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SnCl₄-functionalized nano-Fe₃O₄ encapsulated-silica particles as a novel heterogeneous solid acid for synthesis of 1,4-dihydropyridine derivatives

Abdolhamid Bamoniri*, Sara Fouladgar

A novel type of green heterogeneous solid acid was prepared by the immobilization of SnCl₄ on the surface of Fe₃O₄@SiO₂ (Fe₃O₄@SiO₂-SnCl₄) and characterized by Fourier transform-infrared spectroscopy (FT-IR), X-ray diffraction (XRD), vibrating sample magnetometer (VSM), field emission-scanning electron microscope (FE-SEM), energy dispersive X-ray (EDX), N₂ adsorption-desorption (BET) and transmission electron microscope (TEM). The activity of this solid acid was probed via the synthesis of 1,4-dihydropyridine derivatives of three or four components coupling reaction of aldehyde, 1,3-dicabonyl compound, and ammonium acetate under ultrasonic irradiation and yielded excellent results with easy work-up in short time. 1,4-dihydropyridine derivatives were characterized by FT-IR and ¹HNMR.

Introduction

Industrial chemistry is broadly adopting the conception of green chemistry to meet the essential scientific challenges of protecting the environment and human health while preserving commercial viability.¹ As one of the breakthroughs progresses in the field of green processes based on sonochemistry, it has increasingly been considered as a simple, clean and convenient method²⁻⁵ and so chemists are focusing on its use for the synthesis of organic compounds. Similarly, multicomponent reactions (MCRs) work as an efficient and important tool in modern synthetic organic chemistry. These reactions which consist of two or more synthetic steps, are carried out without the separation of any intermediates, so as to reduce time and to save both energy and raw materials.⁶,⁷ The Hantzsch reaction, which provides 1,4-dihydropyridines as products, is one of the most well-known MCRs. There is always something new on this old topic.⁸ This is mainly due to the fact that the 1,4-dihydropyridines exhibit significant pharmacological and biological functions such as calcium channel blocking⁹, anti-anginal¹⁰, antitumor¹¹, anti-inflammatory¹²,¹³ antitubercular¹⁴, analgesic¹⁵ and antithrombotic activities.¹⁶,¹⁷ Moreover 1,4-dihydropyridine skeleton is the parent nucleus of many commercial drugs such as amlodipine, nifedipin, nimodipin, felodipine, isradipine, and nicardipine. Thus, 1,4-dihydropyridines have attracted the attention of many chemists and pharmacologists. As a result, various methods to prepare these compounds have been reported.¹⁸⁻²⁴

More recently, the design of magnetical catalysts has attracted a great deal of attention because these catalysts improve the efficient separation of catalysts by magnetic decantation after the reaction leading to improved reusability.²⁵⁻²⁷ The combination of this concept with that of nano materials holds a significant potential in advanced catalysts with improved activities and selectivities providing high specific surface area to volume ratio and higher surface area more active sites. Thus making MNPs have emerged as a new class of nano catalysts.²⁸,²⁹ MNPs are one of the most extensively considered materials in research fields including biotechnology, biomedicine and catalysis. These are generally inert and, for this reason, ideal for imaging and separation in biological systems.³⁰,³¹ They have been used as a...
useful support in a variety of heterogeneous catalysts for various organic reactions.\textsuperscript{32-34} MNPs of Fe\textsubscript{3}O\textsubscript{4} are an efficient and important alternative to conventional heterogeneous catalyst supports due to their magnetic properties which facilitate the separation of the catalyst upon reaction and produce a very active surface area for adsorptions or immobilization of metals and ligands.\textsuperscript{35} Nano-Fe\textsubscript{3}O\textsubscript{4} (Fe\textsubscript{3}O\textsubscript{4} NPs) is chemically stable, readily available, and easy to prepare, and low in toxicity and cost. However, pure Fe\textsubscript{3}O\textsubscript{4} NPs suffer from some inherent limitations: they are oxidized and easily lose their magnetism when used under acidic conditions and they are easy to agglomerate and lose dispersibility.\textsuperscript{36, 37} The above inherent limitations of Fe\textsubscript{3}O\textsubscript{4} NPs has led to use of a suitable protective coating. Silica has been considered as one of the most ideal coating layers for Fe\textsubscript{3}O\textsubscript{4} NPs due to its chemical stability, biocompatibility, flexibility and reactivity with numerous coupling agents.\textsuperscript{38} The iron-oxide with a layer of silica not only stabilizes the nanoparticles in solution but also offers sites for surface modification with various biomedical ligands in biological applications.\textsuperscript{39, 40} Bi\textsubscript{2}WO\textsubscript{6}, TiO\textsubscript{2} in photocatalyst application\textsuperscript{41, 42} and y-mercaptopropyl-trimethoxysilane for extracted various ions metal from water in a wide pH range.\textsuperscript{43}

