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Magnesium-iron bimetal oxides as an effective magnetized solid-base catalyst for the synthesis of substituted 2-aminthiophenes

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ABSTRACT

Mg-Fe bi-metal oxide was prepared and utilized as a magnetized renewable solid base catalyst for formation of 2-aminothiophenes by means of Gewald's reaction. The prepared heterogeneous basic solid catalyst can be separated by a magnet and reused without considerable wastage in this activity. The structure of the aforementioned magnetized basic nano-catalyst was studied by XRD (X-ray diffraction), SEM (scanning electron microscopy), TEM (transmission electron microscopy), EDS (energy dispersive x-ray spectroscopy) and VSM (vibrating sample magnetometry) techniques. The present methodology offers several advantages such as high yields of products, shorter reaction times, environmentally friendly conditions, low catalyst dosage, high endurance and facile work-up.

***Keywords**: Solid base catalyst, Magnetic nanoparticles, 2-aminothiophene, Gewald reaction.*

1. Introduction

Substituted thiophenes are significant heterocycles that have drawn specific attention, because of their various pharmaceutical and biologic characteristics [1-5]. 2-aminothiophenes have been progressively used as antitumoral, dyes, antioxidants and agrochemical compounds [6]. Gewald's reaction is a three-component reaction that can simply produce the 2-aminothiophenes with high yields [7]. Effective and appropriate variations to the Gewald reaction have been noted in the literature [8-16]. Base-catalyzed synthetic reactions are significant steps for constructing big and intricate molecules for the synthesis of many chemicals and pharmacological compounds [17, 18]. Compared to the extensive uses of solid acid catalysts in chemical methodology, solid basic catalysts have received significantly less consideration. Solid bases are important type of catalysts providing advantageous possibilities for homogeneous bases replacement. The application of basic solid catalysts instead of liquid ordinary bases may benefit of running costs reduction related to base neutralizing and product purifying, decreasing corrosion and other environment-related challenges, and at the same time permitting simpler isolation and catalysts retrieval. Over the last few years, magnetized substances have appeared as noteworthy alternatives to common heterogeneous beds [19-22]. The magnetic isolation provides many benefits over typical filtering and other purifying procedures. For instance, in the reutilization process, the catalyst could be easily and effectively retrieved from the reaction mixture with the aid of an exterior magnet and may be considered as a benign protocol that prevents the outcomes caused by filtering steps. Magnetic compounds have been utilized in acid-base catalyzed reactions [23], and specially, magnetically removable basic solid catalysts have been noted in the past few years [24-27]. Nevertheless, the insertion of supplementary, magnetized core into basic materials generally causes a lowered effective surface of the catalysts, which may alter the catalyzing character by decreasing the TOF, for instance. To resolve this difficulty, it is essential to significantly enhance the active effective surface of the magnetized catalysts [28-29]. Herein, the preparation of Mg–Fe bimetal oxides as a considerably effective, environmentally friendly, magnetically isolable and recyclable basic solid catalyst is discussed. After complete characterization, the catalyst function was explored in the formation of 2-

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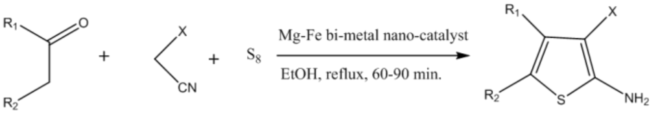
aminothiophenes via Gewald reaction. The general reaction is presented in **Scheme 1**.



Scheme 1. Synthesis of 2-aminothiophenes via Gewald reaction.

2. Experimental

2.1. General

All compounds were bought from Sigma. The metal contents of the synthesized nano catalyst were measured by ICP (inductively coupled plasma). The XRD pattern of the catalyst was investigated by a Bruker D8 Advance (λ = 1.540 Å). TEM micrographs were taken with the help of Zeiss electron microscope, LEO 912AB (120 kV), Germany. SEM images were captured by Zeiss electron microscope DSM-960A, Germany. FT-IR spectra were acquired by a Bruker model 470 spectrophotometer. Magnetic features were studied using a VSM, LDJ9600 device at ambient temperature. EDS examinations were performed using 133 eV resolution (model 7353, Oxford Instruments, UK). NMR spectra were captured in $CDCl_3$ on a Bruker Advance 300 MHz instrument. The melting points were evaluated on an Electrothermal Type 9100 apparatus.

