

## Fe<sub>3</sub>O<sub>4</sub> magnetic nanoparticles (Fe<sub>3</sub>O<sub>4</sub> MNPs): A magnetically reusable catalyst for synthesis of Benzimidazole compounds

Ahmad Sajjadi\*, Reza Mohammadi

Young Researchers and Elite Club, Ilam Branch, Islamic Azad University, Ilam, Iran

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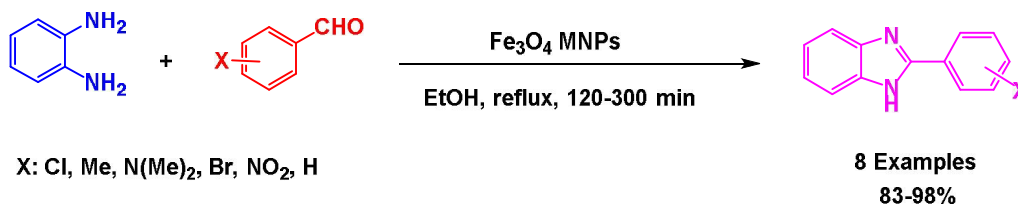
Reusable catalyst

### ABSTRACT

In this paper, Fe<sub>3</sub>O<sub>4</sub> magnetic nanoparticles (Fe<sub>3</sub>O<sub>4</sub> MNPs) were prepared and introduced as an efficient and eco-friendly catalyst for the synthesis of benzimidazole derivatives. The as-synthesized Fe<sub>3</sub>O<sub>4</sub> magnetic nanoparticles were characterized by FT-IR spectroscopy and scanning electron microscopy (SEM). This method afforded the target products in high yields and the catalytic system could be recycled and reused without significant loss of catalytic activity.

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### GRAPHICAL ABSTRACT



### 1. Introduction

Benzimidazoles have emerged as an important class of nitrogenated heterocycles attracting significant synthetic interest because of their pharmacological and therapeutic properties.<sup>1-2</sup> Benzimidazole derivatives are common structural motifs in various biologically active and pharmaceutical molecules for their antioxidant, antibacterial, antitumor, anti-inflammatory, anti-HIV, antidiabetic and antifungal properties.<sup>2-5</sup> The most common method for the synthesis of benzimidazoles is the condensation of o-phenylenediamines with carboxylic acid derivatives or aldehydes.<sup>6</sup> In recent years, a number of protocols have been reported for the synthesis of Benzimidazoles.<sup>6</sup> Catalyst is very important for organic synthesis, it can greatly promote the organic reaction, effectively and sustainably synthesize organic compounds, and many reactions nearly do not occur without it.<sup>7</sup>

In the past decade, magnetic nano-particles (MNPs) have emerged as a new class of catalyst owing to ultrafine size and high surface area, which exhibit higher catalytic activity than conventional heterogeneous catalysts.<sup>4, 8-12</sup> The best advantage of magnetic nanoparticles is their easy separation from reaction mixture using an external magnet.<sup>13-14</sup> Among the various MNPs employed as catalyst, Fe<sub>3</sub>O<sub>4</sub> nanoparticles have been widely studied due to high surface area to bulk ratios,

low toxicity, high activity and thermal stability and the capability of surface modifications and easy dispersion.<sup>15-18</sup> In this paper, we will report the synthesis of benzimidazoles using Fe<sub>3</sub>O<sub>4</sub> magnetic nanoparticles as an efficient reusable catalyst.

### 2. Result and discussion

The as-synthesized Fe<sub>3</sub>O<sub>4</sub> magnetic nanoparticles were characterized by FT-IR spectroscopy and scanning electron microscopy (SEM). The FT-IR spectra of Fe<sub>3</sub>O<sub>4</sub> MNPs are given in Fig. 1. As shown in Fig. 1, the characteristic absorption peaks at 570 are attributed to the Fe-O structure, which confirm the formation of Fe-O band. The SEM image of the Fe<sub>3</sub>O<sub>4</sub> MNPs confirmed the uniformity and spherical morphology of the nanoparticles (Fig. 2) in the prepared material. The size of the nanoparticles was found to be increased in the range of 10-20 nm, due to the aggregation of the nanoparticles.

