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Original Research

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A novel and attractive recoverable nanomagnetic copper catalyst for synthesis of biologically active oxazole derivatives

Zahra Moghadasi *[1] and Ali Noory Fajer [2]

[1] Department of Chemistry, Islamic Azad University, Central Tehran Branch, Tehran, Iran.

[2] Department of chemistry, College of Education, University of AL-Qadisiyah, Iraq.

Corresponding author-mail: z_moghadasi@yahoo.com

ABSTRACT: Oxazole moiety is an important heterocyclic compound as they are being an essential constituent of large number of marketed drugs. In this research paper we found that, copper (II) complex immobilized on the surface of magnetic Fe_3O_4 nanoparticles functionalized with imidazole [Fe_3O_4@SiO_2-IM-$CuCl_2$] is a novel and highly efficient catalyst for the preparation of oxazole derivatives through reaction of benzylamine and benzil derivatives. The structure of nanocatalyst was well characterized by FT-IR, SEM, TEM, XRD, EDX, TGA and VSM techniques. The Fe_3O_4@SiO_2-IM-$CuCl_2$ catalyst can be reused after 6 times of recycling without significant reduction in its catalytic activity.

KEYWORDS: Fe_3O_4@SiO_2-IM-$CuCl_2$ nanocatalyst, Oxazoles, Recoverable catalyst, Organic synthesis.

■ Introduction

With the introduction of nano technology into the industry of catalysts, nanocatalysts have become more visible; during the last decade, nano catalysts have received much attention due to their advantages such as recyclability, easy maintenance, safety, and environmental compatibility [1–3]. In recent years, the immobilization of transition metals on the surface of nanomaterials have presented as an interesting and efficient catalytic strategy in chemistry science especially in organic synthesis [4–7]. Magnetic nanoparticles are one of the types of nanomaterials that has attracted a lot of attention due to its unique characteristics compared to other nanomaterials [8–10]. Magnetic nanoparticles increase the reaction speed due to their high surface-to-volume ratio and the large contact surface they will have with the reactants [11,12]. Also, as a result of using magnetic nanoparticles as a support, the resulting final metallic-catalysts will have magnetic properties and can be easily separated from the reaction medium under the influence of an external magnetic field [13–15]. These nanomagnetic metallic-catalysts have been used in a wide range of catalytic reactions such as hydrogenation, oxidation, C-C, C-S, C-N bond formation reactions, cyclization, etc [16–18].

Every day one of the heterocyclic compounds is recognized as a key component in medicinal and pharmaceutical processes [19]. In heterocyclic chemistry, oxazoles are among the important and valuable compounds that play a significant role in the field of medicine and therapy [20–22]. Oxazoles and their derivatives have a special position, which has increased the attention of organic chemists to these types of compounds for better and greener synthesis with higher efficiency and yield in the last few years [23–25]. These compounds are important units in the structure of many bioactive molecules, drugs and natural products. Some these compounds are outlined in **Figure 1** [26–30]. In this paper, we reported that copper iodide

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immobilized on the surface of Fe_3O_4 nanoparticles functionalized with serine is a highly active nanocatalyst for the synthesis of oxazole derivatives through reaction of benzylamine and benzil derivatives.

