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ORIGINAL PAPER

One-pot synthesis of pyrano[3,2-*c*]quinoline-2,5-dione derivatives by Fe_3O_4@SiO_2-SO_3H as an efficient and reusable solid acid catalyst

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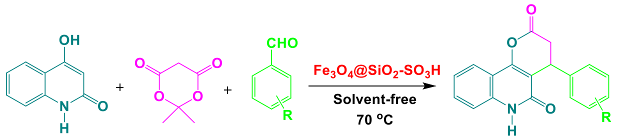
Abstract In this study, Fe_3O_4@SiO_2-SO_3H was prepared as an efficient and reusable solid acid catalyst and its catalytic activity was considered in the synthesis of pyrano[3,2-*c*]quinoline-2,5-dione derivatives by the three-component reaction of 4-hydroxyquinolin-2(1*H*)-one, Meldrum's acid and arylaldehydes under thermal solvent-free conditions at 70 °C. This catalytic system can be reused minimally for five times without any noticeable loss of activity. In addition, the characteristic analysis of Fe_3O_4@SiO_2-SO_3H, such as thermogravimetric analysis, Fourier-transform infrared spectroscopy, vibrating sample magnetometer, scanning electron microscope, and X-ray diffraction was performed.

Graphical abstract



Keywords Heterogeneous catalyst · Pyrano[3,2-*c*]quinoline-2,5-dione · Solvent-free conditions · Three component reaction

Introduction

Heterocyclic compounds have wide applications and their major contribution is clearly evident among various pharmaceutical compounds. Constructing various structures to achieve the desired functions is among the main reasons for the widespread use of heterocyclic compounds [1, 2]. Nitrogen-containing heterocyclic molecules due to massive presence in the nature with regard to the provision of appropriate biological activity are noteworthy and this has caused scientists to consider to this part of organic chemical science more [3–8].

4-Hydroxyquinolones are among quinolines, which are highly beneficial derivatives and develop activities such as analgesic, anti-inflammatory, and anti-allergy with respect to the existing substituents in the structure [9–11]. These compounds as herbicides and dyes have good performance and are used in the synthesis of heterocyclic compounds, for example, oxazinoquinolines, isoxazoloquinolines, and pyranoquinolines [12–14]. Pyranoquinoline is an example of heterocyclic compounds that studying their attributes due to the important biological properties and various medicinal applications is highly important. In addition to the above-mentioned activities for the quinolones derivatives, various biological activities such as antibacterial, antifungal and anti-platelet aggregation has been also reported on them [15–17]. Natural resources for the preparation of these compounds are limited and in most cases, should be handled as a difficult process for their isolation and purification of them [18, 19]. Therefore, in

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order to synthesize of compounds from this group, derivatives development and their medicinal properties have been considered [20–23].

Magnetic nanoparticles (MNPs) have been recently developed as an attractive candidate to support catalysts owing to their unique properties such as easy synthesis and functionalization, good stability, high surface area, and low toxicity [24]. The surface functionalization of magnetic particles has received considerable interest as a picturesque way to bridge the gap between heterogeneous and homogeneous catalysis. This type of heterogeneous catalysis can be easily extracted and recovered from the final product using an external magnet Thus, the development of silica-coated magnetite nanoparticles as an efficient, cheap and eco-friendly catalyst creates a new way to introduce an amazing efficient system to facilitate catalyst recovery in different organic reactions [25–28].

Owing to our interest in the synthesis of heterocyclic compounds and in the performance of reactions with the aid of catalyst [29–31], we reported our results in the efficient and rapid synthesis of pyrano[3,2-*c*]quinoline-2,5-dione derivatives using $Fe_3O_4@SiO_2\text{-}SO_3H$ as an efficient and reusable heterogeneous solid acid catalyst under solvent-free conditions (Scheme 1).

Results and discussion

The thermogravimetric analysis (TGA) of $Fe_3O_4@SiO_2\text{-}SO_3H$ indicates several regions corresponding to different weight lose ranges (Fig. 1). The first weight loss below 150 °C can be due to the loss of adsorbed solvent or trapped water from the catalyst. The second weight loss between 150 and 500 °C can be attributed to the loss of SO_3H groups. The occurrence of further weight losses at the temperature higher than 600 °C was likely a consequence of the decomposition of silica shell [32]. These results demonstrate that the catalyst is stable up to approximately 250 °C, supporting that it could be safely applied in organic reactions at the temperatures range 70–150 °C.

