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# HYPERACTIVE MAGNETICALLY SEPARABLE NANO-SIZED $MgFe_2O_4$ CATALYST FOR THE SYNTHESIS OF SEVERAL FIVE- AND SIX- MEMBERED HETEROCYCLES

***Shobha Bansal[1], Yogendra Kumar[1], Dipak Kumar Das[1], Prabal Pratap Singh[1, *]***

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**Abstract.** $MgFe_2O_4$ nanoparticle ferrites were synthesized by combustion technique using pure ferric nitrate and magnesium carbonate. The magnetically separable $MgFe_2O_4$ MNP's were found to be hyper active catalyst for the synthesis of a wide range of biologically active five and six-membered heterocyclic moieties at refluxing conditions. Reaction times are lowest in comparison to all reported in literature with excellent yields. Strong electron pull of $Fe^{3+}$ is responsible for its hyper activity, which has been substantiated by substitution of $Fe^{3+}$ by other trivalent metal ions. $Mg^{2+}$ has a unique role because replacement of $Mg^{2+}$ has poor catalytic activity. The developed protocol has been efficiently utilized for the synthesis of a series of substituted mono/bis pyrimidines, pyrimidin-2-ol, pyrimidin-2-thiol, pyrazoles and isoxazoles by condensing monochalcones/1,4-bischalcones with various bis-nucleophiles in the presence of catalytic amount of heterogenous magnetic $MgFe_2O_4$ nanoparticles. The structure of these synthesized compounds was determined by FTIR, $^1H$, $^{13}C$ and mass spectra. The catalyst can be removed easily from reaction mixture by using a simple external magnet. Nanoparticles of ferrite were recovered and reused with no appreciable change in the activity even after the five runs. Nanoparticles are characterized by XRD, TEM and IR spectroscopy.

**Keywords:** magnetic $MgFe_2O_4$ nanoparticles, mono chalcones, 1,4-bischalcones, pyrimidines, pyrazolines, isoxazolines, external magnetic separation, heterogeneous and reusable catalyst.

## 1. Introduction

The heterogeneous catalyst has received a remarkable amount of interest from scientific and industrial perspectives because of its enormous impact on world's economy. The use of functionalized magnetic nanoparticle (MNP's) as heterogeneous catalyst has attracted most of the researchers for its easy separation from reaction mixture with the aid of external magnetic field [1-8].

Magnetic nano catalyst [9] is rapidly developing area. Researchers have reported striking novel catalytic properties including greatly enhanced reactivities and selectivities for nanocatalyst compared to bulk counter parts. Recently functionalized magnetic nano particle have been used as efficient catalytic system in many chemical transformation including synthesis of $\alpha$-amino nitriles [10], 1-1 diacetates form aldehyde [11], diazepiene derivatives [12], indazalo[2,1-*b*] phthalazine triones, pyrazoles [1,2-*b*] phthalazine-diones [13], 3,4 dihydro pyrimidines-2(1H)ones [14], 1,4 dihydropyrimidines [15], and pyrrole synthesis [16]. Also a series of organic reaction such as Michael addition [17], Suzuki/Heck cross-coupling [18], asymmetric aldol reaction [19], Suzuki coupling [20], acetalization reaction [21], Ritter reaction [22], cyanosilylation of carbonyl compounds [23], Henry reaction [24], enantioselective direct addition of terminal alkynes to imines [25] have been done using functionalized nanostructure.

In the context of our research of considerable interest is the synthesis of various heterocyclic organic compounds such as substituted pyrimidines, pyrimidin-2-ol, pyrimidin-2-thiol, pyrazoles, and isoxazoles for their biological activities [26-33] including antiproliferative, anticancer, antimalerial, antimicrobial, antihypertensive, herbicidal, ACE inhibitors, antitubercular, and others. We are in the process of development of effective and environment friendly basic nanocatalyst in organic synthesis. Although there are so many reports for the synthesis of heterocylic compounds in the absence of catalyst [34-40], all of them have reported higher reaction time which is a matter of concern for industrial applicability of the procedure.

We herein report a hyperactive heterogenous magnetic nanocatalyst for the synthesis of many biologically active five and six-membered heterocycles such as pyrimidines, pyrimidin-2-ol, pyrimidin-2-thiol,

[1] Department of Chemistry, GLA University,
17km stone, NH-2 Delhi-Mathura Highway,
Chaumuhan, Mathura UP 281406, India
[*] *prabal.singh@gla.ac.in*

pyrazoles, and isoxazoles having lowest reaction time with high yield. The catalyst is recyclable 5-6 times without any change of reaction time and yield.

