

# A simple synthesis of imidazole derivatives under microwave conditions in the presence of MgO nanoparticles supported on periodic mesoporous organosilica based on ionic liquids

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Received: 15 June 2021

Accepted: 05 July 2021

Published: 02 September 2021

## Abstract

A simple synthesis of imidazole derivatives has been prepared through multi-component reaction of 1,2-dicarbonyl compounds, various aldehydes and ammonium acetate in the presence of a highly efficient and reusable nanocatalyst (MgO@PMO-IL) in the solvent-free and microwave reaction conditions. The products were isolated in high yields by simple work-up procedure in short reaction time.

**Keywords:** Solvent-free conditions, Microwave, Multi component reactions, Metal nano-oxide.

## How to cite the article:

A. Afzali, R. Baharfar, S.L. Allahgholipour, A simple synthesis of imidazole derivatives under microwave conditions in the presence of MgO nanoparticles supported on periodic mesoporous organosilica based on ionic liquids, *Medbiotech J.* 2021; 5(3): 31-36. <https://doi.org/10.1001.1.22092528.2021.05.03.6.4>

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## 1. Introduction

Homogeneous catalysts are extremely active due to their high dispersion in the reaction medium. However, the main problem with homogeneous catalysts is their difficult separation from the reaction mixture, which is often associated with high residual generation and large energy consumption. Complex steps such as distillation and extraction must be used to separate homogeneous catalysts. On the other hand, in a heterogeneous catalysis system, the separation problem is solved and done by simple methods such as flatten out [1] and [2].

Ionic liquids (IL) are ionic compounds that resulting from combination of organic cations and various anions. They are also called liquid salts due to their low temperature melting points (<100°C), which are used as media in various chemical

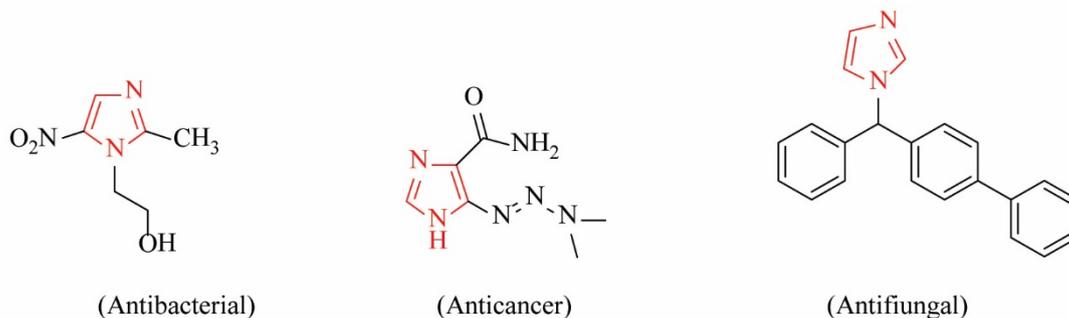
processes. These liquids are replaced as volatile organic solvents and have many advantages, such as high catalytic activity, high ionic conductivity, easy separation, high thermal stability and low vapor pressure [3] to [5]. Currently, ionic liquids have been used in various organic reactions such as Diels-Alder [6], Michael addition [7], N-alkylation [8] and MCRs [9].

Periodic mesoporous organosilicas have attracted much research attention due to a high specific surface area, uniform pore size with high coverage, thermal and mechanical stability. PMO have been prepared by using different functionalized organic precursors and successfully applied as supports for the immobilization and stabilization of organic and inorganic catalysts in chemical processes. Periodic mesoporous organosilica containing ionic liquid (PMO-IL), which has been recently reported by our research group, are as efficient support for metal catalysts, and can be recovered and reused several times without any remarkable decrease in their activity [10] to [13].

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Metal oxide nanoparticles such as magnesium oxide are used as a heterogeneous catalyst in the synthesis of many organic compounds and with their large surface area have created a site of small particles and high concentration of their corners. In addition, magnesium oxide has a dual role that contains a number of (O<sup>2-</sup>/O<sup>-</sup>) as anionic oxidic Lewis basic and OH as a hydroxylic Brønsted basic site along with Mg<sup>2+</sup> as a Lewis acid site [14]. For this reason, we used immobilized MgO nanoparticles on PMO-IL (MgO@PMO-IL) for the synthesis of imidazole ring. Multi-component reactions are processes in which one or more components are combined to form a