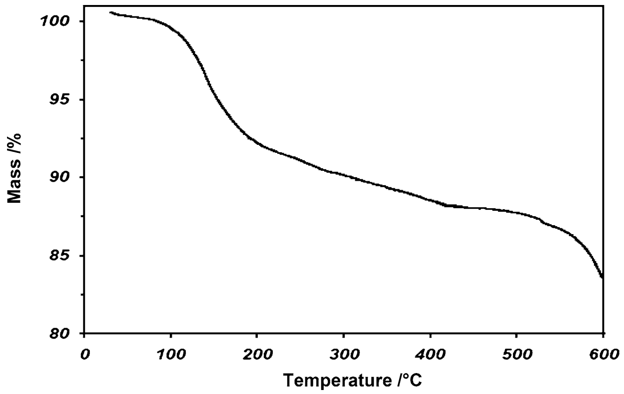


Fig. 1 TGA curve of $Fe_3O_4@SiO_2\text{-}SO_3H$

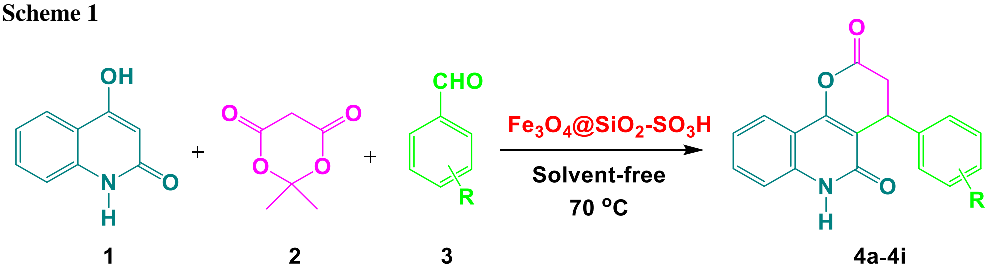
Figure 2 demonstrates the FT-IR spectra of $Fe_3O_4@SiO_2\text{-}SO_3H$ nanoparticles. The FT-IR analysis of the $Fe_3O_4@SiO_2\text{-}SO_3H$ presents the basic characteristic peaks at 578, 1091, 795, and 463 cm^{-1}, which were attributed to the presence of Fe–O vibration, Si–O–Si asymmetric stretching vibration, Si–O–Si symmetric stretching vibration, and Si–O–Si bending vibration, respectively. In addition, the presence of O–H stretching vibration near 3381 cm^{-1} and O–H deformed the vibration near 1637 cm^{-1} were confirmed for $Fe_3O_4@SiO_2\text{-}SO_3H$.

The magnetic feature of the catalyst was investigated by vibrating-sample magnetometer (VSM). The magnetization diagram for the bare Fe_3O_4, $Fe_3O_4@SiO_2$, and $Fe_3O_4@SiO_2\text{-}SO_3H$ nanoparticles are shown in Fig. 3. The saturation magnetization value of $Fe_3O_4@SiO_2$ and $Fe_3O_4@SiO_2\text{-}SO_3H$ nanoparticles appeared to be 38.67 and 16.57 emu/g, respectively, which are much lower than the bare Fe_3O_4 MNPs (61.22 emu/g) [33].

The X-ray diffraction (XRD) patterns of the bare Fe_3O_4 and $Fe_3O_4@SiO_2\text{-}SO_3H$ (Fig. 4), present broad peaks 2θ from 22° to 28°, which is typical for amorphous silica [33]. Some explicit peaks at 2θ values of 30.29, 35.73, 42.84, 53.65, 57.9, and 62.74° are dedicated to the (220), (311), (400), (422), (511), and (440) planes of Fe_3O_4 [34, 35].

