#### SHORT COMMUNICATION



# Efficient synthesis of spirooxindole derivatives by magnetic and recyclable CaFe<sub>2</sub>O<sub>4</sub>@MgAl-LDH

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#### Abstract

A promising chemotherapeutic agent is spirooxindole. Probable targets involve cancers of the lung, liver, breast, colon, stomach, and prostate. Widespread drug discovery applications and biological activity are significant synthetic targets of spirooxindoles. In the present study, the synthesis of  $CaFe_2O_4$  nanoparticles via the sol–gel method is discussed. Vibrating sample magnetometer, scanning electron microscopy, Fourier transform infrared spectroscopy, and X-ray diffraction were used to prepare and characterize  $CaFe_2O_4@MgAl-LDH$  as an effective catalyst for the preparation of spirooxindole derivatives via one-pot, the three-component reaction of malononitrile, CH-acids (1,3-dicarbonyl compounds), and isatin in the presence of  $CaFe_2O_4@MgAl-LDH$  in excellent yields with short reaction times in aqueous media is used to describe a facile and efficient multicomponent synthesis of functionalized spirooxindoles.

Keywords Malononitrile · Spirooxindoles · Multicomponent reaction · 1,3-Dicarbonyl compounds · CaFe<sub>2</sub>O<sub>4</sub>@MgAl-LDH

# Introduction

In a variety of applications such as biomedical applications [1], magnetic fluids [2], and catalyst [3], the magnetic nanoparticles have been mainly used. The shape and size of metal nanoparticles influence the magnetic properties of them [4]. Nowadays, wide applications of magnetic oxide nanoparticles, both in fundamental research and industrial use, have made significant interest [5]. Because of their interesting magnetic, optical, and catalytic properties, CaFe2O4 NPs are among several kinds of nanoparticles that are presently getting a lot of interest [6, 7]. Because of the presence of  $Ca^{2+}$ rather than heavy metals, calcium ferrite, among well-known other ferrites, for example, ZnFe<sub>2</sub>O<sub>4</sub>, NiFe<sub>2</sub>O<sub>4</sub>, MnFe<sub>2</sub>O<sub>4</sub>, CuFe<sub>2</sub>O<sub>4</sub>, and CoFe<sub>2</sub>O<sub>4</sub>, has an important benefit as it is eco-friendly and biocompatible [8]. Also, due to chemical stability and biocompatibility, these particles are potentially beneficial for a wide range of applications [9].

Calcium- and iron-based compounds have been studied for possible uses in optical memory tools as well as the production of steel through dephosphorization, desulfuration, and deoxidization, gas absorbers, high-temperature sensors, and oxidation [10], oxidation catalysts, gas absorbers, among others [11, 12]. The co-precipitation [13], sol–gel, hydro-thermal [14], and aerosolization methods [15], auto combustion [16] can be used to produce magnetic nanoparticles.

It is favorable to use 2D materials as catalyst supports [17] because they have exceptional mechanical robustness and excellent electronic properties. Layered double hydroxide (LDH) is a kind of 2D material, and its advantages include low cost, exclusive structure, easy preparation, high stability, and composition diversity. It has presented countless potential in the synthesis and design of new supported catalysts.

Due to their frequent presence in many synthetic and natural products along with valuable biological activities, oxindoles play a significant role in the area of heterocyclic chemistry. In natural compounds and biological activities including anti-inflammatory activities, antiprotozoal, progesterone receptors (PR) agonists, and antibacterial, oxindole derivatives often appear as significant structural components [18–21].

It has been recently reported in the literature that several procedures of this strategy include reaction of dimedone, isatin, and malononitrile in the presence of GN/SO<sub>3</sub>H [22], CoFe<sub>2</sub>O<sub>4</sub>@SiO<sub>2</sub> [23], Borax [24], sodium stearate [25], Al-ITQ-HB [26], Alum [27], TEBA [28], CoFe<sub>2</sub>O<sub>4</sub>@SiO<sub>2</sub>@

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Co(III) Salen complex [29], DES [30], NEt<sub>3</sub> [31], SBA-PR-NH<sub>2</sub> [32], and Ni NPS [33].

In this work, our research continues on developing environmentally friendly organic synthesis, especially with nanocatalyst [34-44]. CaFe<sub>2</sub>O<sub>4</sub>@ MgAl-LDHs was introduced as an active, recyclable, and effective magnetic nanocatalyst. This nanocatalyst can be used for various organic functional group transformations in green processes. Then, its catalytic efficiency in the preparation of spirooxindoles was investigated by the coupling of malononitrile and various isatins with 1,3-dicarbonyl. High to excellent yield and selectivity of the corresponding delivered products were found. Unique advantages including simple synthesis of the catalyst, high magnetic property, and easy separation of the catalyst with a permanent magnet, the application of available and inexpensive precursors are also presented in this study. Also, under the applied reaction conditions, the catalytic systems exhibited high reusability and durability. The stability, reusability, and reactivity of the catalyst were also enhanced against the reaction processes (Scheme 1).

