Short communication

Design, Preparation and Characterization of MoO_3H-functionalized Fe_3O_4@SiO_2 Magnetic Nanocatalyst and Application for the One-pot Multicomponent Reactions

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Abstract

Molybdic acid-functionalized silica-based Fe_3O_4 nanoparticles (Fe_3O_4@SiO_2-MoO_3H) are found to be a powerful and magnetically recyclable nanocatalyst. The morphology and structure of this nanocatalyst were investigated by Fourier transform infrared spectroscopy (FT-IR), energy dispersive X-ray spectroscopy (EDX), transmission electron microscopy (TEM), field emission scanning electron microscopy (FE-SEM), thermo gravimetric analyses (TGA), X-ray diffraction (XRD) and vibrating sample magnetometer (VSM) techniques. The high catalytic activity of this catalyst was investigated in the synthesis of pyrano[2,3-*c*]chromenes, representing potent biologically active compounds. The catalyst can be readily separated by applying an external magnet device and recycled up to 8 times without significant decrease in its catalytic activity, which makes it highly beneficial to address the industrial needs and environmental concerns. Fe_3O_4@SiO_2-MoO_3H has many advantages, such as low cost, low toxicity, ease of preparation, good stability, high reusability and operational simplicity.

Keywords: Fe_3O_4@SiO_2-MoO_3H, Magnetically recyclable nanocatalyst, Pyrano[2,3-*c*]chromenes, Biological activity

1. Introduction

Nowadays, the design and synthesis of efficient, reusable, easily separable, low toxicity, low cost, and insoluble acidic nanocatalysts have become an important area of research in chemistry.[1] The use of nanoparticles as heterogeneous catalysts has attracted considerable attention because of the interesting structural features and high levels of catalytic activity associated with these materials.[2]

Magnetic nanoparticles (MNP) are widely applied in various fields, such as magnetic resonance imaging (MRI) contrast agents, biomedical science, bioseparation and hyperthermia.[3–6] Transition metal nanoparticles are used as efficient catalysts for various synthetic organic transformations due to their high surface area-to-volume ratio and coordination sites which are mainly responsible for their catalytic activity.[7] Because the Fe_3O_4 nanoparticles will aggregate quickly into large bunches and therefore lose their unique properties, various surface modification methods have been developed to modify the surface of naked Fe_3O_4 nanoparticles to improve the dispersibility, stability, biocompatibility and biodegradability for specific purposes. The resulting modified Fe_3O_4 nanoparticles have been extensively used for various applications.[8] Among them, the silica coating is a very good surface modifier,

because of its excellent stability, biocompatibility, nontoxicity and ease of furthered conjugation with various functional groups, thus enabling the coupling and labeling of biotargets with high selectivity and specificity.[9–11]

Development of MCRs can lead to new efficient synthetic methodologies to afford many small organic compounds in the field of modern organic, bioorganic, and medicinal chemistry.[10] Hence, MCRs are considered as a pivotal theme in the synthesis of many important heterocyclic compounds, such as pyranocoumarin derivatives nowadays.[12]

In continuation of our research on the introduction of recoverable catalysts in organic synthesis,[13–16] recently, we disclosed that Fe_3O_4@SiO_2-MoO_3H can be used as a novel magnetic nanocatalyst for the synthesis of 1,8-dioxodecahydroacridine derivatives.[17] In this work, we demonstrate high catalytic activity of this new catalyst in the synthesis of pyrano[2,3-*c*]chromenes as potent biologically active compounds.

It is also interesting to note that the catalyst can be recovered and reused several times**.**