Figure 5 shows the scanning electron microscope (SEM) images of $Fe_3O_4@SiO_2$ and $Fe_3O_4@SiO_2\text{-}SO_3H$

Scheme 1



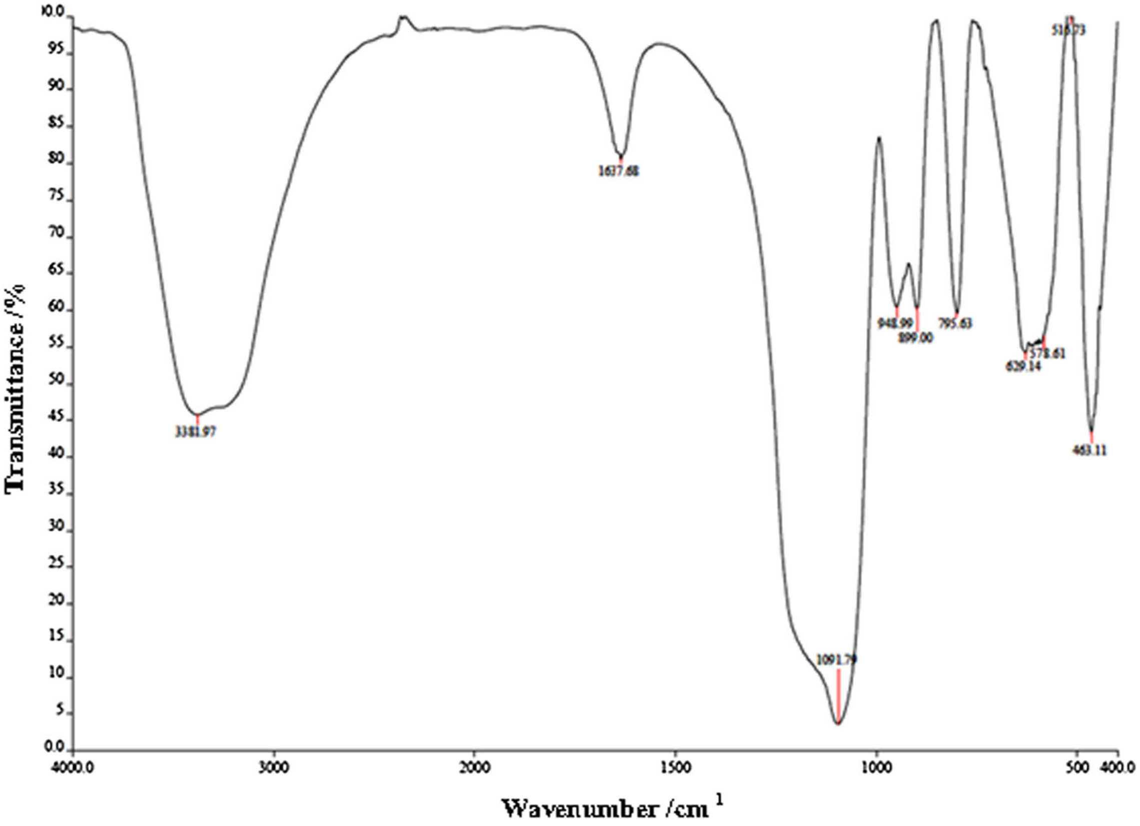


Fig. 2 FT-IR spectra of $Fe_3O_4@$ SiO_2-SO_3H

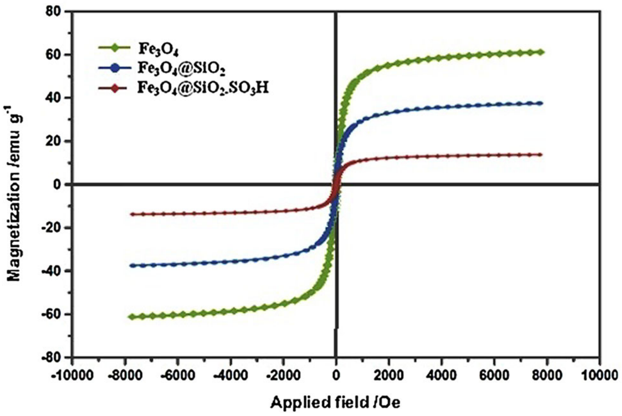


Fig. 3 VSM magnetization curves of the bare Fe_3O_4, $Fe_3O_4@SiO_2$, and $Fe_3O_4@$ SiO_2-SO_3H nanoparticles

