Journal Synthetic Chemistry

Original Research

J. Synth. Chem.

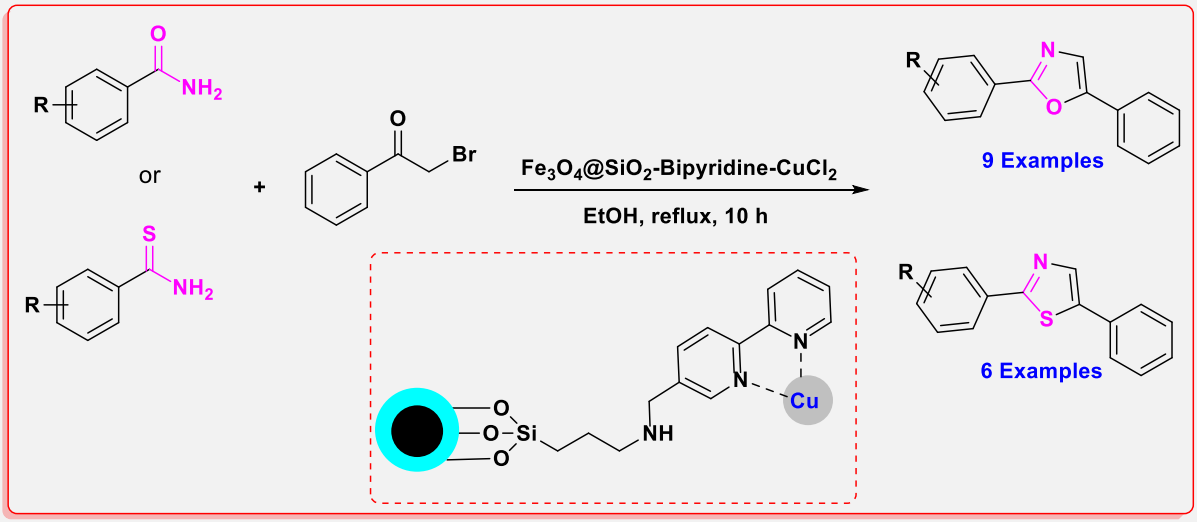
Copper (II) complex immobilized on magnetic nanoparticles catalyzed synthesis of oxazole and thiazole derivatives

Mustafa-Saleh Shafik *

Institute of Chemical Science and Technology, Baghdad, Iraq.

Corresponding author-mail: mustafasalehshafik@gmail.com

ABSTRACT: During the last decade, nanomagnetic catalysts have attracted considerable attentions due to their simple recovery and reusability. Molecules with thiazole or oxazole ring are used as anti-virus, anti-tumor, anti-fungal, anti-bacterial and anti-cancer reagents. Up to now, many synthetic methodologies have been reported in the literature for the synthesis of oxazole and thiazole derivatives. In this research work, we reported that the utilization of Fe_3O_4@SiO_2-Bipyridine-$CuCl_2$ in EtOH under reflux conditions can be considered as a novel and ecofriendly catalytic system for the synthesis of oxazole and thiazole derivatives through the condensation of benzothioamide or benzamide with 2-bromoacetophenone derivatives. The recovered copper nanocatalyst could be reused 7 times without any significant loss of its activity.



KEYWORDS: Fe_3O_4@SiO_2-Bipyridine-$CuCl_2$, Oxazoles, Thiazoles, Medicinal chemistry.

■ Introduction

Magnetic nanoparticles are a class of nanostructured materials of current interest, due largely to their advanced technological and medical applications, envisioned or realized [1–3]. In recent times, nanomagnetic catalysts have attracted considerable attentions due to their simple recovery and reusability [4–7]. Among various magnetic nanoparticles, magnetic Fe_3O_4 nanoparticles have the great interest due to stability, easy work-up, magnetic separation and recyclability which minimize the organic waste generation as compared to the conventional catalytic systems [8–11].

