

Synthesis of Nanostructured sawdust-BF₃: An efficient reagent for synthesis of 2,3,5-substituted-2H-pyrazole derivatives

Hamidreza Molaei, Bahareh Sadeghi*, Mohamadhosaine Moslemin

Department of Chemistry, Yazd Branch, Islamic Azad University, P.O. Box 89195-155, Yazd, Iran

Abstract

Nanostructured sawdust-BF₃ has been prepared and shown to efficiently catalyse the one-pot reaction of 1,3-diketones and hydrazines under solvent-free conditions, to afford the corresponding 2,3,5-substituted-2H-pyrazole derivatives in excellent yields.

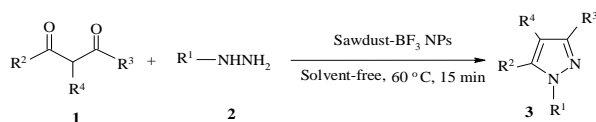
Keywords: sawdust-BF₃ NPs, 1,3-diketones, hydrazines, 2,3,5-substituted-2H-pyrazoles, solid acids.

1 Introduction

Heterocycles are popularly known for displaying a wide range of the biological properties [1]. The recent success of pyrazole based COX-II inhibitors and their applications in medicinal chemistry have amplified the importance of pyrazoles to even a greater extent [2]. Several pharmaceutical drugs including celecoxib [2] and rimonabant [3] utilize the pyrazole as their core molecular entity [4,5]. Pyrazoles are often synthesized by the 1,3-dipolar cycloaddition reaction of nitrilimines with alkynes [6], alkyne surrogates [7], or alkenes [5,6], pyrazoles also can be synthesized *via* 1,3-dipolar cycloadditions of diazo compounds [8], reaction of chalcones [9] and hydrazines, a four-component coupling of terminal alkynes, hydrazine, carbon monoxide, and aryl iodides [10], and the direct condensation of 1,3-diketones and hydrazines in

the presence of an acidic catalyst [11]. The last one is the simplest and most straightforward procedure for the synthesis of pyrazoles. A variety of the catalysts such as H₂SO₄ [12], polystyrene supported sulfonic acid [13], layered zirconium sulfophenyl phosphonate [a-Zr(CH₃PO₃)_{1.2}(O₃PC₆H₄SO₃H)_{0.8}] [14], Sc(OTf)₃ [15], Y-zeolite [16] and magnesium perchlorate Mg(ClO₄)₂ [17] have been employed to affect this transformation.

Application of environmentally benign solvent-free conditions and solid acid catalyst represents powerful green procedure. In this work, the application of solid phase acidic green nano catalyst have investigated for synthesis of 2,3,5-substituted-2H-pyrazole derivatives (Scheme 1).



Scheme 1. Reaction between 1,3-diketones and hydrazines catalyzed by Nanostructured sawdust-BF₃ under solvent-free conditions

2. EXPERIMENTAL

Melting points were determined with an Electrothermal 9100 apparatus. Elemental analyses were performed at the analytical laboratory of Science and Researchs Unite of Islamic Azad University. The morphology of the catalyst were observed using a SEM model VEGA//TESCAN with an accelerating voltage of 15 kV. The chemicals used in this work were purchased from Fluka (Buchs, Switzerland) and were used without further purification.

2.1. Synthesis of sawdust-BF₃ NPs

The nano-sawdust-BF₃ was prepared by combination of BF₃.OEt₂ (0.6 g, 4.2 mmol) drop by drop over 10 min via a syringe to sawdust powder (0.4 g) in a 50 ml flask include 5ml diethyl ether at room temperature. The reaction mixture was then stirred and then after 30 min, the ashy powder was separated and dried in an oven at 60°C for 4h and then pulverized at the mortar [18]. The morphology and size of sawdust-BF₃ NPs was observed by SEM images. As shown in Figure 1, the size of sawdust-BF₃ NPs is below 50 nm.

