



## Original Research Article

# Amine functionalized $\text{SiO}_2@Fe_3O_4$ as a green and reusable magnetic nanoparticles system for the synthesis of Knoevenagel condensation in water

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### KEYWORDS

2-(Aryl)methylenemalononitrile

Various aldehydes

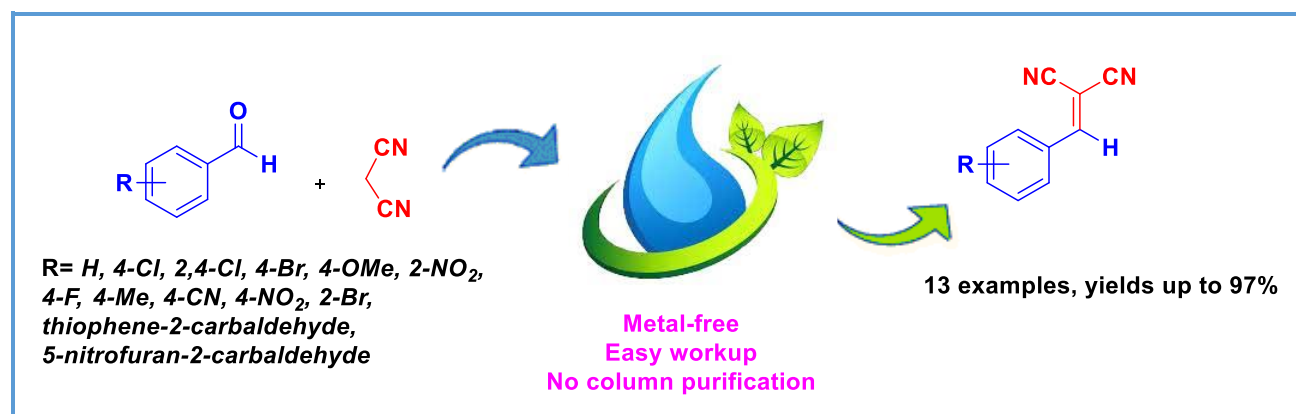
Green methodology

Knoevenagel condensation

### ABSTRACT

Amine functionalized  $\text{SiO}_2@Fe_3O_4$  as an efficient, green, and recyclable catalyst was synthesized using a simple approach. Then, the catalytic activity of the amine-functionalized  $\text{SiO}_2@Fe_3O_4$  was evaluated in the metal-free green synthesis of Knoevenagel condensation from the various aromatic aldehydes and malononitrile in water to give the corresponding 2-(aryl)methylenemalononitrile derivatives in excellent yields with a relatively low catalyst loading. Short reaction times, commercial availability of the starting materials, being environmentally friendly, reusability of catalyst, high yields, low cost, and easy work-up are the attractive features of the present work. The reusability of the catalyst was investigated for the product **3a**. After separation with an external magnet, the recycled catalyst can be reused in 7 consecutive runs. The yield of the product reduced from 97 to 91% over 7 times.

### Graphical Abstract



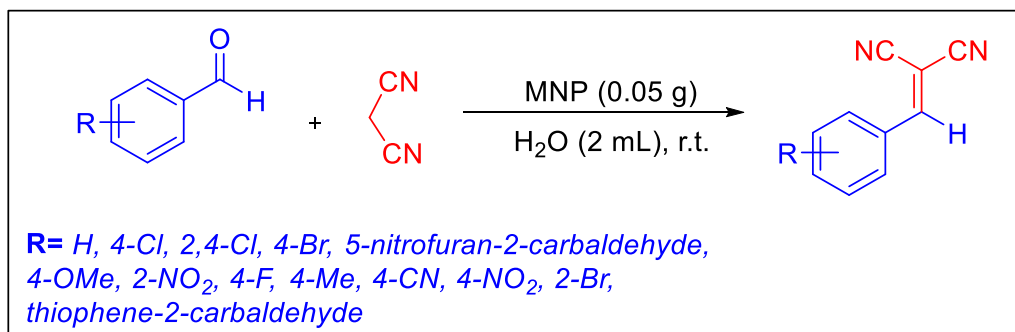
## Introduction

In recent years, much attention has been paid to developing environmentally friendly chemical synthesis using non-toxic reagents, solvents, and catalysts. Generally, ideal methods for synthesizing heterocyclic compounds were defined as one in which the target compound is generated via a one-pot reaction and in the quantitative yield. Moreover, starting materials are readily available and inexpensive in resource-effective and environmentally benign routes. In this context, one-pot synthesis played as an efficient, simple, and significant method for constructing nanoscale inorganic/organic hybrid functional materials [1–3].