2. Experimental

2. 1. General

The chemicals were purchased from Merck and Aldrich chemical companies. The reactions were monitored by TLC (silica gel 60 F 254, hexane : EtOAc). Fourier transform infrared (FT-IR) spectroscopy spectra were recorded on a Shimadzu-470 spectrometer, using KBr pellets and the melting points were determined on a KRUSS model instrument. ^{1}H NMR spectra were recorded on a Bruker Avance II 400 NMR spectrometer at 400 MHz, with DMSO-d_6 used as the solvent and TMS as the internal standard. X-Ray diffraction (XRD) pattern was obtained by Philips X Pert Pro X diffractometer operated with a Ni filtered Cu Kα radiation source. Transmission electron microscopy (TEM) images of the electrocatalyst were recorded using a Philips CM-10 TEM microscope operated at 100 kV. Field emission scanning electron microscopy (SEM) and X-ray energy dispersive spectroscopy (EDS) analyses were carried out on a Philips XL30, operated at a 20 kV accelerating voltage. Thermogravimetric analyses (TGA) were conducted on a Rheometric Scientific Inc. 1998 thermal analysis apparatus under a N_2 atmosphere at a heating rate of 10 °C/min. The magnetic measurement was carried out in a vibrating sample magnetometer (Model 7407 VSM system, Lake Shore Cryotronic, Inc., Westerville, OH, USA) at room temperature.

2. 2. General Procedure for the Preparation of nano-Fe_3O_4 (1)

$FeCl_3 \cdot 6H_2O$ (20 mmol) and $FeCl_2 \cdot 4H_2O$ (10 mmol) were dissolved in distilled water (100 mL) in a three-necked round-bottom flask (250 mL). The resulting transparent solution was heated at 90 °C with rapid mechanical stirring under N_2 atmosphere for 1 h. A solution of concentrated aqueous ammonia (10 mL, 25 wt%) was then added to the solution in a drop-wise manner over a 30 min period using a dropping funnel. The reaction mixture was then cooled to room temperature and the resulting magnetic particles collected with a magnet and rinsed thoroughly with distilled water.

2. 3. General Procedure for the Preparation of nano-Fe_3O_4@SiO_2 (2)

Nano-Fe_3O_4@SiO_2 (**2**) was synthesized according to a previously published literature method. Magnetic nano particles (1.0 g) were initially diluted via the sequential addition of water (20 mL), ethanol (60 mL) and concentrated aqueous ammonia (1.5 mL, 28 wt%). The resulting dispersion was then homogenized by ultrasonic vibration in a water bath. A solution of TEOS (0.45 mL) in ethanol (10 mL) was then added to the dispersion in a drop-wise manner under continuous mechanical stirring. Following a 12 h period of stirring, the resulting product was collected by magnetic separation and washed three times with ethanol.

2. 4. General Procedure for the Preparation of nano-Fe_3O_4@SiO_2-$OMoO_3H$ (3)

To an oven-dried (125 °C, vacuum) sample of nano-Fe_3O_4@SiO_2 60 (2 g) in a round bottomed flask (50 mL) equipped with a condenser and a drying tube, thionyl chloride (8 mL) was added and the mixture in the presence of $CaCl_2$ as a drying agent was refluxed for 48 h. The resulting dark powder was filtered and stored in a tightly capped bottle. To a mixture of Fe_3O_4@SiO_2-Cl (1 g) and sodium molybdate (0.84 g) *n*-hexane (5 mL) was added. The reaction mixture was stirred under refluxing conditions (70 °C) for 4 h. After completion of the reaction, the reaction mixture was filtered and washed with distilled water, and dried and then stirred in the presence of 0.1 N HCl (20 mL) for an hour. Finally, the mixture was filtered, washed with distilled water, and dried to afford nano-Fe_3O_4@SiO_2-$OMoO_3H$.

2. 5. General Procedure for the Preparation of Pyrano[2,3-*c*]coumarin Derivatives 7

Malononitrile **4** (1.1 mmol), aromatic aldehyde **5** (1 mmol), 4-hydroxycoumarin **6** (1 mmol), and nano-Fe_3O_4@SiO_2-$OMoO_3H$ (0.02 g) were added to a 10 mL mixture EtOH/H_2O (50/50) in a 25-mL pyrex flask and refluxed for an appropriate time (Table 3). The reaction progress was controlled by thin layer chromatography (TLC) using hexane/EtOAc (1:1). After completion of the reaction, the solvent was removed under vacuum, the cru-

de products **7** were obtained after recrystalization from EtOH.