## 2. Experimental

### 2.1. General Considerations

All the solvents and reagents were used as supplied from commercial sources. FTIR spectra were recorded in KBr on a Schimadzu FTIR 8401 spectrometer and Perkin Elmer version 10.03.06 for the liquid samples. $^{1}H$ and $^{13}C$ spectra were recorded on a Bruker DRX 300 spectrometer operating at 300 MHz for $^{1}H$ NMR and 75 MHz for $^{13}C$ NMR as solutions in $CDCl_3$ and DMSO$d_6$. The ESI mass spectra were measured on waters UPLC-TDQ spectrometer. TLC was performed on silica coated glass plates; spots were developed in $I_2$ chamber or visualized in UV chamber. The morphology of the catalyst was studied by high resolution electron microscopy HRTEM-300 KV Technai G2 30S TWIN with gold coating equipped with energy dispersive X-ray spectroscopy.

### 2.2. Preparation of Catalyst

Nanoparticles of $MgFe_2O_4$ were synthesized by combustion technique. 2.0 mmol of $Fe(NO_3)_3{\cdot}9H_2O$ and 1.0 mmol of $MgCO_3$ dissolved in $HNO_3$ were taken together. After uniform mixing, 1.0 mmol of monoethanolamine was added to the reaction mixture followed by 1.0 mmol of each of sucrose and excess of nitric acid, respectively. The resulting liquid reaction mixture was then put on a hot plate at 353 K till it completely dried to a black residue. This black residue was then kept in muffle furnace at 1073 K for 4–6 h to obtain nanoparticle of $MgFe_2O_4$.

#### 2.2.1. Typical procedure for the synthesis of 1,4-bis pyrimidines, pyrimidin-2-ol, pyrimidin-2-thiol, pyrazoles and isoxazoles (3d-f, 5d-e)

The starting material monochalcone/1,4-bischalcone **1** (Tables 4 and 5) was prepared as per the reported literature procedure [41] by Claisen-Schmidt condensation between acetophenone and aromatic aldehydes in ethanolic solution of sodium hydroxide.

To a well stirred solution of 3,3'-(1,4-phenylene)bis(1-phenylprop-2-en-1-one) **1** (1 mmol), different bifunctional nucleophiles **2/4** (2 mmol) in 10 ml absolute ethanol, catalyst (10 mmol %) was added and the reaction mixture was refluxed in oil bath for the appropriate period of time. The progress of the reaction was monitored by TLC. On completion, the reaction mixture was allowed to cool at room temperature, the catalyst was separated by using external magnet and the solvent was evaporated up to the dryness under reduced pressure to obtain a crude solid product. The solid obtained was stirred in water, filtered and recrystallized from EtOAc:hexane solution.

#### 2.2.2. Typical procedure for the synthesis of pyrimidines, pyrimidin-2-ol, pyrimidin-2-thiol, pyrazoles and isoxazoles (3a-c, 5a-c)

To a well stirred solution of benzylidineacetophenone **1** (1 mmol), different bifunctional nucleophile **2/4** (1 mmol) in 10 ml absolute ethanol, catalyst (10 mmol %) was added and the reaction mixture was refluxed in oil bath for appropriate period of time. The progress of the reaction was monitored by TLC. The reaction mixture was allowed to cool at room temperature, catalyst was separated by external magnet and solvent was evaporated up to the dryness under reduced pressure to obtain a crude solid product. The solid was stirred in water, filtered and recrystallized from EtOAc:hexane solutions.

## 3. Results and Discussion

From the FTIR spectra of $MgFe_2O_4$ it is depicted that the sample show two prominent absorption bands $\upsilon_1$ and $\upsilon_2$ in the range of 560–420 $cm^{-1}$ (Fig. 1). Band $\upsilon_1$ is caused by stretching of tetrahedral cation and oxygen bonding, while $\upsilon_2$ is due to the vibrations of oxygen in a perpendicular direction to the axis joining the tetrahedron ion and oxygen.

The high-resolution transmission electron microscopy (HRTEM) of NP'S is shown in Fig. 2. The particle size of the magnesium ferrite NP's sample is typically in the range of 100–200 nm. The crystals are irregular in shape and are attached to each other along the grain boundaries. The material was verified by XRD data, which matched very well with standard data (JCPDS file no.737960). The peaks are indexed as (220), (311), (222), (400), (331), and (440), Fig. 3. Size of crystallite was found to be 100 nm from analysis of XRD profile by Debye Sheerer equation $D = \frac{0.9\,l}{b\cos q}$.