To the best of our knowledge, the grafting of SnCl\textsubscript{4} on Fe\textsubscript{3}O\textsubscript{4} coated with SiO\textsubscript{2} has not been reported previously. In this study, we report, for the first time, the successful synthesis of Fe\textsubscript{3}O\textsubscript{4}@SiO\textsubscript{2}-SnCl\textsubscript{4} as a new catalyst for the synthesis of 1,4-dihydropyridines. We attempted to perform one-pot synthesis of 1,4-dihydropyridine derivatives through three and four component coupling reaction of aldehydes, 1,3-dicarbonyl compounds, and ammonium acetate in the presence of Fe\textsubscript{3}O\textsubscript{4}@SiO\textsubscript{2}-SnCl\textsubscript{4} as an efficient eco-friendly catalyst under ultrasound irradiation.

**Experimental**

**Materials and apparatus**

Chemicals and solvents were purchased from Merck and Aldrich companies. FT-IR spectra were run on a Nicolet Magna 550 spectrometer using KBr pellets. NMR spectra were recorded at 400 MHz (\textsuperscript{1}H) on a Bruker DRX-400 Avance spectrometer in CDCl\textsubscript{3} as a solvent. Melting points were obtained with a micro melting point apparatus (Electrothermal, Mk3) and used uncorrected. A multiwave ultrasonic generator (Sonicator 3000; Bandelin MS 72, Germany), equipped with a convertor/transducer and titanium oscillator (horn), 12.5 mm in diameter, operating at 20 kHz with a maximum power output of 60 W, was used for the ultrasonic irradiation. The ultrasonic generator automatically adjusted the power level. The morphology of the synthesized samples and catalyst were studied by a Mira ІІ LMU Tescan FE-SEM made in Czech Republic. XRD patterns were recorded on a Philips Xpert MPD diffractometer equipped with a Cu Ka anode (\textlambda=1.54 A\textdegree) in the 20 range from 10 to 80\textdegree. Magnetization of the samples was recorded as a function of the applied magnetic field sweeping between ±10 kOe at room temperature. All measurements were performed on a vibrating sample magnetometer device (Meghnatis Daghigh Kavir Co., Kashan Kavir, Iran). Fe\textsubscript{3}O\textsubscript{4}@SiO\textsubscript{2}-SnCl\textsubscript{4} average size and distribution were analyzed by TEM using a Philips CM120 with a LaB\textsubscript{6} cathode and accelerating voltage of 120 kV. Elemental composition of the above mentioned MNPs was investigated by EDX spectroscopy (XL30, Philips microscope). The specific surface area was evaluated by the BET method using N\textsubscript{2} adsorption at –196 °C using an automated gas adsorption analyzer (TriStar II 3020 V1.03, Micromeritics).

**Synthesis of Fe\textsubscript{3}O\textsubscript{4}@SiO\textsubscript{2}-SnCl\textsubscript{4} MNPs**

Fe\textsubscript{3}O\textsubscript{4} nanoparticles were prepared by a known procedure, chemical co-precipitation method reported in the literature.\textsuperscript{44, 45} Briefly, FeCl\textsubscript{3}-6H\textsubscript{2}O (2.7 g) and FeCl\textsubscript{2}-4H\textsubscript{2}O (1 g) with molar ratio of 2:1, were dissolved in concentrated HCl, 1.2 M (100 mL, 0.12 mol) through ultrasonic method for 30 min. Then, ammonia 1.25 M (150 mL, 0.19 mol) was injected into the reaction mixture under vigorous stirring at 80 °C for 1 h under atmosphere nitrogen. The black magnetic nanoparticles of Fe\textsubscript{3}O\textsubscript{4} (magnetite) were formed. Afterwards, the reaction mixture was cooled. The precipitate was isolated using the magnetic field and washed thoroughly with water until the supernatant liquid reached neutrality (pH ~7).

