



The 21st International Electronic Conference on Synthetic Organic Chemistry

1–30 November 2017
chaired by Dr. Julio A. Seijas Vázquez



<http://sciforum.net/conference/ecsoc-21>

Imidazole dicarboxylic acid as a new catalyst for the synthesis of 1,4-dihydropyridines in ball mill

Mohaddeseh Shah Hosseini,^a Hossein Ghafuri, ^{*a} Hamid Reza Esmaili Zand^a

^a*Catalysts and Organic Synthesis Research Laboratory, Department of Chemistry, Iran
University of Science and Technology, Tehran, Iran*

**E-mail: Ghafuri@iust.ac.ir*

Abstract

One useful technique which used to combine economic and ecofriendly benefits is the multicomponent reaction (MCR), which contains some synthesis phases to enhance cost-effectiveness and energy savings and are carried out without separation of intermediates. MCRs have shown to be leading techniques in heterocyclic chemistry in the context of green methods. These procedures are atom economic in nature, and forming directed products in high yields. To access green chemistry in synthesis, one promising approach is to replace new green methods with classical methods by means of non-toxic reagents. In order to use green and non-toxic reagent and catalyst, 1-H-imidazole-4,5-dicarboxylic acid was synthesized using previous reported method. By means of this method, 1-H-imidazole-4,5-dicarboxylic acid was synthesized with more acidic properties than normal imidazole. After synthesizing this homogeneous catalyst, an efficient three component procedure was advanced for synthesis of 1,4-dihydropyridines (1,4-DHP) at room temperature in ball-mill and using imidazole

dicarboxylic acid as catalyst. The structures of the new compounds were completely confirmed by useful spectral analyses. Imidazole dicarboxylic acid was synthesized and characterized by FT-IR and its melting point. The key advantages of this process are good to high yields, short reaction times, easy work-up and eco-friendly and non-toxic reagents.

Keywords: Imidazole dicarboxylic acid, 1,4-dihydropyridines, ball-mill

1. Introduction

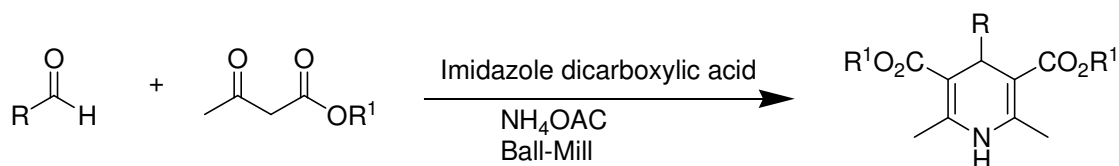
One of the effective tools for an improvement in environmentally benign technique for synthesis of organic structures is the multicomponent reaction (MCR) [1-3]. MCRs have proved to be efficient bond-forming techniques in heterocyclic chemistry in the context of green approaches [4,5]. These protocols are also very flexible in nature [6]. Among other reaction conditions, the nature of the catalyst is very important in determining yield and general applicability [7]. Thus, the development of specific catalysts for MCRs will remain a matter of interest.

One of the promising green chemistry approaches is to use atom-efficient benign materials [8]. Catalysts are required for to make materials more efficient and to reduce the reaction times. Heterogeneous catalysts have also attracted a lot of attention in heterocyclic synthesis [8–10].

imidazole is an aromatic heterocycle compound, classified as a diazole, and having non-adjacent nitrogen atoms. Many natural products, contain the imidazole ring. These imidazoles feature varied substituents. The ring system of imidazole is present in important biological building blocks, such as histidine and the related hormone histamine. Many drugs contain an imidazole

ring, such as certain antifungal drugs, the nitroimidazole series of antibiotics, and the sedative midazolam.

To this purpose, here the scope of imidazole dicarboxylic acid as a heterogeneous catalyst for efficient, convenient and facile green synthesis of functionalized 1,4-dihydropyridine derivatives through the one-pot reaction was described. (Scheme 1).



Scheme 1. Synthesis of 1,4-dihydropyridines

2. Experimental section

2.1. General

Reagents and chemicals were all purchased from Aldrich, Merck and Fluka. Melting points were measured with an Electrothermal 9100 apparatus and are uncorrected. Spectra of FT-IR were recorded by the method of KBr pellet on a Shimadzu IR-470 spectrometer.