Over the past decades, Fe<sub>3</sub>O<sub>4</sub> or  $\gamma$ -Fe<sub>2</sub>O<sub>3</sub> core-shell magnetic nanoparticles have received progressive attention by playing the role of catalyst in organic synthesis. This was due to their commercial availability, the high surface area, environmental stability, inexpensiveness, superparamagnetic properties, ease of handling, eco-friendly nature, high stability, low cost, convenience, and cost-effective synthesis. Also, they have been used in various areas such as environmental remediation [4], magneto thermal therapy [5, 6], MRI contrast agent [7], bioseparation [8], biomolecular sensing [9, 10], enzyme and protein separations [11], drug delivery [12, 13], and data storage [14].

Knoevenagel condensation is highly interesting as demonstrating various application in drugs (like pioglitazone, atorvastatin, and coartem) [15–16], total synthesis [17, 18], construction one-step of molecules (like (S)-(+)-3-aminomethyl 5-methylhexanoic acid) [19, 20]. Although a variety of procedures have been reported for the synthesis of Knoevenagel condensation such as L-Proline [21], NUC-2 [22], iron [23], MgAl-LDH/ZIF-8 [24], ethylenediammonium diacetate [25], magnesium oxide (MgO) [26], KGCN-RGO [27], hydroquinone and benzoquinone [28], Silica-l-proline [29], MOF [30], phosphane [31], Fe<sub>3</sub>O<sub>4</sub>@SiO<sub>2</sub>-3N [32], Nmm-based ionic liquids [33], Montmorillonite KSF [34], composite oxides [35, 36], Ce(III) and Lu(III) MOFs [37], papain [38], nickel MOF [39], organic compounds [40], lipase [41], and DABCO [42]. However, many of these procedures suffer from drawbacks such as toxic solvents, tedious steps for the catalyst preparation, expensive reagents and catalysts, long reaction times, harsh reaction conditions, and tedious work-up procedures. Therefore, the development of new methods and catalysts is still in demand.

Hence, we report herein amine-functionalized SiO<sub>2</sub>@Fe<sub>3</sub>O<sub>4</sub> as a green and reusable catalytic system for the efficient synthesis of Knoevenagel condensation (Scheme 1).



**Scheme 1.** Synthesis of Knoevenagel condensation

## Experimental

### Materials and methods

All the materials were purchased from Sigma-Aldrich, Merck (Germany), and Fluka (Switzerland) and were used without further purification. Melting points were determined with an electrothermal 9100 melting point apparatus. Fourier transform infrared (FT-IR) spectra were recorded on a Bruker Equinox 55 spectrometer using potassium bromide disks. All products were identified by comparing their physical and spectra data with those reported in the literature.

### Preparation of amine-functionalized $\text{SiO}_2@\text{Fe}_3\text{O}_4$

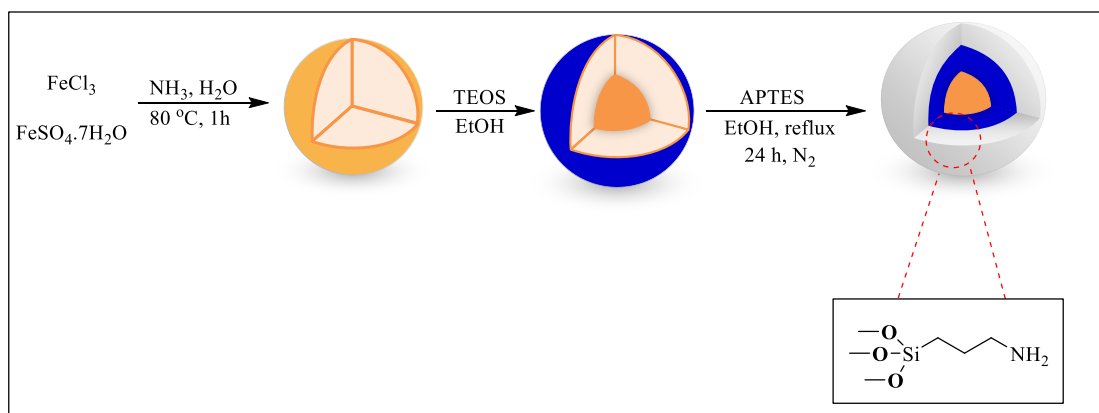
We synthesized the amine-functionalized  $\text{SiO}_2@\text{Fe}_3\text{O}_4$  according to a previous report [43] and characterized by various analyses such as FT-IR, TEM, SEM, XRD, and VSM.