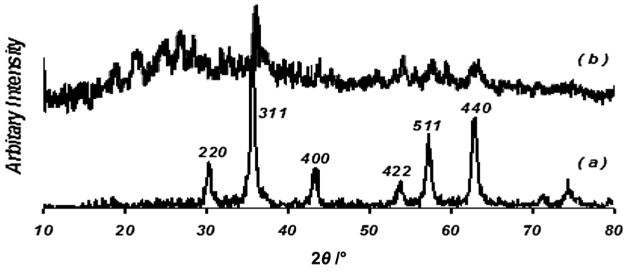
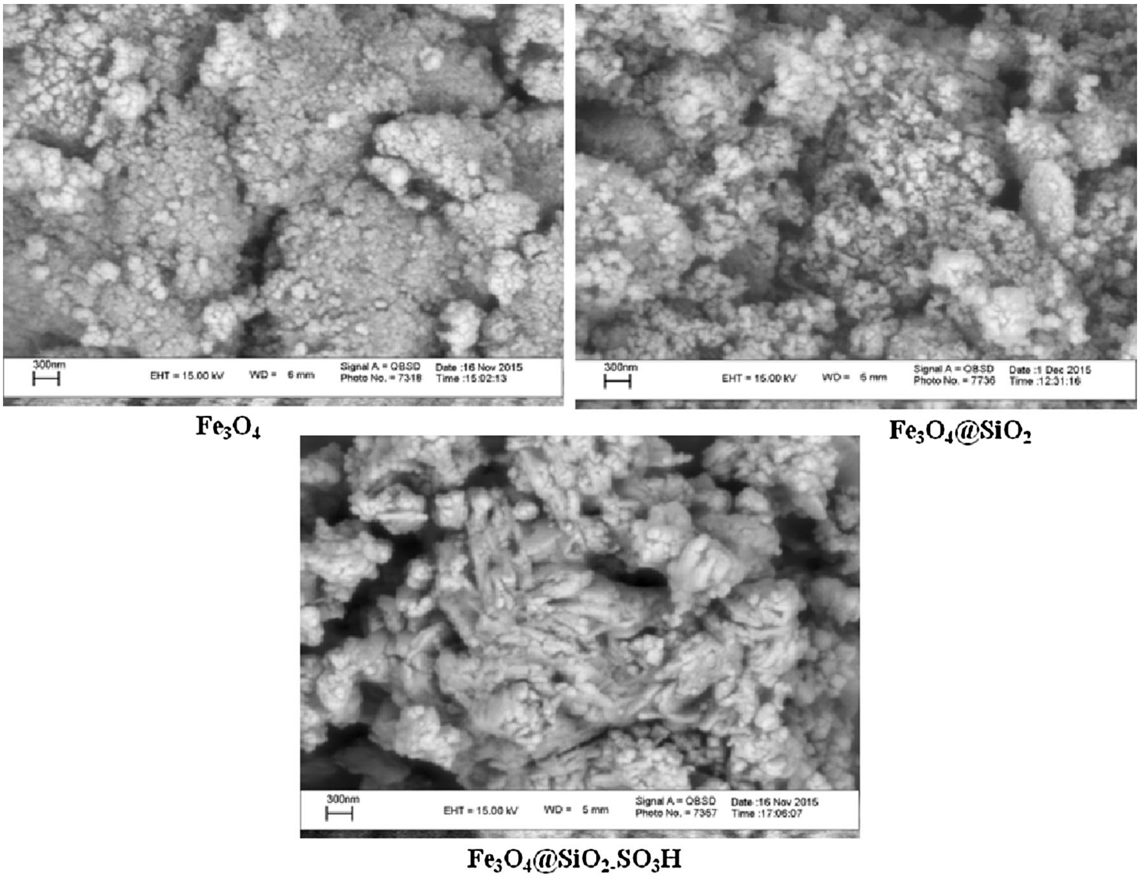


Fig. 4 XRD patterns of *a* Fe_3O_4 and *b* $Fe_3O_4@$ SiO_2-SO_3H

nanoparticles. According to Fig. 5, $Fe_3O_4@$ SiO_2-SO_3H has a spherical shape with nano dimension ranging from 100 to 140 nm in size.