Received: Oct 21, 2022
Revised: Nov 30, 2022
Published: July 3, 2022

DOI: 10.22034/jsc.2023.174117
J. Synth. Chem. 2022, 1, 163-170

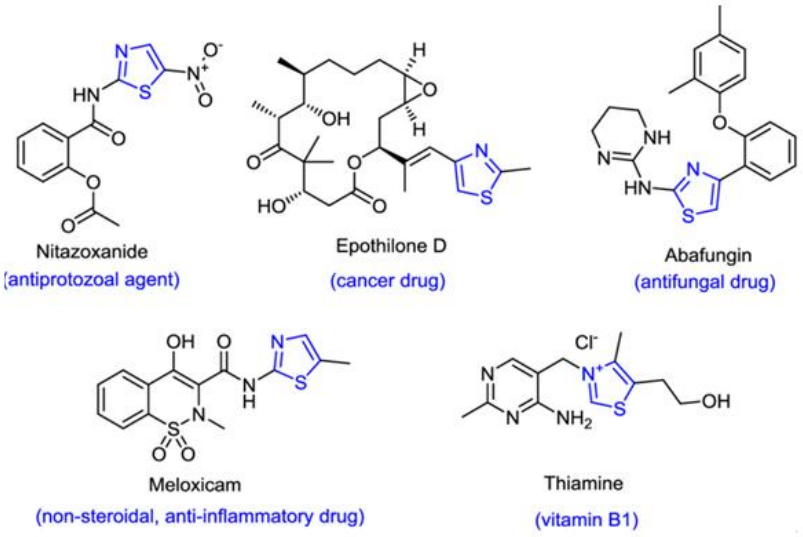


Figure 1. A series of biologically active molecules containing thiazole ring.

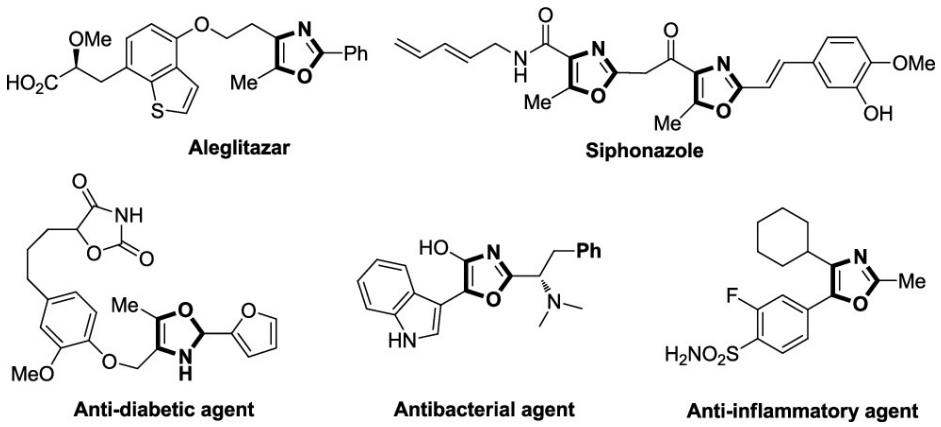


Figure 2. A series of biologically active molecules containing oxazole ring.