### General procedure for the synthesis 2-(aryl)methylenemalononitrile derivatives

A mixture of various aldehyde (1 mmol) and malononitrile (1 mmol) in the presence of catalyst (0.05 g) in water (2 mL) was stirred at room temperature for the specified period. After completing the reaction (monitored by TLC), the catalyst was removed by magnetic separation and washed with  $\text{CH}_2\text{Cl}_2$  to remove the residual product and dried for reuse. The crude products were recrystallized from EtOH to obtain pure Knoevenagel derivatives.

## Results and Discussion

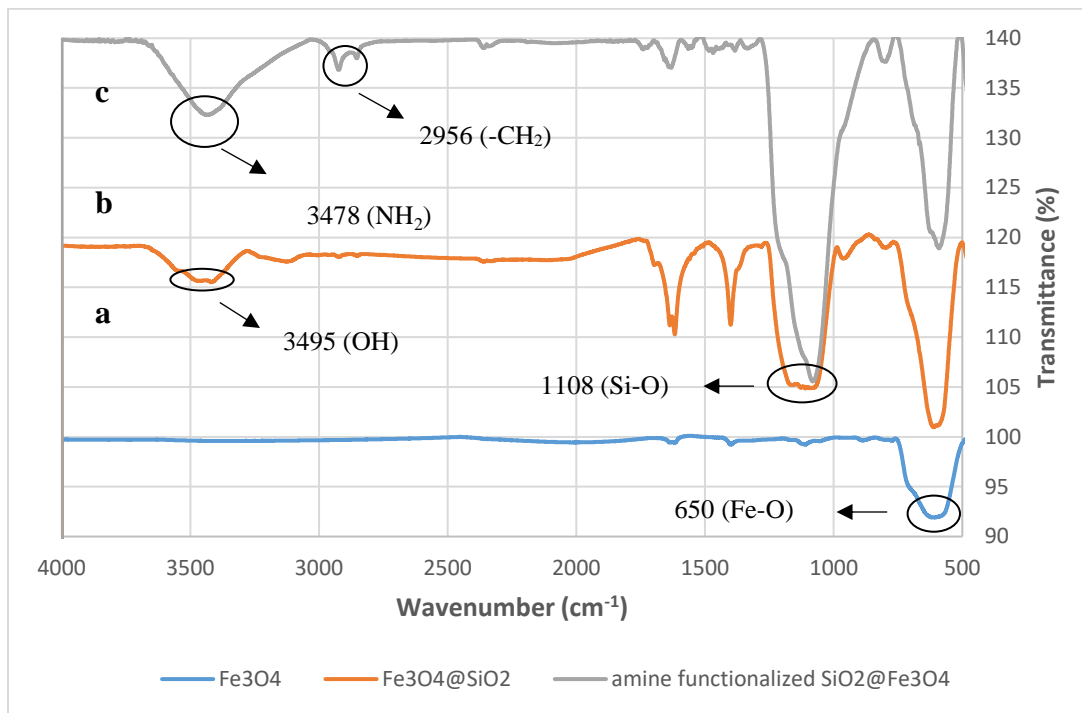
The amine-functionalized  $\text{SiO}_2@\text{Fe}_3\text{O}_4$  was synthesized by a simple approach. To prepare the catalyst,  $\text{Fe}_3\text{O}_4$  was first modified with  $\text{SiO}_2$  to afford the  $\text{SiO}_2@\text{Fe}_3\text{O}_4$ . Then, the treatment of  $\text{SiO}_2@\text{Fe}_3\text{O}_4$  prepared with APTES gives the corresponding superparamagnetic amine functionalized  $\text{SiO}_2@\text{Fe}_3\text{O}_4$  (Scheme 2) [43]. Then, the catalyst characterized by various analyses such as FT-IR, TEM, SEM, and XRD.