2.2. Catalyst synthesis procedure

The Mg-Fe bi-metal oxalate precursors were synthesized according to previously reported procedure [30]. In a general method, 20 mmol magnesium chloride hexahydrate and 10 mmol iron(II) sulfate heptahydrate were solved in 100 mL deionized water. Then, 30 mmol sodium oxalate was solved into 100 mL H_2O at 80 °C under stirring not less than 1 h and afterwards this second solution was gradually dropped into the first solution, during which sedimentary particles were formed. The precipitates were isolated by filtration, and thereafter washed with distilled water and dried at 60 ° C overnight. The Mg-Fe bi-metal oxide catalyst was afforded by calcining the resultant precipitate at 500 °C for 2 h.

2.3. Synthetic typical manner for 2-aminothiophenes

Mg-Fe bi-metal oxide catalyst (0.15 g) and sulfur (5.0 mmol) were added to a solution consisting of ketone or aldehyde (5.0 mmol), malononitrile or ethyl cyanoacetate (5.0 mmol) in dry ethanol (10 mL) under continuing stirring. Then, the reaction mixture was warmed at reflux (80 °C) for 60-90 min. The progression of the reaction was followed by TLC. After completing the reaction, the basic solid catalyst was removed, assisted by a magnet, rinsed with acetone and dried to be ready to react again. The solvent was evaporated under reduced pressure. The raw product was crystallized in ethanol to provide relevant substituted 2-aminothiophenes. The products were identified by their melting points, FT-IR and ^{1}H-NMR spectra.

3. Results and Discussion

The magnetic solid base catalyst was prepared by one-stage oxalate co-precipitation and calcination at 500 °C. The catalyst structure has been qualified by XRD, SEM, TEM, EDS and VSM techniques.

The X-ray diffraction patterns of the synthesized Mg-Fe bi-metal catalyst, $MgFe_2O_4$, Fe_3O_4 and MgO standards are indicated in **Figs. 1a-d** respectively. The diffraction peaks of synthesized catalyst can be well-matched to spinel $MgFe_2O_4$ (JCPDS 17-0464, **Fig. 1b**) with respect to both peak locations and severities, where the diffraction peaks at 30.1, 35.5, 43.1, 53.5, 57.0 and 62.6° can be attributed to the reflections of (220), (311), (400), (422), (511) and (440) planes of $MgFe_2O_4$, respectively. It should be noted that the XRD pattern of synthesized catalyst (**Fig.1a**) is very similar to standard XRD pattern of Fe_3O_4 nanoparticles (**Fig.1c**), because $MgFe_2O_4$ and Fe_3O_4 have spinel crystal structure and their X-ray diffraction pattern is almost similar [31-33]. In comparison to synthesized Mg-Fe bi-metal catalyst, the lines at 43° and 63°, which can be well matched to the (200) and (220) reflectance of magnesium oxide (JCPDS 87-0653, **Fig. 1d**), stating that the production of crystalline magnesium oxide besides spinel $MgFe_2O_4$.

The production of extra crystalline magnesium oxide phase in Mg–Fe bi-metal catalyst agrees well with its high magnesium oxide content as illustrated in **Table 1**. Thus, the combination and phase construction analysis of synthesized Mg–Fe bimetal catalyst was the mixtures of magnesium oxide and $MgFe_2O_4$ [30]. The crystallite dimension of magnesium oxide in synthesized nano catalyst could be approximated very roughly, owing to the peak convergence with those of $MgFe_2O_4$, to be 13.5 nm by Scherrer's equation through the (200) reflectance. Consequently, such a magnesium-rich substance could also be considered as a composite with nano-scale magnesium crystallites on-site charged in the mesoporous framework of spinel $MgFe_2O_4$.

The morphological structure of the synthesized catalyst was investigated under SEM technique. The results showed that the surface of the catalyst was porous and the particle size was less than 100 nm and spherical (**Fig.2**).

TEM image demonstrates that synthesized nano catalyst is mesoporous structured.

