



# Silica aerogel-iron oxide nanocomposites: recoverable catalysts in conjugate additions and in the Biginelli reaction

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**Abstract**—Ferrihydrite silica aerogels containing 11–13% iron and a surface area of 500–600 m<sup>2</sup>/g are catalysts for the title reactions. They are recovered and reused without loss of activity. © 2003 Elsevier Science Ltd. All rights reserved.

## 1. Introduction

Heterogeneous catalysis dominates the industrial scenery mainly due to the facility of recovery and reuse of solid insoluble catalysts.<sup>1</sup> The comparison between heterogeneous and homogeneous catalysis has been deeply discussed.<sup>2</sup> Transition-metal containing catalytic active sites should be anchored to both chemically stable and physically robust frameworks in order to secure recovery without detriment of catalytic properties. Silica gel and silicate-based supports fulfil both conditions.<sup>3–5</sup> Another crucial point is the accessibility of reagents to the active sites. This requires either the active sites to be at the surface of the support or materials of high specific surface and porosity, and aerogels offer these advantages.<sup>6</sup> Some of us have prepared and studied silica aerogels containing iron oxide nanoparticles.<sup>7a,b</sup> Nanoparticles of iron oxide were grown inside the silica aerogel pores by wet chemistry during sol-gel step. They are accessible because of the high open porosity and the aerogel acts as supporter of the active catalyst. The iron oxide particles are round shaped and the average particle size diameter is of 3 nm. Depending on the synthesis conditions as well as on further thermal treatment of the composite aerogels, different phases for the iron oxide have been obtained: maghemite, magnetite, hematite or ferrihydrite.<sup>7</sup>

In order to analyse the catalytic activity of iron-containing aerogels, the ferrihydrite phase was selected as the guest particles due to the known catalytic activity of ferrihydrite.<sup>8</sup> Few references deal with the use of iron aerogels in catalysis in gas phase<sup>9</sup> or in supercritical CO<sub>2</sub>.<sup>10,11</sup> To the best of our

knowledge ferrihydrite silica aerogels have not been used in heterogeneous solid–liquid catalysis.

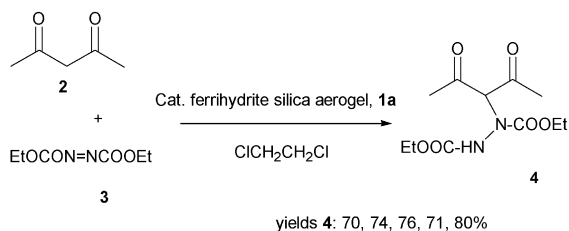
We present our results<sup>12</sup> on the use of nanoparticles of ferrihydrite anchored in a silica aerogel, **1**, having a high specific surface and high porosity, in the conjugate addition of pentane-2,4-dione **2** to diethyl diazenedicarboxylate **3** and in the Biginelli reaction.

## 2. Results

The conjugate addition of  $\beta$ -dicarbonyl compounds to azodiester **3** is an example of electrophilic amination which has been performed before under nickel(II) and ruthenium(II) catalysis.<sup>13</sup> Others have used iron(III) chloride as a catalyst in these reactions.<sup>14</sup> In all cases but one<sup>13c</sup> catalysts were not recovered. We have now performed the reaction of diketone **2** and **3** five consecutive times with the same batch of aerogel **1a** in refluxing 1,2-dichloroethane (Scheme 1). The yields of pure **4** after recrystallization were 70, 74, 76, 71, and 80%. Analysis of the reaction crude indicates a leaching of 3% of the iron present in the aerogel. In the case of ethyl acetoacetate, a complete consumption of the nucleophile was observed but the adduct could not be properly isolated.

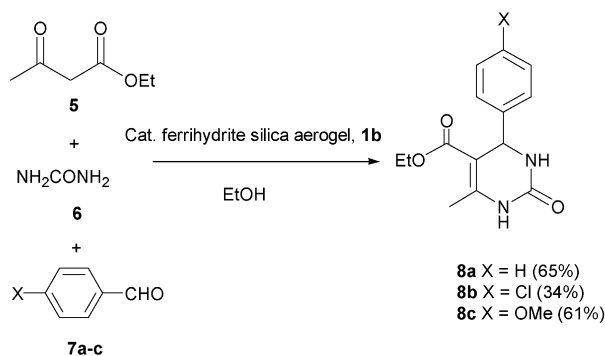
The Biginelli reaction<sup>15</sup> is an old three component condensation reaction which recently has drawn the attention of the chemical community because the resulting 4-aryl-3,4-dihydropyrimidin-2(1*H*)-ones are antihypertensive agents.<sup>16</sup> The Biginelli reaction is catalysed by different Lewis acids, including iron(III) chloride.<sup>17</sup> Now we have found that the three component reaction can be carried out in refluxing ethanol in the presence of iron-containing