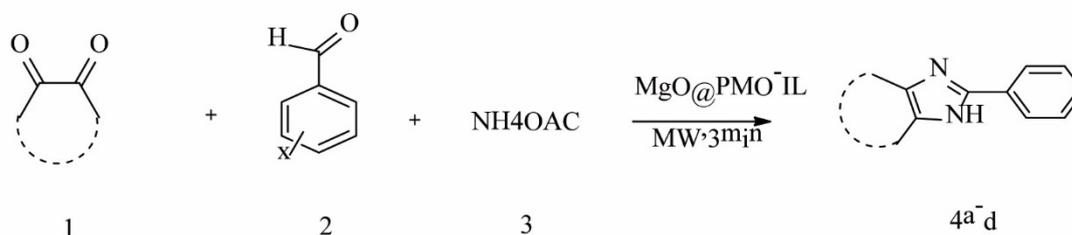
highly functional product that may be biologically active. Recently, multi-component reactions have generally been used in chemistry and the development of a new organic method [15]. Imidazole ring-containing compounds, which are a subset of nitrogen-containing heterocyclic compounds, have been reported to possess wide ranges of biological and pharmacological activities [16]. Also, imidazole derivatives have been used in photography as photosensitive compounds. Pharmacological properties of imidazole derivatives include anticancer [17], antifungal [18], antibacterial [19] and antitumor [20].



**Fig 1:** Drug derivatives of imidazole

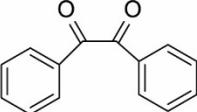
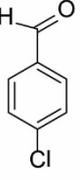
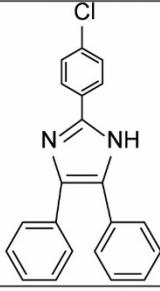
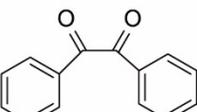
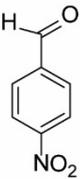
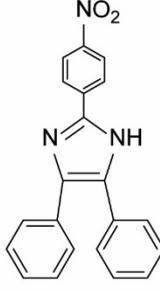
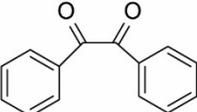
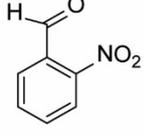
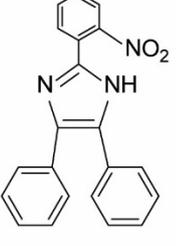
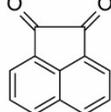
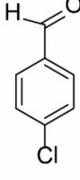
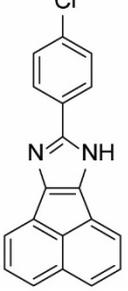
There are several methods that have been used in the synthesis of imidazole ring using various catalytic systems such as acetic acid [21], silica sulfuric acid [22], CAN [23], L-proline [24], HClO<sub>4</sub>-SiO<sub>2</sub> [25] and Fe<sub>3</sub>O<sub>4</sub> [26]. Most of these procedures have drawbacks such as expensive and toxic metal catalyst, long reaction time, hard work-up, large amounts of waste materials, reflux conditions and low yields. Microwave-assisted organic synthesis is a new growing in synthetic organic chemistry. This synthetic technique compared to some organic reactions is much faster and often with higher yields. Many of reactions that normally require to long times, at reflux temperature under classical

conditions can be completed within several minutes or even seconds in a microwave oven [27]. In a continuation of our studies on the synthesis of heterocyclic compounds [28] to [30], we developed a one-pot reaction for the synthesis of imidazoles via three-component reaction of 1,2-dicarbonyl compounds, aldehydes and ammonium acetate under microwave irradiation in the presence of MgO@-PMO-IL as an efficient method (Scheme 1). The products were synthesized under mild reaction conditions with high yields, low reaction time and simple work-up.



