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Silver functionalized on hydroxyapatite-core-shell magnetic γ-Fe₂O₃: An enviromentaly and readily recyclable nanatalyst for the one-pot synthesis of 14H-dibenzo[a,j]xanthenes derivatives

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ABSTRACT

An efficient and simple procedure for the preparation of silver functionalized on hydroxyapatite-core-shell magnetic γ-Fe₂O₃ nanoparticles (γ-Fe₂O₃@HAp-Ag) as an enviromentaly efficient magnetically recoverable and reusable catalyst is described, and it is used for the one-pot synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes via a cost-effective and atom-economical procedure from substituted benzaldehydes and β-naphthol under solvent-free conditions at 60 °C. The attractiveness of this protocol lies in its green approach in that the catalyst is easily recoverable using an external magnet, which makes the process economical.
Graphical Abstract

Ag immobilized on hydroxyapatite-core-shell \( \gamma \)-Fe\(_2\)O\(_3\) nanoparticles

- High yields of product
- Short reaction time
- Low catalyst loadings
- Wide substrate scope
- Green medium

**Introduction**

Xanthenes and Benzoxanthenes are an important category of organic compounds which recently received much attention of organic and medical chemists due to of their wide range of therapeutic and biological properties such as antifungal [1], antibacterial [2] and anti-inflammatory activities [3]. Furthermore, these compounds in laser technologies [4], fluorescent material of visualization of biomolecules [5] and have been widely used as dyes [6]. Many methods using the synthesis of xanthenes and benzoxanthenes have been reported in the literature, including cyclodehydration [7–10], cyclization of polycyclic aryl triflate esters [11], trapping of benzynes by phenols [12], Intermolecular phenyl carbonyl coupling reactions of benzaldehydes and acetophenones [13] and cyclocondensation between 2-hydroxy aromatic aldehydes and 2-tetralone [14]. The synthesis process of the xanthenes has been improved by condensing of aldehydes and 2-naphthol in the presence of an acid catalyst such as ZnO-NPs [15], selectfluor\textsuperscript{TM} [16], sulfamic acid [17], imidazol-1-yl-acetic acid [18], succinimide-\( N \)-sulfonic acid [19], montmorillonite K10 [20], sulfonic acid
functionalized imidazolium salts (SAFIS) [21], Ferric Hydrogensulfate [22], 2,6-Pyridinedicarboxylic acid [23], γ-Fe₂O₃@HAp-Fe²⁺ [24] and silica-bonded imidazolium-sulfonic acid chloride (SBISAC) [25]. Furthermore, most of the reported methods for the synthesis of the title compounds are associated with one or more of the following drawbacks: low yields, long reaction times, the use of large amount of catalyst, and the use of expensive, non-available or toxic catalysts, tedious work-up procedure, performances under certain special conditions, and poor agreement with the green chemistry protocols.

Fe²⁺, Ni²⁺, and Ag functionalized on hydroxyapatite-core-shell γ-Fe₂O₃ (γ-Fe₂O₃@HAp-Fe²⁺, γ-Fe₂O₃@HAp-Ni²⁺, and γ-Fe₂O₃@HAp-Ag) can be easily prepared. Also, various transition metals such as Ni, Fe, Cd, Zn and Ag are know and versatile among catalysts for organic transformations. γ-Fe₂O₃@HAp-Fe²⁺, γ-Fe₂O₃@HAp-Ni²⁺, and γ-Fe₂O₃@HAp-Ag were used in various organic transformations such as synthesis of pyrano[2,3-d] pyrimidinone derivative [26], chemoselective synthesis of 1,1-diacetate [27], synthesis of the dihydropyrimidinones derivatives [28], regioselective azidolysis of epoxides [29], synthesis of benzimidazoles and benzoazazole derivatives [30], synthesis of tetrahydropyridines [31], and chemoselective oxidation of sulfides to sulfoxides [32].

Having the above subjects in mind, and also in continuation of ongoing program to prepare magnetic nanoparticles or solid acid catalysts and apply them as catalysts in organic synthesis [33, 34], we report a synthesis of new core-shell MNPs having a spherical shape. This γ-Fe₂O₃@HAp-Ag NPs is used as an enviromentaly efficient magnetically recoverable and reusable catalyst for the synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes under solvent-free conditions at 60 °C (Scheme 1).

