

ORIGINAL RESEARCH PAPER

## Caffeine-loaded Fe<sub>3</sub>O<sub>4</sub> nanoparticles: A new magnetically recoverable organocatalyst for Knoevenagel condensation reaction

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### ABSTRACT

Caffeine loaded magnetic nanoparticle was successfully synthesized and were characterized by Fourier transform infrared spectroscopy (FT-IR), scanning electron microscopy (SEM), transmission electron microscopy (TEM), energy dispersive X-ray analysis (EDX), thermo gravimetric analysis (TGA), differential thermal analysis (DTA) and vibrating sample magnetometer (VSM). The resulting nanocomposite is shown to be an efficient catalyst in Knoevenagel condensation of various aldehydes under ultrasound irradiation.

**Keywords:** Caffeine; Knoevenagel Condensation; Magnetic Nanoparticles; Ultrasound Assisted  
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## INTRODUCTION

Recently, catalysis with magnetic nanoparticles (MNPs) has been attracting great attention and investigated extensively. Since such catalysts, whose flocculation and dispersion can be reversibly controlled by applying a magnetic field, work under quasi-homogeneous conditions, their performance is usually very good. Reactions are often performed under mild conditions without using solvents or by applying water. The catalysts can be easily separated by magnetic decantation and reused in many cases without losing their activity [1-4]. MNPs were used in a wide range of organic reactions, such as hydrogenation, oxidation, carbon-carbon coupling, cycloaddition, arylation, alkylation, multicomponent "one-pot" synthesis, Fenton-like reaction, etc. [5- 12].

Sonication chemistry has gained considerable attention in recent years and implementation of ultrasound irradiation in organic reactions provides a specific activation based on physical properties such as acoustic cavitation. Therefore, ultrasound can be used as an important tool to

perform a number of chemical reactions in high yields at shorter reaction times and with simpler and easier work -up conditions compared to some conventional methods [13- 16]

The Knoevenagel condensation is the reaction of an aldehyde or ketone with any compound having an active methylene group [17-18]. Because of the mild reaction conditions, and its broad applicability, the Knoevenagel reaction widely an employed method for carbon-carbon bond formation in organic synthesis with numerous applications in the synthesis of fine chemicals, hetero Diels-Alder reactions and in the synthesis of carbocyclic as well as heterocyclic compounds of biological significance [19-20].

Herein; in continuation of our research to develop new magnetic nanoparticle-supported catalysts for organic synthesis [21-25], we describe our results on the preparation and characterization of modified magnetite with caffeine and its catalytic application for Knoevenagel condensation under ultrasonic irradiation.

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## RESULTS AND DISCUSSION

The strategy used to prepare target MNPs<sub>s</sub> is shown in scheme 1. The structure of the nanocomposite was identified by IR, SEM, TEM, VSM, EDAX, and TGA.

FT-IR spectroscopy was used to verify the functional groups of the MNPs as the following peaks: Fe-O stretching vibrations at  $\sim 588\text{ cm}^{-1}$ ; Si-O-Si asymmetric stretching vibrations at  $\sim 1100\text{ cm}^{-1}$ ; C-H stretches vibrations at  $\sim 2900\text{ cm}^{-1}$ ; C=C and C=O stretching vibrations at  $\sim 1620\text{ cm}^{-1}$  and  $\sim 1700\text{ cm}^{-1}$ , respectively (Fig. 1).