Screening of reaction conditions

Initially, we investigated the one-pot condensation of 4-hydroxyquinolin-2(1*H*)-one (**1**), Meldrum's acid (**2**), and 4-chlorobenzaldehyde (**3g**) in the presence of $Fe_3O_4@$-SiO_2-SO_3H as a model reaction. The effect of temperature, amounts of catalyst, and reaction time were surveyed and optimized to develop the optimum conditions for this model reaction. For this purpose, a condensation between 4-hydroxyquinolin-2(1*H*)-one (1 mmol), Meldrum's acid (1 mmol), and 4-chlorobenzaldehyde (1 mmol) were inquired (Table 1). To obtain the optimal reaction solvent, different solvents such as H_2O, CH_2Cl_2, CH_3CN, DMF, toluene, and EtOH in the presence of a certain amount of catalyst were applied. Among these solvents, EtOH produced the highest yield of product (Table 1, entry 6), but the most favorable conditions in terms of rate and yield when obtained that no solvent was used for the reaction



Fe_3O_4

$Fe_3O_4@SiO_2$

$Fe_3O_4@SiO_2$-SO_3H

Fig. 5 SEM images of Fe_3O_4, $Fe_3O_4@SiO_2$, and $Fe_3O_4@$ SiO_2-SO_3H

Table 1 Effect of the solvent, temperature, reaction time, and amount of the catalyst in the synthesis of pyrano[3,2-*c*]quinoline-2,5-dione

Entry	Solvent	Cat/mol%	Temp/°C	Time/min	Yield/%
1	CH_2Cl_2	10	70	80	51
2	CH_3CN	10	80	80	58
3	Toluene	10	70	80	57
4	DMF	10	110	80	61
5	H_2O	10	100	80	68
6	EtOH	10	80	80	72
7	Solvent-free	–	70	80	Trace
8	Solvent-free	10	60	20	83
9	Solvent-free	10	70	20	92
10	Solvent-free	10	90	20	86
11	Solvent-free	5	70	60	53
12	Solvent-free	10	25	80	22
13	Solvent-free	15	70	20	86

[a] 4-Hydroxyquinolin-2(1*H*)-one (1 mmol), Meldrum's acid (1 mmol), and 4-chlorobenzaldehyde (1 mmol)

(Table 1, entry 9). To explore the optimal amount of catalyst, the reactions were carried out at different amount of $Fe_3O_4@SiO_2$-SO_3H ranging from 5 to 15 mol%. It was found that when the concentration of the catalyst was 10 mol%, we obtained an excellent yield of product in a short time. Increasing the amount of catalyst beyond this led to no substantial improvement in the yield (Table 1, entry 13), whereas the lower amount of catalyst leads to reducing the efficiency of the reaction (Table 1, entry 11). In the absence of the catalyst, the yields of the product fell sharply and negligible stain was observed on TLC (Table 1, entry 7). To evaluate the optimum condition, we also performed several experiments at variable temperatures. At room temperature, the reaction rate is extremely and the yield is considered low (Table 1, entry 12). The yield of the product increased up to 70 °C (Table 1, entries 8 and 9). After 70 °C, increasing the reaction temperature did not show any sign of the enhancement (Table 1, entry 10).

The condensation of 4-hydroxyquinolin-2(1*H*)-one, Meldrum's acid, and aryl aldehydes (carrying both electron-donating and electron-withdrawing groups), in the presence of $Fe_3O_4@SiO_2$-SO_3H 10 mol% as a solid acid catalyst under solvent-free conditions using conventional heating at 70 °C, prepared desired pyrano[3,2-*c*]quinoline-2,5-diones in high purity with good to high yields. The reactions required 20–38 min with conventional heating at 70 °C (Table 2, compounds **4a**–**i**). The nature of the functional group on the aryl ring of the aldehyde demonstrated a slightly different on the reaction time and the yield of pyrano[3,2-*c*]quinoline-2,5-dione. More precise analysis shows that aryl aldehydes with electron donating substituents (Table 2, compounds **4b**–**d**) react slower than aryl aldehydes with electron-withdrawing and halogen substituents (Table 2, compounds **4e**–**i**). These results clearly indicate that the reactions can tolerate a wide range of differently substituted aldehydes.

