



## Magnetic Ionic Liquid [bmim][FeCl<sub>4</sub>] as an Efficient Catalyst for the Synthesis of 2-Aryl Benzimidazoles and 2-Aryl Benzothiazoles Derivatives

SOHEIL SAYYAH<sup>1,2\*</sup>, SARA SHABANI<sup>3</sup>, SARA GHASEMI<sup>2</sup>,  
ATENA AZIN<sup>2</sup> and SEYYED MORTEZA HASANI<sup>1</sup>

<sup>1</sup>SAMA Technical and Vocational Training College, Mahshahr Branch,  
Islamic Azad University, Mahshahr, Iran.

<sup>2</sup>Department of Chemistry, Mahshahr Branch, Islamic Azad University, Mahshahr, Iran

<sup>3</sup>Department of Chemistry, Omidieh Branch, Islamic Azad University, Omidieh, Iran

\*Corresponding author E-mail: sayyahi.soheil@gmail.com

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### ABSTRACT

The magnetic ionic liquid (MIL) 1-butyl-3-methylimidazolium tetrachloro ferrate(III) ([bmim][FeCl<sub>4</sub>]) sufficiently catalyzes the one-pot condensation of 1,2-diaminobenzene or 2-aminobenzenethiol with different aromatic aldehydes producing benzimidazoles and benzothiazoles derivatives, respectively. The MIL showed high performance resulting in great yields with appropriate reaction time.

**Key words:** Magnetic ionic liquid, Multicomponent Reactions, Benzimidazoles, Benzothiazoles.

### INTRODUCTION

Ionic liquids (ILs) have been applied in green catalytic technologies and have been studied widely in reactions early after their discovery because of their individual unique properties such as low vapor pressure, wide liquid range, low flammability, high conductivity, excellent stability and large electrochemical window. ILs can perform specific catalytic processes and using them usually

represent the advantages of high catalytic activity and also good selectivity<sup>1,2</sup>.

Otherwise, the term "magnetic ionic liquid" (MIL) was recently proposed by Hamaguchi and co-workers in 2004 to introduce ILs with paramagnetic exclusivity<sup>3,4</sup>. The MILs are primarily based on high-spin d<sup>5</sup> Fe(III) in the form of FeCl<sub>4</sub><sup>-</sup> or FeBr<sub>4</sub><sup>-</sup> with various counter cations. These MILs exhibited a strong response to magnetic fields by

their high single-ion magnetic moments<sup>5</sup>. The catalytic activities of MILs have been studied in Friedel crafts acylation<sup>6</sup>, aryl grignard cross coupling of alkyl halides<sup>7</sup>, preparation of 1,2-azidoalcohols<sup>8</sup>, glycolysis of poly(ethylene terephthalate)<sup>9</sup>, "liquid fixed-bed" catalysts in flow application<sup>10</sup>, oxidative desulfurization of fuels<sup>11</sup> and multi-component synthesis of 1- and 5-substituted 1H-tetrazoles<sup>12</sup>, quinazolines<sup>13</sup> and 1-amidoalkyl-2-naphthols<sup>14</sup> derivatives.

Basically, heteroaromatic bicycles have a wide range of applications in medicinal chemistry because of their pharmaceutical and biological activities<sup>15</sup> which are responsible for antibacterial and antifungal activity observed for benzimidazole derivatives<sup>16</sup>. The substituted benzimidazoles such as 2-Aryl and 2-alkyl benzimidazoles deliver biological activity against several viruses such as HIV, human cytomegalovirus (HCMV)<sup>17</sup>, Herpes (HVS-1)<sup>18</sup>, and influenza<sup>19</sup>. Besides, 2-Aryl benzothiazoles are important molecules due to their use not only as medicinal agents but also as organic functional materials such as fluorescent dyes and liquid crystals<sup>20</sup>. Various derivatives of benzothiazoles are also used as radioactive amyloid imaging agents<sup>21</sup>. Thus, the synthesis of these organic compounds has received considerable attention in diverse areas of chemistry. So far, a number of various synthetic methods have been developed to uncover a variety of new reagents for the preparation of benzimidazoles and benzothiazoles. The most commonly-used synthetic approaches to produce benzimidazoles typically entail the condensation of benzene-1,2-diamine with carbonyl compounds, such as aldehydes, carboxylic acids and their derivatives<sup>22-24</sup>. In addition, there are several reports on benzimidazoles synthesis via the reductive cyclization of benzene-1,2-diamine with aldehydes<sup>25</sup>, cyclization of benzene-1,2-diamine derivatives with aryl isothiocyanates<sup>26</sup>, and Baker's yeast reduction of 2, 4-dinitroacyl anilines<sup>27</sup>. Traditional methods for the synthesis of benzothiazoles typically involve the condensation of 2-amino thiophenols with aryl aldehydes<sup>28, 29</sup>, carboxylic acids<sup>30</sup>, nitriles<sup>31</sup>, acyl chlorides<sup>23, 32</sup>, alcohols<sup>33</sup>, or through Jacobson's potassium ferricyanide mediated cyclization of thiobenzanilides<sup>34</sup>. However, most of the reported methods have several drawbacks including low