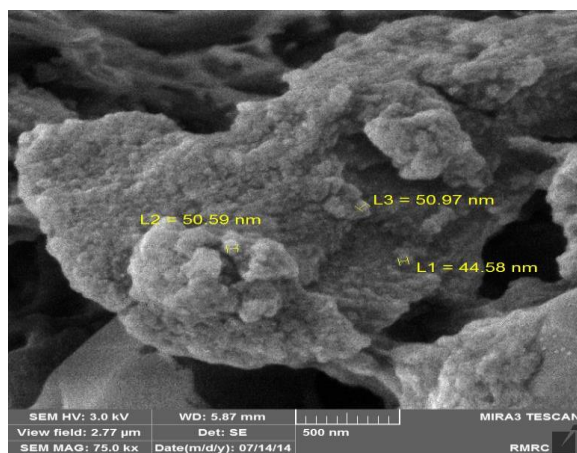


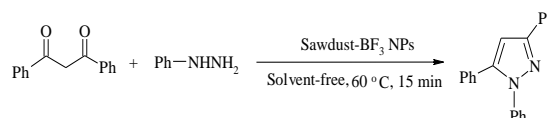
Fig. 1. The SEM image of Nanostructured sawdust-BF₃

2.2. General procedure for preparation of compounds 3a-p

A mixture of 1,3-diketones (2 mmol), hydrazines (2 mmol) and sawdust-BF₃ NPs (0.001 g) were placed in a round bottom flask. The materials were mixed and heated in 60 °C for 15 min. The progress of the reaction was followed by TLC (n-hexane:ethylacetate). After the completion of the reaction, the mixture was filtered to separate the catalyst. After evaporation of the solvent, the crude product was recrystallized from hot ethanol to obtain the pure compound.

3. RESULTS AND DISCUSSION

In continuation of previous research on the use of solid acids in organic synthesis [19-21], the synthesis of 2,3,5-substituted-2H-pyrazole derivatives have investigated by condensation of 1,3-diketones and hydrazines in the presence of sawdust-BF₃ NPs as a inorganic solid acid. To optimize the reaction conditions, the reaction of 1,3-diphenylpropane-1,3-dione and phenylhydrazine was used as a model reaction to pyrazoles synthesis. According to the obtained data, using the sawdust-BF₃ NPs (0.001 g) under solvent-free conditions for the pyrazoles formation is the best reaction conditions (Scheme 2).



Scheme2 Reaction between 1,3diphenylpropane-1,3-dione and phenylhydrazine catalyzed by Nanostructured sawdust-BF₃

The stable catalyst is easily prepared and used for preparation of 2,3,5-substituted-2H-pyrazole derivatives. To prove the better catalytic activity of sawdust-BF₃ NPs, Initially, the reaction has studied with other catalysts under solvent-free conditions at 15 min, and the results are listed in Table 1.

Entry	Catalyst	Time (min)	Yield ^a (%)
1	H ₂ SO ₄	15	35
2	Y-Zeolite	15	45
3	Sc(OTf) ₃	15	83
4	Zr(CH ₃ PO ₃) _{1.2} (O ₃ PC ₆ H ₅) _{0.8}	15	70
5	Mg(ClO ₄) ₂	15	80
6	sawdust-BF ₃ NPs	15	96
7	PSSA*	15	95
			-

Table 1. Reaction between 1,3-diphenylpropane-1,3-dione and phenylhydrazine in different catalytic and under solvent-free conditions

^aIsolated yield *Polystyrene supported sulfonic acid

Table 1 clearly demonstrates that sawdust-BF₃ NPs is an effective catalyst in term of yield of obtained product.

To find out the optimum quantity of sawdust-BF₃ NPs, the model reaction was carried out at 60 °C using different quantities of sawdust-BF₃ NPs (Table 2). According to the obtained data, 0.001 g of sawdust-BF₃ NPs gave excellent yield in 15 min (Table 2, entry 1).

Entry	Solvent	Time /min	Yield ^a /%
1	CHCl ₃	15	57
2	EtOH	15	85
3	EtOAc		22
4	n-hexan	15	Trace
5	Solvent-free	15	96

Table 2. Optimization amount of sawdust-BF₃ NPs on the reaction of 1,3-diketones and hydrazines at 60 °C

The above reaction was also examined in various solvents (Table 3).

The results indicated that different solvents affected the efficiency of the reaction. Most of these solvents required a longer time and gave moderate yields, and the best results were obtained when solvent-free conditions was used (Table 3, entry 5).

