Design, Preparation and Characterization of MoO$_3$H-functionalized Fe$_3$O$_4$@SiO$_2$ Magnetic Nanocatalyst and Application for the One-pot Multicomponent Reactions

Mahtab Kiani, Mehrnoosh Hendijani, Mohammad Mohammadipour and Ali Zamanian

1 Young Researchers and Elite Club, Karaj Branch, Islamic Azad University, Karaj, Iran
2 Department of Chemistry, Kharazmi University, Tehran 15719-14911, Iran
3 Department of Chemistry, Semnan University, Semnan 35131-19111, Iran
4 Department of Nanotechnology and Advance Materials, Materials and Energy Research Center, Karaj, Alborz, Iran

* Corresponding author: E-mail: mahtabkiani47@yahoo.com
Tel: 00989372059283; fax: 00987412242167
Received: 05-01-2017

Abstract
Molybdic acid-functionalized silica-based Fe$_3$O$_4$ nanoparticles (Fe$_3$O$_4@$SiO$_2$-MoO$_3$H) 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$_3$O$_4@$SiO$_2$-MoO$_3$H has many advantages, such as low cost, low toxicity, ease of preparation, good stability, high reusability and operational simplicity.

Keywords: Fe$_3$O$_4@$SiO$_2$-MoO$_3$H, 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. 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.

Magnetic nanoparticles (MNP) are widely applied in various fields, such as magnetic resonance imaging (MRI) contrast agents, biomedical science, bioseparation and hyperthermia. 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. Because the Fe$_3$O$_4$ 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$_3$O$_4$ nanoparticles to improve the dispersibility, stability, biocompatibility and biodegradability for specific purposes. The resulting modified Fe$_3$O$_4$ nanoparticles have been extensively used for various applications. 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 Fe3O4@SiO2-MoO3H can be used as a novel magnetic nanocatalyst for the synthesis of 1,8-dioxodehydroacridine derivatives.17 In this work, we demonstrate high catalytic activity of this new catalyst in the synthesis of pyranocoumarin derivatives 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. 1H NMR spectra were recorded on a Bruker Avance II 400 NMR spectrometer at 400 MHz, with DMSO-d6 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 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 20 kV accelerating voltage. Thermogravimetric analyses (TGA) were conducted on a Rheometric Scientific Inc. 1998 thermal analysis apparatus under a N2 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-Fe3O4 (1)

FeCl3·6H2O (20 mmol) and FeCl2·4H2O (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 N2 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-Fe3O4@SiO2 (2)

Nano-Fe3O4@SiO2 (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-Fe3O4@SiO2·OMoO3H (3)

To an oven-dried (125 °C, vacuum) sample of nano-Fe3O4@SiO2 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 CaCl2 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 Fe3O4@SiO2·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 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-Fe3O4@SiO2·OMoO3H.

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-Fe3O4@SiO2·OMoO3H (0.02 g) were added to a 10 mL mixture EtOH/H2O (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 recrystallization from EtOH.

3. Results and Discussion

3.1. Characterization of Fe₃O₄@SiO₂-OMoO₃H

As can be seen in Scheme 1, from the reaction Fe₃O₄@SiO₂ nanoparticles 2 with thionyl chloride, the Fe₃O₄@SiO₂-Cl has been prepared. The Fe₃O₄@SiO₂-OMoO₃H 3 was prepared from nucleophilic substitution of Fe₃O₄@SiO₂-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 Fe₃O₄@SiO₂-MoO₃H powder reveals the spherical Fe₃O₄@SiO₂-MoO₃H powder with an average particle sizes of about 10–30 nm (Fig. 1a).

Surface morphology, particle shape and size distribution features of Fe₃O₄@SiO₂-MoO₃H 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 Fe₃O₄ particles powder before modification. The following peak signals at $2\theta = 30.1^\circ, 35.4^\circ, 43.1^\circ, 53.6^\circ, 57^\circ, \text{and } 62.8^\circ$ corres-

Scheme 1. Schematic procedure for the preparation of Fe₃O₄@SiO₂-MoO₃H.

Figure 1. TEM image of Fe₃O₄@SiO₂-MoO₃H (a), Histogram of particle size distribution (b), SEM image of Fe₃O₄@SiO₂-MoO₃H (c) and EDAX spectrum of Fe₃O₄@SiO₂-MoO₃H (d)
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 Fe₃O₄@SiO₂-MoO₃H.

