



Research Note

# Pyridylmethylaminoacetic acid functionalized $\text{Fe}_3\text{O}_4$ magnetic nanorods as an efficient catalyst for the synthesis of 2-aminochromene and 2-aminopyran derivatives

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## KEYWORDS

$\text{Fe}_3\text{O}_4$ ;  
 Magnetic nanorods;  
 Three-component reactions;  
 Chromene;  
 Pyran.

**Abstract.** 2-[(2-PyridylMethyl)Amino]Acetic acid (PMAA) functionalized  $\text{Fe}_3\text{O}_4$  superparamagnetic nanorods efficiently catalyzed three-component reaction of malononitrile, aromatic aldehydes, and phenolic or enolic components, such as  $\alpha$ -naphthol,  $\beta$ -naphthol, dimedone, or kojic acid, to synthesize a variety of chromene or pyran derivatives in good to high yields. PMAA functionalized  $\text{Fe}_3\text{O}_4$  magnetic nanorods were prepared via simple coprecipitation in an aqueous solution of  $\text{Fe}^{2+}$  and  $\text{Fe}^{3+}$  ions using  $\text{NH}_4\text{OH}$  in the presence of glycine, followed by subjecting it to 2-pyridine carbaldehyde and then,  $\text{NaBH}_4$ -mediated reduction of in-situ generated imine. Obtained nanorods were characterized by FT-IR, XRD, TGA, SEM, EDX, TEM, BET, and VSM analysis.

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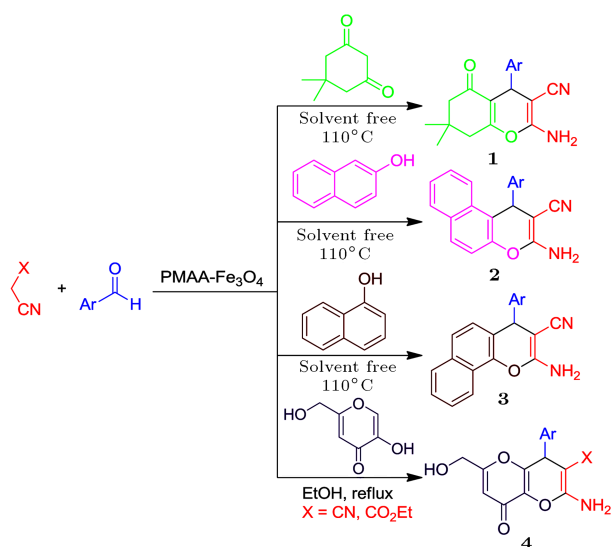
## 1. Introduction

Iron oxide based magnetic nanoparticles have attracted much attention due to their wide range of applications in medicine, such as magnetic separation, especially separation of biomolecules such as DNA, proteins, cells, enzymes, and viruses; tissue repair; magnetic resonance imaging; hyperthermia; drug delivery; molecular diagnostics; and design of biomedical devices [1-6]. Because of easy preparation, functionalization, and separation in using an external magnetic field as well as good dispersion in water and recoverability, iron oxide magnetic nanoparticles have also been widely used as catalyst [7-11]. Therefore, the improvement in the

preparation and functionalization of these nanomaterials is of interest. However, there are some reports for the synthesis of iron oxide based nanomaterials, including coprecipitation of  $\text{Fe}^{2+}$  and  $\text{Fe}^{3+}$  ions with alkaline solution [12,13],  $\text{KNO}_3$  induced oxidation of the ferrous hydroxide gels [14], hydrothermal synthesis [15], microemulsion methods [16], and  $\gamma$ -irradiation [17].

Chromene and pyran cores are broadly found in natural products and pharmaceuticals [18,19] with a wide range of biological activities, such as antimicrobial, antifungal, antiproliferative, antisterility, and anticancer [20-22]. Also, they are vastly used in cosmetics, pigments, and agrochemicals [23,24]. Therefore, the development of new synthetic approaches for these heterocycles by utilizing the synthetic and medicinal chemists is of interest. Three-component reactions of various phenolic or enolic compounds with active methylene and carbonyl compounds were generally reported for construction of these heterocycles, using acidic or basic catalyst, such as  $\text{Et}_3\text{N}$  [25], DBU [26],

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**Scheme 1.** Catalytic activity of PMAA-Fe<sub>3</sub>O<sub>4</sub> in three component synthesis of chromene and pyran derivatives 1-4.