yield, long reaction time, the use of expensive reagents, harsh reaction conditions, tedious workup procedures, involving more than one step in their synthesis, and co-occurrence of several side reactions<sup>35</sup>.

In this paper the catalytic activity of [bmim][FeCl<sub>4</sub>] was practically investigated for the one-pot synthesis of benzimidazoles and benzothiazoles, respectively.

## EXPERIMENTAL

### General

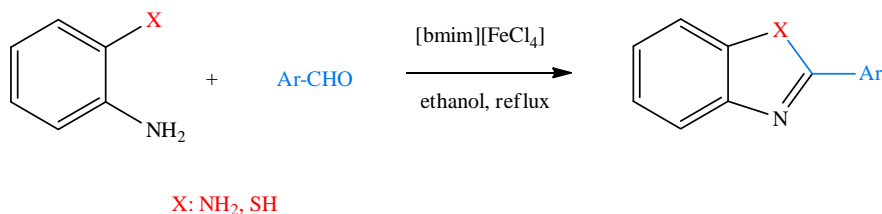
All compounds were purchased from Aldrich and Merck companies and used as received without further purification. Progress of the reaction was monitored by TLC on Merck DC-Alufolien plates pre-coated with silica gel F<sub>254</sub>. Melting points were recorded using a Thermo Fisher Scientific IA 9200 instrument.

### Synthesis of MIL [bmim][FeCl<sub>4</sub>]

The magnetic ionic liquid was synthesized following the same way remarked in literature[36]. 5 mmol [bmim]Cl (0.870g) and 5 mmol FeCl<sub>3</sub> (0.825g) were added to a round bottom flask and stirred with a magnet for 15 minutes. The resulting ionic liquid was dissolved in ethyl acetate (10 mL) and the solution was centrifuged after filtration in order to separate any possible residue of inorganic salts. Afterwards, ethylacetate was evaporated and the obtained dark brown liquid, butyl methyl imidazolium tetrachloroferrate(III) was dried under vacuum at 80 °C overnight.

### General procedure for the synthesis of benzimidazoles and benzthiazoles in the presence of [bmim][FeCl<sub>4</sub>]

A mixture of 2-aminobenzenethiol or 2-aminobenzenethiol (1 mmol), aryl aldehyde (1 mmol), [bmim][FeCl<sub>4</sub>] (0.5 mmol) and ethanol (5 mL) was placed in a round bottom flask and refluxed for the given times recorded in Table 2. After completion of the reaction observed by TLC (using n-hexane/ethylacetate (7:3) as eluent), the mixture was cooled to room temperature, the precipitate was filtered and washed with water for several times. The resultant product purified by column chromatography and characterized by comparison of their physical data