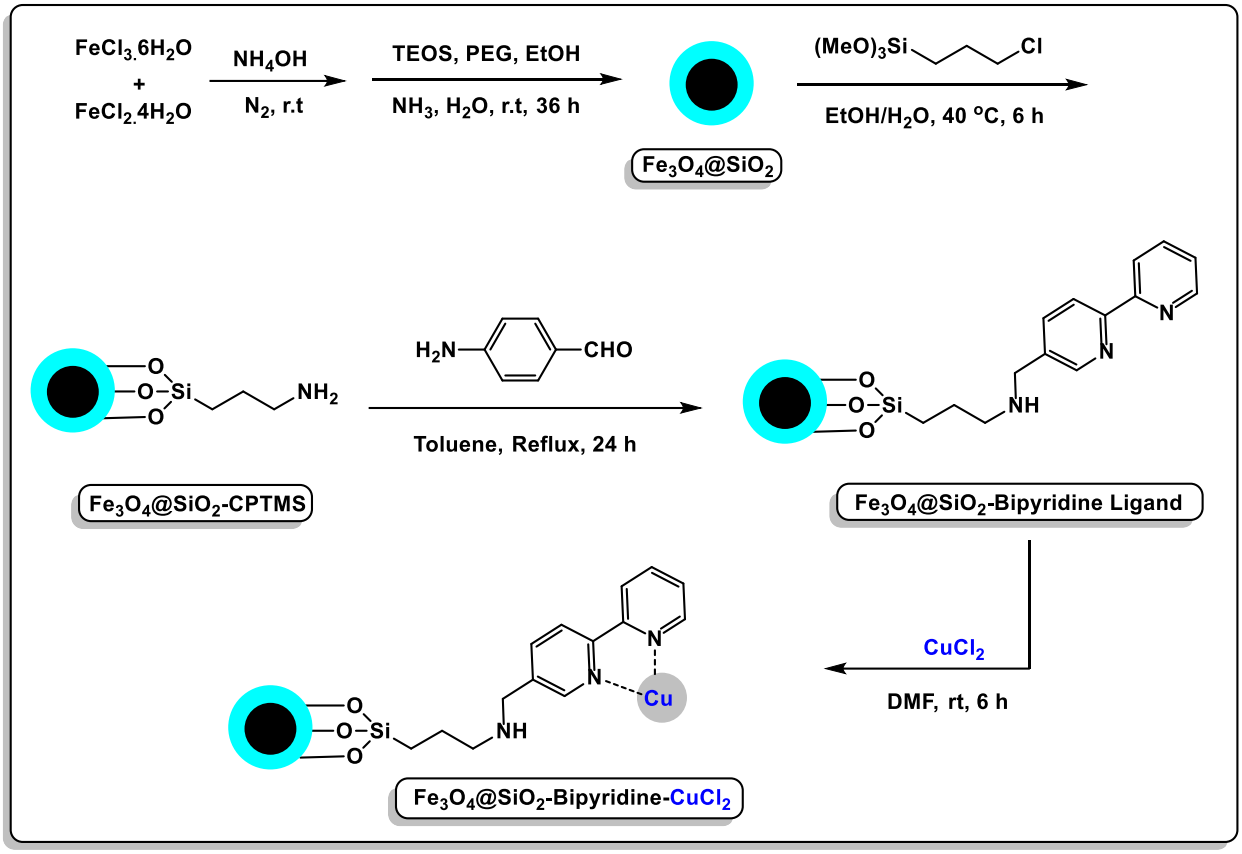
Thiazoles and oxazoles are five-membered heterocycles containing nitrogen-sulfur and nitrogen-oxygen atoms and form a very important group of heterocyclic compounds [12–15]. These compounds are of great interest due to their many medicinal and biological properties [6]. Molecules with thiazole or oxazole ring are used as anti-virus, anti-tumor, anti-fungal, anti-bacterial and anti-cancer reagents [16–18]. Some biologically active molecules with thiazole and oxazole rings are shown in **Figures 1 and 2** [19–22]. Different derivatives of thiazoles and oxazoles have been synthesized and various synthetic methods have been presented for the synthesis of these compounds [23].

■ Results and Discussion

In this research work, we reported that the utilization of Fe_3O_4@SiO_2-Bipyridine-$CuCl_2$ in EtOH under reflux conditions can be considered as a novel and ecofriendly catalytic system for the synthesis of oxazole and thiazole derivatives through the condensation of benzothioamide or benzamide with 2-bromoacetophenone derivatives. Details of the fabrication of Fe_3O_4@SiO_2-Bipyridine-$CuCl_2$ were fully

DOI: 10.22034/jsc.2023.174117
J. Synth. Chem. 2022, 1, 163-170

shown in **Scheme 1**. FT-IR, SEM, TEM, TGA, XPS, XRD, VSM, EDX and ICP-OES techniques were well confirmed the successful fabrication of Fe_3O_4@SiO_2-Bipyridine-$CuCl_2$ nanocatalyst.

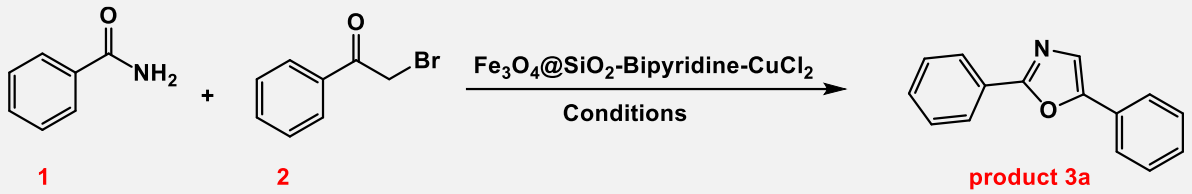


Scheme 1. General route for fabrication of Fe_3O_4@SiO_2-Bipyridine-$CuCl_2$ nanocatalyst.