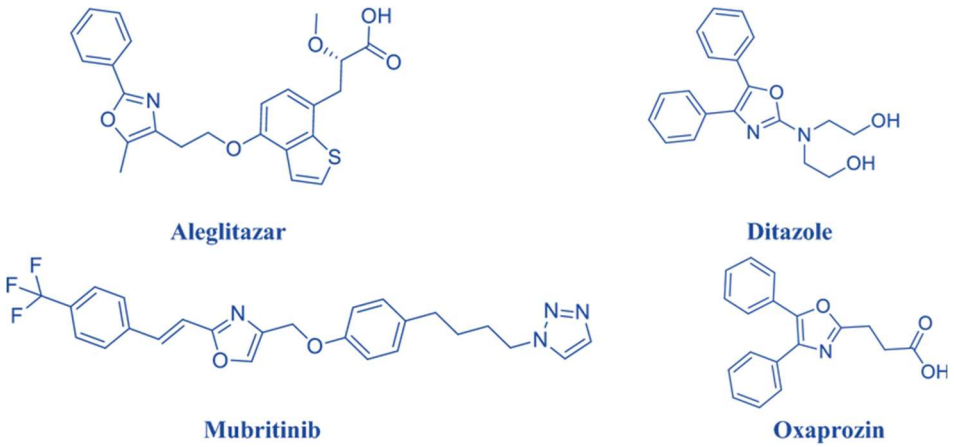

Figure 1. Some bioactive molecules containing oxazole ring.

■ Result and discussion

In this method, copper (II) complex supported on the surface of magnetic Fe_3O_4 nanoparticles functionalized with imidazole [Fe_3O_4@SiO_2-IM-$CuCl_2$] was successfully fabricated and its structure was well characterized by FT-IR, SEM, EDX, TEM, MAP, XRD, TGA, VSM, ICP-OES techniques. Experimental details of the fabrication of Fe_3O_4@SiO_2-IM-$CuCl_2$ nanocatalyst are outlined in **Scheme 1**. Magnetic nanoparticles have been synthesized based on previous methods. In the next step, imidazole was fixed on magnetic nanoparticles, which was accompanied by reaction with copper (II) chloride to form the final Fe_3O_4@SiO_2-IM-$CuCl_2$ catalyst.

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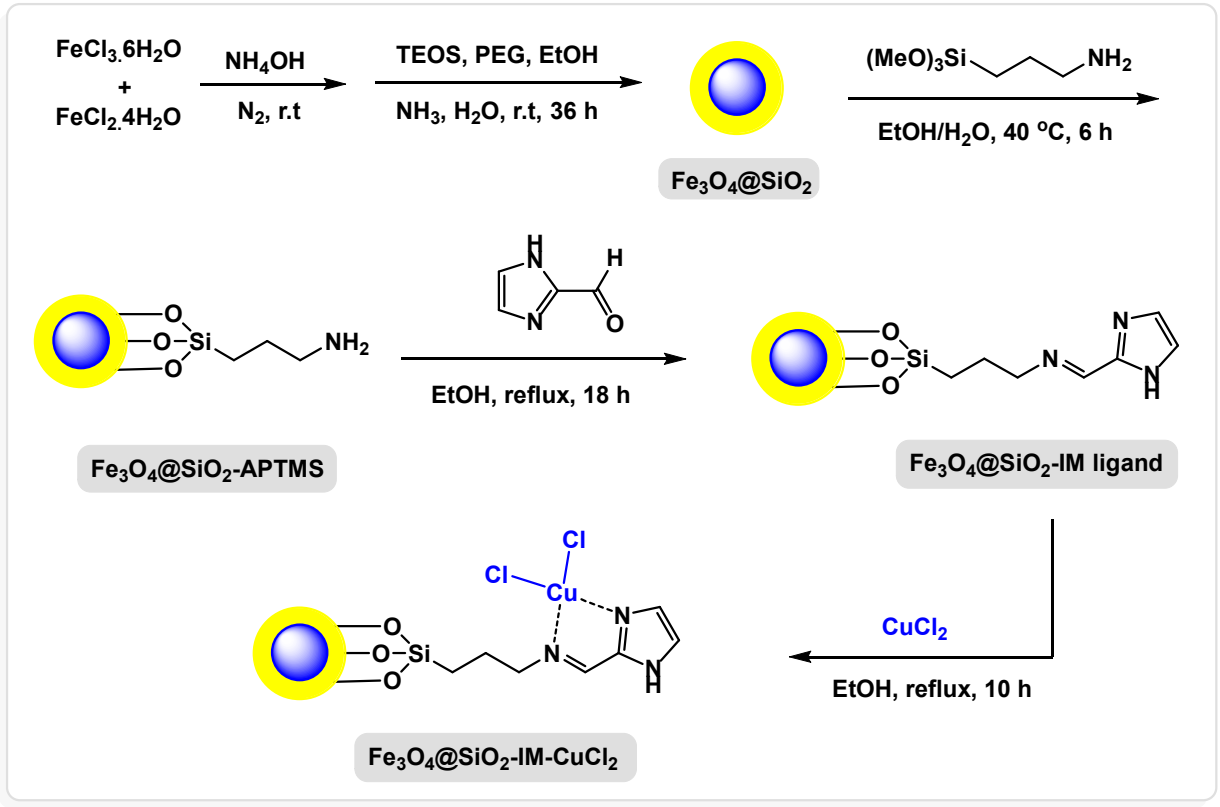
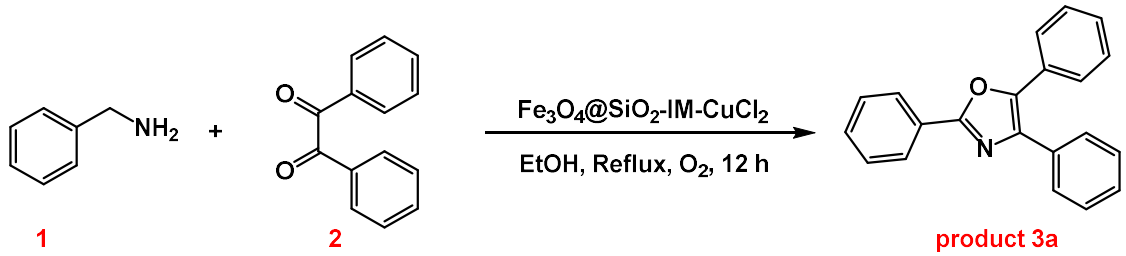