3. Results and Discussion

3. 1. Characterization of Fe_3O_4@SiO_2-$OMoO_3H$

As can be seen in Scheme 1, from the reaction Fe_3O_4@SiO_2 nanoparticles **2** with thionyl chloride, the Fe_3O_4@SiO_2-Cl has been prepared. The Fe_3O_4@SiO_2-$OMoO_3H$ **3** was prepared from nucleophilic substitution of Fe_3O_4@SiO_2-Cl with anhydrous sodium molybdate in *n*-hexane (Scheme 1).

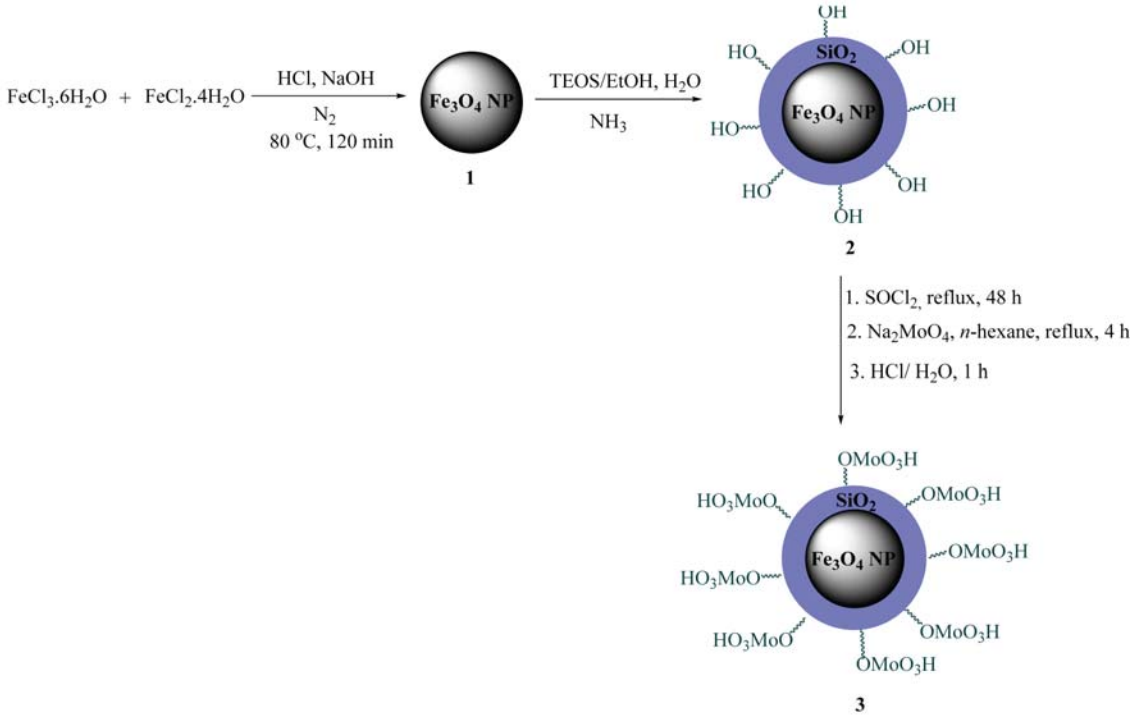
The resulting MNP acid catalyst was characterized by XRD, FT-IR, TEM, SEM, TGA and EDX.[17]

The transmission electron microscopy (TEM) image of Fe_3O_4@SiO_2-MoO_3H powder reveals the spherical Fe_3O_4@SiO_2-MoO_3H powder with an average particle sizes of about 10–30 nm (Fig. 1a).

Surface morphology, particle shape and size distribution features of Fe_3O_4@SiO_2-MoO_3H nanoparticles were examined by FE-SEM (Fig. 1b).

The successful incorporation of molybdate groups was also confirmed by EDAX analysis (Fig. 1c), which showed the presence of Fe, Si, Mo and O elements.

Fig. 2a shows the XRD patterns of Fe_3O_4 particles powder before modification. The following peak signals at 2θ = 30.1°, 35.4°, 43.1°, 53.6°, 57°, and 62.8° corres-



Scheme 1. Schematic procedure for the preparation of Fe_3O_4@SiO_2-MoO_3H.