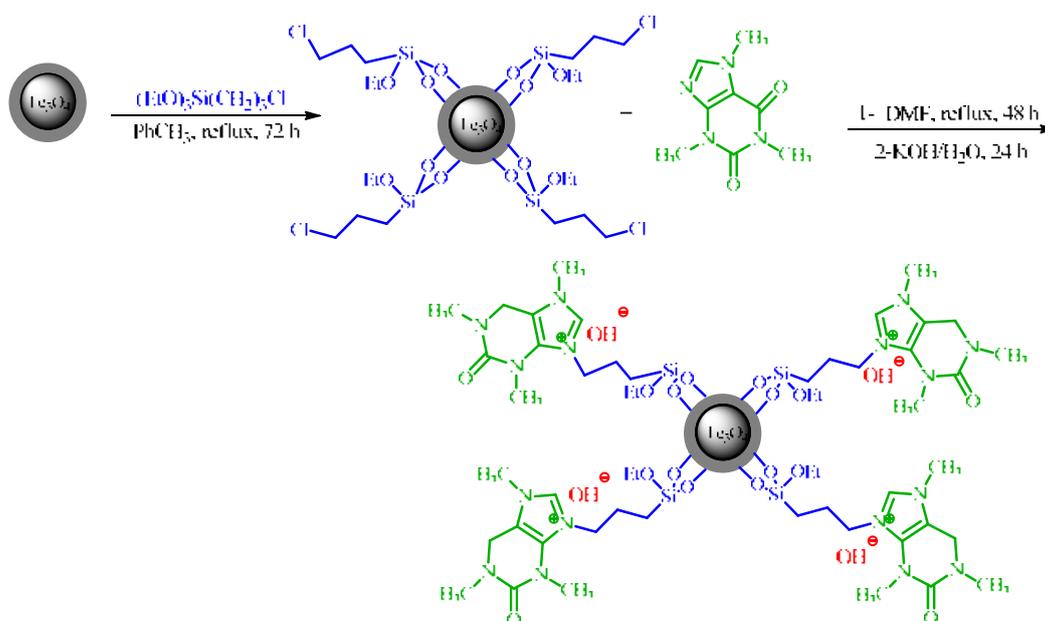
A particle size with about  $\sim 23\text{-}34\text{ nm}$  diameter with a nearly spherical shape was observed in the SEM and TEM images of the MNPs- caffeine. TEM analysis also shows a dark nano- $\text{Fe}_3\text{O}_4$  core surrounded by a gray silica shell thickness.

EDAX analysis of the nanocatalyst confirmed

the presence of the expected elements in its structure (iron, carbon, oxygen, silicon, nitrogen, and chlorine) (Fig. 3).

The magnetic properties of the synthesized MNPs were analyzed using VSM. The saturated magnetization value of the caffeine-loaded  $\text{Fe}_3\text{O}_4$  nanoparticles was  $\sim 26\text{ emu/g}$  (Fig. 4).

The thermo gravimetric analysis (TGA) and differential thermal analysis (DTA) of  $[\text{Fe}_3\text{O}_4@\text{SiO}_2@(\text{CH}_2)_3\text{-caffeine}]\text{OH}$  is shown in Fig. 5. The analysis showed two decreasing peaks. First peak appears at temperature below  $120\text{ }^\circ\text{C}$  due to desorption of water molecules from the catalyst surface. The weight loss is about 3 %. The weight loss (7 %) at  $120\text{-}530\text{ }^\circ\text{C}$  is linked mainly to the loss of the organic spacer group. Thus, the catalyst can be used without danger of decomposition at temperatures below  $120\text{ }^\circ\text{C}$ .



Scheme 1. Preparation of caffeine modified MNPs

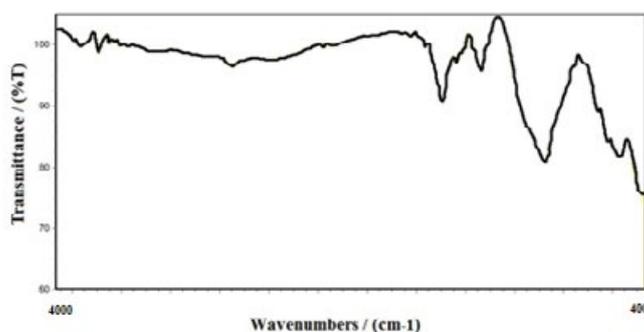


Fig. 1. The FT-IR spectra of MNPs- caffeine

After synthesis of MNPs, to determine the optimal reaction conditions, a typical reaction of benzaldehyde and malononitrile was performed in the presence of the prepared MNPs- caffeine as organocatalyst. Initially, the model reaction under stirring conditions at room temperature under catalyst-free and silent conditions was

investigated. This attempt failed and the materials remained unreacted (Table 1, entry 1). Increasing in the reaction temperature up to 60 °C led to an increase in the yield of product in a 15% yield after 3 h (Table 1, entry 2). Hence, this reaction mixture was carried out using 50 mg of the catalyst, conditions that satisfyingly provided product in a