A reasonable pathway of the reaction of 4-hydroxyquinolin-2(1*H*)-one, Meldrum's acid, and benzaldehyde conducted in the presence of $Fe_3O_4@SiO_2$-SO_3H is presented in Scheme 2. The pyrano[3,2-*c*]quinoline-2,5-dione synthesis probably begins with Knoevenagel condensation of Meldrum's acid (**2**) and aldehyde **3** via the nucleophilic addition of Meldrum's acid on the aldehyde activated by the hydrogen groups of sulfonic acid. The resulting adduct **5** undergoes dehydration to give the intermediate **6**. Double bond in the formed intermediate is highly active due to the presence of presented oxygen groups in the structure of Meldrum's acid and converts it to a strong electrophile. In the next step, 4-hydroxyquinoline **1** attack to the electrophilic intermediate via the Michael-type addition and converts to the transition state **7** that via tautomerization process produced intermediate **8**. The resultant intermediate due to instability produces the final product **4** during a cyclic process which is accompanied by the release of a molecule of acetone and carbon dioxide (Scheme 2).

Table 2 $Fe_3O_4@SiO_2$-SO_3H catalyzed synthesis of pyrano[3,2-*c*]quinoline-2,5-dione derivatives (Scheme 1)

Product	R	Time/min	Yield/%[a]	M.p./°C	References
4a	H	32	91	>300	[29]
4b	4-CH_3	35	89	>300	[29]
4c	4-OCH_3	38	85	>300	[29]
4d	4-OH	30	87	>300	[30]
4e	4-NO_2	25	91	>300	[30]
4f	4-F	27	90	>300	[29]
4g	4-Cl	20	92	>300	[29]
4h	2,4-Cl_2	22	94	>300	[29]
4i	3-Br	28	87	>300	[29]

[a] Yield refers to isolated product

In order to evaluate the performance of the recycled solid acid catalyst, it was reused after five periods of recovery for the preparation of the compound (Table 2, entry **4g**). Negligible change in the reaction efficiency is indicative of recycling solid acid catalyst performance and expressing the cost-effectiveness of this method (Fig. 6).

Furthermore, a comparative evaluation of the catalytic efficacy of $Fe_3O_4@SiO_2$-SO_3H was compared with some of the obtained results in this study with those methodologies which have been reported using other earlier homogeneous catalysts for the synthesis of pyrano[3,2-*c*]quinoline-2,5-dione (Table 3). The present methodology has several merits such as: solvent-free condition, high reaction rates, effective recovery, use of an inexpensive catalyst, and less time consuming for the synthesis of pyrano[3,2-*c*]quinoline-2,5-dione **4b**.