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Scheme 1.

aerogel **1b**. We performed three consecutive albeit not identical reactions with the same batch of **1b**. Indeed, aldehyde **7** was varied in each reaction to afford three different 4-aryl-3,4-dihydropyrimidin-2(1*H*)-ones, **8a–c**, in this order in 65, 34, and 61% unoptimised yields (Scheme 2).



Scheme 2.

### 3. Conclusion

In summary, iron(III)-containing silica aerogels are prepared and used as efficient catalysts for condensation reactions. The aerogels are recovered and reused without decrease of activity.

## 4. Experimental

### 4.1. Preparation and characterization of ferrihydrite silica aerogel (**1**)

$\text{Fe}(\text{NO}_3)_3 \cdot 9\text{H}_2\text{O}$  (7.3 g, 0.018 mol) was dissolved in ethanol (12 mL). Then, tetramethoxysilane (20 mL, 0.09 mol) was added drop-wise while stirring. After 20 min of continuous stirring the solution was kept at 40°C. The resulting sol took a darker colour and gellified after 9 days (gel precursor of **1a**). Another batch was prepared with triple amount of reactants and gellified after 11 days (gel precursor of **1b**). Supercritical drying of the gels was performed at supercritical conditions of ethanol ( $T=516$  K, pressure=100–140 bar). The complete process taking 8 h. They presented the following analyses. Compound **1a**: C, 8.99 and 8.92%; H, 1.29 and 1.25%; Fe, 11.8 and 11.2%. Compound **1b**: C, 6.91 and 6.97; H, 0.95 and 0.93; Fe, 12.9 and 13.0 (carbon comes from non-hydrolysed ethers). Iron has been determined by atomic absorption spectrophotometry. Bulk densities: 0.65 g/mL (for **1a**) and 0.64 g/mL (for **1b**); BET surface area: 603 m<sup>2</sup>/g (for **1a**) and 511 m<sup>2</sup>/g (for **1b**).

X-Ray diffractogram of **1b** shows a broad peak centred at 22° of 2θ, which is typical of silica aerogels (Fig. 1). The remaining peaks are also broad and their position cannot be established with high precision. They could correspond to different iron oxide phases, except the peak located at 45.5°. This one is characteristic of the ferrihydrite phase. X-Ray diffractograms of ferrihydrites largely depend on the sample's crystallinity, but those ferrihydrites showing the whole set of peaks are usually known as '6-line ferrihydrite'.<sup>18</sup> The crystalline structure can be described as hexagonal close-packed layers of O<sup>2-</sup>, OH<sup>-</sup> and H<sub>2</sub>O with the Fe(III) occupying octahedral positions, the structure is identical to that of hematite but in the case of hematite, the hexagonal layers are only of O<sup>2-</sup> and there are no-vacancies.

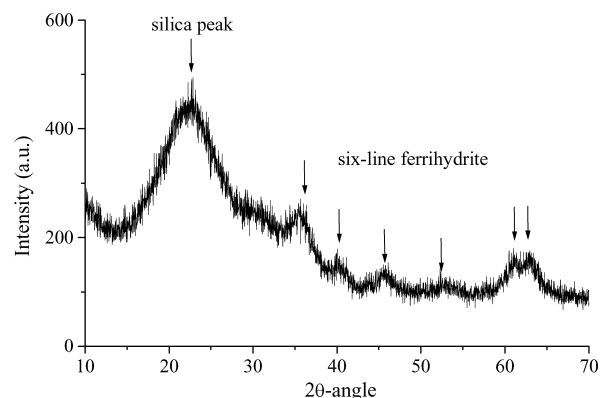


Figure 1.

Mössbauer spectrum (Fig. 2) at 300 K shows a single doublet characteristic of paramagnetic iron sites. At 70 K the magnetic ordering appears. At 4.2 K the spectrum is totally split in six broad lines. The hyperfine parameters correspond to those of ferrihydrite.<sup>19</sup> Mössbauer measurements were also performed at 10 K and under 6 T magnetic field,<sup>7b</sup> hyperfine field distribution agrees with the supermagnetic behaviour of ferrihydrite.