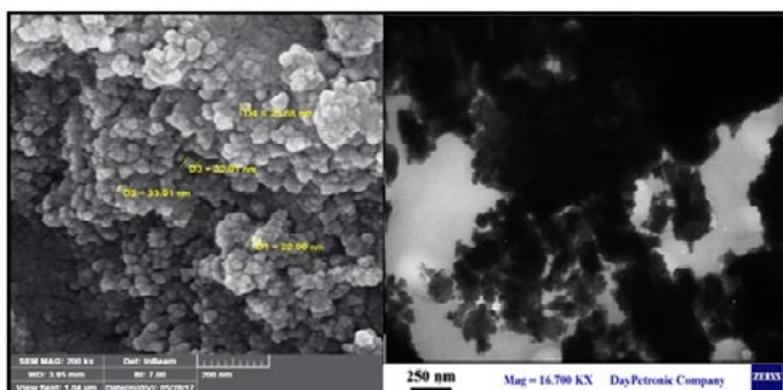


Fig. 2. SEM and TEM images of MNPs- caffeine

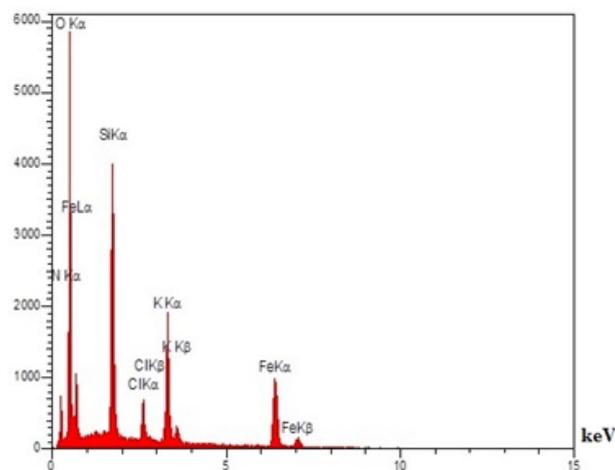


Fig. 3. The energy-dispersive X-ray spectroscopy of MNPs catalyst

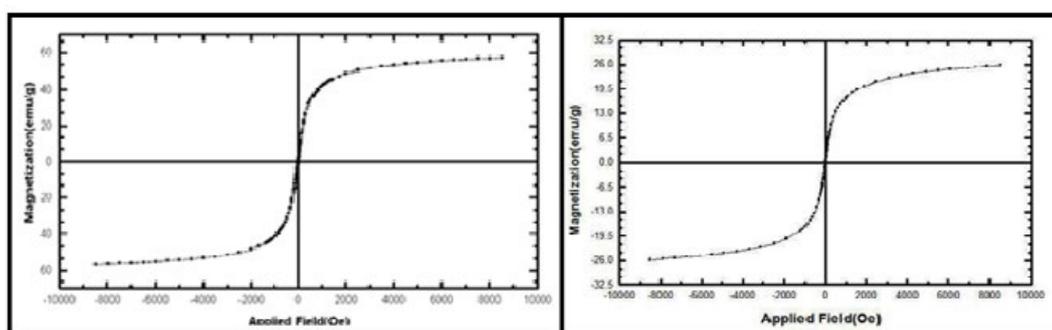


Fig. 4. VSM magnetization curve of  $Fe_3O_4$  (left) and MNPs- caffeine (right)

85% yield after 45 min. The yield of the reaction was not improved by elevating the temperature and the increase in the amount of the catalyst. To investigate the effect of the solvent on the catalytic reaction, the model reaction was carried out in various solvent media (Table 1, entries 4–6). The results show that the H<sub>2</sub>O is the best choice for this reaction. The efficiency of MNP-caffeine-OH was also compared with MNP-caffeine-Cl at 60 °C. The obtained results indicated in the presence of MNP-caffeine-Cl, lower yield was achieved.

In view of the advantages associated with the use of ultrasound irradiation in performing reactions [26], the reaction was investigated under ultrasound irradiation at 60°C in H<sub>2</sub>O. The obtained results indicate the superiority of the present method in terms of yield and reaction time relative to the thermal reaction.

