

## P<sub>2</sub>O<sub>5</sub>/Al<sub>2</sub>O<sub>3</sub>: An efficient and Reusable Catalyst for the Synthesis of Trisubstituted Imidazoles under solvent- free conditions

Mona Esmaeilzadeh, Sadegh Allameh\* and Hossein Behmadi

Department of Chemistry, Mashhad Branch, Islamic Azad University, Mashhad, IRAN

Corresponding Email: [sadegh\\_allameh@yahoo.com](mailto:sadegh_allameh@yahoo.com)

### ABSTRACT

An efficient and simple one-pot multicomponent procedure for the synthesis of imidazoles from the condensation of benzyl, ammonium acetate and aromatic aldehydes in the presence of a catalytic amount of alumina-supported phosphorus pentoxide /Al<sub>2</sub>O<sub>3</sub> (P<sub>2</sub>O<sub>5</sub>/Al<sub>2</sub>O<sub>3</sub>) under solvent- free conditions is reported.

**Keywords:** Imidazoles, P<sub>2</sub>O<sub>5</sub>/Al<sub>2</sub>O<sub>3</sub>, Solvent- free conditions, Reusable catalyst;

### INTRODUCTION

Reusable catalysts attracted considerable amount of interest in organic synthesis owing their easy work-up procedures, easy filtration and minimization of cost and waste generation due to reuse and recycling of these catalysts [1].

Multicomponent reactions (MCRs) have become important tools in modern preparative synthetic chemistry because they increase the efficiency by combining several operational steps without isolation of intermediates or changing the reaction conditions [2, 3]. Multicomponent reactions (MCRs) have emerged as valuable tools for the preparation of structurally diverse chemical libraries of drug-like heterocyclic compounds [4-6].

The imidazole nucleus is an important substructure found in numerous natural products and pharmacologically and biologically active compounds [7-9]. Many of these methods have been reported on for the synthesis of imidazoles in the presence of various catalytic systems such as L-proline [10], ZrCl<sub>4</sub> [11], InCl<sub>3</sub>·3H<sub>2</sub>O [12], HClO<sub>4</sub>/SiO<sub>2</sub> [13], BF<sub>3</sub>/SiO<sub>2</sub> [14], heteropolyacids [15], Yb(OTf)<sub>3</sub>[16], ionic liquids[17] and NiCl<sub>2</sub>·6H<sub>2</sub>O/Al<sub>2</sub>O<sub>3</sub> [18]. Many of these methods suffer from some limitations such as long reaction times, drastic reaction conditions, expensive reagents and low to moderate yields. Hence, the development of simple, efficient, high-yielding and environmentally friendly approaches is desirable.

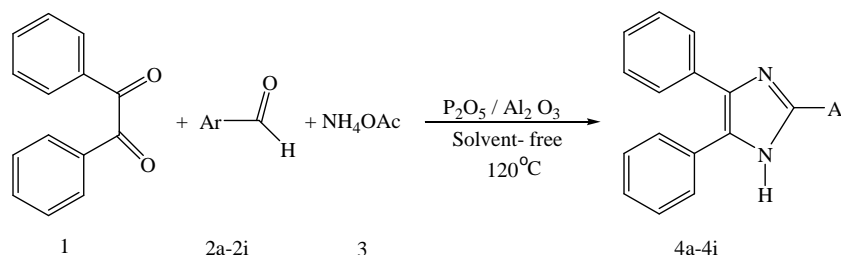


Fig. 1. The catalytic effects of P<sub>2</sub>O<sub>5</sub>/Al<sub>2</sub>O<sub>3</sub> for the synthesis imidazole derivatives

It is therefore of interest to examine the behavior of P<sub>2</sub>O<sub>5</sub>/Al<sub>2</sub>O<sub>3</sub> as catalyst for the synthesis of imidazoles. To the best of our knowledge, synthesis of imidazole derivatives in the presence of a catalytic amount of P<sub>2</sub>O<sub>5</sub>/Al<sub>2</sub>O<sub>3</sub>

under solvent- free conditions has not yet been reported in literatures. During the course of our studies toward the development of new routes to the synthesis of heterocyclic compounds [19-22], herein we report the catalytic effects of P2O5/Al2O3 for the synthesis imidazole derivatives (Figure 1).

Initially, in order to optimize the reaction conditions for preparation of products, the reaction of benzyl (1 mmol), 4-chlorobenzaldehyde (1 mmol) and ammonium acetate (2 mmol) in the presence of various amount of catalyst (P2O5/Al2O3) used as a model reaction. The best result have been obtained at (0.07 g) of catalyst, 120°C and under solvent- free conditions (Table1, Entry 10).