Scheme 1. General route for the fabrication of Fe_3O_4@SiO_2-IM-$CuCl_2$ nanocatalyst.

In order to identify the best conditions for the synthesis of triaryl oxazoles, we have studied the effect of catalyst on the model reaction of benzylamine (**1**) with benzil (**2**) in ethanol under reflux conditions for 12 h (**Figure 2**). The model reaction was not accomplished in the absence of catalyst. Details of these experiments revealed that 25 mg of Fe_3O_4-Serine-CuI nanomaterial is the optimal amount for the synthesis of triaryl oxazoles. Under the standardized conditions, several derivatives of benzylamine reacted with benzil in order to prepare oxazole derivatives which results are listed in **Table 1**. As shown in **Table 1**, the target oxazoles were synthesized with high to excellent yields.



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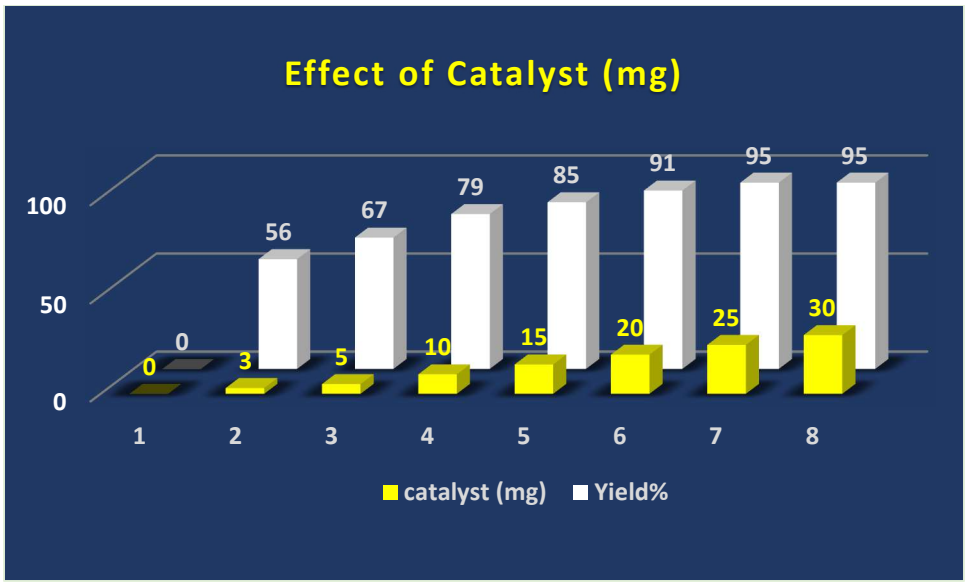