Scheme 1: Synthesis of 2-Aryl Benzimidazoles and 2-Aryl Benzothiazoles

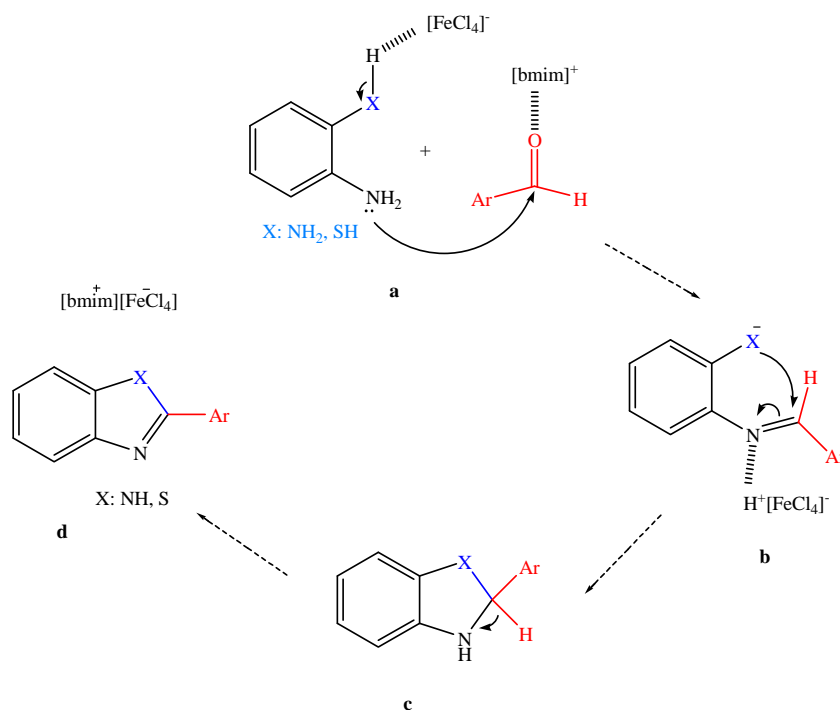
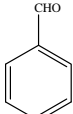
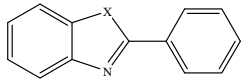
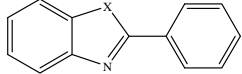
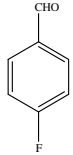
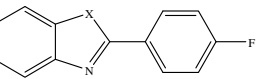
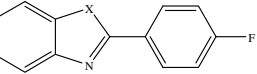
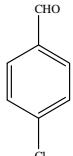
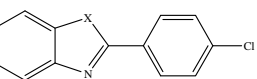
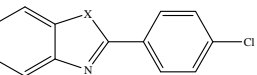
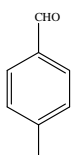
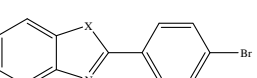
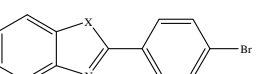
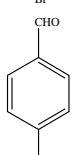
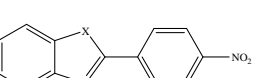
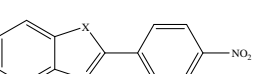
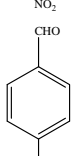
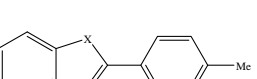
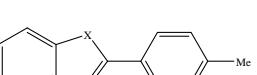
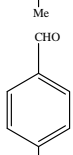
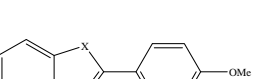
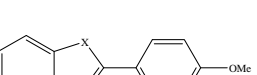
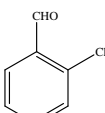
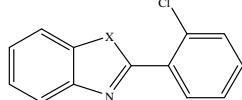
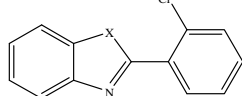
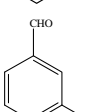
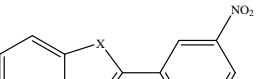
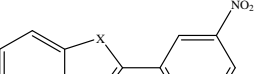
Scheme 2: The suggested mechanism for the synthesis of 2-Aryl Benzimidazoles and 2-Aryl Benzothiazoles derivatives utilizing  $[\text{bmim}][\text{FeCl}_4]$  as catalyst

Table 1: The one-pot condensation reaction of benzene-1,2-diamine (1 mmol) and 4-nitrobenzaldehyde (1 mmol) under different conditions

| Entry | Catalyst (mmol) | Solvent                | Temperature ( $^{\circ}\text{C}$ ) | Time (min) | Result      |
|-------|-----------------|------------------------|------------------------------------|------------|-------------|
| 1     | 0.5             | -                      | 40                                 | 60         | No Reaction |
| 2     | 0.5             | -                      | rt                                 | 60         | No Reaction |
| 3     | 0.5             | n-hexane               | reflux                             | 60         | No Reaction |
| 4     | 0.5             | $\text{CHCl}_3$        | reflux                             | 60         | Uncompleted |
| 5     | 0.5             | $\text{CH}_3\text{CN}$ | reflux                             | 60         | Uncompleted |
| 6     | 0.5             | $\text{H}_2\text{O}$   | reflux                             | 60         | Uncompleted |
| 7     | 0.5             | EtOH                   | reflux                             | 40         | Completed   |
| 8     | 0.25            | EtOH                   | reflux                             | 60         | Uncompleted |
| 9     | 0.5             | EtOH                   | rt                                 | 60         | Uncompleted |