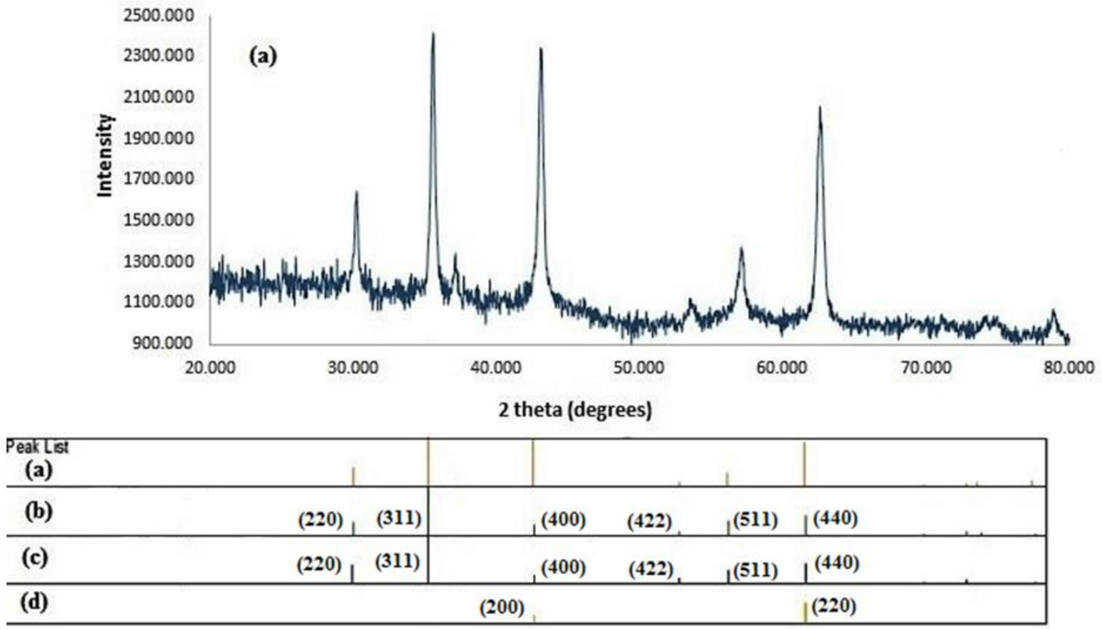


Fig. 1. The powder X-ray diffraction patterns of: a) synthesized Mg-Fe bi-metal catalyst, b) standard $MgFe_2O_4$, c) standard Fe_3O_4 d) standard MgO

Table 1. ICP data for Mg-Fe bi-metal nano-catalyst

Mg/Fe (atom)	Mg (wt%)	Fe (wt%)
1.68	29.35	39.87

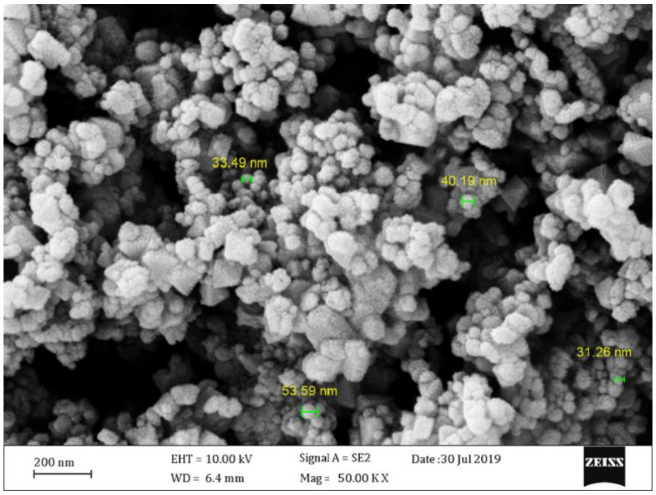


Fig. 2. SEM image of synthesized nano-catalyst

Fig. 3 shows randomized but uniform dispensations of mesopore channels within the overall particles. There was no evidence of clusters separate or particles of magnesium in the TEM image. This displays that the magnesium oxide species prepared uniformly inside the mesoporous framework of the matrix.

The EDS was utilized as a powerful manner to identify the chemical composition of the prepared basic solid catalyst. The EDS analysis confirms the presence of expected elements consisting magnesium, oxygen and iron in the catalyst construction (**Fig. 4**).