**Scheme 2.** Schematic for the synthesis of amine-functionalized  $\text{SiO}_2@\text{Fe}_3\text{O}_4$

The FT-IR spectra of amine-functionalized  $\text{SiO}_2@\text{Fe}_3\text{O}_4$  step by step were studied in the range  $500\text{--}4000\text{ cm}^{-1}$  (Figure 1a-c). As illustrated in Figure 1a, the absorption bands at  $650\text{ cm}^{-1}$  are related to the Fe-O vibrations. After coating  $\text{SiO}_2$  on the iron oxide, the

existence of Si-O of the  $\text{SiO}_2@\text{Fe}_3\text{O}_4$  group in structure was determined by a peak at  $1108\text{ cm}^{-1}$ . Finally, after the reaction between  $\text{SiO}_2@\text{Fe}_3\text{O}_4$  and APTES, new bands according to  $\text{NH}_2$  and  $-\text{CH}(\text{sp}^3)$  were observed at  $3478$  and  $2956\text{ cm}^{-1}$ , respectively (Figure 1c).



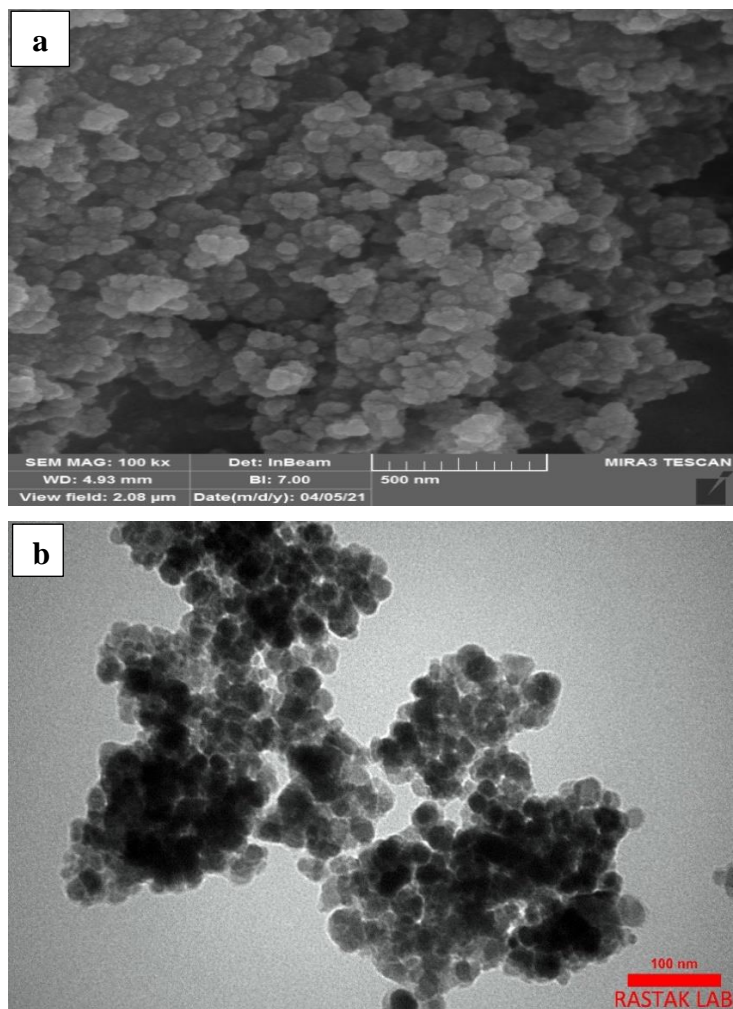
**Figure 1.** FT-IR spectra of a)  $\text{Fe}_3\text{O}_4$ , b)  $\text{SiO}_2@\text{Fe}_3\text{O}_4$ , and c) amine functionalized  $\text{SiO}_2@\text{Fe}_3\text{O}_4$

To the determination the particle size, morphology, and particle aggregation mode of the amine-functionalized  $\text{SiO}_2@\text{Fe}_3\text{O}_4$ , FESEM and TEM analyses were studied (Figures 2a,b). The average size of coated particles was less than 45 nm, and the sphere-like shape was changed due to the complex coating. In the TEM image, the nanometer-sized nature and the core-shell structure of the amine-functionalized  $\text{SiO}_2@\text{Fe}_3\text{O}_4$  were obvious.