After the characterization of Fe_3O_4@SiO_2-Bipyridine-$CuCl_2$ nanocomposite, we decide to study its catalytic activity in the synthesis of thiazoles and oxazoles. First, the condensation of benzamide (**1**) with 2-bromoacetophenone (**2**) was selected as the model reaction and the effect of catalyst loading and solvents and temperature was evaluated. The results of these experiments are shown in **Table 1**. It is noteworthy that the model reaction is not performed in the absence of catalyst. The highest yield was seen in the presence of 20 mg of Fe_3O_4@SiO_2-Bipyridine-$CuCl_2$ nanocatalyst in ethanol under reflux conditions. Then, the scope of this catalytic system was investigated in the synthesis of oxazole and thiazole derivatives through the condensation of benzothioamide or benzamide with 2-bromoacetophenone derivatives. The results of synthesis of oxazole and thiazole derivatives are shown in **Tables 2 and 3**. Under this catalytic system, a broad range of benzothioamide or benzamide derivatives were utilized and the desired products were synthesized with high yields.

DOI: 10.22034/jsc.2023.174117
J. Synth. Chem. 2022, 1, 163-170

Table 1. Optimization of conditions for the preparation of **product 3a**.

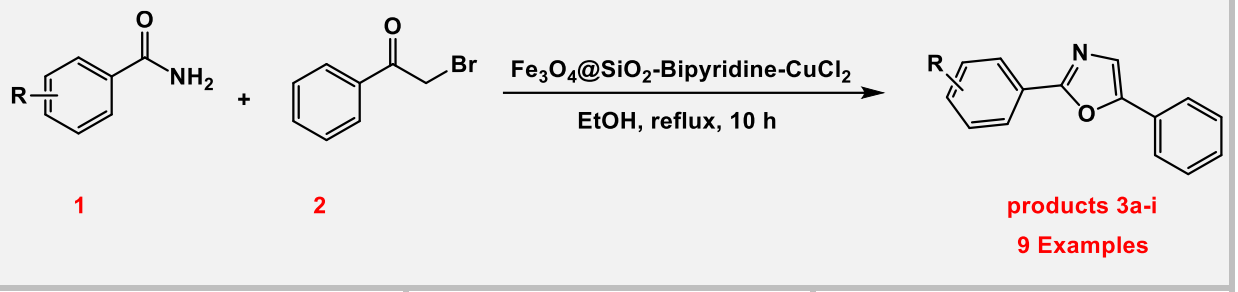


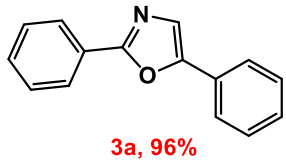
Entry	Catalyst (mg)	Solvent (°C)	Time (h)	Yield % [a]
1	No	DMF (100 °C)	24	No
2	5	DMF (100 °C)	10	62
3	10	DMF (100 °C)	10	76
4	15	DMF (100 °C)	10	83
5	20	DMF (100 °C)	10	90
6	25	DMF (100 °C)	10	90
7	20	water (100 °C)	10	83
8	20	MeCN (reflux)	10	74
9	20	Toluene (100 °C)	10	22
10	**20**	**EtOH (reflux)**	**10**	**96**
11	20	Solvent-Free (100 °C)	10	11

[a] Isolated yields

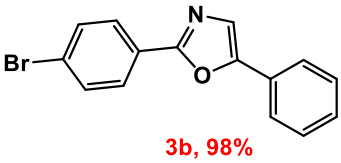
DOI: 10.22034/jsc.2023.174117
J. Synth. Chem. 2022, 1, 163-170

Table 2. Scope of Fe_3O_4@SiO_2-Bipyridine-$CuCl_2$ nanocatalyst in synthesis of oxazole derivatives [a]