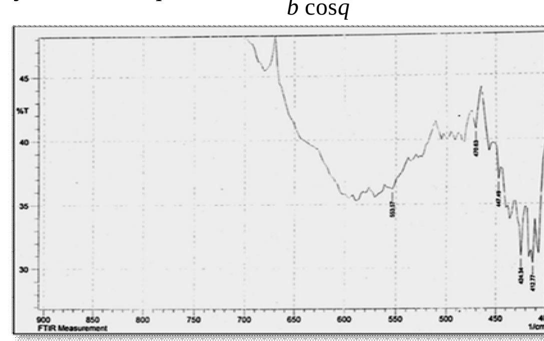



**Fig. 1.** FTIR spectrum of magnesium ferrite MNPs

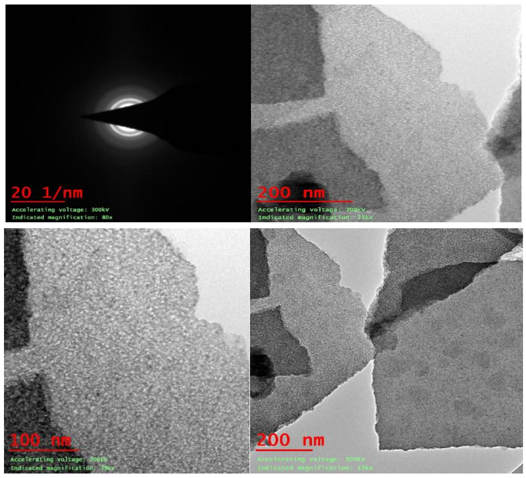



**Fig. 2.** X-ray diffraction pattern
and HRTEM image of $MgFe_2O_4$ MNP's

In order to check the catalytic activity of the magnesium ferrite catalyst benzylidine acetophenone **1** and guanidine nitrate **2** were taken as starting materials (Scheme 1). The reaction was first performed in the presence of catalytic amount of $Fe_2O_3$ (20 mmol %) in the refluxing ethanol to afford the formation of 4,6 diphenyl-pyrimidine-2-ylamine **3c** (Scheme 1, Table 1, Entry 1). However, the synthesis was achieved in poor yields. Then the same reaction was repeated with magnesium ferrite MNP's, and the synthesized product was obtained in the excellent yield and in considerably less time (Table 1, Entry 13). The catalytic study was also carried out in the presence of various other catalysts (Table 1, Entries 2-12) but we got unsatisfactory results with all of them.

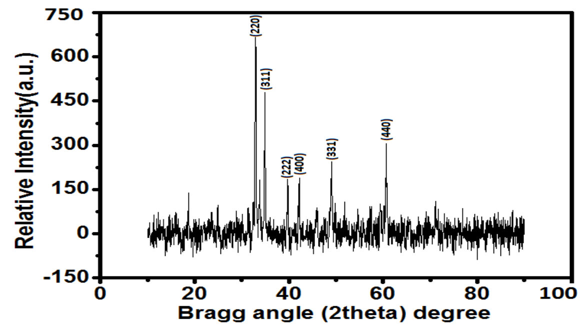
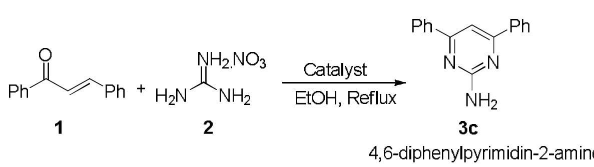



**Fig. 3.** Powder XRD pattern
for the $MgFe_2O_4$ nanoparticle

Only $MgFe_2O_4$ (Table 1, Entry 13) was found to have the best results in comparison with other metal ion oxides catalysts. During the model study the presence of various solvents like MeOH, MeCN, $CHCl_3$, PhMe, and DMF was also investigated using 10 mmol % of $MgFe_2O_4$ MNPs (Table 2). It was observed that ethanol stands out to be the solvent of choice with its fast conversion, high yields and easy removal (Table 2, Entry 2). This is due to efficient solubility of reactants and products and poor coordination with surface metal ions.

We next examined the effect of catalyst loading on to the model reaction (Table 3, Entries 1-5). It was observed that minimum 10 mmol % of $MgFe_2O_4$ MNPs afforded the product with best result (Table 3, Entry 3).