**Experimental**

**Materials and methods**

Reagents and solvents were purchased from Merck, Fluka or Aldrich companies. Melting points were determined in capillary tubes in an electro-thermal C14500 apparatus. The progress of the reaction and the purity of compounds were monitored by TLC using analytical silica gel plates (Merck 60 F250). All known compounds were identified by comparison of their melting points and ¹H NMR and ¹³C NMR data with those of authentic samples. The ¹H NMR (250 MHz) and ¹³C NMR (62.9 MHz) spectra were acquired on a Bruker Avance DPX-250, FT NMR spectrometer. IR spectra were recorded on a Frontier FT-IR (Perkin Elmer) spectrometer using KBr disks. The phases present in the magnetic materials were analyzed using powder XRD on a Philips (Holland) spectrometer, model X0 Pert with X' Pert with CuKα radiation (λ = 1.5401 Å), with the X-ray generator operated at 40 kV and 30 mA. Diffraction patterns were collected from 2θ = 20°–70°.
Preparation of Ag functionalized on hydroxyapatite-core-shell magnetic γ-Fe₂O₃

In this study, hydroxyapatite-core-shell γ-Fe₂O₃ NPs was prepared according to the literature procedure. Then hydroxyapatite-core-shell γ-Fe₂O₃ NPs (0.6 g) was introduced into 150 mL aqueous solution of silver nitrate (6.7×10⁻³ M) and stirred at room temperature for 6 h. The resulting slurry was filtered, washed, and dried at room temperature in vacuum. Next, the γ-Fe₂O₃@HAp NPs containing Ag was treated with an aqueous solution of KBH₄ (5.0×10⁻² M) for 1 h at room temperature. Again, the slurry was filtered, washed, and dried at room temperature in vacuum, giving Ag functionalized on Fe₂O₃@HAp NPs (Scheme 2). The mean size and the surface morphology of the Ag functionalized on hydroxyapatite-core-shell magnetic γ-Fe₂O₃ were characterized by TEM, SEM, VSM, XRD and FT-IR techniques [35].

Typical procedure for the preparation of 14-aryl-14H-dibenzo[a,j]xanthenes

To a mixture of aldehyde (1 mmol) and 2-naphthol (2 mmol), γ-Fe₂O₃@HAp-Ag NPs (15 mg) was added and the mixture was inserted in an oil bath and heated at 60 °C for the appropriate time.
Completion of the reaction was indicated by TLC. After completion of the reaction, the reaction mixture was cooled to room temperature. The reaction mixture was dissolved in ethylacetate and the catalyst was separated out by simple filtration. Excess of solvent was removed under reduced pressure and the crude product was recrystallized with ethanol to afford the pure product in 86–95% yield.

**The pH measurement of the silver immobilized on hydroxyapatite-core-shell γ-Fe₂O₃**

The determination of pH_{pzc} of sorbent was carried out by pH titration procedure. 50 cm³ of NaCl 0.01 M solution was poured into several erlenmeyer flasks. The pH of solution within each flask was adjusted to a value between 2 and 9 by addition of HCl 0.1 M or NaOH 0.1 M solution. Then, 15 mg of catalyst was added to the flasks and the final pH was measured after 24 h. The pH_{pzc} is defined as the point where the curve pH_{final} vs. pH_{initial} crosses the line pH_{final} = pH_{initial}. The point of zero charge of the γ-Fe₂O₃@HAp-Ni^{2+} was 6.8.

**Results and discussion**

**Characterization of catalyst**

In recent years, the use of magnetic nanoparticles has many advantages in organic synthesis. For example, high efficiency and selectivity, operational simplicity, environmental compatibility, nontoxic, reusability, low cost, ease of isolation and benefit for industry as well as environment. In this study, the structure of the γ-Fe₂O₃@HAp-Ag NPs was characterized by TEM, SEM, VSM, XRD and FT-IR techniques [35].

Silver functionalized on hydroxyapatite-core-shell magnetic γ-Fe₂O₃ nanoparticles (γ-Fe₂O₃@HAp-Ag) as an environmentaly efficient magnetically recoverable and reusable catalyst was reported by Abbasi et al. and it was used for the 14-aryl-14H-dibenzo[a,j]xanthenes under solvent-free condition.

The scanning electronic microscopy (SEM) image of Ag functionalized on hydroxyapatite-core-shell magnetic γ-Fe₂O₃ nanoparticles is given in Figure 1. As can be clearly seen, the SEM of the γ-Fe₂O₃@HAp-Ag NPs showed that the particles of the catalyst were observed in nanosize.