# Experimental

# Chemicals

Reagents and solvents were produced in Merck or Fluka chemical companies. An Electrothermal 9100 apparatus was used to measure melting points. A PerkinElmer 781 spectrometer was used to take IR spectra in KBr pellets,

Scheme 1 Preparation of spirooxindole derivatives with  $CaFe_2O_4@$  MgAl-LDHs nanoparticle

which were reported in cm<sup>-1</sup>. A Bruker DPX-250 Avance instrument was used to measure <sup>1</sup>HNMR and <sup>13</sup>CNMR spectra at 250 MHz and 62.9 MHz in CDCl<sub>3</sub> or DMSO-d<sub>6</sub>. The chemical shift was given in ppm relative to TMS as the internal standard. A Bruker D<sub>8</sub>-advance X-ray diffractometer with Cu K $\alpha$  ( $\lambda$  = 0.154 nm) radiation was used to carry out power X-ray diffraction (XRD). Using vibrating sample magnetometer (VSM) leak shore 7200, the magnetic properties were determined at 300 K Vsm leak shore. MIRA 3TESCAN-XMU spectrometer was used for scanning electron microscopy.

## **Catalyst preparation**

#### Preparation of CaFe<sub>2</sub>O<sub>4</sub> nanoparticles

The conventional sol-gel method was used to synthesize the calcium ferrite nanoparticles. A mixture of 1 M solution of  $Ca(NO_3)_2 \cdot 6H_2O$  and 2 M solution of  $Fe(NO_3)_3 \cdot 9H_2O$  was prepared. 2.5 M citric acid solution along with 7 ml of ethylene glycol was added to this mixture. The constantly magnetically stirring was done, and heating was carried out at 80–90 °C. Heat treatment is also significant for drying gel, and finally, the powder was prepared. Ethanol was used to wash the obtained powder thoroughly. In a vacuum oven, it was dried overnight at 60 °C. At 550 °C, the obtained product was calcined for 3 h [45].



#### Preparation of CaFe<sub>2</sub>O<sub>4</sub>@ MgAI-LDHs nanoparticles

The CaFe<sub>2</sub>O<sub>4</sub> particles of 0.50 g were dispersed in deionized water and methanol (80 ml) with a deionized water/methanol molar ratio of 1:1 by an ultrasonic cleaner. CaFe<sub>2</sub>O<sub>4</sub> was created in the form of a suspension in 15 min (solution A). To obtain a metal nitrate solution,  $Al(NO_3)_3 \cdot 6H_2O$ of 1.13 g and Mg(NO<sub>3</sub>)<sub>2</sub>·6H<sub>2</sub>O of 1.96 g were dissolved in 100 ml of deionized water (solution B). NaOH of 0.39 g and Na<sub>2</sub>CO<sub>3</sub> of 2.12 g were dissolved in 100 ml of deionized water (solution C). At room temperature, solution B was dropped into solution A along with solution C until pH to 10 under vigorous stirring. Then, for 24 h, the mixture was heated to 65 °C. Finally, using a magnet, the resulting products were separated and later, washed with ethanol and deionized water several times. Then, to obtain the magnetic precursor CaFe<sub>2</sub>O<sub>4</sub>@MgAl-LDHs, the formed products were dried at 65 °C in a forced air oven for 12 h [46].

## **Catalytic activity**

# General procedure for the preparation of spirooxindole derivatives

CaFe<sub>2</sub>O<sub>4</sub>@MgAl-LDHs of 0.002 g was added to a mixture of 1.0 mmol of 1,3-dicarbonyl compounds, 1.0 mmol of isatin, and 1.0 mmol of malononitrile in water as a solvent. At 70 °C, the mixture was stirred for appropriated reaction time. TLC was used to monitor the progress of the reaction. When the reaction was completed, the mixture was dissolved in ethyl acetate, and an external magnet was used to separate the CaFe<sub>2</sub>O<sub>4</sub>@MgAl-LDHs. Then, under reduced pressure, the solvent was removed from the solution. Using ethanol, the resulting product was purified by recrystallization to obtain the pure spirooxindole product in excellent purity and yield. <sup>1</sup>HNMR, <sup>13</sup>CNMR, and IR spectra of the products are bases of their structural assignments.