After characterization, the catalytic activity of Fe<sub>3</sub>O<sub>4</sub> MNPs was evaluated in the synthesis of benzimidazoles. In order to obtain the best conditions for the synthesis of benzimidazoles, the reaction of benzaldehyde and o-phenylenediamine (as a model reaction) was studied in the presence of Fe<sub>3</sub>O<sub>4</sub> MNPs (Scheme 1). First, the effect of catalyst amount on the

\* Corresponding Author:

E-mail address: [sajadiahmad64@yahoo.com](mailto:sajadiahmad64@yahoo.com) (A. Sajjadi)

reaction was tested. The best performance was obtained when 30 mg of Fe<sub>3</sub>O<sub>4</sub> MNPs was used. Then the influence of a number of solvents was tested.

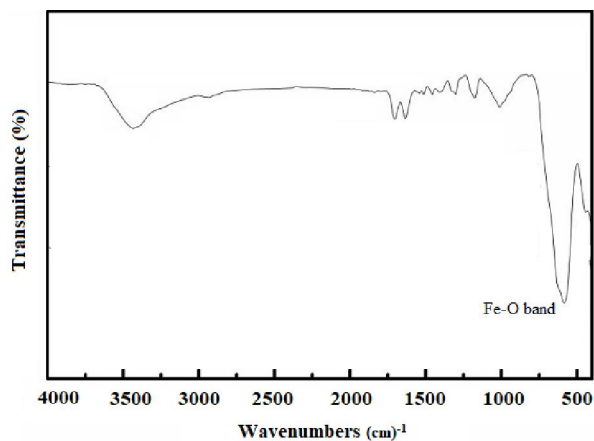


Fig 1. FT-IR spectra of Fe<sub>3</sub>O<sub>4</sub> MNPs.

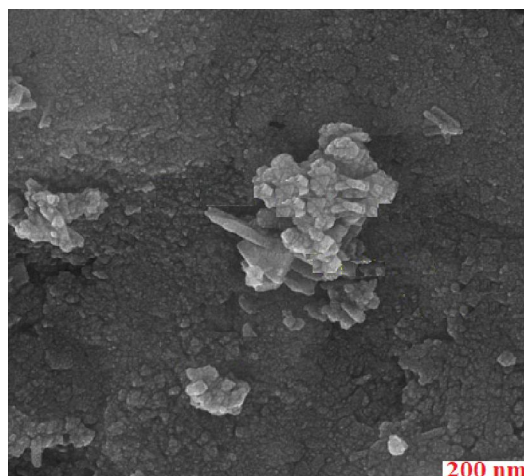
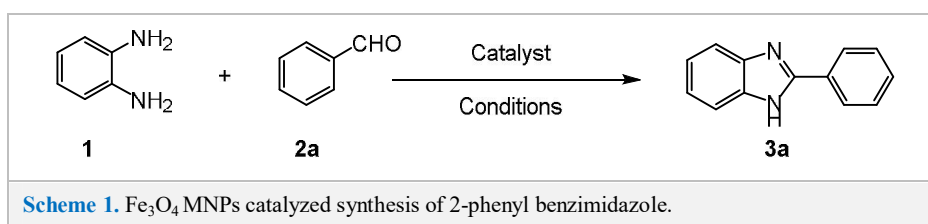


Fig 1. SEM image of Fe<sub>3</sub>O<sub>4</sub> MNPs.

After comprehensive experiments, 30 mg of catalyst in ethanol at reflux temperature was selected as the standardized reaction conditions (Table 1).