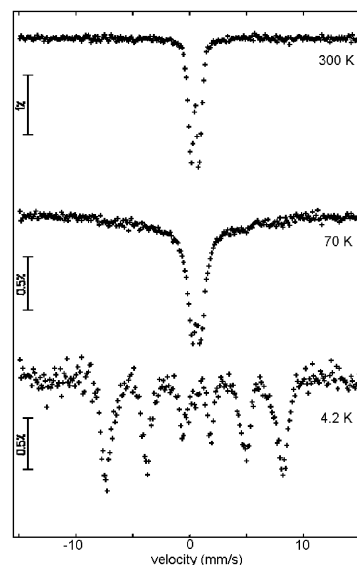


Figure 2.

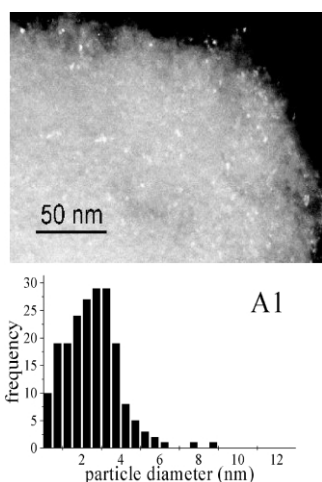


Figure 3.

Dark field TEM image of **1a** (Fig. 3) is the most useful to visualize the iron oxide particles, since those are more crystalline than the silica aerogel matrix then resulting in a brighter contrast. The particles are round shaped, homogeneously distributed and with sizes ranging from 1 to 5 nm, few larger particles having sizes between 6 and 10 nm are also observed. The particle distribution histogram is also shown and the average particle size is of 3 nm of diameter.

**4.1.1. Preparation of 3-[N,N'-bis(ethoxycarbonyl)hydrazino]-2,4-pentane-2,4-dione (4).** A solution of pentane-2,4-dione **2** (1.2 g, 11.6 mmol) and diethyl azodicarboxylate **3** (1.0 g, 5.7 mmol) in 1,2-dichloroethane (30 mL) was refluxed for 72 h under mechanical stirring in the presence of iron-containing aerogel **1a** (0.1 g, 0.21 mmol of iron). Then the solution was decanted and the aerogel washed several times with 1,2-dichloroethane never permitting it to dry. The recovered aerogel was used in the following preparation of **4**. The combined solvent extracts were evaporated and the residue was recrystallized from toluene to afford pure **4** (1.10 g, 70%), mp 122–125°C (lit.<sup>13c</sup> mp 122–125°C): IR (KBr) 3263, 2985, 1760, 1698, 1244 cm<sup>-1</sup>. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 250 MHz) δ major keto tautomer: 1.29 (t, *J*=7.3 Hz, 6H), 2.23 (s, 6H), 4.22 (q, *J*=7.3 Hz, 4H), 6.79 (s, 1H); minor enol tautomer: 1.29 (t, *J*=7.3 Hz, 6H), 2.17 (s, 6H), 4.22 (q, *J*=7.3 Hz, 4H), 16.02 (s, 1H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 62.5 MHz) δ tautomeric mixture 14.4, 14.5, 22.1, 62.3, 63.5, 63.7, 117.9, 155.7, 155.8, 156.3, 191.9. MS (*m/z*, %): 274 (5) [M<sup>+</sup>], 232 (7), 159 (10), 43 (100).

**4.1.2. Preparation of 5-(ethoxycarbonyl)-6-methyl-4-phenyl-3,4-dihydropyrimidin-2(1H)-one (8a): general procedure.** A solution of urea **6** (4.55 g, 75 mmol) and benzaldehyde **7b** (5.1 mL, 50 mmol) in ethanol (15 mL) was added into a suspension of iron-containing aerogel **1b** (1.77 g, 4.0 mmol of iron) in ethyl acetoacetate **5** (8 mL, 62.3 mmol). The mixture was refluxed for 84 h under mechanical stirring. After cooling the solution was decanted and the aerogel was washed with ethanol several times never permitting it to dry. The recovered aerogel was used in the following Biginelli reaction. The combined ethanol extracts were evaporated to afford a residue which was recrystallized from ethanol to afford **8a** (7.92 g, 65%), mp 204–205°C (lit.<sup>20</sup> mp 202–204°C): IR (KBr) 3234, 3110,