Selected spectral data 2-Amino-2',5-dioxo-5,6,7,8-tetrahy drospiro-[chromene-4,3'-indoline]-3-carbonitr ile (Compound 6, Table 1): White solid, mp>250 °C. <sup>1</sup>HNMR (250 MHz, DMSO-d<sub>6</sub>) 1.91 (2H, m, CH<sub>2</sub>), 2.14 (2H, m, CH<sub>2</sub>), 2.59 (2H, m, CH<sub>2</sub>), 6.65 (d,1H, J 7.39 Hz, Ph), 6.87 (t, 1H, J 7.39 Hz, Ph), 7.11 (d, 1H, J 7.39 Hz, Ph), 7.21 (t, 1H, J 7.39 Hz, Ph), 7.37 (s, 2H, NH<sub>2</sub>), 10.66 (s, 1H, NH). <sup>13</sup>CNMR (62.9 MHz, DMSO-d<sub>6</sub>) 195.1 (C=O), 178.2 (C=O), 166.1 (C), 158.7 (C), 142.1 (C), 134.5 (C), 128.5 (CH), 123.3 (CH), 121.8 (CH), 117.4 (CH), 112.9 (C  $\equiv$  N), 109.2 (C), 57.6 (C), 46.9 (C), 36.4 (CH<sub>2</sub>), 26.8 (CH<sub>2</sub>), 19.8 (CH<sub>2</sub>). IR (KBr, cm<sup>-1</sup>) 3354, 3296, 3174, 2952, 2204, 1712, 1655, 1350, 1214, 1075. Anal. Calcd for C<sub>17</sub>H<sub>13</sub>N<sub>3</sub>O<sub>3</sub>: C, 66.44; H, 4.26; N, 13.67%. Found: C, 66.42; H, 4.31; N, 13.72%.

**2-Amino-7,7-dimethyl-2',5-dioxo-5,6,7,8-tetrahydrosp iro** [chromene-4,3'-indoline]-3-carbonitrile (Compound 11, Table 1): White solid, mp > 250 °C. <sup>1</sup>HNMR (250 MHz, DMSO-d<sub>6</sub>) 1.02 (3H, s, CH<sub>3</sub>), 1.12 (3H, s, CH<sub>3</sub>), 2.07-2.12 (2H, m, CH<sub>2</sub>), 2.54 (2H, m, CH<sub>2</sub>), 6.68 (d,1H, J 7.3 Hz, Ph), 6.88 (t, 1H, J 7.3 Hz, Ph), 7.08 (d, 1H, J 7.3 Hz, Ph), 7.23 (t, 1H, J 7.4 Hz, Ph), 7.31 (s, 2H, NH<sub>2</sub>), 10.64 (s, 1H, NH). <sup>13</sup>CNMR(62.9 MHz, DMSO-d<sub>6</sub>) 195.2 (C=O), 178.4 (C=O), 166.5 (C), 159.1 (C), 152.3 (C), 142.4 (C), 134.8 (CH), 128.5 (CH), 123.3 (CH), 122.1 (CH), 117.7 (C), 112.2 (C  $\equiv$  N), 109.6 (C), 57.9 (C), 50.4 (CH<sub>2</sub>), 47.2 (C), 32.3 (CH<sub>2</sub>), 28.0 (CH<sub>3</sub>), 27.0 (CH<sub>3</sub>). IR (KBr, cm<sup>-1</sup>): 3374, 3311, 3143, 2927, 2194, 1723, 1654, 1349, 1225, 1055 cm<sup>-1</sup>. Anal. Calcd for C<sub>19</sub>H<sub>17</sub>N<sub>3</sub>O<sub>3</sub>: C, 68.05; H, 5.11; N, 12.53%. Found: C, 67.86; H, 5.14; N, 12.65%.

# **Results and discussion**

From Fe(NO<sub>3</sub>)<sub>3</sub>·9H<sub>2</sub>O and Ca(NO<sub>3</sub>)<sub>2</sub>·6H<sub>2</sub>O, CaFe<sub>2</sub>O<sub>4</sub> was synthesized. Then, in methanol/deionized water, an appropriate amount of CaFe<sub>2</sub>O<sub>4</sub> nanoparticles was dispersed. Then, to obtain a metal nitrate solution, Al(NO<sub>3</sub>)<sub>3</sub>·6H<sub>2</sub>O and Mg(NO<sub>3</sub>)<sub>2</sub>·6H<sub>2</sub>O were dissolved in 100 ml of deionized water. In 100 ml of deionized water, NaOH and Na<sub>2</sub>CO<sub>3</sub> were dissolved. Then, the solution of Al(NO<sub>3</sub>)<sub>3</sub>·6H<sub>2</sub>O, Mg(NO<sub>3</sub>)<sub>2</sub>·6H<sub>2</sub>O, NaOH, and Na<sub>2</sub>CO<sub>3</sub> was dropped to achieved CoFe<sub>2</sub>O<sub>4</sub>@ MgAl-LDHs (corresponding heterogeneous CaFe<sub>2</sub>O<sub>4</sub>@ MgAl-LDHs, Scheme 2).