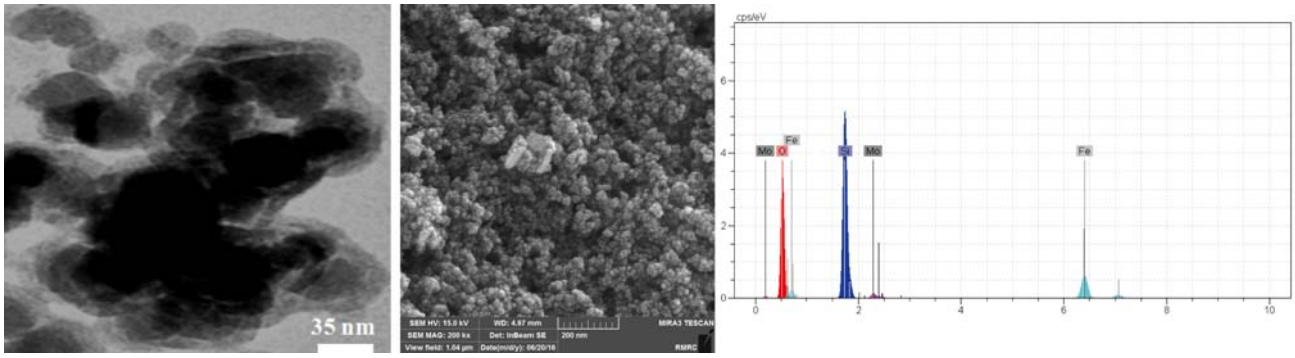


Figure 1. TEM image of Fe_3O_4@SiO_2-MoO_3H (a), Histogram of particle size distribution (b), SEM image of Fe_3O_4@SiO_2–MoO_3H (c) and EDAX spectrum of Fe_3O_4@SiO_2–MoO_3H (d)

pond to the spinel structure of Fe_3O_4, which can be assigned to the diffraction of the (220), (311), (400), (422), (511), and (440) planes of the crystals, respectively.[18] Fig. 2b shows the XRD pattern of Fe_3O_4@SiO_2-$OMoO_3H$ demonstrating that the crystalline structure of the Fe_3O_4 particles was retained after the deposition of SiO_2 layers. The broad peak at around $2\theta = 20°$ to 27° indicates the presence of amorphous silica in Fe_3O_4@SiO_2–$OMoO_3H$. The intensity of this peak increased with the introduction of molybdate on the silica-coated magnetic nanoparticles, which can be attributed to the amorphous molybdate supported on the composite. The XRD results showed that the Fe_3O_4@SiO_2 particles have been successfully coated with molybdate.

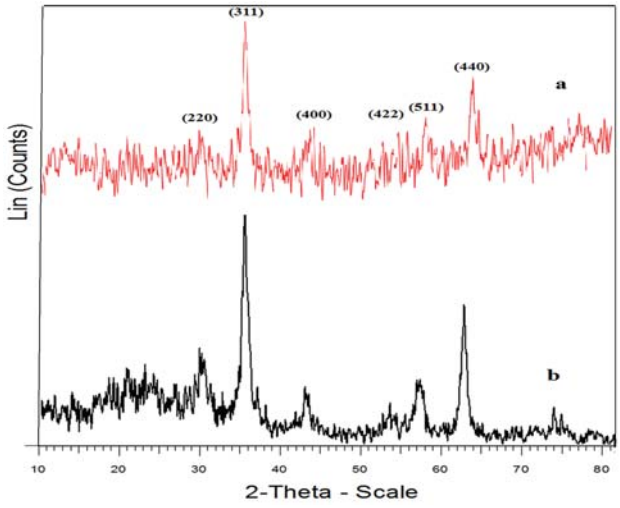


Figure 2. X-ray powder diffraction patterns of (a) Fe_3O_4 NPs, (b) Fe_3O_4@SiO_2-$OMoO_3H$.