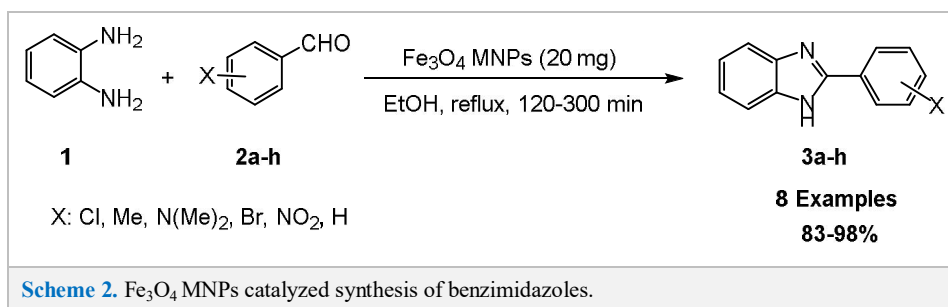


Scheme 1. Fe<sub>3</sub>O<sub>4</sub> MNPs catalyzed synthesis of 2-phenyl benzimidazole.

Table 1. Effect of reaction conditions on the synthesis of 2-phenyl benzimidazole<sup>a</sup>

Entry	Catalyst (mg)	Solvent	Tem (°C)	Yield (%) <sup>b</sup>
1	10	Ethanol	Reflux	84
2	20	Ethanol	Reflux	90
3	30	Ethanol	Reflux	97
4	40	Ethanol	Reflux	96
5	--	Ethanol	Reflux	10
6	30	Water	Reflux	74
7	30	CH <sub>3</sub> CN	Reflux	69
8	30	DMF	Reflux	76
9	30	Ethyl acetate	Reflux	58
10	30	EtOH/H <sub>2</sub> O(1:1)	50 °C	87

<sup>a</sup> Reaction conditions: o-phenylenediamines (5 mmol) and benzaldehyde (5 mmol), catalyst (30 mg), solvent (5 ml). The reaction was stirred for 3 h. <sup>b</sup> Yield of isolated product.



Scheme 2. Fe<sub>3</sub>O<sub>4</sub> MNPs catalyzed synthesis of benzimidazoles.

In order to extend the scope of our methodology for the synthesis of benzimidazoles, we next used a variety of aromatic aldehydes for this cycloaddition reaction (Scheme 2). The results are listed in Table 2. As shown in Table 2, in most cases, o-phenylenediamine reacted smoothly with various benzaldehydes to give the corresponding products with good yields. All reactions were done within 120 to 300 min. The time of reactions was depending on the substituents present on the substrates. The possibility of recovering and recycling of the catalyst is an important process from different

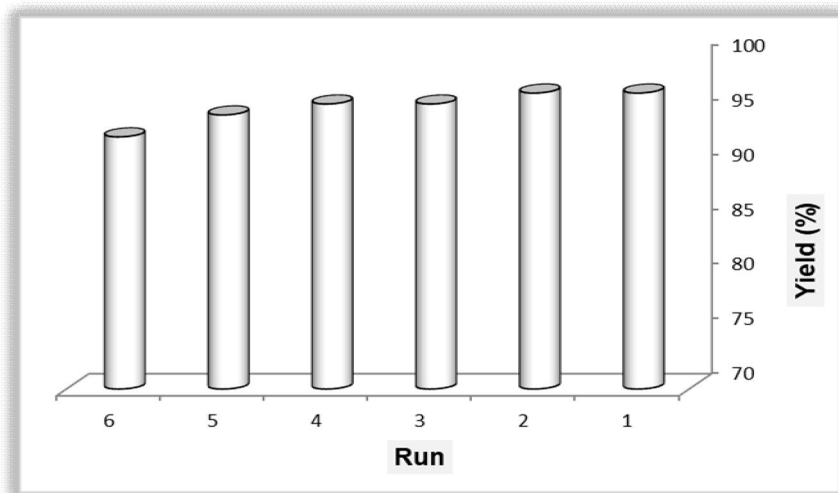
aspects such as environmental concerns, and commercial applicable processes. Then the reusability of Fe<sub>3</sub>O<sub>4</sub> MNPs was investigated by using o-phenylenediamine and benzaldehyde as a model reaction.