Scanning electron microscopy (SEM), vibrating sample magnetometer (VSM), Fourier transform infrared (FTIR) analyses, and powder X-ray diffractometry (XRD) were used to characterize the catalyst.

## **Catalyst characterization**

#### FTIR spectroscopy

FTIR spectroscopy was used to study the FTIR at 4000 to  $400 \text{ cm}^{-1}$  for (a)  $\text{CaFe}_2\text{O}_4$  and (b)  $\text{CaFe}_2\text{O}_4$ @ MgAl-LDHs; the results are shown in Fig. 1. Due to O–H stretching and bending vibrations, the FTIR spectra of calcium ferrite nanoparticles, Fig. 1a exhibits abroad stretch at 3419 cm<sup>-1</sup> cm<sup>-1</sup>. Metal–alloy (Fe–Ca) corresponds to the band at 1094 cm<sup>-1</sup>, and due to the presence of ferrite skeleton, bands at 634 and 585 cm<sup>-1</sup> are attributed to Fe–O bonds [47].

In spectrum 1b, the broad bands which were displayed in the range of  $3130-3627 \text{ cm}^{-1}$  were assigned to OH group stretching, and the absorption band, which was around  $1630 \text{ cm}^{-1}$ , was caused by the flexural oscillation peaks of interlayer water molecules [48]. Also, the absorption peaks around 1384 cm<sup>-1</sup> were considered to be caused by the asymmetric stretching bond of intercalated NO<sub>3</sub><sup>2-</sup> [49]. This

Entry	Product	Substrate 1	Substrate 2	Substrate 3	Time (min)	Yield (%)
1	H <sub>2</sub> N NC NC NC NC NC O H		OH OH OOH	< CN	4	96
2	$\begin{array}{c} H_2N \\ NC \\ F \\ NC \\ H \\ H \\ H \end{array} \\ \begin{array}{c} 0 \\ 0 \\ H \\ H \\ \end{array}$		OH OH	<cn CN</cn 	4	97
3	$H_{2N} \xrightarrow{O} O$	H <sub>3</sub> C		<cn CN</cn 	5	96
4	H <sub>2</sub> N NC Br NC NO CH <sub>3</sub>	Br O N CH <sub>3</sub>	OH OH	<cn CN</cn 	5	95
5	H <sub>2</sub> N O NC O Cl NC O NC O NC O Cl NC O NC O Cl NC O Cl NC O NC O Cl NC O NC O Cl NC O NC O NC O NC O NC O NC O NC O NC O	Cl	OH OH O	< CN CN CN 	10	82
6	H <sub>2</sub> N O NC O NC O H			< CN CN CN 	6	96

#### Table 1 Synthesis of spirooxindole derivatives

#### Table 1 (continued)

Entry	Product	Substrate 1	Substrate 2	Substrate	Time (min)	Yield (%)
7	$H_{3}C$	H <sub>3</sub> C		< CN CN CN 	5	97
8	Br NC NC NC NC NO CH <sub>3</sub>	Br		CN CN	5	94
9	CI NO NC NC NO NO CI NO CI CH <sub>2</sub> Ph	Cl		< CN CN CN 	12	81
10	$\begin{array}{c} H_2N & O \\ NC & \\ F & \\ & \\ & \\ & \\ & \\ & \\ H \end{array} \\ O \\ H \end{array}$	$F \longrightarrow N = 0$ H H		< CN CN	5	96
11	H <sub>2</sub> N NC NC N O CH <sub>3</sub> CH <sub>3</sub> CH <sub>3</sub> H		H <sub>3</sub> C H <sub>3</sub> C O	< CN CN CN 	4	96
12	$\begin{array}{c} H_2N & O \\ NC & CH_3 \\ F & O \\ H \\ H \end{array} $		H <sub>3</sub> C H <sub>3</sub> C O	<cn CN</cn 	4	97

indicates the presence of a small number of carbonate ions

in the LDH phase. Al–OH stretching may be responsible for the bond at 646, 710, and 1160 cm<sup>-1</sup> [50]. The lattice vibration of metal–oxygen bonds (M–O) was responsible for the absorption peaks around 550–770 cm<sup>-1</sup>.