**Scheme 1.** Optimized (model) reaction condition
for synthesis of 4,6-diphenylpyrimidine-2-amine (3c)

*Table 1*

**Screening of catalyst for the synthesis of 3c**

| Entry | Catalyst* | Time, min | Yield, %** |
|---|---|---|---|
| 1 | $Fe_3O_4$ | 120 | 20 |
| 2 | $SrFe_2O_4$ | 120 | 10 |
| 3 | ZnO | 120 | <10 |
| 4 | $ZnO@Fe_2O_4$ | 120 | NP |
| 5 | $MgSO_4$ | 120 | NP |
| 6 | $SrCr_2O_4$ | 120 | Traces |
| 7 | $Bi(NO_3)_3.5H_2O$ | 120 | NP |
| 8 | $CoFe_2O_4$ | 120 | NP |
| 9 | $CaFe_2O_4$ | 120 | 70 |
| 10 | $CuFe_2O_4$ | 120 | NP |
| 11 | $ZnCr_20_4$ | 120 | 20 |
| **13** | **$MgFe_2O_4$** | **25** | **92** |

Notes: *reaction conditions: chalcone (1 mmol), guanidine nitrate (1 mmol) and catalyst (10 mmol %) refluxed in ethanol (10 ml) solvent for the mentioned time; ** isolated yields.

*Table 2*

**The model study in various solvents using $MgFe_2O_4$ MNP's for the synthesis of 3c**

| Entry | Solvent* | Time, min | Yield, %** |
|---|---|---|---|
| 1 | EtOH | 25 | 72 |
| 2 | MeOH | 25 | 92 |
| 3 | MeCN | 180 | <20 |
| 4 | $CHCl_3$ | 180 | <20 |
| 5 | PhMe | 180 | <10 |
| 6 | DMF | 35 | 60 |

Notes: *reaction conditions: chalcone (1 mmol), guanidine nitrate (1 mmol) and catalyst (10 mmol %) refluxed in ethanol (10 ml) solvent for the mentioned time; ** isolated yields.

*Table 3*

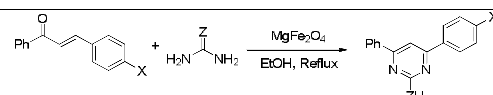
**The effect of catalyst loading on the model reaction**

| Entry | Catalyst, mmol % | Time, min | Yield, %** |
|---|---|---|---|
| 1 | 20 | 30 | 92 |
| 2 | 15 | 32 | 91 |
| 3 | 10 | 25 | <92 |
| 4 | 5 | 50 | <80 |
| 5 | 3 | >60 | 45 |

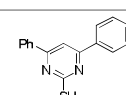
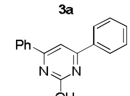
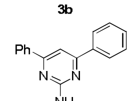
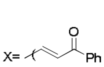
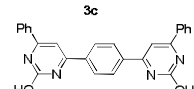
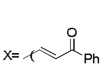
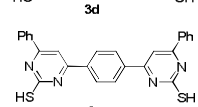
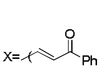
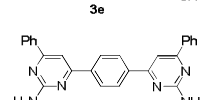
Notes: *reaction conditions: benzalidene acetophenone **1** (1 mmol), **2** (1 mmol), $MgFe_2O_4$, ethanol reflux; ** isolated yields.

*Table 4*

**Synthesis of substituted mono and bis pyrimidines, pyrimidin-2-ol and pyrimidin-2-thiol (3a-f)**




**1** **2** **3**

| Entry | Chalcone | 2 | Product | Time (min) | Yield (%)[a] |
|---|---|---|---|---|---|
| 1 | X=H | Z=S |  **3a** | 40 | 70 |
| 2 | X=H | Z=O |  **3b** | 45 | 67 |
| 3 | X=H | Z=$NH_2.NO_3$ |  **3c** | 25 | 92 |
| 4 | X=  | Z=O |  **3d** | 200 | 86 |
| 6 | X=  | Z=S |  **3e** | 200 | 90 |
| 7 | X=  | Z=$NH_2.NO_3$ |  **3f** | 55 | 85 |

[a]Isolated yiled

To check the scope and generality of this methodology, several diverse chalcones were treated with various bifunctional nucleophiles to give substituted six-membered mono- and bis-pyrimidines, pyrimidin-2-ol and pyrimidin-2-thiol heterocycles in good to excellent yields in lesser reaction time. The results of the experiments are listed in Table 4. It was observed that present methodology could be applied to various substrates successfully.