After completion of the reaction, the catalyst can be easily removed using an external magnetic from the reaction mixture. Then the recovered catalyst was used in the next run. This catalyst was recycled and reused at least for six times without significant loss of its catalytic activity (Fig. 3).

**Table 2.** Synthesis of benzimidazoles from aldehydes in the presence of Fe<sub>3</sub>O<sub>4</sub> MNPs <sup>a</sup>

Entry	Aldehyde	Product	Time (min)	Yield (%) <sup>b</sup>
1	C <sub>6</sub> H <sub>5</sub> CHO	<b>3a</b>	180	97
2	4-ClC <sub>6</sub> H <sub>4</sub> CHO	<b>3b</b>	130	98
3	4-BrC <sub>6</sub> H <sub>4</sub> CHO	<b>3c</b>	145	95
4	4-MeC <sub>6</sub> H <sub>4</sub> CHO	<b>3d</b>	120	94
5	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CHO	<b>3e</b>	210	89
6	4-NMe <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CHO	<b>3f</b>	300	83
7	3-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub> CHO	<b>3g</b>	285	91
8	2-ClC <sub>6</sub> H <sub>4</sub> CHO	<b>3h</b>	170	93

<sup>a</sup> All the isolated products were characterized on the basis of their physical properties and IR, <sup>1</sup>H- and <sup>13</sup>C-NMR spectral analysis and by direct comparison with authentic materials. <sup>b</sup> Isolated yield.



**Fig 3.** Reusability of catalyst in the model reaction (3a).

### 3. Conclusion

In summary, Fe<sub>3</sub>O<sub>4</sub> MNPs was prepared, characterized and found to be an efficient and recyclable nanocatalyst for the synthesis of benzimidazoles. Our inexpensive catalytic system exhibited a great functional group tolerance in the presence of multiple potentially reactive groups at moderate temperature. Furthermore, the Fe<sub>3</sub>O<sub>4</sub> MNPs catalyst can be easily recovered by an external magnetic field and reused for subsequent run for at least 6 times with less deterioration in catalytic activity.

### 4. Experimental

#### 4.1. Preparation of magnetic nanoparticles (Fe<sub>3</sub>O<sub>4</sub> MNPs)

A solution of FeCl<sub>2</sub>·4H<sub>2</sub>O (0.86 g) and FeCl<sub>3</sub> (1.40 g) in deionized water (40 mL) was stirred at 85 °C for 30 minutes under nitrogen gas. Then, 3 mL ammonium hydroxide (25 %, 3 mL) was added, and the reaction mixture was stirred for 20 minutes. The solution was cooled to room temperature followed by filtration. The magnetite precipitate was washed twice with H<sub>2</sub>O and sodium chloride (0.02M) solution.

#### 4.2. General procedure for synthesis of benzimidazoles

o-Phenylenediamine (5mmol) and aldehyde (5mmol) were thoroughly mixed in ethanol (5 mL) in a 25 mL three-necked flask equipped with a water-cooled condenser and a gas inlet with vigorous stirring at reflux temperature. Then, Fe<sub>3</sub>O<sub>4</sub> nanoparticles (30 mg) was added, and air was continuously

bubbled by a small pump at an average speed of 60 bubbles per minute. When the reaction was complete, as monitored by TLC analysis, Fe<sub>3</sub>O<sub>4</sub> nanoparticles were collected by magnetic force, subsequently washed with ethanol and dried under vacuum to give recycled Fe<sub>3</sub>O<sub>4</sub> nanoparticles. The reaction mixture was extracted with ether three times, and the organic layer was dried using anhydrous magnesium sulfate and rotary evaporation under reduced pressure. The residue was purified by column chromatograph on a silica gel using *n*-hexane–ethyl acetate (10:1) as eluent to afford the pure products.<sup>4</sup>

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