Time

(min)

Substrate

3

Substrate 2

Yield

(%)

Deringer

By the prominent use of XRD measurement, crystalline structures of the CaFe2O4 particles could be clearly understood. The crystalline nature of the samples is determined by the sharp peaks from diffraction patterns. As shown in Fig. 2, the good match of the XRD pattern of the synthesized calcium ferrite powder with the documented XRD data of CaFe<sub>2</sub>O<sub>4</sub> (JCPDS card No. 32-0168) indicated that wellcrystallized catalyst had been obtained.

Scheme 2 Preparation of CaFe<sub>2</sub>O<sub>4</sub>@ MgAl-LDHs

X-ray diffraction (XRD) analysis

In the case of  $CaFe_2O_4$  (Fig. 2a), the most prominent peaks present at 23.41°, 30.33°, 32.40°, 38.47°, and  $48.87^{\circ}$  which are corresponding to the (2 1 0), (21 2), (2 0 2), (2 0 3) and (4 0 2) planes of CaFe<sub>2</sub>O<sub>4</sub>, respectively. Thus, the sample is identified as orthorhombic CaFe<sub>2</sub>O<sub>4</sub> corresponding to reported data (DB card number 9013281). There are also peaks present at 43.01° and 78.24°, which are corresponding to the (133) and (0 8 3) planes of CaFe<sub>5</sub>O<sub>7</sub>, which indicates the complex nature of the sample. Typically, an intergrowth between

Reaction conditions: H<sub>2</sub>O (0.5 cc), 70 °C, 0.002 g CaFe<sub>2</sub>O<sub>4</sub>@MgAl-LDHs





Substrate 1

0

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Table 1 (continued)
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Entry

Product

H<sub>2</sub>N



Fig. 1 FTIR spectra for the a  $CaFe_2O_4$ , b  $CaFe_2O_4$ @ MgAl-LDHs

one  $CaFe_2O_4$  unit and 3 units of FeO wustite-type structures forms  $CaFe_5O_7$  [51]. This is common for  $CaFe_2O_4$ because it naturally exists as a system comprising the different oxidation states of Fe.

The characteristic diffraction peaks of a well-crystallized LDH phase (JCPDS NO. 22-0452) were presented by MgAl-LDH at 20 of 11.71°, 34.33°, 61.34°, and 62.68°, corresponding to the reflections of planes (001), (100), (110), and (111), respectively. The successful synthesis of the LDH was determined by the diffraction peaks.

#### Vibrating sample magnetometer (VSM)

By a vibrating sample magnetometer (VSM), the magnetic properties of  $CaFe_2O_4$  and  $CaFe_2O_4$ @ MgAl-LDHs nanoparticles were studied at 300 K (Fig. 3). For  $CaFe_2O_4$ @ MgAl-LDHs nanoparticles, the saturation magnetization value decreased compared to the  $CaFe_2O_4$ .



Fig. 2 XRD results of a  $CaFe_2O_4$ , b  $CaFe_2O_4$ @ MgAl-LDHs



Fig. 3 VSM pattern of CaFe<sub>2</sub>O<sub>4</sub> and CaFe<sub>2</sub>O<sub>4</sub>@MgAl-LDH

#### Scanning electron microscopy (SEM)

The size and morphology information of  $CaFe_2O_4$  nanoparticle is provided by SEM analysis of the products (Fig. 4). The results presented that the average product size of  $CaFe_2O_4$  nanoparticle was 26.36–57.76 nm.

# The catalytic activity of CaFe<sub>2</sub>O<sub>4</sub>@MgAl-LDHs for the synthesis of spirooxindoles

For the first time,  $CaFe_2O_4@MgAl-LDHs$  was used as an efficient and recyclable nanocatalyst for the synthesis of spirooxindoles by the coupling of various isatins with 1,3-dicarbonyls and malononitrile to show the merit of synthesized nanocatalyst in organic reactions. The model substrates were isatins, dimedone, and malononitrile. The reaction was examined in various solvents (Fig. 5). The results indicate that the efficiency of the reaction is affected by different solvents. Low yield (60%) was afforded by acetonitrile, while the yields could be improved using solvents such as water, ethanol, and DMSO. Finally, using water as a solvent, the yield increased to 97%, which is better than any other solvents examined here. The yield of model reaction decreased to 5% in the absence of solvent.

A fundamental strategy for constructing MCRs is the electrophilic reaction of isatin with two different nucleophiles, water, and protic solvent which helps in the enolization of dimedone as well as its action as a solvent by making hydrogen bonds with the OH. This increases the nucleophilic



**Fig. 5** The effect of several solvents in the preparation of spirooxindole by  $CaFe_2O_4@MgAl-LDHs$ . Reaction conditions: dimedone (1.0 mmol), isatin (1.0 mmol), and malononitrile (1 mmol), at 70 °C, 0.002 g CaFe\_2O\_4@MgAl-LDHs

character of the methylene carbon (C-2) of dimedone. Thus, it helps to increase the reaction rate [30].

