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Synthesis of Benzimidazole and Benzthiazole Derivatives By Using Ionic Liquids

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ABSTRACT: Ionic liquid efficiently catalysed the synthesis of benzimidazoles and benzthaizoles derivatives form o-phenyldiamine/2-aminothiaophenol and aldehydes in an aqueous media as a green solvent at reflux condition. This method provides a novel and efficient route for the synthesis of benzimidazole and benzthiazole derivatives in good to excellent yields with catalytic amount of ionic liquid.

KEYWORDS: Ionic liquid, o-phenyldiamine, 2-aminothiophenol, Benzaldehyde..

I. INTRODUCTION

Organic chemists synthesize hundreds of new heterocyclic compounds every week. In most cases the chemist has specific reasons for synthesizing a particular compound, usually based on theoretical considerations, medicinal chemistry, biological mechanisms or a combination of all three. The heterocyclic compounds are very widely distributed in nature and are very essential to living organisms. They play a vital role in the metabolism of all the living cells. Among large number of heterocycles found in nature, nitrogen heterocycles are the most abundant specially those containing oxygen or sulphur [1] due to their wide distribution in nucleic acid illustration and their involvement in almost every physiological process of plants and animals.

Benzimidazole is a group of substances have found practical applications in organic synthesis [2] and a significant structural element in medicinal chemistry owing to its diverse biological activities [3,4]. Benzimidazoles are also being developed as DNA minor groove binding agents with antitumor activity [5]. These act as ligand to transition-metal for modeling biological systems[6].

A wide range of methods are available for the synthesis of benzimidazole derivatives including condensation of either o-phenylenediamine, o-aminobenzenethiol, and/or o-aminophenol with aldehydes, acid chloride, esters, carboxylic acids, and orthoesters in the presence of various acid catalysts .Also, syntheses of these compounds have been reported using ILs [7-9]. Although these procedures provide improvement, many of these catalysts or activators suffer from disadvantages such as the use of organic solvents or toxic reagents, harsh reaction conditions, long reaction times, need to excess amounts of the reagent, and non-recoverability of the catalyst.

Taking in view of the applicability of heterocyclic compounds, the present work was undertaken to synthesize some heterocycles like benzimidazole and benzthiazole derivatives by using the [Bmim]PF_6 in an aqueous media as a green solvent (**Scheme 01**).

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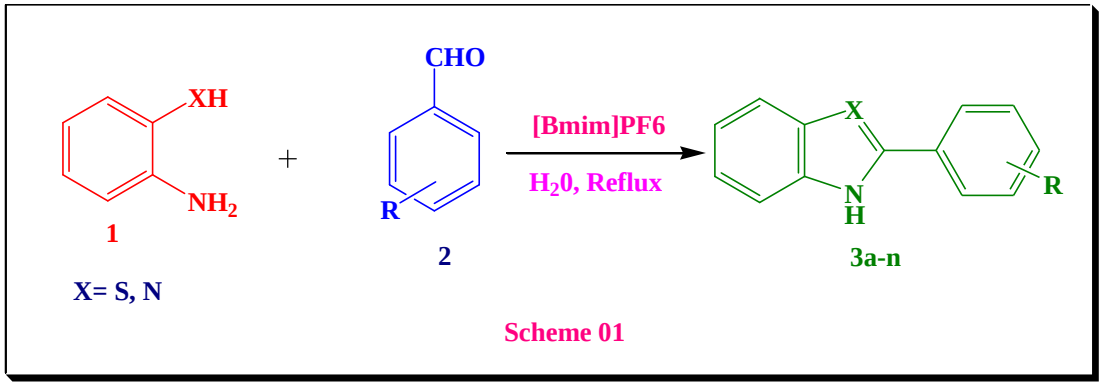

Scheme 01

II. RESULT AND DISCUSSION

In recent years, ionic liquids have gained importance in several organic transformations due to their interesting reactivity as well as for economic and environmental reasons. In continuation of our work to develop greener alternatives for organic transformations, organic reactions in an aqueous media and using ionic liquids have attracted immense interest as green alternative and environmentally benign conditions. Thus, here we report the formation of 2-arylbenzimidazole and 2-arylbenzthiazole by a direct condensation reaction of aryl aldehyde with o-phenylenediamine / 2-aminothiophenol in the presence of [Bmim]PF_6 ionic liquid under reflux condition in an aqueous media as a greener protocol.