The transmission electronic microscopy (TEM) image of Ag functionalized on hydroxyapatite-core-shell magnetic γ-Fe₂O₃ nanoparticles is given in Figure 2. As can be clearly seen, the TEM micrograph of the γ-Fe₂O₃@HAp-Ag NPs clearly proved that the particles were in nanosize. These nanoparticles consist of relatively small, nearly spherical particles, which is nicely consistent with the value obtained from XRD measurements. Also, diameters of approximately 30 nm for the catalyst.
**Scheme 2.** Schematic representation of the synthesis of $\gamma$-Fe$_2$O$_3$@HAp-Ag NP

**Figure 1.** SEM images of $\gamma$-Fe$_2$O$_3$@HAp-Ag NPs
As shown in Figure 3, X-ray diffraction (XRD) patterns of the synthesized Ag supported on hydroxyapatite-core-shell magnetic γ-Fe₂O₃ nanoparticles display several relatively strong reflection peaks in the 2h region of 20°–70°. Figure 3, shows the XRD for Ag functionalized on hydroxyapatite-core-shell magnetic γ-Fe₂O₃ nanoparticles. The crystallinity of the prepared γ-Fe₂O₃@HAp NPs was confirmed by the reflections observed at 2θ values of 31.2, 32.31, 33.12, 34.32, 45.87 and 49.19. It is also found the metallic Ag phase at 2θ of 32.19 and 45.32 are found over Ag doped catalysts.

In another investigation, magnetic measurements of Ag functionalized on hydroxyapatite-core-shell magnetic γ-Fe₂O₃ nanoparticles was performed at room temperature using a vibrating sample magnetometer (VSM). The magnetization curve in Figure 4 gives a saturation magnetization value of 13.21 emu/g.

The structural properties of synthesized γ-Fe₂O₃@HAp-Ag MNPs a), HAp supported with Fe₃O₄ MNPs, b) HAp, C) were analyzed by FT-IR spectra (Figure 5). The band at 3570 cm⁻¹ corresponds to O–H Stretching in the hydroxyapatite structure. The bands at 1095 cm⁻¹, 1025, and 958 corresponds to asymmetric and symmetric stretching vibration of the phosphate group (PO₄³⁻). The peak located at ~ 2344 cm⁻¹ is due to asymmetric stretching C–H. Stretching modes of C–O and C=O are observed at ~ 1388 cm⁻¹ and 1521 cm⁻¹. On doping, stronger and wider absorption bands are observed in the region ~ 1170–698 cm⁻¹due to the organic capping of silver.

*Study of the efficiency of γ-Fe₂O₃@HAp-Ag NPs in the synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes*
Silver functionalized on hydroxyapatite-core-shell ...

Figure 3. XRD pattern of a) γ-Fe$_2$O$_3$@HAp and b) γ-Fe$_2$O$_3$@HAp-Ag NPs

Figure 4. Magnetization curve of γ-Fe$_2$O$_3$@HAp-Ag NPs
Figure 5. FT-IR spectra of a) γ-Fe$_2$O$_3$@HAp-Ag NPs, b) γ-Fe$_2$O$_3$@HAp, and c) HAp

For this purpose, as a model reaction, the condensation of benzaldehyde (1 mmol) and β-naphthol (2 mmol) was tested using different amounts of γ-Fe$_2$O$_3$@HAp-Ag NPs at range of 60–100 °C in the absence of solvent (Table 1). As it is shown in Table 1, 15 mg of the catalyst was sufficient to promote the reaction efficiently at 60 °C, and give the product in excellent yield and in short reaction time (Table 1, entry 4).

To compare the efficiency of solution conditions versus the solvent-free procedure, the reaction between benzaldehyde (1 mmol) with β-naphthol (2 mmol) using γ-Fe$_2$O$_3$@HAp-Ag NPs (15 mg) was checked in some solvents (5 mL) under reflux conditions. The results are summarized in Table 2. As this Table indicates, low yields of the product were obtained in solution conditions even after elongated reaction times.

To assess the efficiency and the scope of γ-Fe$_2$O$_3$@HAp-Ag NPs in the preparation of 14-aryl-14H-dibenzo[a,j]xanthenes, different aldehydes were reacted with β-naphthol under the optimal reaction conditions; the respective results are displayed in Table 3. As it can be seen in Table 3, both aromatic aldehydes containing electron-donating as well as electron-withdrawing groups were utilized in the present case to form corresponding 14-aryl-14H-dibenzo[a,j]xanthenes in high yields and short
reaction time. However, the reaction conducted by α-naphthol instead of β-naphthol did not afford any product.