Following the obtained results, benzylidene malonitrile derivatives were obtained by the reaction of various aromatic aldehydes and

malonitrile in the presence of 50 mg MNPs- caffeine under ultrasound irradiation at 60 °C in high yields (Table 2).

It is estimated that the nature and electronic properties of the substituents on the aromatic ring are effective in terms of yields and reaction rates. Aromatic aldehydes with electron-withdrawing groups react faster than those containing electron-releasing groups and lead to an increase in isolated yield.

To investigate reusability of the catalyst, synthesis of 3b was selected as the model reaction. The catalyst was magnetically recovered after each run, washed with water and ethanol and dried at ambient temperature. Pleasingly, the catalyst did not suffer from a significant change in structure or decrease in reactivity after five consecutive runs.

## EXPERIMENTAL

All chemicals were of analytical grade and used without further purification. Fe<sub>3</sub>O<sub>4</sub> and Fe<sub>3</sub>O<sub>4</sub>@

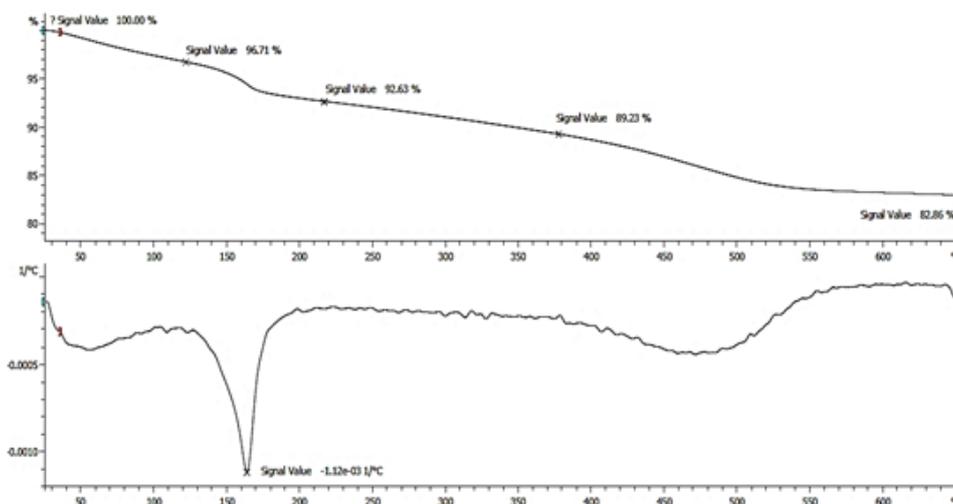
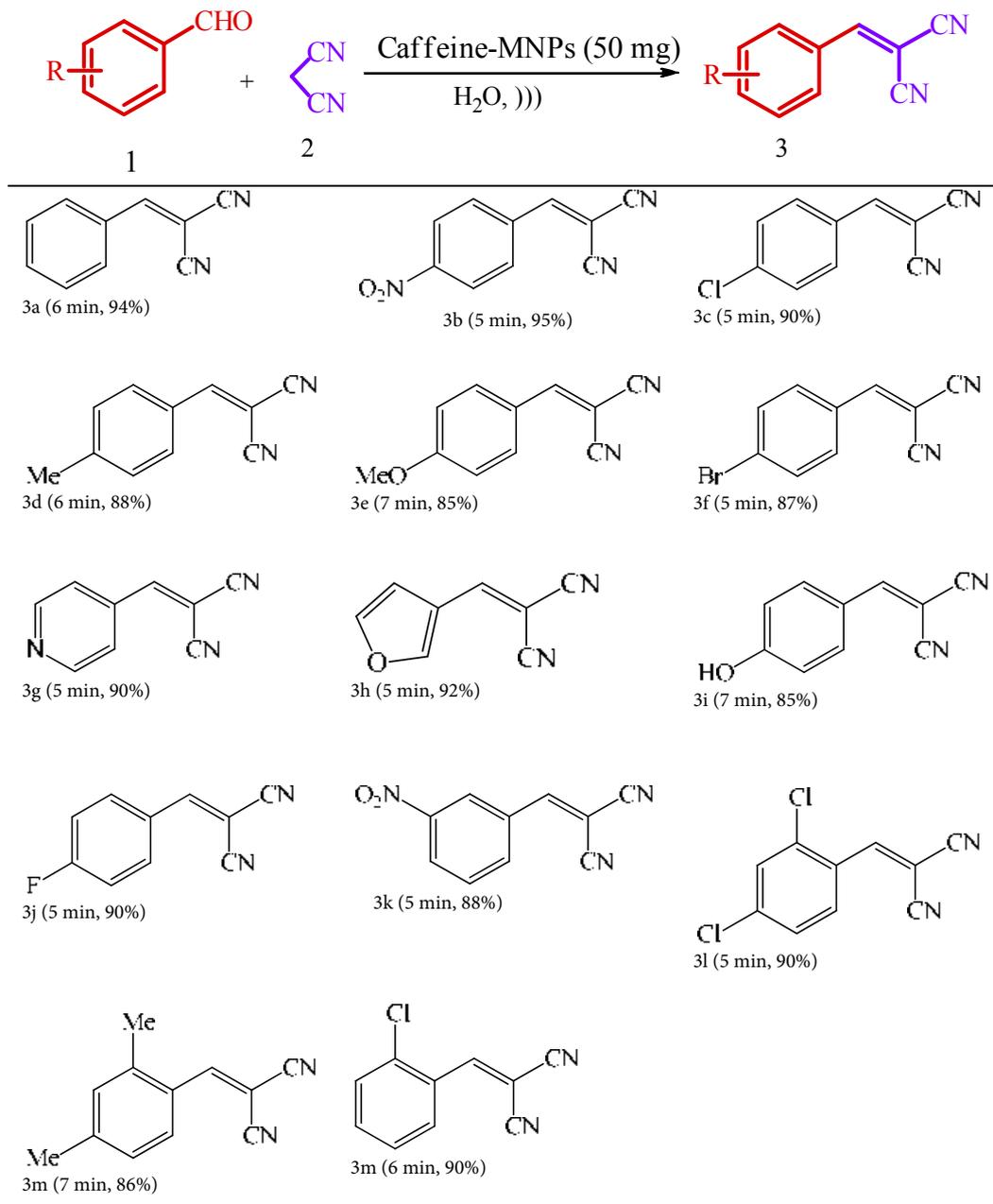