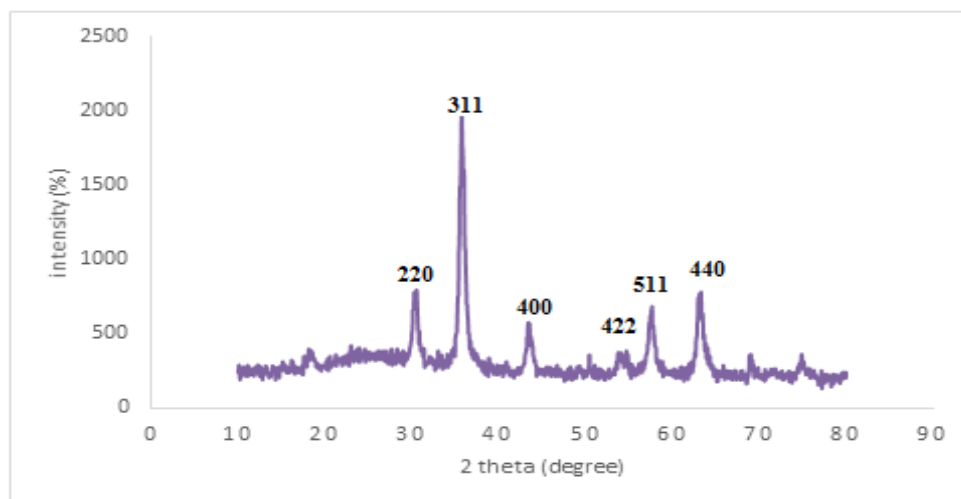
The X-ray diffraction (XRD) analysis was used to determine the crystalline and the size of amine-functionalized  $\text{SiO}_2@\text{Fe}_3\text{O}_4$  (Figure 3). The intense Bragg's peaks were observed at  $2\theta=30.6, 37.4, 44.5, 58.4, 63.2^\circ$ , which are the plates (220), (311), (400), (422), (511), and (440) respectively. These peaks are related to the crystal planes in the  $\text{Fe}_3\text{O}_4$  lattice and according to the standard XRD pattern of cubic  $\text{Fe}_3\text{O}_4$  (JCPDS 88-0866) [44].

The magnetic behavior of amine-functionalized  $\text{SiO}_2@\text{Fe}_3\text{O}_4$  was investigated using the VSM analysis (Figure 4). As can be seen, the specific saturation magnetizations of amine-functionalized  $\text{SiO}_2@\text{Fe}_3\text{O}_4$  is measured to be  $32 \text{ emu g}^{-1}$ .

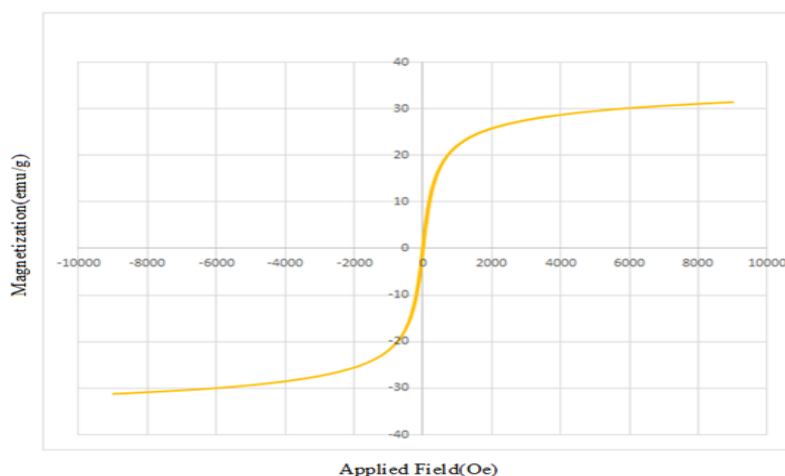
To explore the practicability of our investigation, a model reaction was performed between benzaldehyde (**1a**) and malononitrile (**2**) using various amounts of catalyst and various solvents at room temperature to gives the corresponding **3a**. The model reaction was evaluated using various amounts of catalyst (0.01, 0.03, 0.05, 0.07, and 0.1 g) at room temperatures and a various solvents such as  $\text{H}_2\text{O}$ , EtOH, MeOH,  $\text{CH}_2\text{Cl}_2$ , and THF. When the reaction was carried out without amine-functionalized  $\text{SiO}_2@\text{Fe}_3\text{O}_4$ , the product was obtained in a trace amount (Table 1, entry 1). Increasing the reaction yield in the presence of catalyst was obtained (Table 1, entry 2-6).