The thermogravimetric analysis (TGA) was used to study the thermal stability of the acid catalyst (Fig. 3). The first weight loss which occurred below 150 °C, displayed a mass loss that was attributable to the loss of adsorbed solvent or trapped water from the catalyst. A weight loss of approximately 5% weight occurred between 300 and 500 °C which can be attributed to the loss of molybdate groups covalently bound to silica surface. Thus, it can be concluded that the catalyst is stable up to 300 °C.

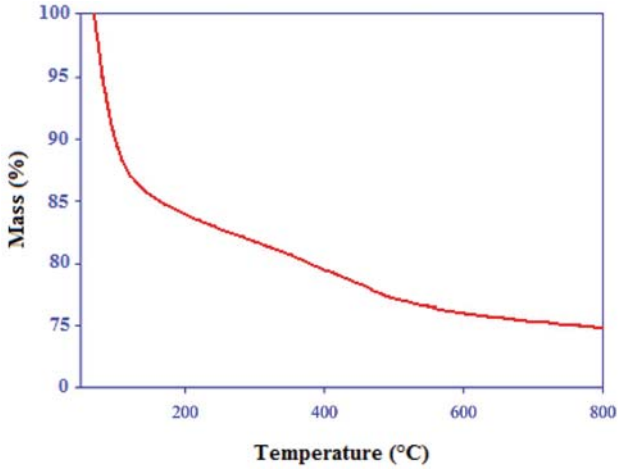


Figure 3. TGA curve of Fe_3O_4@SiO_2-MoO_3H.

Typical magnetization curves for Fe_3O_4 nanoparticles and Fe_3O_4@SiO_2-MoO_3H are shown in Fig. 4. Room temperature specific magnetization (*M*) versus applied magnetic field (*H*) curve measurements of the sample indicate a saturation magnetization value (Ms) of 20.30 emu g^{-1}, lo-

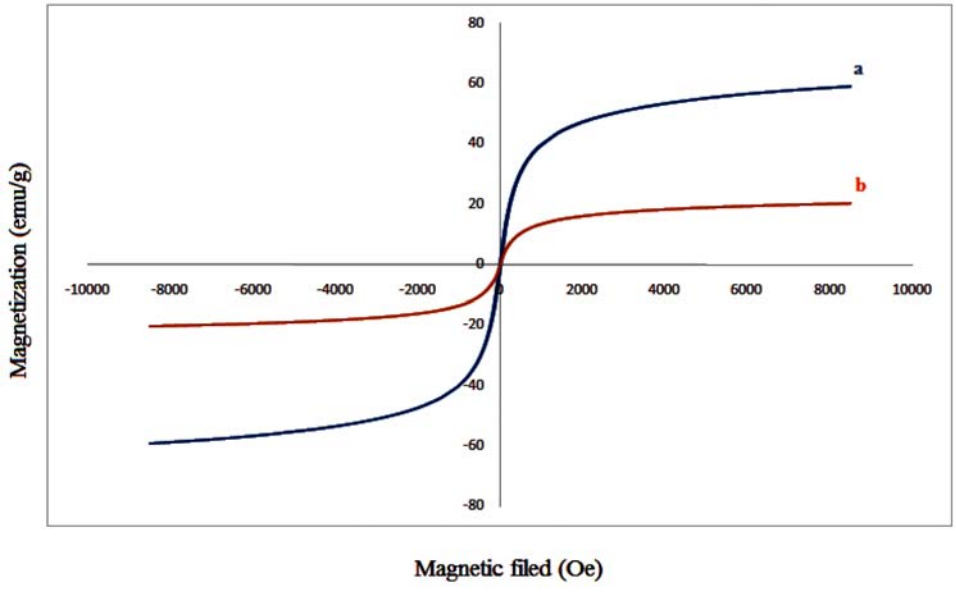
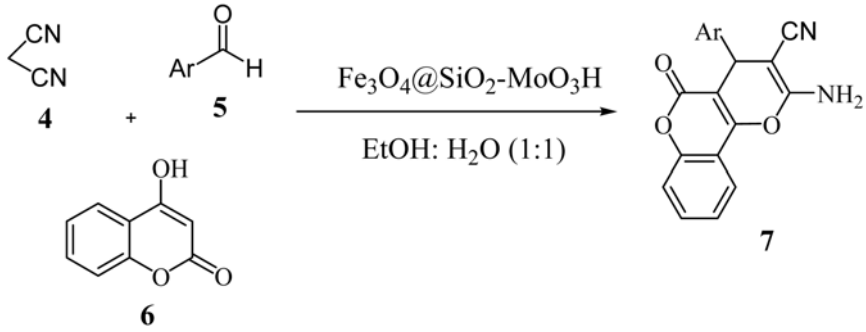