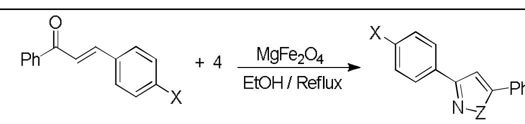
After successful synthesis of six-membered heterocylces we next targeted to synthesize five membered heterocycles like substituted pyrazoles and isoxazoles. Interestingly, using the same protocol we were able to synthesize the desired products in very good yield with lesser reaction time (Table 5).

In order to check the advantages of developed strategy we compared our protocol with the various published reports and it has been found that the catalyst reduced the reaction time drastically from 2–12 h (in the reported processes) to 30–120 min for all reactions with good yields in the present process. The following few examples illustrate the advantages of the process over using the different catalyst Table 6.

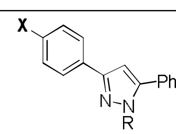
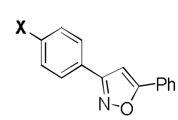
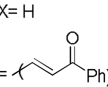
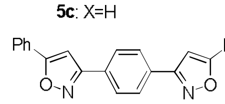
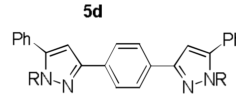
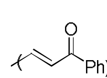
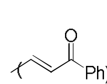
In the mechanistic study of chalcone reaction with guanidine nitrate in the presence of $MgFe_2O_4$MNP's, it is believed that Mg has a well established spinel. In the crystal structure there are two sites of accommodation of metal ions: one is octahedral site and another one – tetrahedral site. Tetrahedral site is occupied by $Mg^{2+}$ and octahedral site is occupied by $Fe^{3+}$ ions. All the metal ions are bridged through oxide anions. Thus $Mg^{2+}$is bridged with $Fe^{3+}$ through oxide ion ($O^{2-}$). $Mg^{2+}$ and $Fe^{3+}$ ions both are Lewis acids but the $Fe^{3+}$ ion is a stronger Lewis acid than $Mg^{2+}$ion. As a result, electron cloud of oxygen anion moves towards $Fe^{3+}$ ion depriving partially $Mg^{2+}$. Thus $Mg^{2+}$ become more electron deficient leading to its hyperactivity. Role of $Fe^{3+}$ ion is well understood through its substitution by $Cr^{3+}$ and $Mn^{2+}$, where the catalytic activity of spinel is found to be very poor. The role of $Mg^{2+}$ is very dominant, which is understood by substitution of $Mg^{2+}$ by $Ca^{2+}$ and $Sr^{2+}$ producing no catalytic activity. Therefore, the combination of Mg and Fe is unique for its hyper catalytic activity.

*Table 5*

**Synthesis of substituted mono and bis pyrazoles and isoxazoles (5a-f)**




1 5

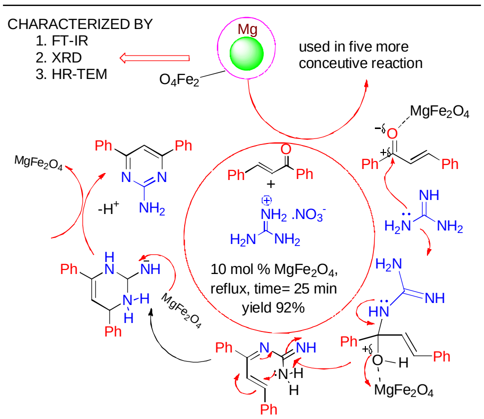
| Entry | Chalcone | 4 | Product | Time (min) | Yield(%)[a] |
|---|---|---|---|---|---|
| | | $RNHNH_2$ |  | | |
| 1 | X= H | R = Ph | **5a**: X=H, R=Ph | 120 | 85 |
| 2 | X= H | R = H | **5b**: X=H, R=H | 120 | 70 |
| | | |  | | |
| 3 | X= H | $NH_2OH.HCl$ | **5c**: X=H | 290 | 45 |
| 4 | X=  | $NH_2OH.HCl$ |  **5d** | 240 | 79 |
| | | |  | | |
| 5 | X=  | R = H | **5e**: R=H | 120 | 60 |
| 6 | X=  | R = Ph | **5f**: R=Ph | 140 | 74 |