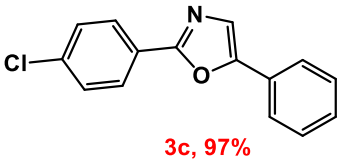




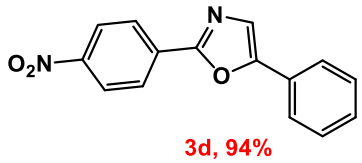
3a, 96%



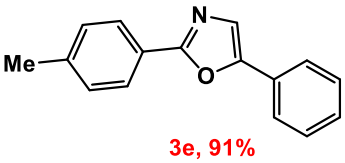
3b, 98%



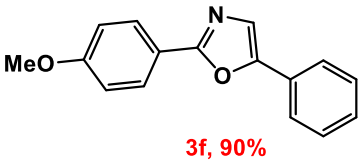
3c, 97%



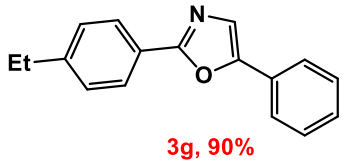
3d, 94%



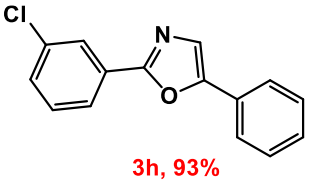
3e, 91%



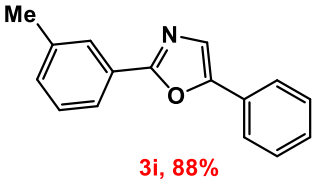
3f, 90%



3g, 90%



3h, 93%

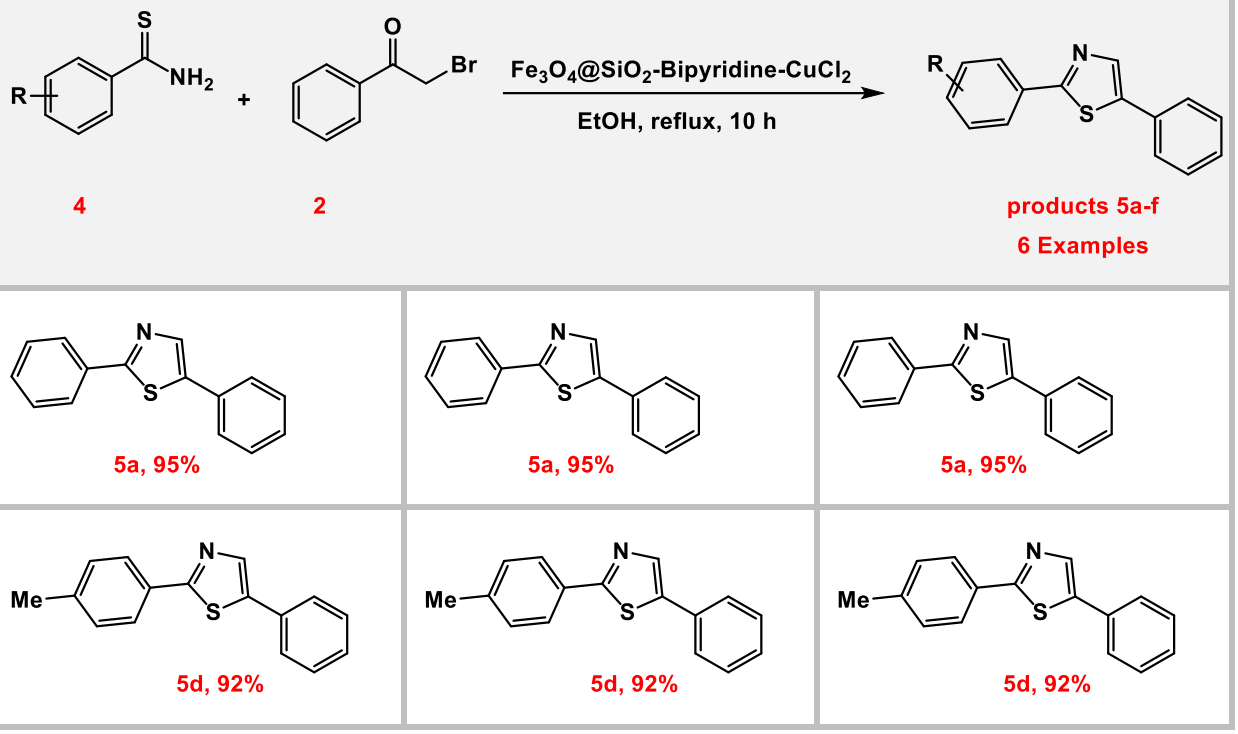


3i, 88%

[a] Isolated yields

DOI: 10.22034/jsc.2023.174117
J. Synth. Chem. 2022, 1, 163-170

Table 3. Scope of $Fe_3O_4@SiO_2$-Bipyridine-$CuCl_2$ nanocatalyst in synthesis of thiazole derivatives [a]