Figure 4. Magnetization curves for the prepared Fe_3O_4 MNPs (a) and Fe_3O_4@SiO_2-MoO_3H (b)

wer than that of bare MNPs (59.14 emu g^{-1}) due to the presence of coated shell.

3. 2. Application of Fe_3O_4@SiO_2-MoO_3H for the Synthesis of Pyrano[2,3-*c*] chromenes

In continuation of our studies on developing novel, efficient, and green procedures for the synthesis of organic compounds using safe catalysts,[19–21] we decided to prepare pyrano[2,3-*c*]chromenes **7** via the synthesis by condensation between malononitrile **4**, aromatic aldehydes **5**, and 4-hydroxycoumarin **6** in the presence of catalytic amounts of Fe_3O_4@SiO_2-MoO_3H (Scheme 2).



Scheme 2. Synthesis of 1,8-dioxo-octahydroxanthene derivatives **7** by Fe_3O_4@SiO_2-MoO_3H.

In order to explore the catalytic efficiency of Fe_3O_4@SiO_2-MoO_3H, the model reaction was carried out under the catalyst-free conditions and compared with the one carried out in the presence of Fe_3O_4@SiO_2-MoO_3H and nano-Fe_3O_4. The obtained results showed higher yields for the reaction with the addition of Fe_3O_4@SiO_2-MoO_3H (94% yield) compared to the catalyst-free reaction (13% yield) and with the reaction with the addition of nano-Fe_3O_4 (86% yield).

The influence of the solvent was studied when the model reaction was performed using Fe_3O_4@SiO_2-MoO_3H nanoparticles, a mixture of H_2O/EtOH (1:1) was opted as the reaction medium. It should be noted that the reaction progress in pure water and/or absolute ethanol was considerable, however it was not better than in the mixture of these two solvents. From different ratios of H_2O/EtOH mixtures, equal mixture H_2O/EtOH (1:1) was considered as the most effective ratio.

After optimization of the reaction conditions, in order to extend the scope of this reaction, a wide range of aromatic aldehydes was used with **3** and **5** (Table 2). All the products were characterized by comparison of their spectra and physical data with those reported in the literature.[22–25]

As shown in Table 2, the new catalyst fortunately also works very well for the preparation of a vast variety of pyrano[2,3-*c*]coumarin derivatives **7a**–**n**. The present method not only affords the products **7** in excellent yields, but also avoids the problems associated with catalyst cost, handling, safety and pollution.

Table 1. Optimization of the model reaction by using various solvents and amount of Fe_3O_4@SiO_2-MoO_3H

Entry	Catalyst (mol%)	Solvent	Yield (%)
1	5	CH_2Cl_2	60
2	5	CH_3Cl	65
3	5	EtOH	90
4	5	MeOH	80
5	5	H_2O	70
6	–	H_2O/EtOH	Trace
7	1	H_2O/EtOH	94
8	3	H_2O/EtOH	88
9	5	H_2O/EtOH	86
10	10	H_2O/EtOH	85

Table 2. Synthesis of pyrano[2,3-*c*]coumarin derivatives **7** using Fe_3O_4@SiO_2-MoO_3H

Product	Ar	Time (min)	Yield[a] (%)	Mp (°C)
7a	C_6H_5	30	96	262–264
7b	4-MeO-C_6H_4	18	92	240–242
7c	2-Cl-C_6H_4	25	78	260–262
7d	3-NO_2-C_6H_4	35	81	255–257
7e	4-NO_2-C_6H_4	75	73	248–250
7f	4-Me-C_6H_4	70	87	250–252
7g	4-Cl-C_6H_4	50	90	258–260
7h	thiophene-2-yl	75	70	234–236
7i	3-Br-C_6H_4	20	91	272–274
7j	2-Cl-6-F-C_6H_3	30	95	288–290
7k	4-benzyloxy-C_6H_4	450	84	275–277
7l	1-naphthyl	90	90	260–262
7m	4-isopropyl-C_6H_4	40	92	239–241
7n	cyclohexyl	25	86	265–267

[a] Isolated yields.