The amount of catalyst was also changed. Figure 6 summarizes the results. The results presented that the catalyst concentration reaction affects the yield crucially. Under the same conditions, decreasing the catalyst concentration resulted in lower yields. The product significantly reduced, with catalyst concentration increasing (more 0.002 g). Consequently, because the reaction was completed within high



Fig. 4 SEM images of CaFe<sub>2</sub>O<sub>4</sub>



**Fig.6** The effect of diverse catalysts in the preparation of spirooxindole by  $CaFe_2O_4@MgAl-LDHs$ . Reaction conditions: dimedone (1.0 mmol), isatin (1.0 mmol), and malononitrile (1 mmol) in H<sub>2</sub>O (0.5 cc), at 70 °C

yield, this condensation was best catalyzed by 0.002 g of  $CaFe_2O_4@MgAl-LDHs$ . The reaction was performed in the presence of  $CaFe_2O_4$  and efficiency was 20%.

By carrying out the model reaction at different temperatures, the effect of the temperature of the reaction was studied. The best result was obtained within 70  $^{\circ}$ C (Fig. 7).

By carrying out the model reaction at various times, the effect of time of reaction was investigated. The best outcome was obtained within 4 min (Fig. 8).

This coupling was carried out in the absence of catalysts to study the catalytic activity of  $CaFe_2O_4@MgAl-LDHs$ . In this case, over model reaction time, the reaction proceeded in low yield (6%). Using 0.002 g of the



**Fig. 7** The effect of different temperatures in the preparation of spirooxindole by  $CaFe_2O_4@MgAl-LDHs$ . Reaction conditions: dimedone (1.0 mmol), isatin (1.0 mmol), and malononitrile (1 mmol) in  $H_2O(0.5 \text{ cc})$ 



**Fig. 8** The effect of different time in the preparation of spirooxindole by  $CaFe_2O_4@MgAl-LDHs$ . Reaction conditions: dimedone (1.0 mmol), isatin (1.0 mmol), and malononitrile (1 mmol) in H<sub>2</sub>O (0.5 cc), 70 °C

catalyst within 4 min in  $H_2O$  as a solvent, spirooxindole was achieved with an excellent yield (97%).

Evaluation using various 1,3-dicarbonyl and isatin compounds was carried out to explore further the scope and limitation of this protocol under the optimized conditions, particularly regarding library construction. Table 1 summarizes the results. In all cases, to afford the corresponding spirooxindoles in good to excellent yields (81–97%) in short reaction times, the reaction proceeded readily.

In comparison with most of the reported works, this catalyst showed good catalytic activity and good yields (97%) in shorter times (see Table 2).

Herein, in Scheme 3, a mechanism was proposed for the  $CaFe_2O_4@MgAl$ -LDHs catalyzed preparation of spirooxindole. Thus, it is demonstrated that the  $CaFe_2O_4@MgAl$ -LDHs induces the polarization of the carbonyl group of isatin, which is followed by the nucleophilic addition of malononitrile to isatin. Then, this intermediate subsequently undergoes elimination via Knoevenagel condensation. The spirooxindole derivatives are afforded by the addition of dimedone to intermediate [29].

A permanent external magnet could recover the catalyst at the end of the reaction. Ethanol was used to wash the recycled catalyst, which is then subjected to a second reaction process. According to the results, the yield of the product was only slightly reduced after five runs (Fig. 9). After five runs, the reused catalyst characterization (FTIR spectra (Fig. 10)) was obtained where no important variation was seen in the structure of the recovered catalyst with the fresh catalyst. Table 2Comparison of resultsutilizing CaFe2O4@MgAl-LDHs with different catalysts

Entry	Catalyst	Solvent/ $T$ (°C)	Time (min)	Yield (%)	References
1	GN/SO <sub>3</sub> H	EtOH/water (1:1)/ref.	40	95	[22]
2	Borax (10 mol%)	EtOH/ref.	120	94	[24]
3	(SB-DBU)Cl	EtOH/r.t	150	97	[52]
4	SBA-PR-NH <sub>2</sub>	H <sub>2</sub> O/ref.	5	80	[32]
5	β-Cyclodextrin	H <sub>2</sub> O/60 °C	480	88	[53]
6	CaFe <sub>2</sub> O <sub>4</sub> @MgAl-LDH	H <sub>2</sub> O/70 °C	4	97	This work