Figure 2. Optimization amount of the Fe_3O_4@SiO_2-IM-$CuCl_2$ catalyst for the synthesis of **product 3a**.

Table 1. Scope of Fe_3O_4@SiO_2-IM-$CuCl_2$ nanocomposite system for synthesis of triaryl oxazoles [a]

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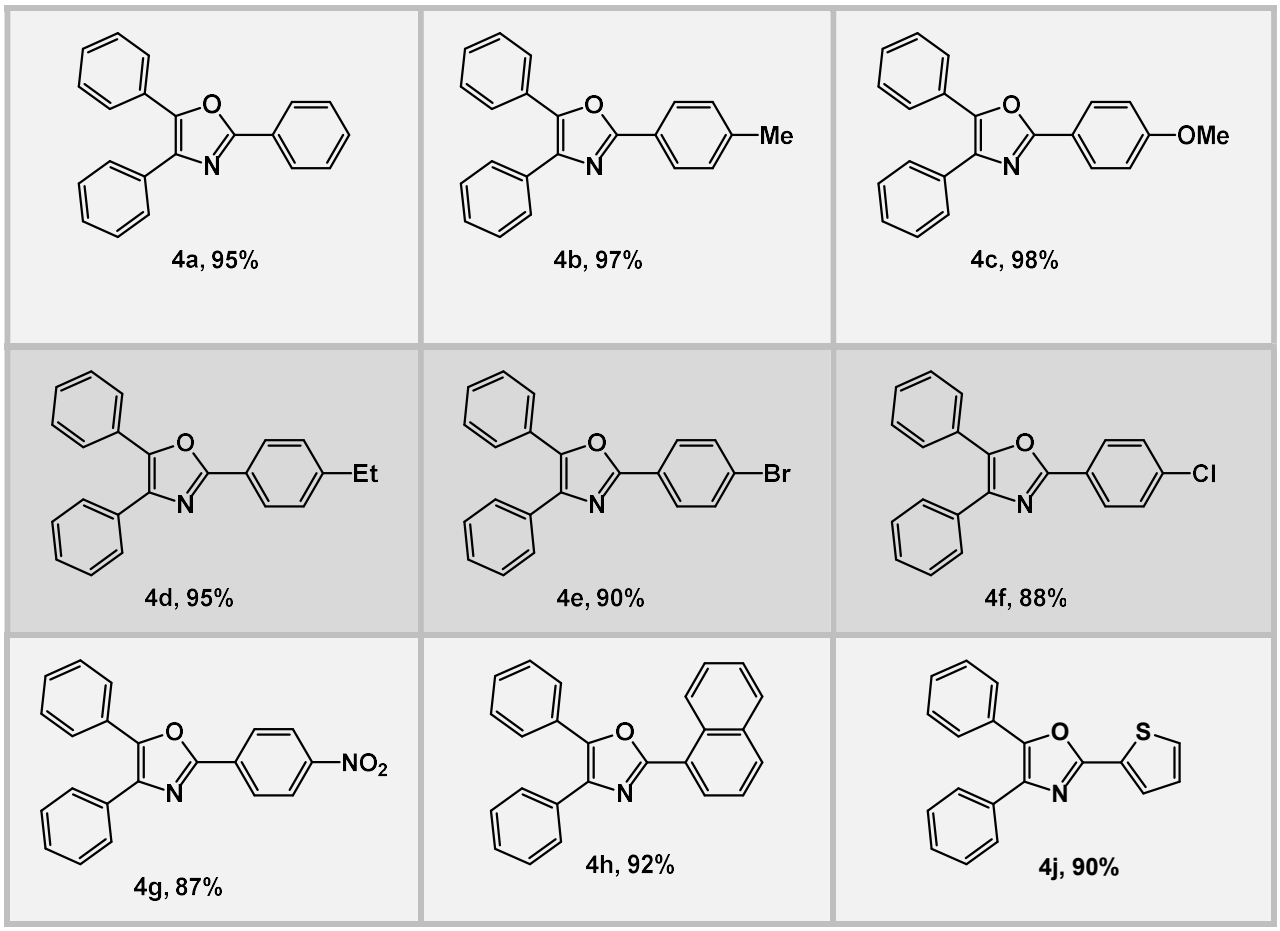