**Table 2: Synthesis of 2-Aryl Benzimidazoles and 2-Aryl Benzothiazoles catalyzed by bmim[FeCl<sub>4</sub>]**

| Entry | Aldehyde  | Product <sup>a</sup>  | Time (min) | Yield <sup>b</sup> (%) | M.p. (°C) (Lit.)     | Ref. |
|-------|---|---|------------|------------------------|----------------------|------|
| 1     |    |  x: NH   | 10         | 93                     | 282-291<br>(292-294) | [22] |
|       |   |  x: S    | 50         | 87                     | 130-132<br>(112-114) | [28] |
| 2     |    |  x: NH   | 45         | 93                     | 240-242<br>(248)     | [38] |
|       |   |  x: S    | 70         | 82                     | 110-113<br>(102-103) | [28] |
| 3     |    |  x: NH   | 20         | 94                     | 288-290<br>(290-292) | [35] |
|       |   |  x: S    | 80         | 94                     | 110-111<br>(114-116) | [39] |
| 4     |   |  x: NH   | 20         | 93                     | 261-263<br>(261-263) | [40] |
|       |   |  x: S    | 45         | 94                     | 107-109<br>(129-132) | [39] |
| 5     |  |  x: NH | 40         | 95                     | 317-319<br>(315-317) | [35] |
|       |   |  x: S  | 70         | 91                     | 118-120<br>(143-145) | [39] |
| 6     |  |  x: NH | 30         | 91                     | 258-260<br>(268-270) | [35] |
|       |   |  x: S  | 80         | 87                     | 122-123<br>(87-88)   | [41] |
| 7     |  |  x: NH | 10         | 85                     | 176-178<br>(180-182) | [42] |
|       |   |  x: S  | 90         | 82                     | 120-122<br>(122-123) | [28] |
| 8     |  |  x: NH | 10         | 93                     | 232-235<br>(231-233) | [35] |
|       |   |  x: S  | 85         | 92                     | 104-106<br>(84-85)   | [43] |
| 9     |  |  x: NH | 75         | 92                     | 200-203<br>(200-203) | [35] |
|       |   |  x: S  | 30         | 91                     | 124-126              | [35] |

<sup>a</sup> All products are known and were identified by comparing their physical and spectral data with literature<sup>b</sup> Isolated yields

with benzimidazole or benzthiazole derivatives reported in literature.

### Spectral data for 2-(4-nitrophenyl)-1H-benzo[d]imidazole

<sup>1</sup>HNMR was taken on a Bruker BioSpin GmbH. (400 MHz, DMSO-d<sub>6</sub>), 2.50 (s, 1H, NH), 8.42–8.41 (d, 2H, Ar–H), 7.68–7.67 (d, 2H, Ar–H), 7.66 (s, 2H, Ar–H), 7.27–7.26 (d, 2H, Ar–H).

## RESULTS AND DISCUSSIONS

In order to investigate the catalytic ability of the MIL, the condensation of benzene-1,2-diamine with 4-nitrobenzaldehyde was chosen as the model reaction in different conditions. As seen in Table 1, the most appropriate condition among the candidate ones giving excellent yield in a proper time is the 7<sup>th</sup> process using ethanol as solvent under reflux condition.

Then, to study the scope and limitation of these optimized procedures a wide variety of aryl benzaldehydes were exerted and the results showed a highly effective performance of the catalyst in the preparation of 2-Aryl Benzimidazoles and 2-Aryl Benzothiazoles (Scheme 1, Table 2).

It has been assumed that, magnetic ionic liquids could act as efficient catalysts due to the synergic effect of the cation and anion[37]. The catalytic operation of [bmim][FeCl<sub>4</sub>] is explained in the proposed mechanism (Scheme 2). Initially, the carbonyl group in aldehyde is activated by the [bmim] cation and meanwhile [FeCl<sub>4</sub>]<sup>-</sup> anion interacts with the hydrogen in X (NH<sub>2</sub> or SH) of either benzene-1,2-diamine or 2-aminobenzenethiol. Hence, the nucleophilic attack and ring closure becomes easier to obtain the intermediate (c). Ultimately, the product is formed.

## CONCLUSION

We have established an efficient method demonstrating the high catalytic activity of the magnetic ionic liquid [bmim][FeCl<sub>4</sub>] optimizing the synthesis of 2-Aryl Benzimidazole and 2-Aryl Benzothiazole derivatives, respectively. Furthermore, the synthesis procedure exhibited well to excellent yields under semi-mild conditions.

## ACKNOWLEDGMENTS

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