**Table 1.** Effect of the catalyst amount and temperature on the reaction between β-naphthol (1 mmol) with β-naphthol (2 mmol) under solvent-free conditions

<table>
<thead>
<tr>
<th>Entry</th>
<th>Loading catalyst (mg)</th>
<th>Temperature (°C)</th>
<th>Time (min)</th>
<th>Yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Catalyst-free</td>
<td>-</td>
<td>60</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>5</td>
<td>60</td>
<td>50</td>
<td>78</td>
</tr>
<tr>
<td>3</td>
<td>10</td>
<td>60</td>
<td>30</td>
<td>81</td>
</tr>
<tr>
<td>4</td>
<td>15</td>
<td>60</td>
<td>15</td>
<td>95</td>
</tr>
<tr>
<td>5</td>
<td>20</td>
<td>60</td>
<td>20</td>
<td>95</td>
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<tr>
<td>6</td>
<td>25</td>
<td>60</td>
<td>20</td>
<td>91</td>
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<td>80</td>
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<td>94</td>
</tr>
<tr>
<td>8</td>
<td>15</td>
<td>90</td>
<td>15</td>
<td>94</td>
</tr>
<tr>
<td>9</td>
<td>15</td>
<td>100</td>
<td>18</td>
<td>92</td>
</tr>
</tbody>
</table>

<sup>a</sup>Yield of isolated products

**Table 2.** Effect of various solvents on the reaction of benzaldehyde (1 mmol) with β-naphthol (2 mmol), in the presence of γ-Fe₂O₃@HAp-Ag NPs (15 mg)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Time (min)</th>
<th>Yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>EtOH</td>
<td>45</td>
<td>53</td>
</tr>
<tr>
<td>2</td>
<td>CH₂Cl₂</td>
<td>45</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>EtOAc</td>
<td>45</td>
<td>50</td>
</tr>
<tr>
<td>4</td>
<td>CHCl₃</td>
<td>45</td>
<td>50</td>
</tr>
<tr>
<td>5</td>
<td>H₂O</td>
<td>45</td>
<td>45</td>
</tr>
</tbody>
</table>

<sup>a</sup>Yield of isolated products

**Table 3.** Conversion of aldehyde to xanthene using γ-Fe₂O₃@HAp-Ag NPs under solvent-free condition

<table>
<thead>
<tr>
<th>Entry</th>
<th>Product</th>
<th>Time (min)</th>
<th>Yield (%)&lt;sup&gt;a&lt;/sup&gt;</th>
<th>M.p. (°C) (Lit.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image" alt="Chemical Structure" /></td>
<td>15</td>
<td>95</td>
<td>189-190 191-193 [24]</td>
</tr>
</tbody>
</table>
2

3

4

5

6

7

12  91  307-308  309-311 [24]

12  94  209-210  210-212 [24]

18  86  258-259  260-262 [24]

17  95  187-189  186-187 [25]

17  92  225-225  226-228 [24]

18  89  204-206  203-205 [24]
Silver functionalized on hydroxyapatite-core-shell ...
In Table 4, our results are compared with the results of any other procedures, for the synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes are described. It is clear that in Table 4 the current method is simpler, more efficient, and less time-consuming for the synthesis of 14-aryl-14H-dibenzo[a,j]xanthene derivatives. The data presented in this table show the comparison between the
promising features of this method in terms of the molar ratio of the catalyst, reaction time and yield of product with those reported in the literature.

The reusability of catalyst is of major importance in green chemistry and also is of major importance for large scale operations and an industrial point of view. Thus the recovery and reusability of γ-Fe$_2$O$_3$@HAp-Ag NPs were investigated. From the magnetic separation and isolation of the MNPs catalyst on reaction completion (The reaction between 2-naphthol with benzaldehyde), the additional possibility to reuse and recycle the MNPs catalyst for various runs was too investigated. Results showed in Figure 6 confirm that the magnetically separable MNPs catalyst could be reused and recycled seven runs without any significant loss of its first catalytic activity. In seven runs, the yields of product were 95%, 94%, 94%, 92%, 90%, 88% and 85%, respectively, which verify that the activity of the catalyst remained unchanged throughout these seven runs.

The suggested mechanism for the γ-Fe$_2$O$_3$@HAp-Ag NPs catalyzed transformation is shown in Scheme 3. According to the mechanism, γ-Fe$_2$O$_3$@HAp-Ag NPs catalyzed the readily in situ formation of 14-aryl-14-H-dibenzo[a,j]xanthenes 9. The an activated aromatic aldehyde 1 reacts with one molecule of 2-naphthol 2 to provide intermediate 3, which can be regarded as a fast Knoevenagel addition. Then the active methylene of the second molecule of 2-naphthol reacted with intermediate 3 via conjugate Michael addition to produce the intermediate 7, which undergoes intramolecular cyclodehydration to give the 14-aryl-14-H-dibenzo[a,j]xanthenes 9.