Fig. 5. TG-DTG analysis for MNPs- caffeine

Table 1. Optimization of reaction conditions for the Knoevenagel reaction of benzaldehyde and malonitrile catalyzed by MNPs-caffeine

No	Catalyst amount (mg)	Solvent	Temperature (°C)	Conventional		Sonication	
				Time (min)	Yield <sup>a</sup> (%)	Time (min)	Yield <sup>a</sup> (%)
1	-	H <sub>2</sub> O	25	180	-	10	-
2	-	H <sub>2</sub> O	60	180	15	10	35
3	50	H <sub>2</sub> O	60	45	85	6	94
4	50	EtOH	60	45	58	6	70
5	50	THF	60	45	71	6	78
6	50	CH <sub>3</sub> CN	60	45	78	6	85
7	50 <sup>b</sup>	H <sub>2</sub> O	60	120	86	12	94

<sup>a</sup>Isolated yields; <sup>b</sup>MNP-caffeine-Cl

Table 2. MNPs-caffeine catalyzed Knoevenagel reaction promoted by ultrasonic irradiation<sup>a</sup><sup>a</sup>Isolated yields

SiO<sub>2</sub> were prepared according to the procedure described in the literature [26]. The reaction was monitored by thin-layer chromatography (TLC) on aluminum-backed silica gel 60 F254 plates (0.2mm thickness, Merck). Scanning electron microscopy (SEM) and energy dispersive X-ray (EDX) analyses were carried out using a Philips XL30 instrument for the elemental analysis of the nanoparticles. The magnetic properties were investigated with a

vibrating magnetometer (4 in., Daghigh Meghnatis Kashan Company, Kashan, Iran). The transmission electron microscopy (TEM) image was recorded using a Zeiss-EM10C at 80 kV. FT-IR spectra were acquired on a BOMEM MB-Series 1998 FT-IR spectrometer using KBr pellets. An ultrasonic bath of type SONOREX DIGIPLUS DL 102 H (Bandelin electronic, Berlin, Germany) at 35 kHz of frequency and 120 W of power was used. The thermal stability