[a]Isolated yield

*Table 6*

**A comparative study of the developed protocol with the earlier reported methods**

| Compound No | Our protocol | | Reported methods | | Reaction conditions | Ref. |
|---|---|---|---|---|---|---|
| | Time, min | Yield, % | Time, min | Yield, % | | |
| 3c | 25 | 92 | 60 | 45 | $H_2O_2$/KOH/EtOH/Reflux | [42] |
| 3f | 55 | 85 | 720 | 69 | EtONa/EtOH/Reflux | [43] |
| 3b | 45 | 67 | 360 | 90 | Amberlyst 15/EtOH/Reflux | [44] |
| 5a | 120 | 85 | 200 | 90 | PW12/PA/EtOH/318 K | [45] |
| 5a | 120 | 85 | 300 | 92 | H3PW12O40/EtOH/318 K | [46] |
| 5a | 120 | 85 | 100 | 90 | $Fe_2O_3$@$SiO_2$/$PW_{12}$NP/EtOH/Reflux | [47] |
| 5a | 120 | 85 | 25 | 82 | $PhNHNH_2$/HCOOH/EtOH/353 K | [48] |
| 5b | 120 | 70 | 1440 | 57 | $NH_2NH_2$/MeOH/Reflux | [49] |
| 5b | 120 | 70 | 540 | 70 | $NH_2NH_2$/EtOH/Reflux | [50] |




**Scheme 2.** A mechanistic pathway for the formation of 4,6-diphenylpyrimidine-2-amine in presence of $MgFe_2O_4$ MNPs

The separation of $MgFe_2O_4$ nano catalyst from reaction mixture could be very easily achieved by applying external magnetic field owing to the supermagnetic nature of $Fe_2O_3$ nanoparticles at room temperature. The reusability is one of the important criteria of heterogeneous magnetic catalyst. The recyclability of magnesium ferrite NP's was investigated for the model reaction of Scheme 1. After completion of reaction, the separated catalyst was reused after washing with acetone and drying at 343 K for 5 h. The reusability of the catalyst was examined by repetitive use of catalyst. It was found that catalyst showed no appreciable change in activity even after five cycles (Fig. 4).

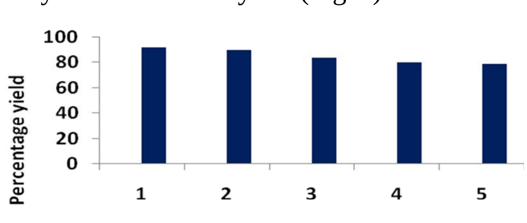



**Fig. 4.** Recyclability of catalyst for the formation of various heterocycles

## 4. Conclusions

We have synthesized magnesium ferrite MNP's through facile and simple combustion method that act as highly efficient and reusable heterogeneous catalyst. This MNP are highly active to catalyse hetero condensation of mono- as well as bis-chalcones and various bifunctional nucleophiles to give five- and six-membered heterocylces. The advantages of this catalytic system are milder reaction conditions, shorter reaction times, high yield, easy catalyst preparation, simple and clean work up, and reusability.

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## References

[1] Gardimalla H., Mandal D., Stevens P. *et al.*: Chem. Commun., 2005, 4432. https://doi.org/10.1039/b504128g
[2] Abu-Rezig R., Alper H., Wang D., Post M.: J. Am. Chem. Soc., 2006, **128**, 5279. https://doi.org/10.1021/ja060140u
[3] Phan N., Gill C., Nguyen J. *et al.*: Angew. Chem. Int. Ed., 2006, **45**, 2209. https://doi.org/10.1002/anie.200503445
[4] Baruwati B., Guin S.: Org. Lett., 2007, **9**, 5377. https://doi.org/10.1021/ol702064x
[5] Shokouhimehr M., Piao Y., Kim J. *et al.*: Angew. Chem. Int. Ed., 2007, **46**, 7039. https://doi.org/10.1002/anie.200702386
[6] Chouhan G., Wang D., Alper H.: Chem. Commun., 2007, 4809. https://doi.org/10.1039/b711298j
[7] Liu J., Peng X., Sun W. *et al.*: Org. Lett., 2008, **10**, 3933. https://doi.org/10.1021/ol801478y
[8] Zheng X.,. Luo S., Zhang L., Cheng J.: Green Chem., 2009, **11**, 455. https://doi.org/10.1039/b823123k
[9] Lu A-H., Salabas E., Schuth F.: Angew. Chem. Int. Ed., 2007, **46**, 1222. https://doi.org/10.1002/anie.200602866
[10] Kassaee M., Masrouri H., Movahedi F.: Appl. Catal. A, 2011, **395**, 28. https://doi.org/10.1016/j.apcata.2011.01.018
[11] Esmaeilpour M., Sardarian A., Javidi J.: Appl. Catal. A, 2012, **445-446**, 359. https://doi.org/10.1016/j.apcata.2012.09.010