Entry	Catalyst (g)	Time (min)	Yield ^a (%)
1	0.001	15	96
2	0.0005	15	49
3	0.0007	15	73
4	0.0015	15	96

^aIsolated yield

Table 3. Solvent effect on the reaction between 1,3-diketones and hydrazines catalyzed by sawdust-BF₃ NPs

To study the scope of the reaction, a series of 1,3-diketones and hydrazines catalyzed by sawdust-BF₃ NPs were applied. The results are shown in Table 4. In all cases, hydrazines

substituted with either electron-donating or electron-withdrawing groups underwent the reaction smoothly and gave the products in excellent yields.

Table 4. Reaction between 1,3-diketones and hydrazines catalyzed by sawdust-BF₃ NPs

Entry	R ¹	R ²	R ³	R ⁴	Product	Yield% ^a	m.p. (°C)	
							found	reported (Ref.)
1	2,4-NO ₂ C ₆ H ₄	C ₆ H ₅	C ₆ H ₅	H	3a	95	148-149	149-150 ¹⁷
2	2,4-NO ₂ C ₆ H ₄	C ₆ H ₅	CH ₃	H	3b	67	129-131	128-130 ¹⁴
3	2,4-NO ₂ C ₆ H ₄	CH ₃	CH ₃	H	3c	93	122-124	122-123 ¹⁵
4	2,4-NO ₂ C ₆ H ₄	CH ₃	CH ₃	Cl	3d	94	166-167	167-168 ¹⁷
5	C ₆ H ₅	C ₆ H ₅	C ₆ H ₅	H	3e	96	134-136	137-138 ¹⁶
6	C ₆ H ₅	C ₆ H ₅	CH ₃	H	3f	91	56-58	55-57 ¹⁵
7	C ₆ H ₅	CH ₃	CH ₃	H	3g	91	oil	oil ¹⁵
8	C ₆ H ₅	CH ₃	CH ₃	Cl	3h	87	oil	oil ¹³
9	H	C ₆ H ₅	CH ₃	H	3i	80	203-205	203-205 ¹²
10	4-BrC ₆ H ₄	CH ₃	CH ₃	Cl	3j	93	88-90	87-88 ¹⁷
11	4-BrC ₆ H ₄	C ₆ H ₅	C ₆ H ₅	H	3k	90	118-120	117-119 ¹⁷
12	4-BrC ₆ H ₄	C ₆ H ₅	CH ₃	H	3l	89	178-179	178-180 ¹⁷
13	4-MeC ₆ H ₄	C ₆ H ₅	C ₆ H ₅	H	3m	92	104-106	104-105 ¹⁷
14	4-MeC ₆ H ₄	C ₆ H ₅	CH ₃	H	3n	85	84-86	82-84 ¹⁷
15	4-MeOC ₆ H ₄	C ₆ H ₅	C ₆ H ₅	H	3o	82	oil	oil ¹⁷
16	4-MeOC ₆ H ₄	C ₆ H ₅	CH ₃	H	3p	86	oil	oil ¹⁷

^a Yields refer to the pure isolated products.

All products were known and were identified by comparing their physical or spectral data with other literature [12-17].

To examine the reusability of sawdust-BF₃ NPs under solvent free condition, after each run, the product was dissolved to CHCl₃ and filtered to separate the catalyst and then dry the solid residue. This process repeated for three cycles and the yield of product **3e** did not change significantly (Table 5).

Table 5. Recycling studies of reaction between 1,3-diphenylpropane-1,3-dione and phenylhydrazine in the presence of sawdust-BF₃ NPs to give product **3e**

Entry	Catalyst	Time (min)	Yield % ^a
1	fresh	15	92
2	1	15	90
3	2	15	89
4	3	15	85

^a Yields refer to isolated products.

4. CONCLUSIONS

In summary, sawdust-BF₃ NPs has synthesised and shown that it has advantages in the preparation of 2,3,5-substituted-2H-pyrazoles such as shorter reaction times, simple work-up, and affords excellent yield. The solid phase acidic catalyst was re-usable for a number of times without appreciable loss of activity. The present method does not involve any hazardous organic solvent. Therefore, this procedure could be classified as green chemistry.