Malononitrile (1 mmol), isatin (1 mmol), dimedone (1 mmol)



Scheme 3 An acceptable mechanism for the synthesis of spirooxindole with CaFe<sub>2</sub>O<sub>4</sub>@MgAl-LDHs

# Conclusion

In conclusion, using  $CaFe_2O_4@MgAl-LDHs$ , a facile methodology was developed to prepare spirooxindole derivative nanoparticles as an efficient heterogeneous catalyst. At 70 °C, the catalyst represents an outstanding activity in water. For a wide variety of substrates, a good to high yield of products was obtained within short reaction times. FTIR, SEM, VSM, and XRD analyses were used to characterize the catalyst. With the negligible loss of efficiency, the catalyst was recycled for at least five consecutive runs. The advantages of the catalyst include the performance, preparation from cheap and accessible materials, environmentally benign nature, and cost-effectiveness. These advantages make it a suitable alternative for the preparation of spirooxindole. Moreover, separation and recovery of the catalyst for another catalytic recycling are easy.



Fig.9 Recyclability of CaFe<sub>2</sub>O<sub>4</sub>@MgAl-LDHs in the preparation of spirooxindole. Reaction conditions: dimedone (1.0 mmol), isatin (1.0 mmol), and malononitrile (1 mmol) in H<sub>2</sub>O (0.5 cc), at 70 °C, 4 min



Fig.10 FTIR spectra of fresh  $CaFe_2O_4@MgAl-LDHs$  (a) and  $CaFe_2O_4@MgAl-LDHs$  after the fifth run (b)

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# References

- 1. T. Zargar, A. Kermanpur, Ceram. Int. 43, 5794 (2017)
- R. Taylor, S. Coulombe, T. Otanicar, P. Phelan, A. Gunawan, W. Lv, G. Rosengarten, R. Prasher, H. Tyagi, J. Appl. Phys. 113, 011301 (2013)
- S.F. Wang, X.T. Zu, G.Z. Sun, D.M. Li, C.D. He, X. Xiang, W. Liu, S.B. Han, S. Li, Ceram. Int. 42, 19133 (2016)