2976, 1724, 1695, 1647, 1219, 1085 cm<sup>-1</sup>; <sup>1</sup>H NMR (*d*<sub>6</sub>-DMSO, 250 MHz) δ 1.09 (t, *J*=7.0 Hz, 3H), 2.24 (s, 3H), 3.99 (q, *J*=7.0 Hz, 2H), 5.14 (d, *J*=3.2 Hz, 1H), 7.22–7.32 (m, 5H), 7.73 (s, 1H), 9.19 (s, 1H). <sup>13</sup>C NMR (*d*<sub>6</sub>-DMSO, 62.5 MHz) δ 14.2, 17.9, 54.1, 59.3, 99.4, 126.4 (2C), 127.4, 128.5 (2C), 145.0, 148.5, 152.3, 165.5.

#### 4.1.3. Preparation of 5-(ethoxycarbonyl)-6-methyl-4-(4-chlorophenyl)-3,4-dihydropyrimidin-2(1H)-one (8b).

The title compound **8b** was prepared following the same procedure as for **8a**. Urea (4.2 g, 70 mmol), *p*-chlorobenzaldehyde (7 g, 50 mmol) and ethyl acetoacetate (8 mL, 62.3 mmol) were added to the recovered aerogel in 15 mL of EtOH. When the reaction was finished the aerogel was washed several times with hot ethanol and with hot tetrahydrofuran. The recovered aerogel was used in the following Biginelli reaction. The combined extracts were evaporated and the residue was recrystallized in tetrahydrofuran to afford **8b** (4.7 g, 34%), mp 214°C (lit.<sup>20</sup> mp 210–212°C): IR (KBr) 3234, 3110, 2966, 1714, 1700, 1647, 1219, 1085 cm<sup>-1</sup>; <sup>1</sup>H NMR (*d*<sub>6</sub>-DMSO, 250 MHz) δ 1.10 (t, *J*=7.2 Hz, 3H), 2.24 (s, 3H), 3.98 (q, *J*=7.2 Hz, 2H), 5.13 (d, *J*=3.2 Hz, 1H), 7.24 (d, *J*=8.3 Hz, 2H), 7.39 (d, *J*=8.3 Hz, 2H), 7.78 (s, 1H), 9.25 (s, 1H). <sup>13</sup>C NMR (*d*<sub>6</sub>-DMSO, 62.5 MHz) δ 14.9, 18.6, 54.3, 60.1, 99.7, 129.02 (2C), 129.2 (2C), 132.6, 144.6, 149.5, 152.7, 166.1.

#### 4.1.4. Preparation of 5-(ethoxycarbonyl)-6-methyl-4-(4-methoxyphenyl)-3,4-dihydropyrimidin-2(1H)-one (8c).

The title compound **8c** was prepared following the same procedure as for **8a**. Urea (4.5 g, 75 mmol), *p*-methoxybenzaldehyde (6 mL, 50 mmol) and ethyl acetoacetate (6.4 mL, 50 mmol) were added to the recovered aerogel in 15 mL of EtOH. When the reaction was finished the aerogel was washed several times with hot ethanol and with hot tetrahydrofuran. The recovered aerogel was used in the following Biginelli reaction. The combined extracts were evaporated and the residue was recrystallized in tetrahydrofuran to afford **8c** (8.9 g, 61%), mp 204–205°C (lit.<sup>20</sup> mp 191–193°C): IR (KBr) 3234, 3100, 2947, 1723, 1704, 1647, 1223, 1090 cm<sup>-1</sup>; <sup>1</sup>H NMR (*d*<sub>6</sub>-DMSO, 250 MHz) δ 1.10 (t, *J*=7.2 Hz, 3H), 2.24 (s, 3H), 3.72 (s, 3H), 3.98 (q, *J*=7.2 Hz, 2H), 5.09 (d, *J*=1.0 Hz, 1H), 6.88 (d, *J*=8.6 Hz, 2H), 7.14 (d, *J*=8.6 Hz, 2H), 7.67 (s, 1H), 9.16 (s, 1H). <sup>13</sup>C NMR (*d*<sub>6</sub>-DMSO, 62.5 MHz) δ 14.9, 18.6, 54.2, 55.9, 60.0, 100.4, 114.54, 128.21 (2C), 137.9 (2C), 148.8, 152.9, 159.29, 166.1.

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