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REFERENCES

- [1] Shen, D., Shu, M., Chapman, K. T., (2000). *Org. Lett.*, vol. 2, p. 2789-2792.
- [2] Penning, T. D., Talley, J. J., Bertenshaw, S. R., Carter, J. S., Collins, P. W., Docter, S.; Graneto, M. J., Lee, L. F., Malecha, J. W., Miyashiro, J. M., Rogers, R. S., Rogier, D. J., Yu, S. S., Anderson, G. D., Burton, E. G., Cogburn, J. N., Gregory, S. A., Koboldt, C. M., Perkins, W. E. Seibert, K., Veenhuizen, A. W., Zhang Y. Y., Isakson, P. C., (1997). *J. Med. Chem.*, vol. 40, p. 1347-1365.
- [3] Deng X., Mani, N. S., (2008) *Org. Lett.*, vol. 10, p. 1307-1310.
- [4] Katritzky, A. R., Wang, M., Zhang S., Voronkov, M. V.,(2001). *J. Org. Chem.*, vol. 66, p.6787-6791.
- [5] Deng X., Mani, N. S.,(2006) *Org. Lett.*, vol. 8, p. 3505-3508.
- [6] Hu isgen, R. *Angew. (1980). Chem., Int. Ed. Engl.* , vol. 19, p. 947-973.
- [7] Donohue, A. C., Pallich S., McCarthy, T. D., (2001). *J. Chem. Soc., Perkin Trans,vol. 1,* p. 2817-2822.
- [8] Aggarwal, V. K., Vicente, D. V., Bonnert, R. V., (2003). *J. Org. Chem.*,vol. 68, p. 5381-5383.
- [9] Bhat, B. A., Puri, S. C., Qurishi, M. A., Dhar, K. L., Qazi, G. N., (2005). *Synth. Commun.*, vol. 35, p. 1135-1142.

- [10] Ahmed, M. S. M., Kobayashi, K., Mori, A., (2005). *Org. Lett.*, vol. 7, p. 4487-4489.
- [11] Fustero, S., Roman, R., Sanz-Cervera, J. F., Simon-Fuentes, A. X., Cunat, A. C., Villanova, S., Murguia, M., (2008). *J. Org Chem.*, vol. 73, p. 3523-3529.
- [12] Wang, Z.; Qin, H. (2004). *Green Chem.*, vol.6, p. 90-92.
- [13] Polshettiwar, V., Varma, R. S. (2008). *Tetrahedron Lett.*, vol. 49, p. 397-400.
- [14] Curini, M., Rosati, O., Campagna, V., Montanari, F., Cravotto, G., Boccalini, M. (2005). *Synlett*, vol. 19, p. 2927-2929.
- [15] Xiong, W., Chen, J-X., Liu, M-C., Ding, J-C., Wu, H-Y., Su, W-K, J. Braz. (2009). *Chem. Soc.*, vol. 20, p. 367-370.
- [16] Sreekumar, R., Padmakumar, R. (1998). *Synth. Commun*, vol. 28, p. 1661-1665.
- [17] Mirjalili, B. F., Bamoniri, A. H., Amrollahi M. A., Emtiazi, H. (2010). *Digest J. Nanomaterials and Biostructures*, vol. 5, p. 897-902.
- [18] Sadeghi, B., Zarepour, I. (2015). Nano-sawdust-BF₃ as a new, cheap and effective nano catalyst for one-pot synthesis of 2-amino benzo[h]chromene derivatives. *Journal of Nanostructure in Chemistry*, vol. 5, p. 305-311.
- [19] Sadeghi, B., Mirjalili, B. F., Bidaki, S. and Ghasemkhani, M. (2011). SbCl₅.SiO₂: an efficient alternative for one-pot synthesis of 1,2,4,5-tetrasubstituted imidazoles in solvent or under solvent-free condition. *Journal of the Iranian Chemical Society*, vol. 8, p. 648-652.
- [20] Sadeghi, B. (2014). Silica supported boron trifluoride nanoparticles (BF₃-SiO₂ NPs): An efficient and reusable catalyst for one-pot synthesis of benzo[a]xanthene-11-one derivatives. *Scientia Iranica C*, vol. 21, p. 708-714.
- [21] Sadeghi, B. FarokhiNezhad, P. Hashemian, S. (2014). SiO₂-OSO₃H Nanoparticles: an efficient, versatile and new reagent for the one-pot synthesis of 2-amino-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile derivatives in water, a green protocol. *Journal of Chemical Research*, vol. 38, p. 54-57.