**Figure 2.** The a) SEM, and b) TEM analysis for the amine functionalized  $\text{SiO}_2@Fe_3O_4$



**Figure 3.** XRD analysis for the amine functionalized  $\text{SiO}_2@Fe_3O_4$



**Figure 4.** VSM analysis for the amine-functionalized SiO<sub>2</sub>@Fe<sub>3</sub>O<sub>4</sub>

When the catalyst was gradually increased to 0.05 g in water as green solvent, the reaction was completed in a short time, and the product yield was obtained to 96% (Table 1, entry 4). After optimized reaction conditions, using 0.05 g of catalyst in water at room temperature was the best condition for the reaction.

To study the generality and scope of the magnetic nanocatalyst, we extended our study

with various aromatic aldehydes with electron-withdrawing groups and electron-donating groups with malononitrile to give 2-(aryl)methylenemalononitrile derivatives **3a-m** in optimized conditions (Table 2). As shown in Table 2, all desired products were produced in good to excellent yields in short reaction times without formation of any by-products.

**Table 1.** Effect of different amounts of catalyst and solvent at room temperature<sup>a</sup>

Entry	Loading of catalyst (g)	conditions	Time (min)	Yield (%) <sup>b</sup>
1	-	-	90	Trace
2	0.01	Water	90	33
3	0.03	Water	60	65
4	0.05	Water	30	96
5	0.07	Water	30	92
6	0.1	Water	40	93
7	0.05	EtOH	35	92
8	0.05	CH <sub>2</sub> Cl <sub>2</sub>	60	71
9	0.05	THF	90	65
10	0.05	MeOH	60	55

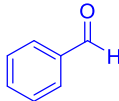
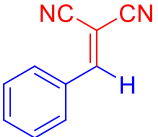
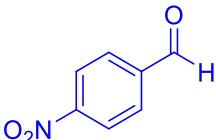
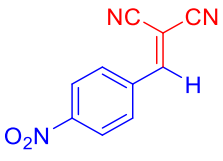
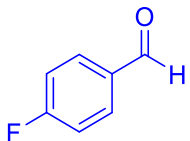
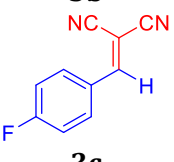
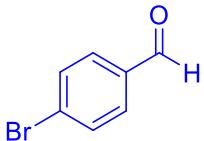
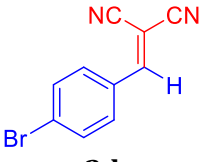
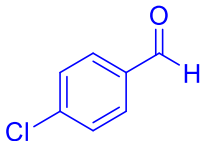
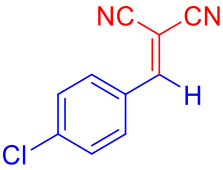
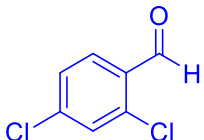
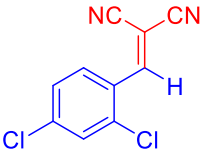
<sup>a</sup> Reaction conditions: benzaldehyde (1 mmol), malononitrile (1 mmol), catalyst, and solvent (2 mL)