- A. Abedini, A. Rajabi, F. Larki, M. Saraji, M.S. Islam, J. Alloys Compd. 711, 190 (2017)
- M. Goodarz Naseri, E.B. Saion, A. Kamali, ISRN Nanotechnol. 2012, 1 (2012)
- S. Ida, K. Yamada, T. Matsunaga, H. Hagiwara, Y. Matsumoto, T. Ishihara, J. Am. Chem. Soc. 132, 17343 (2010)
- 7. S.K. Pardeshi, R.Y. Pawar, Mater. Res. Bull. 45, 609 (2010)
- 8. L. Khanna, N.K. Verma, J. Magn. Magn. Mater. 336, 1 (2013)
- R.A. Candeia, M.I.B. Bernardi, E. Longo, I.M.G. Santos, A.G. Souza, Mater. Lett. 58, 569 (2004)
- M. Dadwal, Polymeric Nanoparticles as Promising Novel Carriers for Drug Delivery: An Overview (2014)
- D. Hirabayashi, T. Yoshikawa, K. Mochizuki, K. Suzuki, Y. Sakai, Catal. Lett. 110, 155 (2006)
- 12. N.O. Ikenaga, Y. Ohgaito, T. Suzuki, Energy Fuels 19, 170 (2005)
- 13. Y. Zhao, Z. Qiu, J. Huang, Chin. J. Chem. Eng. 16, 451 (2008)
- J. Wan, X. Chen, Z. Wang, X. Yang, Y. Qian, J. Cryst. Growth 276, 571 (2005)
- E. Ruiz-Hernández, A. López-Noriega, D. Arcos, I. Izquierdo-Barba, O. Terasaki, M. Vallet-Regí, Chem. Mater. 19, 3455 (2007)
- 16. M. Faraji, Y. Yamini, M. Rezaee, J. Iran Chem. Soc. 7, 1 (2010)
- Y. Xu, C. Cheng, S. Du, J. Yang, B. Yu, J. Luo, W. Yin, E. Li, S. Dong, P. Ye, X. Duan, ACS Nano 10, 4895 (2016)
- 18. G. K. Jnaneshwar and V. H. Deshpande, J. Chem. Res. S 632 (1999)
- 19. H. Pajouhesh, R. Parson, F.D. Popp, J. Pharm. Sci. 72, 318 (1983)
- Y. Kamano, H. Ping Zhang, Y. Ichihara, H. Kizu, K. Komiyama, G.R. Pettit, Tetrahedron Lett. 36, 2783 (1995)
- 21. C. Fischer, C. Meyers, E.M. Carreira, Helv. Chim. Acta **83**, 1175 (2000)
- A. Allahresani, B. Taheri, M.A. Nasseri, Res. Chem. Intermed. 44, 6979 (2018)
- K. Hemmat, M.A. Nasseri, A. Allahresani, S. Ghiami, J. Organomet. Chem. 903, 120996 (2019)
- A. Molla, S. Ranjan, M.S. Rao, A.H. Dar, M. Shyam, V. Jayaprakash, S. Hussain, ChemistrySelect 3, 8669 (2018)
- 25. L.M. Wang, N. Jiao, J. Qiu, J.J. Yu, J.Q. Liu, F. Lou Guo, Y. Liu, Tetrahedron **66**, 339 (2010)
- P. García-García, J.M. Moreno, U. Díaz, M. Bruix, A. Corma, Nat. Commun. 7, 1 (2016)
- 27. A.R. Karimi, F. Sedaghatpour, Synthesis (Stuttg). **2010**, 1731 (2010)
- 28. S.L. Zhu, S.J. Ji, Y. Zhang, Tetrahedron 63, 9365 (2007)
- M.A. Nasseri, K. Hemmat, A. Allahresani, Appl. Organomet. Chem. 33, e4743 (2019)
- N. Azizi, S. Dezfooli, M. Mahmoudi Hashemi, J. Mol. Liq. 194, 62 (2014)
- V.Y. Mortikov, Y.M. Litvinov, A.A. Shestopalov, L.A. Rodinovskaya, A.M. Shestopalov, Russ. Chem. Bull. 57, 2373 (2008)
- G. Mohammadi Ziarani, A. Badiei, S. Mousavi, N. Lashgari, A. Shahbazi, Chin. J. Catal. 33, 1832 (2012)
- 33. J.M. Khurana, S. Yadav, Aust. J. Chem. 65, 314 (2012)
- M.A. Nasseri, B. Zakerinasab, M.M. Samieadel, RSC Adv. 4, 41753 (2014)
- M.A. Nasseri, F. Kamali, B. Zakerinasab, RSC Adv. 5, 26517 (2015)
- H. Hassani, B. Zakerinasab, H. Hossien Poor, Appl. Organomet. Chem. 32, e3945 (2018)
- M.A. Nasseri, B. Zakerinasab, Res. Chem. Intermed. 41, 5261 (2015)
- M.A. Nasseri, F. Ahrari, B. Zakerinasab, RSC Adv. 5, 13901 (2015)
- M.A. Nasseri, S.A. Alavi, B. Zakerinasab, J. Chem. Sci. 125, 109 (2013)
- 40. M. A. Nasseri and M. Salimi, (n.d.)

- 41. M.A. Nasseri, S.M. Sadeghzadeh, J. Iran. Chem. Soc. 11, 27 (2014)
- M.A. Nasseri, F. Ahrari, B. Zakerinasab, Appl. Organomet. Chem. 30, 978 (2016)
- 43. H. Hassani, M.A. Nasseri, B. Zakerinasab, F. Rafiee, Appl. Organomet. Chem. **30**, 408 (2016)
- H. Hassani, B. Zakerinasab, M.A. Nasseri, M. Shavakandi, RSC Adv. 6, 17560 (2016)
- 45. N.H. Sulaiman, M.J. Ghazali, B.Y. Majlis, J. Yunas, M. Razali, Biomed. Mater. Eng. 26, S103 (2015)
- 46. Y. Chen, T. Liu, H. He, H. Liang, Appl. Organomet. Chem. **32**, e4330 (2018)

- 47. S. Rana, J. Philip, B. Raj, Mater. Chem. Phys. 124, 264 (2010)
- S. Aisawa, H. Hirahara, H. Uchiyama, S. Takahashi, E. Narita, J. Solid State Chem. 167, 152 (2002)
- Q. Wu, A. Olafsen, Ø.B. Vistad, J. Roots, P. Norby, J. Mater. Chem. 15, 4695 (2005)
- 50. J.T. Kloprogge, R.L. Frost, J. Solid State Chem. 146, 506 (1999)
- C. Delacotte, F. Hüe, Y. Bréard, D. Pelloquin, Key Eng. Mater. 617, 237 (2014)
- 52. S. Riyaz, A. Indrasena, A. Naidu, P.K. Dubey, Indian J. Chem. Sect. B **53B**, 1442 (2014)
- R. Sridhar, B. Srinivas, B. Madhav, V.P. Reddy, Y.V.D. Nageswar, K.R. Rao, Can. J. Chem. 87, 1704 (2009)