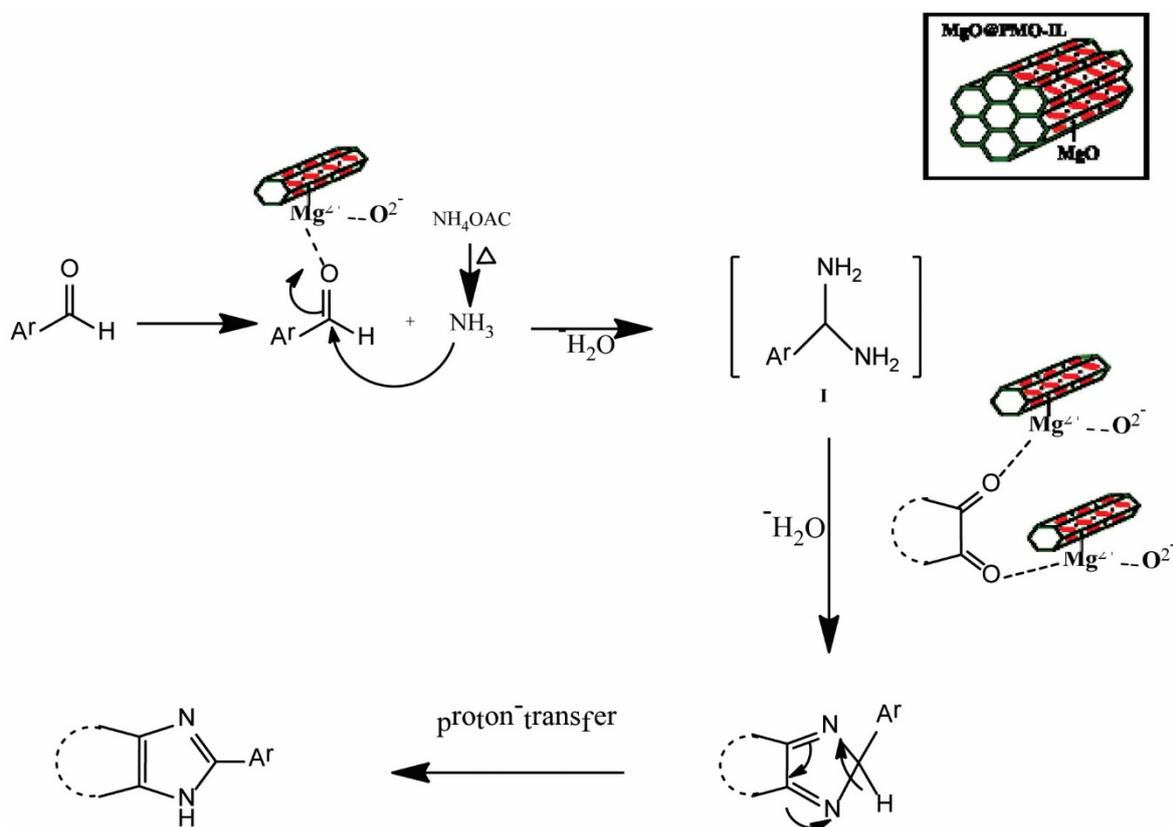
**Scheme 1:** Reaction of 1,2-dicarbonyl compound with aryl aldehydes and ammonium acetate in the presence of MgO@PMO-IL

**Table 1:** synthesis of the imidazole derivatives in the presence of MgO@PMO-IL under microwave irradiation.

Entry	1,2-dicarbonyl compound	Aldehyde	Product	Yield (%)
4a				95
4b				95
4c				95
4d				98

A plausible mechanism is shown in Scheme 2 [31]. Initially, carbonyl group of aldehyde is activated in the presence of MgO@PMO-IL and forms a diamine intermediate (I). In the next step, diamine intermediate (I) attacks to 1,2-dicarbonyl

compound, then intramolecular cyclization and subsequently [1,5] proton transfer leads to imidazole ring derivatives.



**Scheme 2:** Proposed mechanism for the synthesis of imidazoles using MgO@PMO-IL as heterogeneous nanocatalyst

**General procedure for the synthesis of compounds 4a-c:** A mixture of 1,2-dicarbonyl compound

(0.5 mmol), aldehyde (0.5 mmol), ammonium acetate (3 mmol) in the presence of 1% mole of MgO@PMO-IL were mixed thoroughly in a mortar. The reaction mixture was then irradiated in a domestic microwave oven. After completion of the reaction (followed by TLC), the product was obtained by recrystallization from diethylether. The synthesized compounds were analyzed by  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR.

Physical and spectral data for 2-(4-chlorophenyl)-4,5-diphenyl-1H-imidazole (4a)

With powder, mp: 262-264°C; yield (96%);  $^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ ),  $\delta_{\text{H}}$  (ppm): 7.23 (t, 1H,  $^3J_{\text{HH}} = 7.2$  Hz,  $\text{CH}_{\text{Ar}}$ ), 7.31 (t, 2H,  $^3J_{\text{HH}} = 7.2$  Hz,  $\text{CH}_{\text{Ar}}$ ), 7.38 (t, 1H,  $^3J_{\text{HH}} = 6.8$  Hz,  $\text{CH}_{\text{Ar}}$ ), 7.45 (t, 2H,  $^3J_{\text{HH}} = 7.2$  Hz,  $\text{CH}_{\text{Ar}}$ ), 7.49-7.53 (m, 4H,  $\text{CH}_{\text{Ar}}$ ), 7.55 (d, 2H,  $^3J_{\text{HH}} = 8.4$  Hz,  $\text{CH}_{\text{Ar}}$ ), 8.10 (d, 2H,  $^3J_{\text{HH}} = 8.8$  Hz,  $\text{CH}_{\text{Ar}}$ ), 12.79 (s, 1H, N-H);  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ),  $\delta_{\text{C}}$  (ppm):

127.0, 127.2, 127.5, 128.3, 128.6, 128.8, 129.0, 129.1, 129.6, 131.3, 133.2, 135.4, 137.7, 144.8 ( $\text{C}_{\text{Ar}}$ )

In conclusion, we were able to synthesize imidazole derivatives under microwave and solvent-free reaction conditions using a high-efficiency heterogeneous catalyst with a short reaction time. We were also able to recover and reuse the catalyst seven times without reducing its efficiency.

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