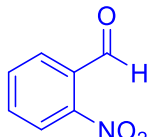
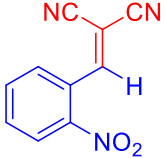
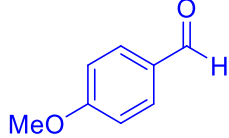
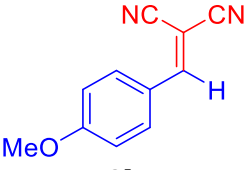
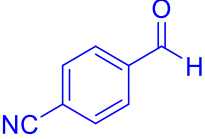
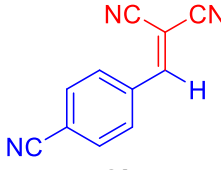
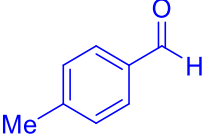
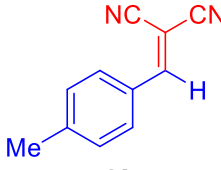
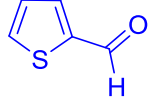
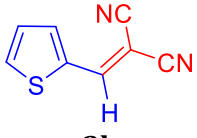
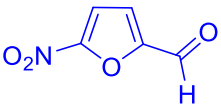
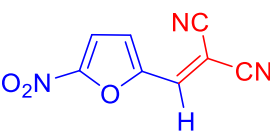
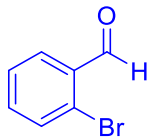
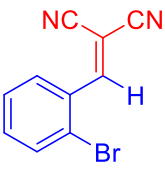
<sup>b</sup> Isolated yields

As expected, it is recyclable and could be reused without any significant activity loss. For this purpose, the reaction between 4-nitrobenzaldehyde (1 mmol) and malononitrile (1 mmol) in the presence of a catalyst (0.05 g) in water (2 mL) at room temperature has been investigated. Upon completion of the reaction, amine-functionalized  $\text{SiO}_2@Fe_3O_4$  can be easily separated and recovered with a permanent external magnet and then reused in the next

run. The results have revealed that the recovered catalyst does not significantly lose its activity after 7 times, and the nano catalyst's catalytic activity was nearly the same as that of the freshly used catalyst (Figure 5a). After 7 runs, the TEM and FT-IR analyses for the catalyst were investigated (Figures 5b,c). As shown in Figure 5b,c the functional groups, morphology, and size are the same with fresh catalyst.