DABCO [27], piperidine [28], InCl<sub>3</sub> [29], nanozeolite clinoptilolite [30], ionic liquids [31], cetyltrimethylammonium bromide [32], nano-Bi<sub>2</sub>O<sub>3</sub>-ZnO [33], Mg/Al hydrotalcite [34], basic alumina [35], Na<sub>2</sub>HPO<sub>4</sub> [36], KF/alumina [37] and poly(4-vinylpyridine) [38], simple grinding [39], etc. However, they suffer from some disadvantages, including complex workup, low yield, expensive and toxic catalyst, and organic solvents.

In continuing our research on nanocatalysts [10,11,40,41] and heterocyclic chemistry [42-44], in this paper, we wish to report the preparation and characterization of Pyridyl Methyl Aminoacetic Acid (PMAA) functionalized Fe<sub>3</sub>O<sub>4</sub> magnetic nanorods (PMAA-Fe<sub>3</sub>O<sub>4</sub>) and their use as an efficient catalyst in the synthesis of chromene and pyran derivatives 1-4 via three-component reaction of enolic or phenolic component, such as dimedone,  $\alpha$ -naphthol,  $\beta$ -naphthol, or kojic acid, with malononitrile and aromatic aldehydes (Scheme 1).

## 2. Experimental

### 2.1. Material and methods

FeCl<sub>3</sub>·6H<sub>2</sub>O, FeCl<sub>2</sub>·4H<sub>2</sub>O, glycine, and all other chemicals were purchased from Merck or Fluka and used without any further purification. Deionized (DI) water was used in all experiments. Win-Bomem spectrometer version 3.04 from Galatic Industries Corporation was used to measure FT-IR spectra as a KBr disc. X-Ray Diffraction (XRD) patterns were measured using a Bruker D8 Advance with CuK ( $\alpha$ ) radiation ( $\lambda = 0.15406$  nm) in the range of  $4^\circ < 2\theta < 70^\circ$ . NETZSDT TG 209 F1 Iris was used for TGA analysis of samples under N<sub>2</sub> atmosphere. Scanning Electron Microscope (SEM) images and EDX analysis were obtained using

a VWGA3 TESCAN (20.0 KV) microscope. A Philips CM120 microscope was used to obtain Transmission Electron Microscopy (TEM) images. The Vibrating Sample Magnetization (VSM) analysis was conducted to study the magnetic properties using Meghnatis Daghigh Kavir Co. vibrating sample magnetometer, Kashan Kavir, Iran, at room temperature. BET analysis was performed using a BELSORP Mini II analyzer.

### 2.2. Synthesis of PMAA-Fe<sub>3</sub>O<sub>4</sub>

To a preheated mixture of FeCl<sub>3</sub>·6H<sub>2</sub>O (4.8 mmol, 1.3 g) and FeCl<sub>2</sub>·4H<sub>2</sub>O (2.4 mmol, 0.48 g) in 20 mL of DI water at 40°C, glycine (6.1 mmol, 0.46 g) was added and the pH was adjusted to 11 using ammonia solution, and it was refluxed for 6 h under N<sub>2</sub> flow. By separation of the obtained precipitate using an external magnetic field and then washing with DI water, and drying in oven at 60°C for 3 h, glycine capped Fe<sub>3</sub>O<sub>4</sub> magnetic nanoparticles were obtained. 0.25 g of glycine capped Fe<sub>3</sub>O<sub>4</sub> magnetic nanoparticles were dispersed in 10 mL EtOH using ultrasonic bath, and then pyridine-2-carbaldehyde (3.74 mmol, 0.4 g) was added and stirred at room temperature for 4 h. After cooling the mixture to 0-4°C using an ice bath, a solution of NaBH<sub>4</sub> (3.65 mmol, 0.138 g) in 5 mL water was added and stirred for 3 h at the same temperature. The obtained PMAA-Fe<sub>3</sub>O<sub>4</sub> was separated using an external magnetic field and thoroughly washed with DI water, and dried in oven at 60°C for 3 h.