The synthesized Fe\textsubscript{3}O\textsubscript{4} MNPs were used for coating with a silica shell following the reported method.\textsuperscript{46} Fe\textsubscript{3}O\textsubscript{4} MNPs (1 g) were diluted by the consecutive addition of water (20 mL), ethanol (60 mL), and concentrated aqueous ammonia (2 mL, 25 wt%). The resultant dispersion was homogenized through ultrasonic method. A solution of tetraethylorthosilicate (TEOS) (0.5 mL) in ethanol (10 mL) was then added to the dispersion in a drop-wise manner at room temperature under vigorous stirring for 16 h. Fe\textsubscript{3}O\textsubscript{4}@SiO\textsubscript{2} was collected by an external magnet, washed three times with ethanol (30 mL) and dried under vacuum at 70 °C for 6 h.

In the last step, Fe\textsubscript{3}O\textsubscript{4}@SiO\textsubscript{2} (0.65 g) was dispersed in CHCl\textsubscript{3} (10 mL) using ultrasonic method for 30 min. Subsequently, SnCl\textsubscript{4} (0.16 mL, 0.001 mol) was added drop-wise to dispersed solution of Fe\textsubscript{3}O\textsubscript{4}@SiO\textsubscript{2} at room temperature under vigorous stirring over a period of 30 min. The resulting suspension was separated using an external magnet, washed with chloroform (20 mL) and dried at room temperature to obtain the brown solid presented nano Fe\textsubscript{3}O\textsubscript{4}@SiO\textsubscript{2}-SnCl\textsubscript{4}.

**Acidic capacity of Fe\textsubscript{3}O\textsubscript{4}@SiO\textsubscript{2}-SnCl\textsubscript{4}**

100 mg of Fe\textsubscript{3}O\textsubscript{4}@SiO\textsubscript{2}-SnCl\textsubscript{4} accurately weighted placed in conical flask containing about 10 mL of water and 3 drops of phenolphthalein TS and then titrated with NaOH (0.1 M) VS until solution remained light pink for 30 seconds.

**General procedure for the synthesis of 1,4-dihydropyridines**

**Method I (∆)**

A mixture of an aryl aldehyde (1 mmol), 1,3-dicarbonyl compound (2 mmol), ammonium acetate (1.5 mmol) and Fe\textsubscript{3}O\textsubscript{4}@SiO\textsubscript{2}-SnCl\textsubscript{4} (25 mg) was refluxed in ethanol (5 mL) near 75 °C for the stipulated time mentioned in table 3. The progress of the reaction was monitored by TLC (EtOAc: petroleum ether 7: 3). After completion of the reaction, the catalyst was separated by an external magnet and reused for the next experiment. The filtrate was poured into crushed ice obtaining solid product, recrystallized from ethanol to get pure crystalline 1,4-dihydropyridines derivative.
Method II (US)
In a round-bottom flask, a mixture of an aryl aldehyde (1 mmol), 1,3-dicarbonyl compound (2 mmol), ammonium acetate (1.5 mmol) and Fe₃O₄@SiO₂-SnCl₃ (18 mg) in ethanol (5 mL) was sonicated at 20 kHz frequency and 40 W power at room temperature for the stipulated time which was confirmed by TLC and worked-up as described in method I.