The generality of this process was demonstrated by the wide range of aromatic aldehydes to synthesize the corresponding products in high to excellent yields (Table 2).

**Table 1. Effect of amount of catalyst, solvent and temperature in the model reaction**

Entry	Catalyst (g)	Solvent	Temp (°C)	Time (min)	Yield (%)
1	---	---	120	60	38
2	0.03	---	100	20	44
3	0.03	---	110	15	58
4	0.03	---	120	10	65
5	0.05	---	100	20	75
6	0.05	---	110	15	78
7	0.05	---	120	10	80
8	0.07	---	100	10	83
9	0.07	---	110	15	87
10	0.07	---	120	20	92
11	0.10	---	120	20	92
12	0.07	EtOH	Reflux	120	21
13	0.07	DMF	Reflux	120	25

**Table 2. Synthesis of trisubstituted imidazole derivatives under optimized conditions**

Entry	Ar	Product	Yield (%)	Time (min)	Melting pint (°C)[23]	
					Found	Reported
1	3-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	4a	80	20	312-314	311-312
2	4-MeOC <sub>6</sub> H <sub>4</sub>	4b	85	30	221-223	223-224
3	4-MeC <sub>6</sub> H <sub>4</sub>	4c	83	20	232-234	233-234
4	4-ClC <sub>6</sub> H <sub>4</sub>	4d	92	10	263-265	260-261
5	4-HOC <sub>6</sub> H <sub>4</sub>	4e	90	20	244-246	245-247
6	4-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	4f	80	30	233-235	232-233
7	3-HOC <sub>6</sub> H <sub>4</sub>	4g	88	15	255-256	257-258
8	4-BrC <sub>6</sub> H <sub>4</sub>	4h	88	15	251-253	254-256
9	C <sub>6</sub> H <sub>5</sub>	4i	85	10	276-277	275-276

In summary, we wish, reporting the use of P2O5/Al2O3 as green recyclable and heterogeneous catalyst for the synthesis of trisubstituted imidazoles.

## MATERIALS AND METHODS

All chemicals were obtained from Merck Company and used as received. Melting points were determined on a SMP3 melting point apparatus. The IR spectra were obtained on a Tensor 27 Bruker spectrophotometer as KBr disks. The 1H NMR (300 MHz) spectra were recorded using Bruker 300 spectrometer. The compounds were identified by the comparison of their physical and spectroscopic data with those of known compounds.

### Preparation of catalyst (P2O5/Al2O3)

A mixture of alumina (3 g) and phosphorus pentoxide (3 g) was stirred at room temperature for 10 min to adsorb P2O5 on surface of support. The mixture dried at 120 °C for 1 h and solid powder was obtained in good yield.

### General procedure for the synthesis of trisubstituted imidazoles (4a-4i)

A mixture of benzil 1 (1 mmole), aromatic aldehydes 2a-2i (1 mmole), ammonium acetate 3 (2 mmol) and P2O5/Al2O3 (0.07 g) was heated in the oil bath at 120°C for 10-30 min. After completion of reaction (monitored by TLC) the mixture was cooled to room temperature and then hot ethanol (10 mlit) was added. Due to the fact that the catalyst was insoluble in hot ethanol, it could therefore be recycled by a simple filtration. The separated catalyst reused in model reaction without appreciable reduction in the catalytic activity. The results of the first experiment and subsequent experiments were almost consistent in yields (92, 88 and 84%).

**Selected Spectral data****2-(3-nitrophenyl)-4,5-diphenyl-1H-imidazole(4a)**

<sup>1</sup>H NMR (300 MHz, DMSO- d<sub>6</sub>): δ 7.04-7.57 (m, 10H, arom-H) , 7.79 (t, 1H, arom-H), 8.22 (d, 1H, arom-H), 8.53 (d, 1H, arom-H), 8.97 (s, 1H , arom- H), 13.10 (s, 1H, N-H). FT- IR (KBr disc): ν 3400, 3057, 1522, 1348, 699 cm<sup>-1</sup>.

**2-(4-methoxyphenyl)-4,5-diphenyl-1H-imidazole(4b)**

<sup>1</sup>H NMR (300 MHz, DMSO- d<sub>6</sub>): δ 3.83 (s, 3H ,CH<sub>3</sub>) , 7.06 (d, 2H, arom-H), 7.31- 7.54 (m, 10H, arom-H), 8.03 (d, 2H, arom-H), 12.52 (s, 1H , N- H). FT- IR (KBr disc): ν 3400, 3058, 1611, 1492, 695 cm<sup>-1</sup>.