[a] Isolated yields

In order to study the reusability of the $Fe_3O_4@SiO_2$-Bipyridine-$CuCl_2$ nanocatalyst in the synthesis of oxazole and thiazole derivatives, we decide to examine this catalytic system in the preparation of **product 3a and 5a** as the model reaction. After the compilation of the reaction, the $Fe_3O_4@SiO_2$-Bipyridine-$CuCl_2$ nanocatalyst was separated by an external magnet, washed with hot ethanol, dried in air and reused for a subsequent similar reaction. The recovered catalyst was reused for seven consecutive cycles without any significant loss in its catalytic activity (**Figure 3**).

DOI: 10.22034/jsc.2023.174117
J. Synth. Chem. 2022, 1, 163-170

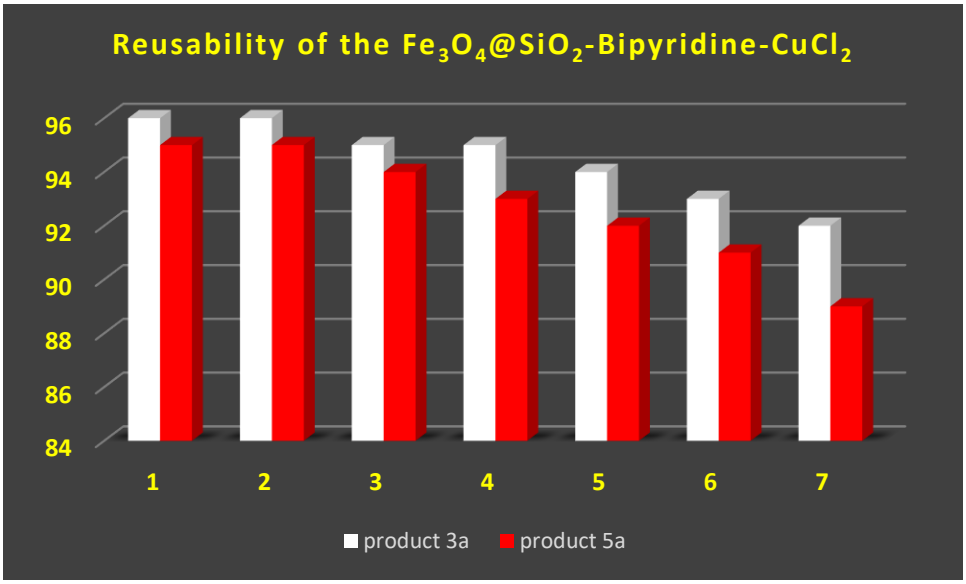


Figure 3. reusability of the Fe_3O_4@SiO_2-Bipyridine-$CuCl_2$ nanocatalyst in the preparation of **product 3a** and **5a.**

■ Summary and Outlook

Summary, we shown that the copper (II) complex immobilized on the surface of magnetic nanoparticles functionalized with Bipyridine as ligand [Fe_3O_4@SiO_2-Bipyridine-$CuCl_2$] is a novel and highly efficient nanocatalyst for the oxazole and thiazole derivatives through the condensation of benzothioamide or benzamide with 2-bromoacetophenone. FT-IR, SEM, TEM, TGA, XPS, XRD, VSM, EDX and ICP-OES techniques were well confirmed the successful fabrication of Fe_3O_4@SiO_2-Bipyridine-$CuCl_2$ nanocatalyst. It is noteworthy that the recovered Fe_3O_4@SiO_2-Bipyridine-$CuCl_2$ catalyst was reused for seven consecutive cycles without any significant loss in its catalytic activity.