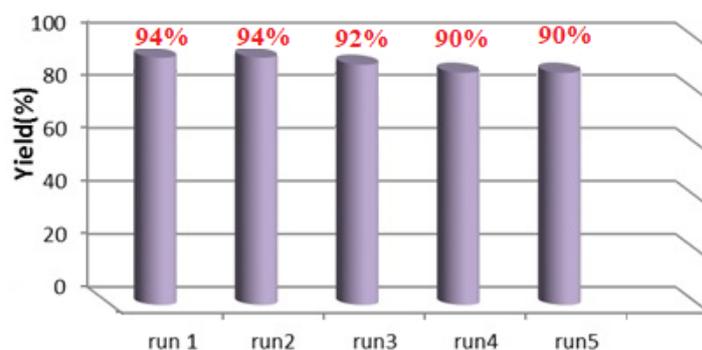


Fig. 6. Recyclability of MNPs-caffeine

of the MNPs- caffeine composite was assessed using a PerkinElmer Pyris diamond TGA/DTA by heating the sample from room temperature to 600 °C at a heating rate of 10 °C/min<sup>-1</sup> under nitrogen.

#### Preparation of [Fe<sub>3</sub>O<sub>4</sub>@SiO<sub>2</sub>-(CH<sub>2</sub>)<sub>3</sub>-caffeine]Cl

First of all, SiO<sub>2</sub>@Fe<sub>3</sub>O<sub>4</sub> (0.5 g) was dispersed in dry toluene (20 mL), sonicated for 15 min, and then (3-chloropropyl) triethoxysilane (1.5 mL, 6.25 mmol) was added. The whole mixture was stirred and refluxed for 48 h under nitrogen atmosphere. The solid materials were filtered off, washed with acetone and dried under reduced pressure. Then, a solution of caffeine (0.388 g, 2 mmol) in N,N-dimethylformamide (15 mL) was added drop wise to the suspension of Fe<sub>3</sub>O<sub>4</sub>@SiO<sub>2</sub>-(CH<sub>2</sub>)<sub>3</sub>Cl (1 g) and the reaction mixture was refluxed for 48 h. Finally, the modified nanoparticles [Fe<sub>3</sub>O<sub>4</sub>@SiO<sub>2</sub>-(CH<sub>2</sub>)<sub>3</sub>-caffeine]Cl were obtained after filtering, washing with acetone and drying.

#### Anion exchange in the immobilized chloride MNPs-caffeine

Immobilized chloride caffeine on MNPs and an excess amount of KOH were added into the deionized water and stirred for 24 h at room temperature. KCl which was prepared during the exchange of chloride anion with OH<sup>-</sup>, was removed by washing with deionized water. Immobilized hydroxide caffeine on Fe<sub>3</sub>O<sub>4</sub> nanoparticles was obtained as a brownish black powder.

#### Knoevenagel condensation catalysed by [Fe<sub>3</sub>O<sub>4</sub>@SiO<sub>2</sub>-(CH<sub>2</sub>)<sub>3</sub>-caffeine]OH

A mixture of aldehyde (1 mmol), malononitrile (1.2 mmol), organocatalyst (50 mg) and water (5 mL) was irradiated under sonication at 60 °C for appropriate time as shown in Table 2. After

completion of the reaction (monitored by TLC, eluent; *n*-hexane: EtOAc, 4:1), the catalyst was separated by a magnet and washed with hot ethanol. After evaporation of the solvent, the crude products were recrystallized from ethanol-water (10:1) to give pure products.

#### CONCLUSIONS

In this work, we have successfully prepared, characterized and applied a new organocatalyst (caffeine-SiO<sub>2</sub>@Fe<sub>3</sub>O<sub>4</sub>) in the Knoevenagel condensation of a variety of aldehydes with malononitrile under ultrasonic irradiation. The catalyst showed a good performance and can be easily retrieved from the reaction mixture by external magnet and reused without any significant loss in catalytic activity.

#### ACKNOWLEDGMENTS

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#### CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this manuscript.

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