[12] Maleki A.: Tetrahedron Lett., 2013, **54**, 2055. https://doi.org/10.1016/j.tetlet.2013.01.123
[13] Kiasat A., Davarpanah J.: J. Mol. Catal. A, 2013, **373**, 46. https://doi.org/10.1016/j.molcata.2013.03.003
[14] Zamani F., Izadi E.: Catal. Commun., 2013, **42**, 104. https://doi.org/10.1016/j.catcom.2013.08.006
[15] Gawande M., Bonifácio V., Varma R. *et al*.: Green Chem., 2013, **15**, 1226. https://doi.org/10.1039/c3gc40375k
[16] Mahmoudi H., Jafari A.: Chem. Cat. Chem., 2013, **5**, 3743. https://doi.org/10.1002/cctc.201300623
[17] Nemati F., Heravi M., Rad R.: Chin. J. Catal., 2012, **33**, 1825. https://doi.org/10.1016/S1872-2067(11)60455-5
[18] Du Q., Zhang W., Ma H. *et al*.: Tetrahedron, 2012, **68**, 3577. https://doi.org/10.1016/j.tet.2012.03.008
[19] Yang H., Li S., Wang X. *et al*.: J. Mol. Catal. A, 2012, **363–364**, 404. https://doi.org/10.1016/j.molcata.2012.07.017
[20] Li W., Zhang B., Li X. *et al*.: Appl. Catal. A, 2013, **459**, 65. https://doi.org/10.1016/j.apcata.2013.04.010
[21] Hu A., Yee G., Lin W.: J. Am. Chem. Soc., 2005,**127**, 12486. https://doi.org/10.1021/ja053881o
[22] Wang P., Kong A., Wang W. *et al*.: Catal. Lett., 2010, **135**, 159. https://doi.org/10.1007/s10562-010-0271-x
[23] Gawande M., Rathi A., Nogueira I. *et al*.: Green Chem., 2013, **15**, 1226. https://doi.org/10.1039/c3gc40375k
[24] Atashkar B., Rostami A., Tahmasbi B.: Catal. Sci. Tech., 2013, **3**, 2140. https://doi.org/10.1039/c3cy00190c
[25] Alizadeh A., Khodaei M., Beygzadeh M. *et al*.: Bull. Korean Chem. Soc., 2012, **33**, 2546. https://doi.org/10.5012/bkcs.2012.33.8.2546
[26] Cheng L., Li H., Sun J. *et al*.: Bioorg. Med. Chem., 2010, **18**, 4606. https://doi.org/10.1016/j.bmc.2010.05.034
[27] Bhatt R.: J. Global Pharma. Tech., 2010, **2**, 110.
[28] Kappe C., Shishkin O., Uraya G., Verdinoa P.: Tetrahedron, 2000, **56**, 1859. https://doi.org/10.1016/S0040-4020(00)00116-2
[29] Amrutkar S., Bhagat U., Pargharmol P. *et al*.: Int. Pharm. Pharm. Sci.ence 2010, **2**, 84.
[30] Atwal K., Swanson B., Unger S. *et al*.: J. Med. Chem. 1991, **34**, 2248. https://doi.org/10.1021/jm00106a048
[31] Kudo N., Futura S.: Chem. Pharma. Bull., 1999, **47**, 857. https://doi.org/10.1248/cpb.47.857
[32] Bonsei M., Loizzo M., Statti G. *et al*.: Bioorg. Med. Chem. Lett., 2010, **20**, 1990. https://doi.org/10.1016/j.bmcl.2010.01.113
[33] Yar M., Abdullah M., Majeed J.: World Acad. Sci. Eng. Tech., 2006, **55**, 593.
[34] Siddiqui S., Azam A.: Med. Chem. Res., 2014, **23**, 2976. https://doi.org/10.1007/s00044-013-0877-9
[35] Kanagarajan V., Thanusu J., Gopalakrishna M.: Eur. J. Med. Chem., 2010, **45**, 1583. https://doi.org/10.1016/j.ejmech.2009.12.068
[36] Thanh N., Mai N.: Carbohyd. Res., 2009, **344**, 2399. https://doi.org/10.1016/j.carres.2009.09.002
[37] Bhat A., Arshad M., Lee E. *et al*.: Chem. Biodiver., 2013, **10**, 2267. https://doi.org/10.1002/cbdv.201300009
[38] Hasan A., Khaleeq M., Raizi U.: J. Org. Chem., 2010, **22**, 5581.
[39] Butta R., Donthamsetty S., Adivireddy P., Venkatapuram P.: J. Heterocycl. Chem., 2017, **54**, 524. https://doi.org/10.1002/jhet.2615
[40] Kanagarajan V., How G. A., Siu C. N., Gopalkrishnan M.: J. Heterocycl. Chem., 2013, **50**, 396. https://doi.org/10.1002/jhet.1046.
[41] Singh J., Dulawat M., Jaitawat N. *et al*.: Ind. J. Chem., 2012, **51B**, 1623.
[42] Varga L., Nagy T., Kovesdi I. *et al*.: Tetrahedron, 2003, **59**, 655. https://doi.org/10.1016/S0040-4020(02)01560-0
[43] Ghoneim A., El-Farargy A.: Org. Chem Curr. Res., 2016, **5**, 1. https://doi.org/10.4172/2161-0401.1000159
[44] Jetti S., Verma D., Jain S.: ISRN Org. Chem., 2012. https://doi.org/10.5402/2012/480989
[45] Fazaeli R., Aliyan H., Mallakpour S. *et al*.: Chin. J. Catal., 2011, **32**, 582. https://doi.org/10.1016/S1872-2067(10)60203-3
[46] Fazaeli R., Aliyan H., Bordbar M., Mohammadi E.: The Open Catal. J., 2010, **3**, 79. https://doi.org/10.2174/1876214X01003010079
[47] Aliyan H., Fazaeli R., Tajsaeed N.: Iranian J. Catal. 2013, **3**, 99.
[48] Maleki B., Azarifar D., Moghaddam A. *et al*.: J. Serb. Chem. Soc., 2009, **74**, 1371. https://doi.org/10.2298/JSC0912371M
[49] Pinto D., Silva A., Cavaleiro J., Elguero J.: Eur. J. Org. Chem., 2003, **4**, 747. https://doi.org/10.1002/ejoc.200390117
[50] Kavitha N., Divekar K., Priyadarshani B., Gajanan S., Manjunath M.: Der Pharma Chemica, 2011, **3**, 55.