■ Experimental

Typical procedure for Fe_3O_4@SiO_2-Bipyridine-$CuCl_2$nanocomposite synthesis of thiazoles and oxazoles

A mixture of benzothioamide or benzamide (0.5 mmol), 2-bromoacetophenone. (0.5 mmol) and Fe_3O_4@SiO_2-Bipyridine-$CuCl_2$ nanocatalyst (20 mg) in EtOH (3 mL) was stirred under reflux conditions for 10 h. 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 combined organics were washed with a saturated solution of brine (4 mL), dried (Na_2SO_4), filtered, and purified by flash chromatography or preparative TLC.

References

1 H. R. Sonawane, J. V. Deore and P. N. Chavan, *ChemistrySelect*, , DOI:10.1002/slct.202103900.

2 I. Fatimah, G. Fadillah, G. Purwiandono, I. Sahroni, D. Purwaningsih, H. Riantana, A. N. Avif and S. Sagadevan, *Inorg. Chem. Commun.*, 2022, 137, 109213.

3 P. Kumar, V. Tomar, D. Kumar, R. K. Joshi and M. Nemiwal, *Tetrahedron*, 2022, 106–107,

DOI: 10.22034/jsc.2023.174117
J. Synth. Chem. 2022, 1, 163-170

132641.

4 M. Ghobadi, M. Kargar Razi, R. Javahershenas and M. Kazemi, *Synth. Commun.*, 2021, 51, 647–669.

5 M. Kazemi, *Synth. Commun.*, , DOI:10.1080/00397911.2020.1720740.

6 M. Ghobadi, P. Pourmoghaddam Qhazvini, M. Eslami and M. Kazemi, *Synth. Commun.*, , DOI:10.1080/00397911.2020.1829646.

7 M. Kazemi, M. Ghobadi and A. Mirzaie, *Nanotechnol. Rev.*, 2018, 7, 43–68.

8 A. Arabmarkadeh, R. Javahershenas and M. Kazemi, *Synth. Commun.*, , DOI:10.1080/00397911.2020.1864646.

9 Q. Li, L. Xu and D. Ma, *Angew. Chemie*, , DOI:10.1002/ange.202210483.

10 M. Kidwai, A. Jain and S. Bhardwaj, *Mol. Divers.*, 2012, 16, 121–128.

11 L. M. Rossi, N. J. S. Costa, F. P. Silva and R. Wojcieszak, *Green Chem.*, 2014, 16, 2906.

12 M. Kazemi, *Synth. Commun.*, 2020, 50, 2095–2113.

13 M. Kazemi, *Synth. Commun.*, 2020, 50, 2079–2094.

14 D. J. Ritson, C. Spiteri and J. E. Moses, *J. Org. Chem.*, 2011, 76, 3519–3522.

15 Y. I. Asiri, A. Alsayari, A. B. Muhsinah, Y. N. Mabkhot and M. Z. Hassan, *J. Pharm. Pharmacol.*, 2020, 72, 1459–1480.

16 S. A. Fazeli-Attar and B. B. F. Mirjalili, *Res. Chem. Intermed.*, 2018, 44, 6419–6430.

17 T. A. Rossa, N. S. Suveges, M. M. Sá, D. Cantillo and C. O. Kappe, *Beilstein J. Org. Chem.*, 2018, 14, 506–514.

18 A. Saito, N. Hyodo and Y. Hanzawa, *Molecules*, 2012, 17, 11046–11055.

19 M. Kaspady, V. Narayanaswamy, M. Raju and G. Rao, *Lett. Drug Des. Discov.*, 2009, 6, 21–28.

20 C. Spiteri, D. J. Ritson, A. Awaad and J. E. Moses, *J. Saudi Chem. Soc.*, 2011, 15, 375–378.

21 M. Gorjizadeh and S. Sayyahi, *Russ. J. Gen. Chem.*, 2018, 88, 1899–1903.

22 M. A. Bodaghifard and S. Shafi, *J. Iran. Chem. Soc.*, 2021, 18, 677–687.

23 X. Zhang, M. Aqeel Ashraf, Z. Liu and D. Zhang, *Synth. Commun.*, 2020, 50, 2705–2734.

DOI: 10.22034/jsc.2023.174117
J. Synth. Chem. 2022, 1, 163-170