Spectral data for selected compounds

<table>
<thead>
<tr>
<th>Compounds</th>
<th>FT-IR (KBr, cm⁻¹)</th>
<th>H NMR (CDCl₃, 300 MHz)</th>
<th>H NMR (CDCl₃, 400 MHz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yellowish solid, FT-IR (KB, v cm⁻¹):</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2,6-Dimethyl-4-(phenyl)-1,4-dihydropyridine-3,5-diethylcarboxylate (compound 4a)</td>
<td>3342 (NH), 1689 (C=O, ester), 1487 (C=C, aromatic), 1212 (C=O)</td>
<td>7.28 (d, J = 7 Hz, 2H, Ar-H), 7.13 (d, J = 6.9 Hz, 1H, Ar-H), 5.54 (s, 1H, NH), 4.99 (s, 1H, CH), 4.00 (q, J = 7.4 Hz, 2H, OCH₃), 2.34 (s, 6H, 2CH₃), 1.22 (t, J = 6.8 Hz, 6H, 2CH₂CH₃).</td>
<td></td>
</tr>
<tr>
<td>2,6-Dimethyl-4-(methoxy)-1,4-dihydropyridine-3,5-diethylcarboxylate (compound 4c)</td>
<td>3342 (NH), 1689 (C=O, ester), 1487 (C=C, aromatic), 1211 (C=O)</td>
<td>7.23 (d, J = 7.5 Hz, 2H, Ar-H), 6.75 (d, J = 7.9 Hz, 2H, Ar-H), 5.54 (s, 1H, NH), 4.99 (s, 1H, CH), 4.00 (q, J = 7.4 Hz, 2H, OCH₃), 2.34 (s, 6H, 2CH₃), 1.22 (t, J = 6.8 Hz, 6H, 2CH₂CH₃).</td>
<td></td>
</tr>
<tr>
<td>2,6-Dimethyl-4-(alkyl)-1,4-dihydropyridine-3,5-diethylcarboxylate (compound 4b)</td>
<td>3342 (NH), 1689 (C=O, ester), 1487 (C=C, aromatic), 1212 (C=O), 1117 (C-Cl)</td>
<td>7.22 (d, J = 7.8 Hz, 2H, Ar-H), 6.75 (d, J = 7.9 Hz, 2H, Ar-H), 5.55 (s, 1H, NH), 4.96 (s, 1H, CH), 4.08 (q, J = 7.2 Hz, 2H, OCH₃), 2.34 (s, 6H, 2CH₃), 1.22 (t, J = 7.2 Hz, 6H, 2CH₂CH₃).</td>
<td></td>
</tr>
<tr>
<td>2,6-Dimethyl-4-(4-methylphenyl)-1,4-dihydropyridine-3,5-diethylcarboxylate (compound 4d)</td>
<td>3342 (NH), 1689 (C=O, ester), 1487 (C=C, aromatic), 1212 (C=O), 1117 (C-Cl)</td>
<td>7.28 (d, J = 7.8 Hz, 2H, Ar-H), 6.75 (d, J = 7.9 Hz, 2H, Ar-H), 5.55 (s, 1H, NH), 4.96 (s, 1H, CH), 4.08 (q, J = 7.2 Hz, 2H, OCH₃), 2.34 (s, 6H, 2CH₃), 1.22 (t, J = 7.2 Hz, 6H, 2CH₂CH₃).</td>
<td></td>
</tr>
</tbody>
</table>

Results and discussion

This research was performed in two steps. Firstly, Fe₃O₄@SiO₂-SnCl₃ MNPs were prepared and identified by FT-IR, XRD, VSM, FE-SEM, EDS, and TEM techniques. In the second step, 1,4-dihydropyridine derivatives were synthesized by aryl aldehyde (1 mmol), 1,3-dicarbonyl compound (2 mmol), ammonium acetate (1.5 mmol) and Fe₃O₄@SiO₂-SnCl₃ (18 mg) in ethanol (5 mL) was sonicated at 20 kHz frequency and 40 W power at room temperature for the stipulated time which was confirmed by TLC and worked-up as described in method I.
aldehydes, 1,3-dicarbonyl compounds, and ammonium acetate under reflux and ultrasound irradiation methods and then characterized by their melting points using FT-IR, ^1^H NMR spectroscopy.

**Preparation and characterization of Fe_3O_4@SiO_2–SnCl_4**

Fe_3O_4@SiO_2–SnCl_4 was prepared by a simple, low cost and convenient method (Figure 1).