In order to study the generality of this procedure, the applicability of the [Bmim]PF_6 ionic liquid in an aqueous media at reflux condition was then examined for the reaction of a series of aromatic aldehydes with o-phenylenediamine/2-aminothiophenol under the optimized reaction conditions. As shown, a variety of substituted aromatic aldehydes, bearing either electron-donating **(Table 01, entry 3,6,7,11,14)** or electron-withdrawing **(Table 01, entry 2,4,5,10,12,13)** substituent's, afforded the products in excellent yields and high purities. The reuse of the catalyst is a major factor in a new synthetic green procedure. The ionic liquid can be reused after simple distillation to remove water and remaining ionic liquids was dried under vacuum and reuse for further reactions.

Table 1: Synthesis of benzimidazole and benzthiazole derivatives using[Bmim]PF_6 **:**

Entry	Amines	Ar	Product	Yield(%)	Time(Hr)
1	o-phenylenediamine	-C_6H_5	3a	92	2
2	o-phenylenediamine	4-OH-C_6H_4	3b	94	1.5
3	o-phenylenediamine	4-OCH_3-C_6H_4	3c	88	3
4	o-phenylenediamine	4-Cl-C_6H_4	3d	95	1
5	o-phenylenediamine	4-Br-C_6H_4	3e	96	1
6	o-phenylenediamine	4-CH_3-C_6H_4	3f	88	3
7	o-phenylenediamine	4-C_2H_5-C_6H_4	3g	87	4
8	o-phenylenediamine	3-OCH_3-4-OH-C_6H_3	3h	89	2.5
9	2-aminothiophenol	-C_6H_5	3i	90	3
10	2-aminothiophenol	4-OH-C_6H_4	3j	93	2
11	2-aminothiophenol	4-OCH_3-C_6H_4	3k	89	4
12	2-aminothiophenol	4-Cl-C_6H_4	3l	95	2
13	2-aminothiophenol	4-Br-C_6H_4	3m	95	2
14	2-aminothiophenol	4-CH_3-C_6H_4	3n	88	3

III. GENERAL PROCEDURE

In a 50 ml round bottom flask, a mixture of o-phenyldiamine (1 mmol) / 2-aminothiophenol (1.5 mmol) and aldehydes (1 mmol) in water (5 ml) were mixed and refluxed on water bath in the presence of [Bmim]PF_6 Ionic liquid (20 mol %) for appropriate time given in a table 27. The progress of the reaction was monitored by using TLC. After completion of the reaction mixture was cooled and filtered. Wash the precipitate with distilled water (5 X 5ml) to recover the catalyst

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and dried it over vacuum. Recrystallise the crude product in ethanol to obtain the pure product. If necessary crude product was purified by silica gel column chromatography using ethyl acetate: pet-ether (2:8) as an eluent.

Spectral data of some compounds:

Entry 3: IR (KBr): 833, 1035, 1125, 1342, 1536, 1628, 2988, 3478 cm-1; H^1NMR (300MHz,DMSO): δ = 3.25 (s, 3H), 7.52(s, broad, 2H), 7.68 (d, 2H, J=7.6Hz, 2H) ; 7.93 (m, 2H); 8.12(d,J=7.6Hz, 2H); 11.92 (s, 1H) .

Entry 2: IR (KBr): 732, 815, 1036, 1537, 1627, 2929, 3329, 3478 cm-1; H^1NMR (300MHz, DMSO): δ = 5.2 (s, 1H), 7.3(s, broad, 2H), 7.5 (d, 2H, J=7.6Hz, 2H) ; 7.8 (m, 2H); 8.2(d, J=7.6Hz, 2H); 12.1 (s, 1H)

IV. CONCLUSION

In conclusion, we have developed an efficient and green procedure for the selective synthesis of benzimidazoles and benzthaizoles derivatives using commercially available ionic liquid in an aqueous media at reflux condition. The present methodology has several advantages such as catalyst reusability, high yield of product, short reaction time, simple work-up procedure and easy isolation.

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