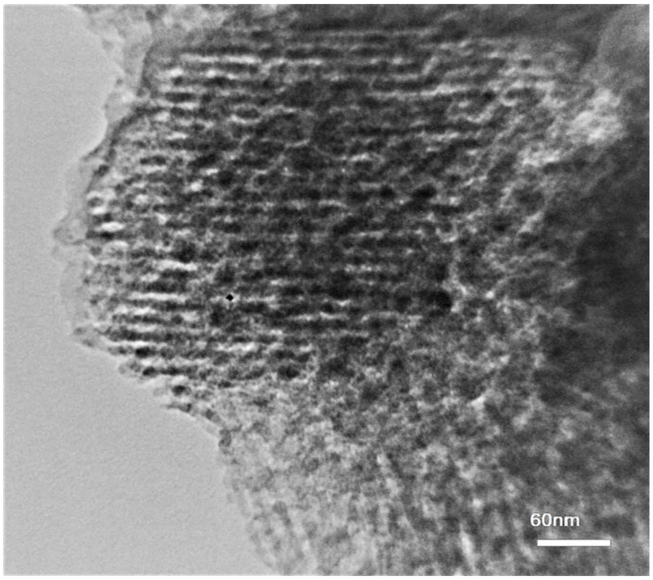


Fig. 3. TEM image of synthesized nano-catalyst

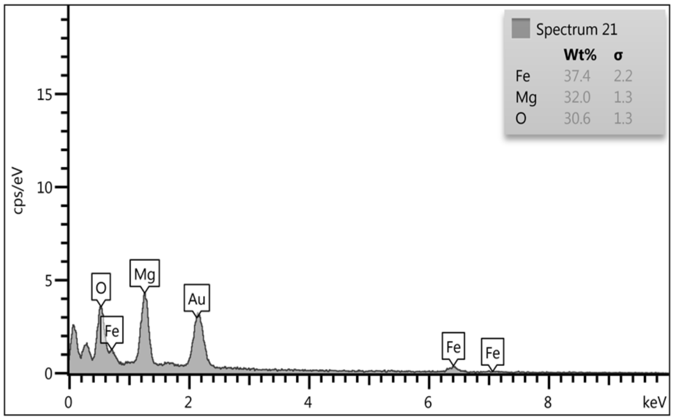


Fig. 4. The EDS analysis of synthesized nano-catalyst

The magnetic characteristic of the synthesized Mg-Fe bi-metal catalyst was examined by VSM. As illustrated in **Fig. 5**, the amount of the saturation magnetising of synthesized Mg-Fe bi-metal nano-catalyst is about 25 emu.g^{-1}. The magnetic character is supported by the spinel ferrite $MgFe_2O_4$ phase in the catalyst structure which designates that the prepared catalyst has magnetic properties and its magnetic characteristic is so high that it could be separated by an ordinary magnet.