![Figure 1](image1.png)

*Fig. 1. The schematic diagram for synthesis and suggested structure of Fe_3O_4@SiO_2–SnCl_4*

In order to recognize the molecular structures of Fe_3O_4, Fe_3O_4@SiO_2, and Fe_3O_4@SiO_2–SnCl_4 MNPs, FT-IR analysis of the three mentioned samples was performed (Figure 2). Fe_3O_4 was identified by bands at 443 and 582 cm\(^{-1}\) due to Fe–O vibrations in octahedral and tetrahedral sites (Figure 1a). The FT-IR spectrum of Fe_3O_4@SiO_2 (Figure 2b) displays characteristic peaks at 1094 and 802 cm\(^{-1}\) corresponding to symmetrical and asymmetrical vibrations of Si–O–Si, respectively. Weak band at 469 cm\(^{-1}\) corresponds to the Si–O–Fe stretching vibrations of the Fe_3O_4@SiO_2. These outcomes indicate that SiO_2 is immobilized on the surface of Fe_3O_4. The successful covalent linking of the SnCl_4 on the surface of Fe_3O_4@SiO_2 was confirmed by the appearance of a new band at 563 cm\(^{-1}\), which originates from the absorption of O-Sn (Figure 2d).

![Figure 2](image2.png)

*Fig. 2. FT-IR spectra of (a) Fe_3O_4, (b) Fe_3O_4@SiO_2, (c) SnCl_4 and (d) Fe_3O_4@SiO_2–SnCl_4*

The phase and purity of the different stepwise synthesized materials in this work from magnetite Fe_3O_4 to final catalyst Fe_3O_4@SiO_2–SnCl_4 were determined by XRD patterns (Figure 3). XRD pattern of Fe_3O_4 exhibited peaks at 2θ = 30.43, 35.80, 43.40, 53.98, 57.46, 62.99, and 74.51° (Figure 3a). The diffraction peaks in this pattern can be in accord with standard pattern of an inverse cubic spinel of Fe_3O_4.\(^{50}\) The strong and sharp peaks indicated phase purity of Fe_3O_4 nanoparticles. Silica coated magnetite nanoparticles exhibited a broadened pattern due to the non-crystalline nature at 2θ = 20-30 corresponding to amorphous phase of SiO_2 and also 30.33, 35.79, 43.36, 53.82, 57.36, 62.99 and 74.62° which corresponded to Fe_3O_4 structure (Figure 3b). The XRD pattern of Fe_3O_4@SiO_2–SnCl_4 in figure 3c showed a much broader diffraction pattern and increased the noise to that of figure 3b, which seems to link to SnCl_4 on the surface of Fe_3O_4@SiO_2. Moreover, characteristic peaks of Fe_3O_4 were observed in three samples, indicating that the binding process did not induce any phase change.

![Figure 3](image3.png)

*Fig. 3. XRD patterns of (a) Fe_3O_4, (b) Fe_3O_4@SiO_2 and (c) Fe_3O_4@SiO_2–SnCl_4*

The energy dispersive X-ray (EDX) from the Fe_3O_4@SiO_2–SnCl_4 (Figure 4) provided the presence of the expected elements in the structure of this catalyst and confirmed supporting of SnCl_4 on Fe_3O_4@SiO_2. The elemental compositions of Fe_3O_4@SiO_2–SnCl_4 were found to be 52.80, 31.33, 0.82, 5.30 and 9.76% for Fe, O, Si, Sn and Cl, respectively.

![Figure 4](image4.png)

*Fig. 4. EDX patterns of Fe_3O_4@SiO_2–SnCl_4*

The BET specific surface area of Fe_3O_4@SiO_2–SnCl_4 in this study was 59.0467 m\(^2\)/g. In order to identify the possible structure of Fe_3O_4@SiO_2–SnCl_4, we determined acidic capacity of this catalyst by...
titration producing HCl in water. We found that 0.1 g of the catalyst produced 0.324 mmol of H⁺ or Cl⁻. Also, for the determination of the loading amounts of the Sn on the Fe₃O₄@SiO₂-SnCl₄ by the addition of 1 mL aqueous solution of NaOH (0.2 M) to 0.1 g of catalyst and hot water. The nanomagnetic catalyst was separated with an external magnet from the obtained Sn(OH)₄ solution. The solution was evaporated to obtain a dry Sn(OH)₄ powder. The calculated loading amount of Sn in the catalyst was 0.138 mmol g⁻¹.

According to the above data and EDX data, the molar ratio of Sn:Cl, calculated loading amount of Sn in the catalyst was 0.138 mmol g⁻¹. Also, for the determination of Sn on the Fe₃O₄@SiO₂-SnCl₄ was proposed as shown in figure 5.