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## ГІПЕРАКТИВНИЙ МАГНІТО-СЕПАРАБЕЛЬНИЙ НАНО-КАТАЛІЗАТОР $MgFe_2O_4$ ДЛЯ СИНТЕЗУ П‘ЯТИ- ТА ШЕСТИЧЛЕННИХ ГЕТЕРОЦИКЛІЧНИХ СПОЛУК

***Анотація.*** *З використанням чистого нітрату заліза та карбонату магнію методом горіння синтезовано наночастки фериту $MgFe_2O_4$. Виявлено, що магніто-сепарабельний $MgFe_2O_4$ є гіперактивним каталізатором для синтезу широкого спектру біологічно активних п'яти та шестичленних гетероциклічних компонентів за умов дефлегмації. Встановлено, що вихід сполук є високим, а час реакції найменшим у порівнянні з літературними даними. Сильний електронний натяг $Fe^{3+}$ відповідає за гіперактивність каталізатора, що було доведено заміщенням $Fe^{3+}$ іншими тривалентними йонами металів. Показано, що заміна $Mg^{2+}$ негативно впливає на каталітичну активність. За допомогою розробленої методики синтезовано ряд заміщених моно/біспіримідинів, піримідин-2-ол, піримідин-2-тіол, піразоли та ізоксазоли внаслідок конденсації монохалконів/1,4-бісхалконів з різними біс-нуклеофілами у присутності гетерогенних магнітних наночастинок $MgFe_2O_4$ як каталізатора. Структуру синтезованих сполук визначено за допомогою спектроскопії Фур‘є, $^1H$, $^{13}C$ та мас-спектроскопії. Каталізатор можна легко видалити з реакційної суміші за допомогою простого зовнішнього магніту. Показано можливість відновлення та повторного використання наночастинок фериту без помітної зміни в активності навіть після п'яти циклів. Проведено аналіз наночастинок за допомогою рентгено-дифракційного аналізу, трансмісійної електронної та ІЧ-спектроскопії.*

***Ключові слова:*** *магнітні наночастки $MgFe_2O_4$, монохалкони, 1,4-бісхалкони, піримідин, піразолін, ізоксазолін, зовнішнє магнітне відділення, гетерогенний відновлювальний каталізатор.*