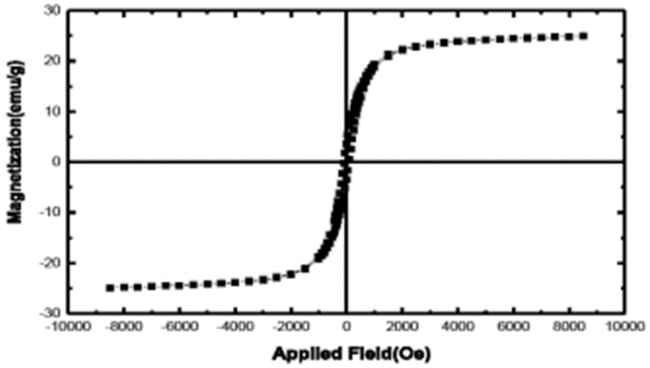


Fig. 5. The VSM curve of synthesized nano-catalyst

After affirming the satisfactory preparation of solid base catalyst by miscellaneous procedures, its catalyzing competence was checked out in the preparation of substituted 2-aminothiophenes. For this purpose, the reaction of malononitrile (5 mmol), cyclohexanone (5 mmol), and sulfur (5 mmol) catalyzed by synthesized nano catalyst were selected as a model reaction to make the best use of the reaction factors comprising solvent, catalyst dosage and temperature. At the initial stage, the aforementioned reaction was also performed in the absence of and in the existence of different amounts of the catalyst (**Table 2**). The findings demonstrated that the lack of catalyst in some non-polar and polar solvents even after 24 h, no progress was observed in the reaction process (entries 1-5). Where the nano catalyst exists, the foremost outcomes were obtained in ethanol (entries 6-10). Raising the nano catalyst portion to 0.15 g enhanced the reaction performance (entries 11-14). Incrementing the dose of catalyst beyond that did not raise the efficacy of the reaction (entry 15). In conclusion, the greatest efficacy was acquired when the sample reaction was carried out in ethanol in the existence of 0.15 g of nano catalyst under reflux conditions (entry 14). Also, the sample reaction was performed in the existence of commercial pure MgO for 1 h at 80 °C. The results revealed that the reaction was 99% efficient (entry 16). This means that the magnesium oxide part in the synthesized Mg-Fe bi-metal nano-catalyst is responsible for the reaction. The function of Fe_3O_4 was also investigated in the reaction under optimized situations. The findings are shown in **Table 2** (entry 17). As can be seen, no progress was observed in the sample reaction when applying Fe_3O_4. After establishing of the optimized reaction situations, the field of the reaction was developed to various aldehydes and ketones. Along with using the different aldehydes and ketones as the main reaction components, malononitrile or ethyl cyanoacetate as another element of the Gewald reaction was also studied. The findings are summarized in **Table 3**.

Table 2. Optimization of solvent, temperature, and nano-catalyst dosage

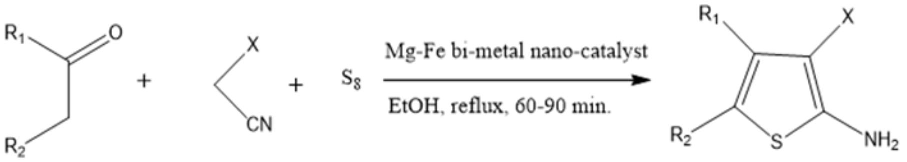
Entry	Condition	Cat. (g)	T (°C)	Time (h)	Yield (%)^a
1	H_2O	-	rt	24	Trace
2	DMF	-	rt	24	Trace
3	$CHCl_3$	-	rt	24	Trace
4	CH_3CN	-	rt	24	Trace
5	EtOH	-	rt	24	Trace
6	H_2O (Mg-Fe catalyst)	0.005	80	4	Trace
7	DMF (Mg-Fe catalyst)	0.005	80	4	20
8	$CHCl_3$ (Mg-Fe catalyst)	0.005	80	4	trace
9	CH_3CN (Mg-Fe catalyst)	0.005	80	4	30
10	EtOH (Mg-Fe catalyst)	0.005	80	4	45
11	EtOH (Mg-Fe catalyst)	0.010	80	4	64
12	EtOH (Mg-Fe catalyst)	0.050	80	3	74
13	EtOH (Mg-Fe catalyst)	0.100	80	2	90
14	EtOH (Mg-Fe catalyst)	0.150	80	1	95
15	EtOH (Mg-Fe catalyst)	0.200	80	1	95
16	EtOH (MgO)	0.150	80	1	99
17	EtOH (Fe_3O_4)	0.150	80	1	None

a: On the basis of isolated yield

All the investigated carbonyl compounds indicated good reaction capability using Gewald's reaction and effectively produced the corresponded products. All the products are known and were identified by checking their melting points and spectra (FT-IR, ^{1}HNMR) with those of authentic samples (ESI). However, malononitrile was revealed to be a preferable reactant than ethyl cyanoacetate due to its greater electron-accepting capability.

The reusability of the catalyst (Mg-Fe bimetal) was checked in the pattern reaction. To realize that objective, after completion of the reaction, the solid basic catalyst was removed, assisted by a magnet and rinsed with acetone and water to obliterate remaining product, dried

Table 3. Mg-Fe bi-metal nano-catalyzed synthesis of 2-aminothiophenes



1a: $R_1 = CH_3$, $R_2 = CH_3$
1b: $R_1 = Ph$, $R_2 = CH_3$
1c: $R_1 = Ph$, $R_2 = H$
1d: $R_1 = CH_3$, $R_2 = COCH_3$
1e: R_1, R_2 = $-(CH_2)_4-$
1f: R_1, R_2 = $-(CH_2)_3-$
1g: R_1 = 4-BrPh, $R_2 = H$
1h: $R_1 = H$, $R_2 = H$