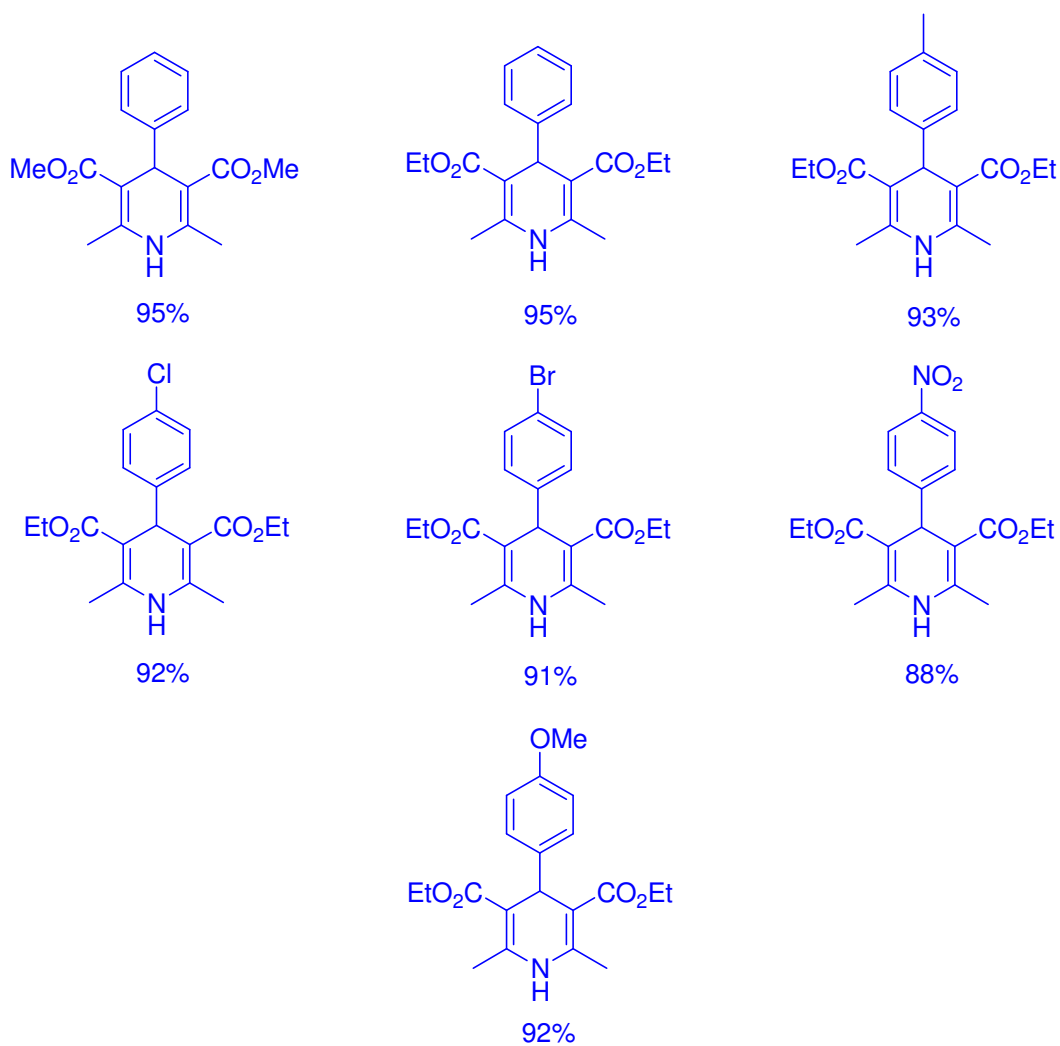
2.1. General synthesis of functionalized 1,4-dihydropyridine derivatives

Initially, 1 mmol of substituted aldehyde, 1.1 mmol of dicarbonyl compound and 50 mg Imidazole dicarboxylic acid (50 mg) as catalyst (30 mg) was added to ball-mill and mixed for 5 min. Subsequently, 1 mmol of ammonium acetate was added to it and milling continued for another 15 min. The reaction progress was monitored by TLC. After completion of the reaction, the catalyst was filtered, and the solvent was evaporated to obtain the crude product. The crude was recrystallized by ethanol to obtain pure product.

3. Results and discussion

The synthesis reaction of 1,4-dihydropyridine can be done by combination of benzaldehyde with various dicarbonyls (table 1). The optimized conditions for the reaction was using 0.05 g of Imidazole dicarboxylic acid in ball-mill.

Table 3. Synthesis of 1,4-dihydropyridines in optimal conditions.



4. Conclusion

In summary, we used an acidic imidazole derivative as a catalyst to synthesize 1,4-dihydropyridines. We provide a simple and green method for the synthesis of 1,4-dihydropyridine derivatives in presence of environmentally friendly catalyst.

Acknowledgements

The authors gratefully acknowledge the partial support from the Research Council of the Iran University of Science and Technology.

References

- [1] B.G. Manoj, D.B.B. Vasco, L. Rafael, S.B. Paula, S.V. Rajender, *Chem. Soc. Rev.* 42 (2013) 5522–5551.
- [2] S. Maddila, S. Rana, R. Pagadala, S. Kankala, S.N. Maddila, S.B. Jonnalagadda, *Catal. Commun.* 61 (2015) 26–30.
- [3] S.N. Maddila, S. Maddila, W.E. van Zyl, S.B. Jonnalagadda, *RSC Advances*. 5 (2015) 37360–37366.
- [4] R. Pagadala, S. Maddila, S. Rana, S.B. Jonnalagadda, *Curr. Org. Synth.* 12 (2015) 163–167.
- [5] B.B. Toure, D.G. Hall, *Chem. Rev.* 109 (2009) 4439–4486.
- [6] D. Reinhardt, F. Ilgen, D. Kralisch, B. Konig, G. Kreisel, *Green Chem.* 10 (2008) 1170–1181.
- [7] Y. Gu, F. Jerome, *Green Chem.* 12 (2010) 1127–1138.

- [8] T.A. Paul, M.K. Mary, *Acc. Chem. Res.* 35 (2002) 686–694.
- [9] B.M. Reddy, A. Khan, *Catal. Rev. Sci. Eng.* 47 (2005) 257–296.
- [10] A. Dandia, V. Parewa, A.K. Jain, K.S. Rathore, *Green Chem.* 13 (2011) 2135–2145.