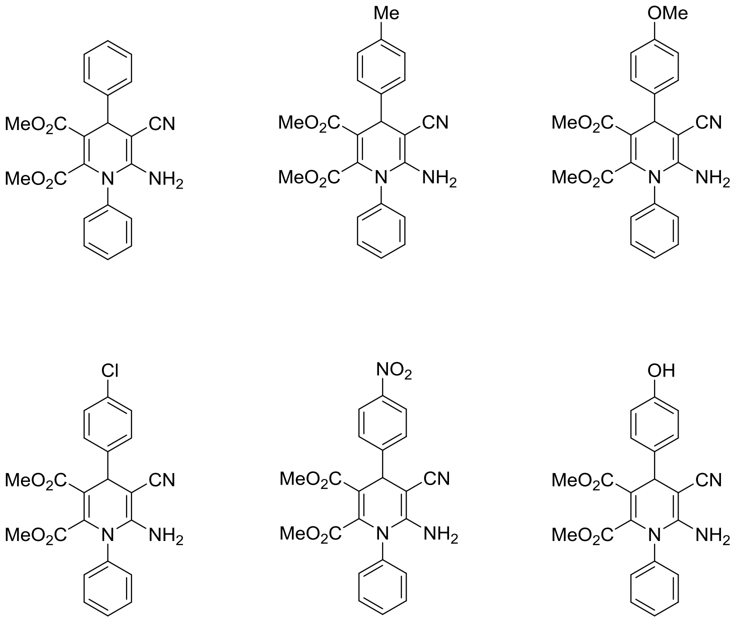


Figure 1. FT-IR of synthesized TEA-Im-Zn

3.2. 1-benzamino-1,4-dihydropyridine derivatives

The synthesis reaction of 1-benzamino-1,4-dihydropyridine can be done by combination of various aryl aldehydes (scheme 1). The optimized conditions for the reaction was using 200 mL of IL as catalyst and solvent at room temperature.



Scheme 1. Various synthesized 1-benzamino-1,4-dihydropyridine

3.3. Spectral data of dimethyl 6-amino-5-cyano-1,4-diphenyl-1,4-dihydropyridine-2,3-dicarboxylate

^1H NMR (500 MHz, DMSO-*d*$_6$) δ (ppm): 7.99—7.91 (m, 2H, CH_{Ar}), 7.69—7.65 (m, 1H, CH_{Ar}), 7.60—7.55 (m, 2H, CH_{Ar}), 7.42-7.45 (m, 3H, CH_{Ar}), 7.19—7.17 (m, 2H, CH_{Ar}), 6.32 (br, 2H, NH_2), 4.25 (br, 1H, CH), 3.72 (s, 3H, OCH_3), 3.35 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, DMSO-*d*$_6$) δ (ppm): 38.9, 53.1, 57.8, 117.7, 122.6, 122.9, 125.1, 125.8, 127.5, 128.4, 129.3, 142.1, 145.2, 145.5, 165.2, 166.3, 168.3.

4. Conclusions

In conclusion, a highly efficient TEA-Im-Zn IL was synthesized and used for the synthesis of 1-benzamino-1,4-dihydropyridine in mild condition reactions. The process was simple and generated a diverse range of 1-benzamino-1,4-dihydropyridine in excellent yields.

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