The magnetization curve for synthesized Fe₃O₄, Fe₃O₄@SiO₂, and Fe₃O₄@SiO₂-SnCl₄ nanoparticles is shown in figure 6. Room temperature specific magnetization (M) versus applied magnetic field (H) indicated the magnetization as a function of applied magnetic field. The saturation magnetization of the Fe₃O₄ nanoparticles was about 53.52 emu/g, which decreased to 40.98 emu/g after supporting Fe₃O₄ with SiO₂ and to 31.05 emu/g after supporting Fe₃O₄@SiO₂ with SnCl₄. The decrease of the saturation magnetization after surface coating of Fe₃O₄ confirms the presence of a diamagnetic outer shell (SiO₂ or SiO₂-SnCl₄).

The FE-SEM images of the Fe₃O₄@SiO₂-SnCl₄ nanoparticles are displayed in figure 7. These images evidently show the surface morphology of three kinds of synthesized MNPs with a nearly spherical shape. Although Fe₃O₄@SiO₂ and Fe₃O₄@SiO₂-SnCl₄ still keep the morphological of Fe₃O₄, they are slightly larger in particle size.

Transmission electron microscopy (TEM) image of the synthesized catalyst was recorded as depicted in figure 8. According to this image, the catalyst was approximately 28 nm in size.

**Evaluation of the catalytic activity of Fe₃O₄@SiO₂-SnCl₄**

To obtain appropriate conditions for the synthesis of 1,4-dihydropyridines, different reaction conditions have been examined. At the outset, the reaction was carried out with benzaldehyde, ethyl acetoacetate, dimedone and ammonium acetate as a model reaction (Scheme 1).

![Scheme 1. Standard model reaction](image)

We studied the effect of various solvents such as H₂O, EtOH, DMF, CH₂CN, and CHCl₃ on a model reaction under ultrasound irradiation (40W power). The results are summarized in table 1. It was found that ethanol was the best choice for the model reaction.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Time (min)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CH₂CN</td>
<td>5</td>
<td>74</td>
</tr>
<tr>
<td>2</td>
<td>CHCl₃</td>
<td>5</td>
<td>75</td>
</tr>
<tr>
<td>3</td>
<td>DMF</td>
<td>5</td>
<td>85</td>
</tr>
<tr>
<td>4</td>
<td>Water</td>
<td>5</td>
<td>89</td>
</tr>
<tr>
<td>5</td>
<td>EtOH</td>
<td>5</td>
<td>98</td>
</tr>
</tbody>
</table>

*Isolated yields. Benzaldehyde (1 mmol), ethyl acetoacetate (1 mmol), dimedone (1 mmol), ammonium acetate (1.5 mmol) and Fe₃O₄@SiO₂-SnCl₄ (30 mg).*
In order to study the effects of Fe₄O₄@SiO₂-SnCl₄ on the model reaction, catalytic behaviour of Fe₄O₄@SiO₂-SnCl₄ was compared under reflux or and ultrasound irradiation conditions (Table 2). The obtained results showed that, in the absence of catalyst, no significant product was obtained and in the presence of Fe₄O₄@SiO₂-SnCl₄ the reaction was carried out with high yields (Entry 1). Also the results in table 1 exhibit the optimum amount of the catalyst was 25 mg under reflux and ultrasound irradiation (Entry 6). Notably, the increase of the catalyst in reflux and ultrasound irradiation conditions did not show any significant changes in yield and time of reaction (Entry 7).