[a] Isolated yields.

A plausible pathway for Fe_3O_4@SiO_2-IM-$CuCl_2$ nanocomposite system for synthesis of triaryl oxazoles is shown in **Scheme 2**. First, 1a and O_2 activate the formation of [Cu] and then intermediate **A** is formed after the addition of benzil; its enolizational isomer coordination of copper ions provide intermediate **B**. compound **B** undergoes an intramolecular cyclization via an oxygen atom attacking the double bonds and gives the intermediate **C**. After an intramolecular hydrogen transfer, compound **D** is formed. And then the reaction proceeds via the copper catalyzed generation of a possible imine-type intermediate **E** with half of an oxygen molecule. Further dehydration of intermediate **E** affords the **product 3a**.

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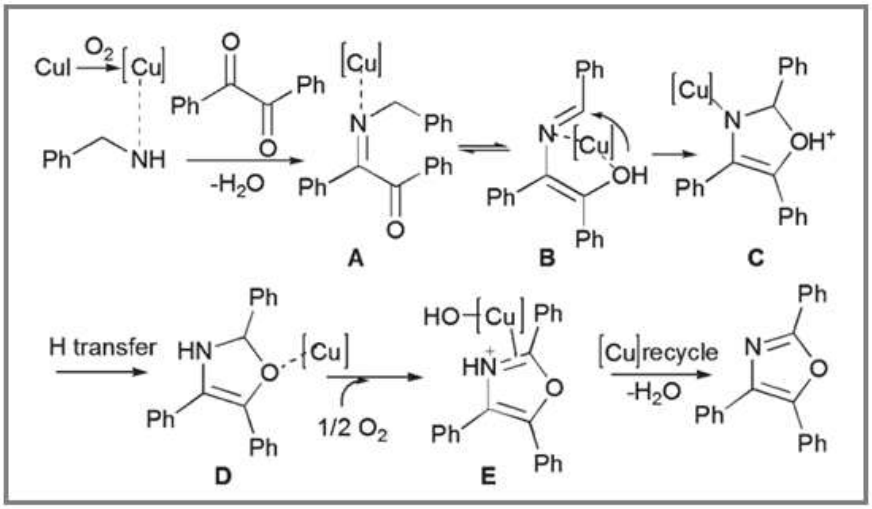

Scheme 2. Plausible pathway for Fe_3O_4@SiO_2-IM-$CuCl_2$ nanocomposite system for synthesis of triaryl oxazoles.

The recovery and reusability are an important characteristic in catalysis. In this respect, we decide to evaluate the reusability of Fe_3O_4@SiO_2-IM-$CuCl_2$ nanocatalyst in the model reaction of benzylamine (**1**) with benzil (**2**) [synthesis of **product 3a**]. The results confirmed that Fe_3O_4@SiO_2-IM-$CuCl_2$ catalyst have been recycled for 6 catalytic cycles without showing much drop in its catalytic activity (**Figure 3**).