2a: $X = CO_2Et$
2b: $X = CN$

3

Entry	Substrates	Product	Time (min)	Yield (%) [a]	Turnover frequency (TOF) (min^{-1})	M.P. (°C) (Lit.)
1	**1a** + **2a**	**3aa**	90	85	6.29	90 (91) [34]
2	**1b** + **2a**	**3ba**	80	90	7.5	92 (93) [34]
3	**1c** + **2a**	**3ca**	90	85	6.29	98 (98) [34]
4	**1d** + **2a**	**3da**	90	80	5.93	160 (161) [34]
5	**1e** + **2a**	**3ea**	70	94	8.95	114 (115) [35]
6	**1f** + **2a**	**3fa**	80	85	7.08	90 (91) [35]
7	**1g** + **2a**	**3ga**	80	85	7.08	122 (120) [36]
8	**1h** + **2a**	**3ha**	75	80	7.11	42 (42) [36]
9	**1a** + **2b**	**3ab**	80	90	7.50	142 (141) [34]
10	**1b** + **2b**	**3bb**	80	88	7.33	141 (142) [35]
11	**1e** + **2b**	**3eb**	60	95	10.56	147 (147) [11]
12	**1f** + **2b**	**3fb**	70	90	8.57	146 (148) [11]
13	**1g** + **2b**	**3gb**	75	88	7.82	190 (190) [37]
14	**1h** + **2b**	**3hb**	70	89	8.48	108 (110) [36]

[a] Isolated yield. All the products are known and were identified by comparison of their physical and spectroscopic data (FT-IR, ^{1}HNMR) with those of authentic samples.

and reutilized in subsequent reactions. The findings indicated that the catalyst could be consistently recovered without any substantial wastage in its function (**Fig. 6**).

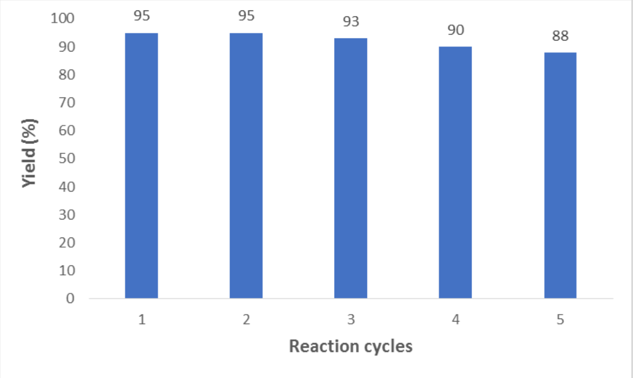


Fig. 6. The reusability of the synthesized nano-catalyst

To validate the advantage of the present research, application of Mg-Fe bimetal nano-catalyst in producing substituted 2-aminotiophenes, with reference to other previously published heterogeneous catalysts is depicted in **Table 4**. Based on results, the presented catalyst illustrates more satisfactory catalytic performance rapidly under green and cost-effective conditions.

4. Conclusions

We have effectually prepared a magnetic solid base heterogeneous nano-catalyst as a highly efficient and retrievable catalyst for the generation of substituted 2-aminothiophenes via Gewald reaction. The reaction is recommended, with the configured Mg-Fe bimetal nano-catalyst as a retrievable catalyst, adapted with the foundations of green catalysis as a consequence of the succeeding characteristics: no contamination, high endurance, recycle ability, shortened reaction times and great products efficiencies. More than the others, the magnetic solid base catalyst could be recycled five turns without any significant failing in its productivity. For this reason, the magnetic heterogeneous catalyst is could have been profitable in relevant branches of industry.

Table 4. Comparison of Mg-Fe bi-metal nano-catalyst with other heterogeneous catalysts in synthesis of substituted 2-aminotiophenes

Entry	Catalyst	Solvent	Temp. (°C)	Time (h)	Yield (%)[a]	Ref.
1	Fe_3O_4@rGO-NH	DMF	80	6	86	[11]
2	$ZnFe_2O_4$	EtOH	Reflux	4	80	[8]
3	TiO_2/nanoclinoptilolite	Solvent-free	100	2	90	[9]
4	ZnO	Solvent-free	100	10	70	[38]
5	ZnO/nanoclinoptilolite	Solvent-free	100	4	76	[39]
6	Mg-Fe bi-metal nano-catalyst	EtOH	Reflux	1	95	This study

[a] Isolated yield of the model reaction

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