Table 2 Optimization of the model reaction using Fe₄O₄@SiO₂-SnCl₄ under reflux (I) and ultrasound irradiation (II)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Method I (∆)</th>
<th>Method II (US)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Catalyst/ (g)</td>
<td>Catalyst/ (g)</td>
</tr>
<tr>
<td>1</td>
<td>none</td>
<td>none</td>
</tr>
<tr>
<td>2</td>
<td>SnCl₄ / 0.13</td>
<td>SnCl₄ / 0.13</td>
</tr>
<tr>
<td>3</td>
<td>BF₃Et₂O / 0.13</td>
<td>BF₃Et₂O / 0.13</td>
</tr>
<tr>
<td>4</td>
<td>TiCl₄ / 0.13</td>
<td>TiCl₄ / 0.13</td>
</tr>
<tr>
<td>5</td>
<td>SnCl₄-SiO₂ / 0.50</td>
<td>SnCl₄-SiO₂ / 0.50</td>
</tr>
<tr>
<td>6</td>
<td>Fe₄O₄@SiO₂-SnCl₄ / 0.005</td>
<td>Fe₄O₄@SiO₂-SnCl₄ / 0.005</td>
</tr>
<tr>
<td>7</td>
<td>Fe₄O₄@SiO₂-SnCl₄ / 0.010</td>
<td>Fe₄O₄@SiO₂-SnCl₄ / 0.010</td>
</tr>
<tr>
<td>8</td>
<td>Fe₄O₄@SiO₂-SnCl₄ / 0.020</td>
<td>Fe₄O₄@SiO₂-SnCl₄ / 0.015</td>
</tr>
<tr>
<td>9</td>
<td>Fe₄O₄@SiO₂-SnCl₄ / 0.025</td>
<td>Fe₄O₄@SiO₂-SnCl₄ / 0.018</td>
</tr>
<tr>
<td>10</td>
<td>Fe₄O₄@SiO₂-SnCl₄ / 0.030</td>
<td>Fe₄O₄@SiO₂-SnCl₄ / 0.025</td>
</tr>
</tbody>
</table>

*Isolated yields. benzaldehyde (1 mmol), ethyl acetoacetate (1 mmmol), dimedone (1 mmol) and ammonium acetate (1.5 mmol) in ethanol (5 mL)

In order to examine the scope and generality of this procedure in these methodologies, a number of aromatic aldehydes containing both electron-withdrawing and electron-donating groups in the para position were used with ammonium acetate and ethyl acetoacetate or/and dimedone in the presence of Fe₄O₄@SiO₂-SnCl₄ in ethanol under reflux and ultrasound irradiation conditions. By comparing obtained data for different condition from Table 3, reveal that ultrasound irradiation method leads to interesting effect concerning the synthesis of 1,4-dihydropyridines.

In all cases, when the reactions were carried out under ultrasound irradiation, the times of the reactions were shorter and the yields of the products were higher than reflux method. Also, the amount of catalyst was decreased under ultrasound irradiation. This should be explained based on the phenomenon of cavitation produced by ultrasound irradiation. Moreover this method, particularly when considering the basic green chemistry concepts, is more environmentally friendly. As can be seen from the results in Table 3, aromatic aldehydes with substituents carrying either electron-donating or electron-withdrawing groups reacted successfully with 1,3-dicarbonyl compounds to afford the corresponding 1,4-di-1hdroxypyridines in excellent yields. However, using dimedone instead of ethyl acetoacetate affects the yield and reaction time due to acidity of the methylenic protons.

The proposed mechanism for the formation of 1,4-di-1hdroxypyridines in the presence of Fe₄O₄@SiO₂-SnCl₄, which can act as Lewis acid catalyst (empty π orbital of Sn in Fe₄O₄@SiO₂-SnCl₄) is depicted in scheme 2.

As can be seen, an acid–base interaction between Fe₄O₄@SiO₂-SnCl₄ and oxygen in carbonyl bond forms corresponding Knoevenagel product (I) and enamine (II). In the following, Michael addition is occurred between enamine and Knoevenagel product for the formation of an open chain intermediate (III). The dipolar transition state is undergone cyclodehydration to furnish the desired product. Moreover, reaction in heterogeneous systems which proceeds via ionic intermediate is influenced predominantly through the mechanical effects of cavitation.