**2-(4-methylphenyl)-4,5-diphenyl-1H-imidazole(4c)**

<sup>1</sup>H NMR (300 MHz, DMSO- d<sub>6</sub>): δ 2.36 (s, 3H, CH<sub>3</sub>) , 7.23-7.57 (m, 10H, arom-H), 7.29 (d, 2H, arom-H), 7.99 (d, 2H, arom-H), 12.60 (s, 1H, N- H). FT- IR (KBr disc): ν 3400, 3028, 1493, 695 cm<sup>-1</sup>.

**RESULTS AND DISCUSSION**

Treatment of benzyl, aromatic aldehydes and ammonium acetate under solvent-free conditions in the presence of a catalytic amount of P2O<sub>5</sub>/Al<sub>2</sub>O<sub>3</sub> gave products which were identified as imidazoles. All products gave satisfactory spectral data in accord with the assigned structures.

**CONCLUSION**

In conclusion, we have reported the synthesis of some trisubstituted imidazoles through reaction of benzyl, aromatic aldehydes and ammonium acetate under solvent-free conditions in the presence of a catalytic amount of P2O<sub>5</sub>/Al<sub>2</sub>O<sub>3</sub>.

**REFERENCES**

- [1] M. H. Alizadeh, H. Razavi, F.F. Bamoharram. *J. Mol. Catal.*, **2003**; 206, 89.
- [2] J. Zhu, H. Bienayme, H. *Multicomponent Reactions. Wiley-VCH: Weinheim*, **2005**.
- [3] V. P. Litvinov, *Russ. Chem. Rev.*, **2003**; 72, 69.
- [4] I. Ugi, A. Domling, W. *Horl. Endeavour*. **1994**; 18, 115.
- [5] L. F. Tietze, A. Modi, *Med. Res. Rev.*, **2000**; 20, 304.
- [6] I. Ugi, A. Dömling, B. Werner, *J. Heterocycl. Chem.* **2000**; 37, 647.
- [7] S. A. Laufer, W. Zimmermann, K. J. Ruff, *J. Med. Chem.*, **2004**; 47, 6311.
- [8] S. E. Wolkenberg, D. D. Wisnoski, W. H. Leister, Y. Wang, *Org. Lett.*, **2004**; 6, 1453.
- [9] J. G. Lombardino, E. H. Wiseman, *J. Med. Chem.*, **1974**; 17, 1182.
- [10] S. Samai, G. C. Nandi, P. Singh, M.S. Singh, *Tetrahedron*. **2009**; 65.
- [11] G. V. M. Sharma, Y. Jyothi, P. S. Lakshmi, *Synth. Commun.* **2006**; 36.
- [12] S. D. Sharma, P. Hazarika, D. Konwar, *Tetrahedron Lett.* **2008**; 49.
- [13] S. Kantevari, S. V. N. Vuppapalapati, D. O. Biradar, L. Nagarapu, *J. Mol. Catal.* **2007**; 266.
- [14] B. Sadeghi, B.B.F. Mirjalili, M.M. Hashemi, *Tetrahedron Lett.* **2008**; 49.
- [15] M. M. Heravi, F. Derikvand, F. F. Bamoharram, *J. Mol. Catal.*, **2007**; 263.
- [16] L. M. Wang, Y. H. Wang, H. Tian, *J. Fluor. Chem.*, **2006**; 127.
- [17] A. Hasaninejad, A. Zare, M. Shekouhy, J. Ameiri Rad, *J. Comb. Chem.* **2010**; 12.
- [18] M. M. Heravi, K. Bakhtiari, H. A. Oskooie, S. Taheri, *J. Mol. Catal.*, **2007**; 263.
- [19] S. Allameh, M. M. Heravi, M. M. Hashemi, F. Bamoharram, *Chines Chemical Letters*. **2011**; 22, 131.
- [20] A. Davoodnia, S. Allameh, S. Fazli, N. Tavakoli- Hoseini, *Chemical papers.*, **2011**; 65, 5.
- [21] G. Yasaghi, A. Davoodnia, S. Allameh, A. Zare- Bidaki, N. Tavakoli- Hoseini, *Bull. Korean Chem Soc.*, **2012**; 33, 8.
- [22] M. Roshani, S. Allameh, E. Darkooti, *Asian Journal of Chemistry*, **2013**; 125, 4.
- [23] M. Ashrafi, A. Davoodnia, N. Tavakoli- Hoseini, *Bull. Korean Chem Soc.*, **2013**; 34, 5.