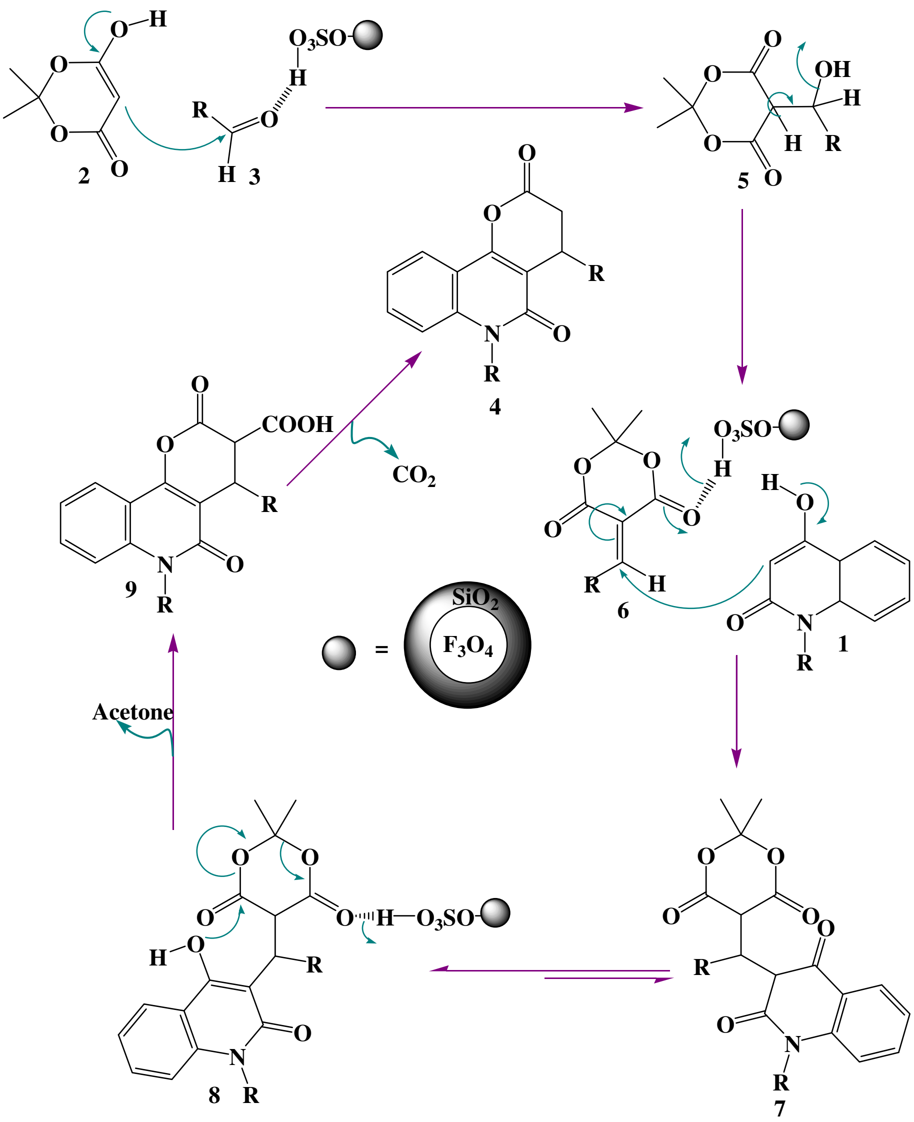
Conclusion

In summary, a simple, efficient, and green procedure for the one-pot preparation of pyrano[3,2-*c*]quinoline-2,5-dione derivatives in the presence of eco-friendly and reusable solid acid catalyst ($Fe_3O_4@SiO_2$-SO_3H) was described. The use of green catalyst, lower loading of catalyst, lack of organic solvent, easy work-up, and good-to-excellent yields are the advantages of the procedure.

Experimental

All the pure chemicals were purchased from Merck and Fluka Chemical Companies and used in the reaction. The separation and purification of the products were performed with extraction and recrystallization techniques. Melting points were measured with an electrothermal-9100 apparatus. ^1H and ^{13}C NMR spectra were recorded on Bruker DRX-400 Avance spectrometer at 400.22 and 100.63 MHz, respectively. Mass spectra were determined

Scheme 2



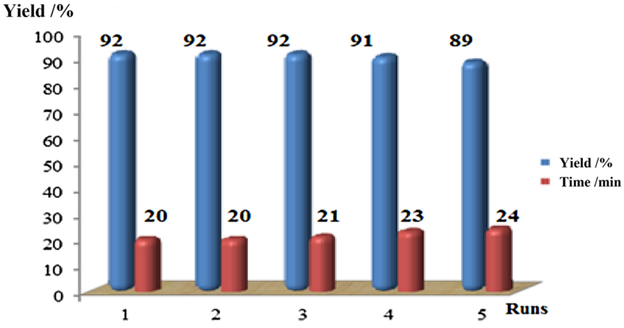


Fig. 6 Recycling of Fe_3O_4@SiO_2-SO_3H as a catalyst under solvent-free conditions

on a Shimadzu QP1100EX mass spectrometer operating at an ionization potential of 70 eV. Thermogravimetric analyses (TGA) were conducted using a TGA thermoanalyzer (PerkinElmer) instrument. Samples were heated from 25 to 800 °C at ramp 10 °C min^{-1} under N_2 atmosphere. FT-IR spectra were recorded on a Bruker Alfa FTIR spectrometer. XRD was performed on a Philips X-Pert diffractometer using CO tube. SEM was achieved on a PHILIPS XL30 electron microscope. The magnetic properties of catalyst were accomplished using vibrating sample magnetometer/Alternating Gradient Force Magnetometer (VSM/AGFM, MDK Co, Ltd, Iran).