3. 3. Reusability of the Fe_3O_4@SiO_2-MoO_3H

The main disadvantage for many of the reported methods is that the catalysts are destroyed in the work-up procedure and cannot be recovered or reused. In this process, as outlined in Fig. 5., the recycled catalyst can be used in up to eight cycles, during which there are negligible losses in the catalytic activity.

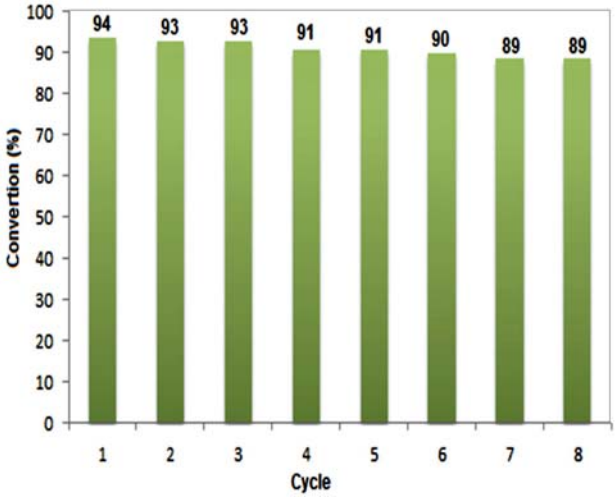


Figure 5. Reusability of Fe_3O_4@SiO_2–MoO_3H for the synthesis of **7a**.

4. Conclusions

In summary, we found Fe_3O_4@SiO_2-$OMoO_3H$ to be an effective acidic magnetic nanocatalyst which successfully catalyzed the reaction between 4-hydroxycoumarin, various aromatic aldehydes and malononitrile to produce new and known pyrano[2,3-*c*] chromens of potential synthetic and pharmaceutical interest. High catalytic activity under solvent free conditions, high yields, a clean process, reusable several times without loss of activity or selectivity simple catalyst preparation, easy separation after the reaction by a magnet and green conditions are the advantages of these protocols.

5. Acknowledgement

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6. References

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Povzetek

Z molibdenovo kislino funkcionalizirani Fe_3O_4 nanodelci, ki temeljijo na silicijevem dioksidu (Fe_3O_4@SiO_2-MoO_3H), so se izkazali kot učinkoviti nanokatalizatorji, ki se jih lahko reciklira z magnetom. Morfologijo in strukturo tega nanokatalizatorja smo raziskali s Fourierjevo transformacijsko infrardečo spektroskopijo (FT-IR), energijsko disperzivno rentgensko spektroskopijo (EDX), transmisivno elektronsko mikroskopijo (TEM), »field emission« vrstično elektronsko mikroskopijo (FE-SEM), termogravimetrično analizo (TGA), rentgensko difrakcijo (XRD) in vibracijsko magnetometrično tehniko (VSM). Veliko katalitsko aktivnost teh katalizatorjev smo preverili na primeru sinteze pirano[2,3-*c*] kromenov, ki predstavljajo biološko zelo aktivne spojine. Katalizator je možno enostavno ločiti iz reakcijske zmesi z uporabo zunanjega vira magnetnega polja in reciklirati vsaj osemkrat brez opazne izgube katalitske aktivnosti; to bi lahko bil razlog za njegovo uporabo v industrijskih procesih, kar bi zmanjšalo okoljske obremenitve. Fe_3O_4@SiO_2-MoO_3H ima torej mnoge prednosti, med drugim nizko ceno, majhno strupenost, enostavnost ločevanja iz reakcijskih zmesi, dobro stabilnost, veliko možnost ponovne uporabe in enostavnost izvedbe reakcij.