**Table 2.** Synthesis of 2-(aryl)methylenemalononitrile derivatives<sup>a</sup>

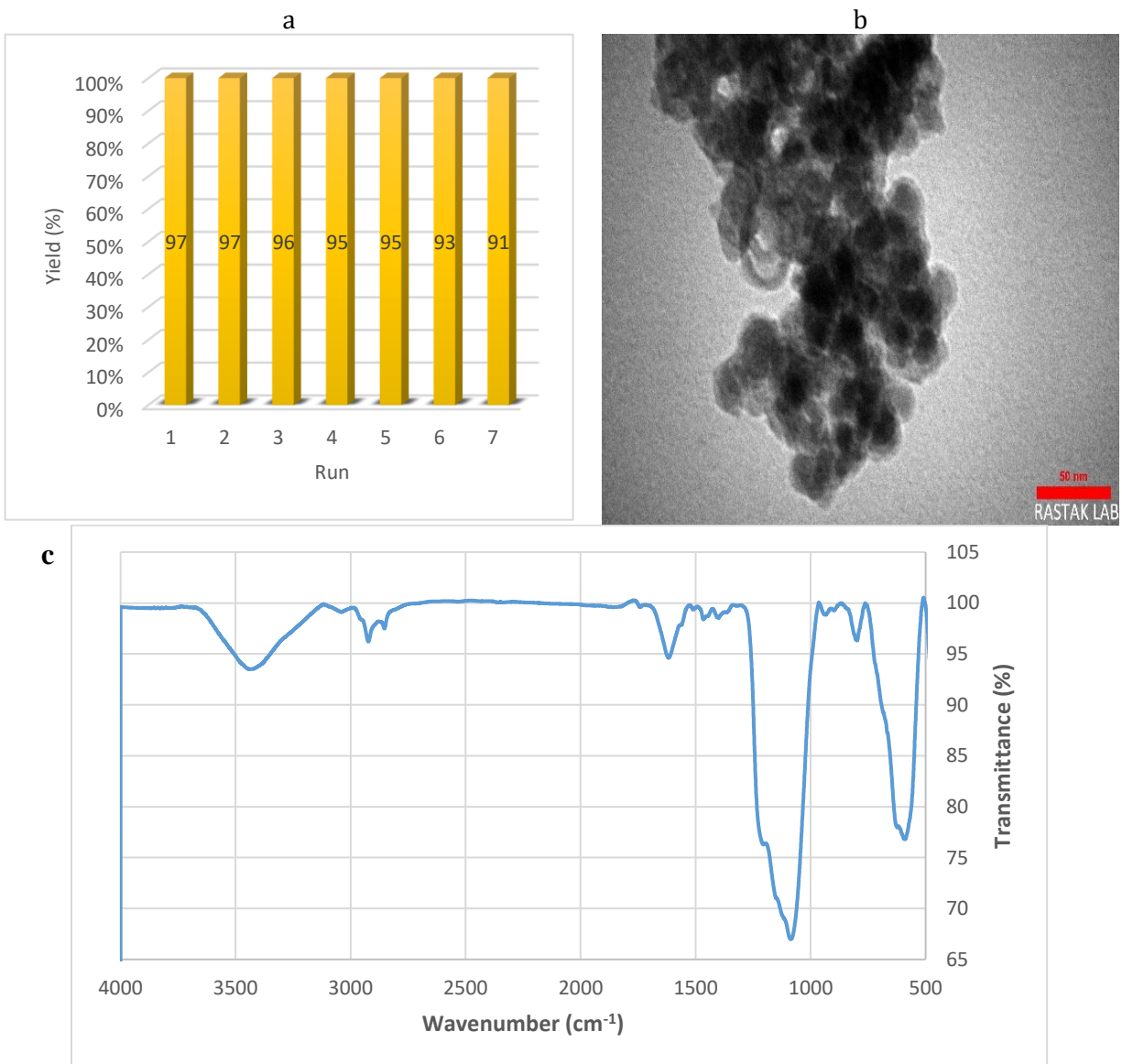
Entry	Aldehyde	Product	Time (min)	Yield (%) <sup>b</sup>	Found	m.p. (°C) Reported
1		 <b>3a</b>	30	96	80-82	81-82 [45]
2		 <b>3b</b>	10	97	158-160	159-160 [45]
3		 <b>3c</b>	15	92	130-132	129-130 [45]
4		 <b>3d</b>	20	90	160-162	159-161 [45]
5		 <b>3e</b>	20	88	162-164	161-162 [45]
6		 <b>3f</b>	15	90	148-150	150-152 [45]

7			10	94	139-141	140-142 [45]
		<b>3g</b>				
8			30	89	112-114	113-114 [45]
		<b>3h</b>				
9			10	95	155-157	156-157 [45]
		<b>3i</b>				
10			30	87	135-137	134-136 [45]
		<b>3j</b>				
11			15	90	98-100	97-99 [45]
		<b>3k</b>				
12			15	91	17-180	177-180 [45]
		<b>3l</b>				
13			25	88	92-93	90-92 [45]
		<b>3m</b>				

<sup>a</sup> Reaction conditions: various aldehyde (1 mmol), malononitrile (1 mmol), and catalyst (0.05 g) in water (2 mL) at room temperature

<sup>b</sup> Isolated yields





**Figure 5.** a) Reusability of amine-functionalized  $\text{SiO}_2@Fe_3O_4$ , b) TEM image, and c) FT-IR spectra after 7 recycling experiment

## Conclusions

In this work, we have reported an efficient and green catalytic system including amine-functionalized  $\text{SiO}_2@Fe_3O_4$  for the one-pot metal-free green synthesis of Knoevenagel condensation in high yields. The amine-functionalized  $\text{SiO}_2@Fe_3O_4$  was evaluated using FT-IR, SEM, TEM, XRD, and VSM analysis. The presented method is a safe, clean procedure and avoids using any toxic solvents. Other

advantages of this method are simplicity in process, ease of work-up, and simple product separation. Moreover, this catalytic system could be reused for seven consecutive runs without any significant catalytic activity loss.

## Acknowledgments

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