Table 3 Comparison of the present method with other reported strategies for the synthesis of compound **4b**

Entry	Conditions	Catalyst loading	Time/min	Yield/%	References
1	[Bmim]HSO_4/rt	0.5 cm^3	80	85	[29]
2	L-Proline/EtOH/80 °C	50 mol%	150	78	[29]
3	[Hmim]HSO_4/ultrasonic	1 cm^3	60	87	[30]
4	Fe_3O_4@SiO_2-SO_3H/70 °C	10 mol%	35	89	This work

General procedure for the synthesis of Fe_3O_4 nanoparticles (Fe_3O_4)

Fe_3O_4 MNPs were synthesized using simple chemical co-precipitation described in the literature [36]. Typically, 2.7 g of $FeCl_3·6H_2O$ and 1 g of $FeCl_2·4H_2O$ were dissolved in 100 cm^3 of 1.2 mmol aqueous HCl (1:1) by ultrasonic bath for 30 min. Thereafter, under rapid mechanical stirring, 150 cm^3 of NaOH (1.25 mol dm^{-3}) was added under vigorous stirring and a black precipitate was immediately formed. The resulting transparent solution was heated at the 80 °C with rapid mechanical stirring and ultrasound treatment under continuous N_2 atmosphere bubbling. After vigorous stirring for 2 h, the resulting black MNPs were magnetically separated and washed three times with deionized water and then, the dried under vacuum at 60 °C for 12 h.

General procedure for the synthesis of silica functionalized Fe_3O_4 nanoparticles (Fe_3O_4@SiO_2)

The synthesized Fe_3O_4 nanoparticles (1 g) were initially diluted with 20 cm^3 water, 60 cm^3 ethanol, and 2 cm^3 concentrated aqueous ammonia (25 wt%). The suspension was homogenized under ultrasonification for 25 min. Then, under continuous mechanical stirring, a solution of 0.5 cm^3 TEOS in 10 cm^3 ethanol was slowly added to this dispersion for 16 h. In the final step, the coated particles were finally separated from the liquid by a magnetic decantation and washed three times with ethanol. Then, the dried under vacuum at 70 °C for 5 h [37].

General procedure for the synthesis of sulfuric acid functionalized Fe_3O_4 nanoparticles (Fe_3O_4@SiO_2-SO_3H)

Fe_3O_4@SiO_2-SO_3H microspheres were prepared as follows; initially, a 500 cm^3 suction flask was charged with 1 g Fe_3O_4@SiO_2 MNPs and dispersed in 10 cm^3 dry CH_2Cl_2 by ultrasonic bath for 30 min. Subsequently, 1 cm^3 chlorosulfonic acid (in dry CH_2Cl_2) was added drop-wise to a cooled (ice-bath) solution over a 30 min at room temperature. After the addition was completed, the mixture was stirred for a further 6-h period until HCl gas evolved from the reaction vessel. The resulted brown solid MNPs were collected using an external magnet and washed with ethanol and water before being dried in an oven at 70 °C.

General procedure for the preparation of 4-chlorophenyl-3,4-dihydro-6H-pyrano[3,2-c]quinoline-2,5-diones (**4g**)

To the mixture of 0.161 g 4-hydroxyquinoline (1 mmol), 0.144 g Meldrum's acid (1 mmol), and 0.119 g 4-chlorobenzaldehyde (1 mmol) in a vial containing a magnetic stirring bar was added Fe_3O_4@SiO_2-SO_3H (10 mg) as a catalyst and stirred at 70 °C under solvent-free conditions. After the completion of the reaction, the mixture was washed with water (2 × 15 cm^3) and then recrystallized from EtOAc/*n*-hexane (1:3) to afford the pure product (92 %).

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