**Table 4.** Comparison of efficiency of various catalysts in synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst/solvent/temperature</th>
<th>Time (h)</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Cellulose sulfuric acid (0.08 g)/ solvent-free/ 110 °C</td>
<td>1.5–3</td>
<td>81–97</td>
</tr>
<tr>
<td>2</td>
<td>Amberlyst-15 (1 mmol)/ solvent-free/ 125 °C</td>
<td>0.5–2</td>
<td>80–94</td>
</tr>
<tr>
<td>3</td>
<td>Silica sulfuric acid (0.05 g)/ solvent-free/ 80 °C</td>
<td>15–120</td>
<td>80–96</td>
</tr>
<tr>
<td>4</td>
<td>Yb(OTf)$_3$/ [BPy]BF$_3$ (0.01 mmol)/ 110 °C</td>
<td>5–7</td>
<td>80–95</td>
</tr>
<tr>
<td>5</td>
<td>PVPP-BF$_3$/ solvent-free (0.05 g)/ 120 °C</td>
<td>1.5–2</td>
<td>92–98</td>
</tr>
<tr>
<td>6</td>
<td>ZnO-NPs (0.3 mmol)/ solvent-free/ 150 °C</td>
<td>40–80</td>
<td>82–92</td>
</tr>
<tr>
<td>7</td>
<td>p-Toluene sulfonic acid (0.1 equiv)/ CH$_2$Cl$_2$/ reflux</td>
<td>15–24</td>
<td>83–95</td>
</tr>
<tr>
<td>8</td>
<td>p-Toluene sulfonic acid (0.1 equiv)/ solvent-free/ 125 °C</td>
<td>2.5–6</td>
<td>80–96</td>
</tr>
<tr>
<td>9</td>
<td>PFPAT (10 mol%)/ toluene/ 25-30 °C</td>
<td>3–5</td>
<td>85–97</td>
</tr>
<tr>
<td>10</td>
<td>Poly(AMPS-co-AA) (0.04 g)/ solvent-free/ 110 °C</td>
<td>20–30</td>
<td>75–92</td>
</tr>
<tr>
<td>11</td>
<td>γ-Fe$_2$O$_3$@HAp-Ag NPs (15 mg)/ solvent-free/ 60 °C</td>
<td>8–30</td>
<td>86–95</td>
</tr>
</tbody>
</table>

*In minute*
Figure 6. Recoverability of $\gamma$-Fe$_2$O$_3$@HAp-Ag NPs

Scheme 3. The plausible mechanism for the condensation reaction of 2-naphthol with aldehydes catalyzed by the $\gamma$-Fe$_2$O$_3$@HAp-Ag NPs
Conclusion

In summary, this method is an efficient, economical and ‘green’ method for the synthesis of xanthenes under solvent-free condition using γ-Fe₂O₃@HAp-Ag NPs as a newly catalyst prepared reagent. This simple method is significant from both environmental and economical point of views as it creates little waste. The important features of this procedure such as excellent yield, short reaction times, non-toxicity of reagent, eco-friendly, simplicity of reaction and reusability of catalyst are the advantages of the present method. The catalyst is readily available, inexpensive and can conveniently be handled and removed from the reaction mixture. This protocol could serve as a valuable alternative to known reactive systems.

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References

[12]. Knight D.W., Little P.B. Synlett, 1998, 10:1141
[19]. Shirini F., Ghaffari Khaligh N. *Dyes Pigm.*, 2012, **95**:789
[23]. Rezayati S., Mirzajanzadeh E., Seifournia H. *Asian J. Green Chem.*, 2017, **1**:24
[25]. Moosavi-Zare A.R., Zolfigol M.A., Zare M., Zare A., Khakyzadeh V. *Journal Molecular Liquids*, 2015, **211**:373
[28]. Rezaee Nezhad E., Abbasi Z., Sajjadifar S. *Sci. Iran.*, 2015, **22**:903
[33]. Soleiman-Beigi M., Arzehgar Z. *Monatsh Chem.*, 2016, **147**:1759
[34]. Sajjadifar S., Arzehgar Z., Ghayuri A. *J. Chin. Chem. Soc.*, 2018, **65**:205