### 2.3. General procedure for the synthesis of tetrahydro-4H-chromene-3-carbonitriles 1

PMAA-Fe<sub>3</sub>O<sub>4</sub> (0.020 g) was added to a mixture of aromatic aldehyde (0.5 mmol), malononitrile (0.5 mmol, 0.033 g), and dimedone (0.5 mmol, 0.070 g) and heated at 110°C for 10-25 min. The reaction progress was monitored by TLC using EtOAc/*n*-hexane (3/7) as eluent. After completion of the reaction, the mixture was cooled to room temperature and extracted by acetone, and evaporated to dryness. The obtained solid was recrystallized in hot EtOH to give corresponding benzochromenes in good to high yields. For example:

- 2-Amino-7,7-dimethyl-5-oxo-4-(thiophen-2-yl)-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile:  
FT-IR (KBr):  $\nu = 3382, 3318$  (NH<sub>2</sub>), 3108 (sp<sup>2</sup>C-H), 2964, 2875 (sp<sup>3</sup>C-H), 2199 (C≡N), 1679 (C=O), 1659, 1603 (C=C), 1373 (CH<sub>3</sub>-bending), 1216 (C-O), 1136 (C-N) cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>):  $\delta = 0.98$  (s, 3H, CH<sub>3</sub>), 1.05 (s, 3H, CH<sub>3</sub>), 2.16 (d,  $J = 16.1$  Hz, 1H, CH<sub>2</sub>), 2.31 (d,  $J = 16.2$  Hz, 1H, CH<sub>2</sub>), 2.44 (d,  $J = 17.7$  Hz, 1H, CH<sub>2</sub>), 2.55 (d,  $J = 17.8$  Hz, 1H, CH<sub>2</sub>), 4.53 (s, 1H, CH), 6.86 (d,  $J = 3.2$  Hz, 1H, CH<sub>Ar</sub>), 6.91 (dd,  $J = 3.5, 4.9$  Hz, 1H, CH<sub>Ar</sub>), 7.12 (s, 2H, NH<sub>2</sub>), 7.32 (d,  $J = 5.0$  Hz, 1H, CH<sub>Ar</sub>) ppm.

- *2-Amino-7,7-dimethyl-4-(naphthalene-2-yl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile*: FT-IR (KBr):  $\nu = 3410, 3340$  (NH<sub>2</sub>), 3097 (sp<sup>2</sup>C-H), 2964 (sp<sup>3</sup>C-H), 2187 (C≡N), 1667 (C=O), 1651, 1555 (C=C), 1365 (CH<sub>3</sub>-bending), 1216 (C-O), 1135 (C-N) cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>):  $\delta = 0.97$  (s, 3H, CH<sub>3</sub>), 1.06 (s, 3H, CH<sub>3</sub>), 2.10 (d,  $J = 16.1$  Hz, 1H, CH<sub>2</sub>), 2.27 (d,  $J = 16.2$  Hz, 1H, CH<sub>2</sub>), 2.47-2.57 (m, 2H, CH<sub>2</sub>), 4.37 (s, 1H, CH), 7.05 (s, 2H, NH<sub>2</sub>), 7.29 (d,  $J = 8.5$  Hz, 1H, CH<sub>Ar</sub>), 7.46-7.52 (m, 2H, CH<sub>Ar</sub>), 7.68 (s, 1H, CH<sub>Ar</sub>), 7.84-7.88 (m, 2H, CH<sub>Ar</sub>), 7.89 (d,  $J = 8.0$  Hz, 1H, CH<sub>Ar</sub>) ppm.