Typical magnetization curves for Fe₃O₄ nanoparticles and Fe₃O₄@SiO₂-MoO₃H 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-
The magnetization of Fe\(_3\)O\(_4\)@SiO\(_2\)-MoO\(_3\)H nanoparticles, a mixture of H\(_2\)O/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\(_2\)O/EtOH mixtures, equal mixture H\(_2\)O/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 2. Synthesis of pyrano[2,3-c]coumarin derivatives 7 using Fe\(_3\)O\(_4\)@SiO\(_2\)-MoO\(_3\)H

<table>
<thead>
<tr>
<th>Product</th>
<th>Ar</th>
<th>Time (min)</th>
<th>Yield* (%)</th>
<th>Mp (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7a</td>
<td>C(_6)H(_5)</td>
<td>30</td>
<td>96</td>
<td>262–264</td>
</tr>
<tr>
<td>7b</td>
<td>4-MeO-C(_6)H(_4)</td>
<td>18</td>
<td>92</td>
<td>240–242</td>
</tr>
<tr>
<td>7c</td>
<td>2-Cl-C(_6)H(_4)</td>
<td>25</td>
<td>78</td>
<td>260–262</td>
</tr>
<tr>
<td>7d</td>
<td>3-NO(_2)-C(_6)H(_4)</td>
<td>35</td>
<td>81</td>
<td>255–257</td>
</tr>
<tr>
<td>7e</td>
<td>4-NO(_2)-C(_6)H(_4)</td>
<td>75</td>
<td>73</td>
<td>248–250</td>
</tr>
<tr>
<td>7f</td>
<td>4-Me-C(_6)H(_4)</td>
<td>70</td>
<td>87</td>
<td>250–252</td>
</tr>
<tr>
<td>7g</td>
<td>4-Cl-C(_6)H(_4)</td>
<td>50</td>
<td>90</td>
<td>258–260</td>
</tr>
<tr>
<td>7h</td>
<td>thiophene-2-yl</td>
<td>75</td>
<td>70</td>
<td>234–236</td>
</tr>
<tr>
<td>7i</td>
<td>3-Br-C(_6)H(_4)</td>
<td>20</td>
<td>91</td>
<td>272–274</td>
</tr>
<tr>
<td>7j</td>
<td>2-Cl-6-F-C(_6)H(_3)</td>
<td>30</td>
<td>95</td>
<td>288–290</td>
</tr>
<tr>
<td>7k</td>
<td>4-benzyloxy-C(_6)H(_4)</td>
<td>450</td>
<td>84</td>
<td>275–277</td>
</tr>
<tr>
<td>7l</td>
<td>1-naphthyl</td>
<td>90</td>
<td>90</td>
<td>260–262</td>
</tr>
<tr>
<td>7m</td>
<td>4-isopropyl-C(_6)H(_4)</td>
<td>40</td>
<td>92</td>
<td>239–241</td>
</tr>
<tr>
<td>7n</td>
<td>cyclohexyl</td>
<td>25</td>
<td>86</td>
<td>265–267</td>
</tr>
</tbody>
</table>

* Isolated yields.

### Table 1. Optimization of the model reaction by using various solvents and amount of Fe\(_3\)O\(_4\)@SiO\(_2\)-MoO\(_3\)H

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (mol%)</th>
<th>Solvent</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5</td>
<td>CH(_2)Cl(_2)</td>
<td>60</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>CH(_3)Cl</td>
<td>65</td>
</tr>
<tr>
<td>3</td>
<td>5</td>
<td>EtOH</td>
<td>90</td>
</tr>
<tr>
<td>4</td>
<td>5</td>
<td>MeOH</td>
<td>80</td>
</tr>
<tr>
<td>5</td>
<td>5</td>
<td>H(_2)O</td>
<td>70</td>
</tr>
<tr>
<td>6</td>
<td>–</td>
<td>H(_2)O/EtOH</td>
<td>Trace</td>
</tr>
<tr>
<td>7</td>
<td>1</td>
<td>H(_2)O/EtOH</td>
<td>94</td>
</tr>
<tr>
<td>8</td>
<td>3</td>
<td>H(_2)O/EtOH</td>
<td>88</td>
</tr>
<tr>
<td>9</td>
<td>5</td>
<td>H(_2)O/EtOH</td>
<td>86</td>
</tr>
<tr>
<td>10</td>
<td>10</td>
<td>H(_2)O/EtOH</td>
<td>85</td>
</tr>
</tbody>
</table>
3.3. Reusability of the Fe₃O₄@SiO₂-MoO₃H

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 Fe₃O₄@SiO₂-MoO₃H for the synthesis of 7a.](image)

4. Conclusions

In summary, we found Fe₃O₄@SiO₂-OMoO₃H 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 pyranochromens 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

We acknowledge the research council of Yasouj University.

6. References

Povzetek

Z molibdenovo kislino funkcionalizirani Fe₃O₄ nanodelci, ki temeljijo na silicijevem dioksidu (Fe₃O₄@SiO₂-MoO₃H), 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. Fe₃O₄@SiO₂-MoO₃H 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.