Table 3 Synthesis of 1,4-dihydropyridine derivatives under reflux conditions and sonication (methods I and II)
<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>1,3-dicarbonyls</th>
<th>Time(min) / Yield (%)</th>
<th>M. P. (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Product</td>
<td>Method I (Δ)</td>
<td>Method II (US)</td>
</tr>
<tr>
<td>1</td>
<td>C₆H₅</td>
<td>Ethyl acetoacetate</td>
<td>25 / 91</td>
<td>6 / 96</td>
</tr>
<tr>
<td>2</td>
<td>4-MeOC₆H₄</td>
<td>Ethyl acetoacetate</td>
<td>18 / 89</td>
<td>6 / 92</td>
</tr>
<tr>
<td>3</td>
<td>4-ClC₆H₄</td>
<td>Ethyl acetoacetate</td>
<td>23 / 95</td>
<td>5 / 96</td>
</tr>
<tr>
<td>4</td>
<td>4-NO₂C₆H₄</td>
<td>Ethyl acetoacetate</td>
<td>20 / 92</td>
<td>4 / 97</td>
</tr>
<tr>
<td>5</td>
<td>C₆H₅</td>
<td>Dimedone</td>
<td>22 / 93</td>
<td>4 / 96</td>
</tr>
<tr>
<td>6</td>
<td>4-MeOC₆H₄</td>
<td>Dimedone</td>
<td>12 / 94</td>
<td>4 / 93</td>
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<tr>
<td>7</td>
<td>4-ClC₆H₄</td>
<td>Dimedone</td>
<td>15 / 93</td>
<td>3 / 97</td>
</tr>
<tr>
<td>8</td>
<td>4-NO₂C₆H₄</td>
<td>Dimedone</td>
<td>15 / 95</td>
<td>3 / 98</td>
</tr>
<tr>
<td>9</td>
<td>C₆H₅</td>
<td>Ethyl acetoacetate</td>
<td>14 / 95</td>
<td>5 / 98</td>
</tr>
<tr>
<td>10</td>
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<td>Ethyl acetoacetate</td>
<td>15 / 90</td>
<td>5 / 94</td>
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<td>11</td>
<td>4-ClC₆H₄</td>
<td>Ethyl acetoacetate</td>
<td>18 / 96</td>
<td>4 / 96</td>
</tr>
<tr>
<td>12</td>
<td>4-NO₂C₆H₄</td>
<td>Ethyl acetoacetate</td>
<td>18 / 95</td>
<td>3 / 98</td>
</tr>
</tbody>
</table>

*Isolated yields, arylaldehyde (1 mmol), 1,3-dicarbonyl compounds (2 mmol), ammonium acetate (1.5 mmol) in ethanol (5 mL).*  
²Fe₃O₄/SiO₂-SnCl₄(25mg).  
³Fe₃O₄/SiO₂-SnCl₄(18mg).
Consequently, it is essential for the solid acid to maintain strong acidity even after recycling and the most important benefits for commercial applications. Thus, after the completion of the reaction, the catalyst was separated by an external magnet. The recovered catalyst was washed with chloroform (30 mL) and dried at room temperature without further purification to use for the next run in current reaction under identical condition. It was found that the catalyst could be reused for five times without any appreciable loss of its activity (Figure 9).

The XRD of the recovered magnetic nanocatalyst was shown in figure 10 and so there is no considerable change in its magnetic phase. The leaching of catalyst also be examined. Any leaching of catalyst was not observed in this protocol. Therefore, the nanocatalyst is stable during synthesis of 1,4-dihydropyridine under ultrasound irradiation.

**Conclusions**

In conclusion, a convenient and efficient method for the synthesis of 1,4-dihydropyridine derivatives in the presence of Fe₃O₄@SiO₂–SnCl₄ as a novel heterogeneous solid acid catalyst has been developed through ultrasound irradiation. This reaction under ultrasound irradiation not only gave excellent yield of products with lesser reaction time but it also required mild reaction conditions and exhibited operational simplicity. In addition, low cost, availability, recyclability and low toxicity of the catalyst make this methodology a valid contribution to the existing processes in the field of one-pot multicomponent Hantzsch reaction.

**Acknowledgements**

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**Notes and references**

SnCl$_4$-functionalized nano-Fe$_3$O$_4$ encapsulated-silica particles as a novel heterogeneous solid acid for synthesis of 1,4-dihydropyridine derivatives

Abdolhamid Bamoniri*, Sara Fouladgar

*Department of Organic Chemistry, Faculty of Chemistry, University of Kashan, Kashan, 8731751167, Iran

E-mail: bamoniri@kashanu.ac.ir

A simple and general synthetic method for the synthesis of 1,4-dihydropyridines via three- or four-component condensation of aldehydes, 1,3-dicarbonyl compounds, and ammonium acetate under ultrasonic irradiation were developed by using Fe$_3$O$_4$@SiO$_2$-SnCl$_4$ as an efficient catalyst.