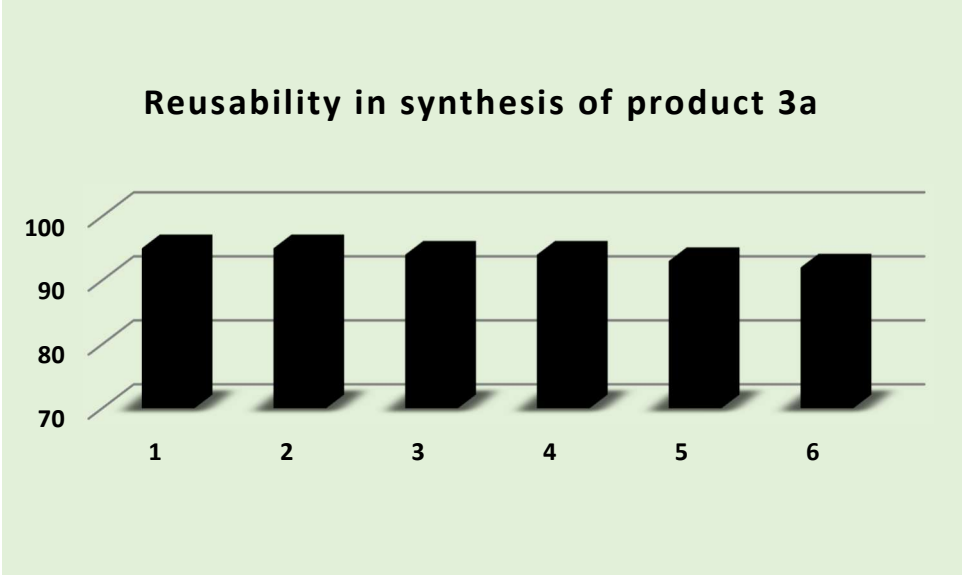

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Figure 3. Reusability of in Fe_3O_4@SiO_2-IM-$CuCl_2$ nanocatalyst in the model reaction of benzylamine (**1**) with benzil (**2**) [synthesis of **product 3a**].

■ Summary and Outlook

This methodology presented an attractive and ecofriendly catalytic system for the preparation of highly functionalized oxazole derivatives through reaction of benzylamine and benzil derivatives in ethanol under reflux conditions. The SEM and TEM images show that the nano-catalyst particles have been synthesized on a scale of less than 20 nm. Also, this image shows that the nano catalyst particles are synthesized in uniform and equal sizes and their shape is spherical. It is noteworthy that Fe_3O_4@SiO_2-IM-$CuCl_2$ nanocatalyst could be easily recovered by a simple magnetic separation and recycled at least 6 times without deterioration in catalytic activity.

■ Experimental

Chemicals were purchased from Fisher and Merck. The reagents and solvents used in this work were obtained from Sigma-Aldrich, Fluka or Merck and used without further purification.

Typical procedure for Fe_3O_4@SiO_2-IM-$CuCl_2$ nanocomposite catalyzed C-O cross-coupling reactions

A mixture of benzylamine (0.5 mmol), benzil (1 mmol), and Fe_3O_4@SiO_2-IM-$CuCl_2$ nanocatalyst (25 mg) in EtOH (3 mL) was stirred at 8 ºC for 12 h under molecular oxygen. The reaction progress was followed by TLC. At the end of the reaction, the mixture was cooled to room temperature, ethyl acetate (10 mL) was added and the catalyst was separated by an eternal magnet. The solvent was evaporated and the resulting crude material was purified by recrystallization from ether and ethyl acetate to afford the pure product. All the products reported here are known compounds and the spectroscopic data was matched literature values.

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