#### 2.4. General procedure for the synthesis of benzochromene-2-carbonitrile 2 and benzochromene-3-carbonitriles 3

The reaction was conducted same as above, using  $\alpha$ -naphthol or  $\beta$ -naphthol (0.5 mmol, 0.072 g) instead of dimedone component, for 30-45 min. For example:

- *3-Amino-1-(p-tolyl)-1H-benzof[f]chromene-2-carbonitrile*: FT-IR (KBr):  $\nu = 3422, 3338$  (NH<sub>2</sub>), 3080 (sp<sup>2</sup>C-H), 2965 (sp<sup>3</sup>C-H), 2185 (C≡N), 1639 (C=O), 1591 (C=C), 1406 (CH<sub>3</sub>-bending), 1233 (C-O), 1130 (C-N) cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>):  $\delta = 2.20$  (s, 3H, CH<sub>3</sub>), 5.25 (s, 1H, CH), 6.93 (s, 2H, NH<sub>2</sub>), 7.06 (m, 4H, CH<sub>Ar</sub>), 7.33 (d,  $J = 8.9$  Hz, 1H, CH<sub>Ar</sub>), 7.42-7.44 (m, 2H, CH<sub>Ar</sub>), 7.83 (d,  $J = 7.8$  Hz, 1H, CH<sub>Ar</sub>), 7.90-7.94 (m, 2H, CH<sub>Ar</sub>) ppm.
- *2-Amino-4-(2-chlorophenyl)-4H-benzo[h]chromene-3-carbonitrile*: FT-IR (KBr):  $\nu = 3418, 3328$  (NH<sub>2</sub>), 3070 (sp<sup>2</sup>C-H), 2910 (sp<sup>3</sup>C-H), 2198 (C≡N), 1663 (C=O), 1631, 16.0, 1573 (C=C), 1377, 1257 (C-O), 1183 (C-N) cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>):  $\delta = 5.42$  (s, 1H, CH), 7.01 (d,  $J = 8.5$  Hz, 1H, CH<sub>Ar</sub>), 7.21 (s, 2H, NH<sub>2</sub>), 7.26-7.31 (m, 3H, CH<sub>Ar</sub>), 7.46 (dd,  $J = 8.0, 1.3$  Hz, 1H, CH<sub>Ar</sub>), 7.58-7.61 (m, 2H, CH<sub>Ar</sub>), 7.65 (t,  $J = 7.8$  Hz, 1H, CH<sub>Ar</sub>), 7.90 (d,  $J = 8.0$  Hz, 1H, CH<sub>Ar</sub>), 8.26 (d,  $J = 8.3$  Hz, 1H, CH<sub>Ar</sub>) ppm.

#### 2.5. General procedure for the synthesis of dihydropyrano[3,2-b]pyran-3-carbonitriles 4

To a solution of aromatic aldehyde (0.5 mmol), malononitrile (0.5 mmol, 0.020 g), and kojic acid (0.5 mmol, 0.042 g) in 5 mL EtOH, PMAA-Fe<sub>3</sub>O<sub>4</sub> (0.020 g) was added and heated under reflux conditions for 2-3 h. The reaction progress was monitored by TLC using EtOAc/*n*-hexane (3/7) as eluent. After completion of the reaction, magnetic nanomaterials were isolated from hot reaction solution using an external magnetic field. By cooling the mixture to room temperature, the desired products were crystallized. The obtained

products were filtered and washed with cold EtOH. For example:

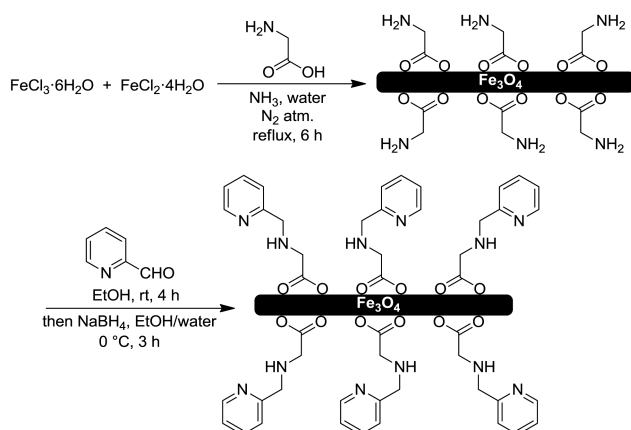
- *2-Amino-6-(hydroxymethyl)-4-(naphthalen-2-yl)-8-oxo-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile*: FT-IR (KBr):  $\nu = 3393$  (O-H), 3299, 3193 (NH<sub>2</sub>), 3061 (sp<sup>2</sup>C-H), 2961 (sp<sup>3</sup>C-H), 2188 (C≡N), 1644 (C=O), 1592 (C=C), 1412 (CH<sub>2</sub>-bending), 1267, 1216 (C-O), 1090 (C-N) cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>):  $\delta = 4.09$ -4.16 (m, 2H, CH<sub>2</sub>), 4.98 (s, 1H, CH), 5.64 (s, 1H, OH), 6.34 (s, 1H, CH), 7.27 (s, 2H, NH<sub>2</sub>), 7.41 (m, 1H, CH<sub>Ar</sub>), 7.54 (m, 2H, CH<sub>Ar</sub>), 7.85 (s, 1H, CH<sub>Ar</sub>), 7.96 (m, 3H, CH<sub>Ar</sub>) ppm; <sup>13</sup>C NMR (125 MHz, DMSO-*d*<sub>6</sub>):  $\delta = 41.0, 57.3, 60.1, 114.6, 119.3, 124.5, 126.2, 126.5, 126.6, 127.0, 127.7, 128.5, 131.8, 133.7, 140.5, 141.3, 155.7, 159.2, 166.7, 179.1$  ppm; Anal. Calcd. for C<sub>20</sub>H<sub>14</sub>N<sub>2</sub>O<sub>4</sub>: C, 69.36; H, 4.07; N, 8.09. Found: C, 69.07; H, 4.07; N, 8.13.
- *2-Amino-4-(benzo[d][1,3]dioxol-5-yl)-6-(hydroxymethyl)-4,8-dihydropyrano[3,2-b]pyran-3-carbonitrile*: FT-IR (KBr):  $\nu = 3408$  (br., O-H, NH<sub>2</sub>, sp<sup>2</sup>C-H), 2964 (sp<sup>3</sup>C-H), 2194 (C≡N), 1637 (C=O), 1592 (C=C), 1415 (CH<sub>2</sub>-bending), 1209 (C-O), 1054 (C-N) cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, DMSO-*d*<sub>6</sub>):  $\delta = 4.12$ -4.23 (m, 2H, CH<sub>2</sub>), 4.72 (s, 1H, CH), 5.68 (s, 1H, OH), 6.03 (s, 2H, CH<sub>2</sub>), 6.33 (s, 1H, CH), 6.76 (d,  $J = 7.0$  Hz, 1H, CH<sub>Ar</sub>), 6.83 (s, 1H, CH<sub>Ar</sub>), 6.91 (d,  $J = 7.1$  Hz, 1H, CH<sub>Ar</sub>), 7.19 (s, 2H, NH<sub>2</sub>) ppm; <sup>13</sup>C NMR (125 MHz, DMSO-*d*<sub>6</sub>):  $\delta = 40.3, 56.2, 59.7, 101.3, 107.7, 108.9, 114.5, 119.3, 126.7, 140.5, 141.1, 146.7, 148.1, 155.9, 159.1, 169.3, 169.9$  ppm; Anal. Calcd. for C<sub>17</sub>H<sub>12</sub>N<sub>2</sub>O<sub>6</sub>: C, 60.00; H, 3.55; N, 8.23. Found: C, 59.97; H, 3.58; N, 8.19.

### 3. Results and discussion

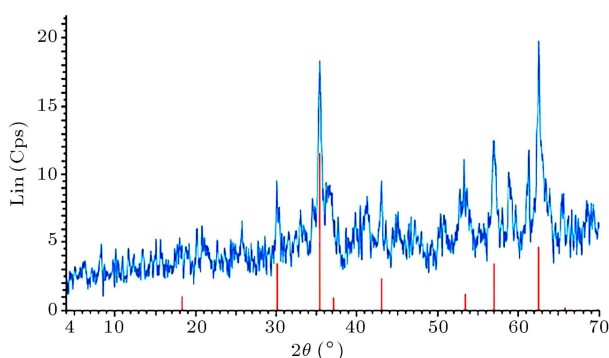
#### 3.1. Synthesis and characterization of PMAA-Fe<sub>3</sub>O<sub>4</sub>

As shown in Scheme 2, the glycine capped Fe<sub>3</sub>O<sub>4</sub> magnetic nanorods were prepared by glycine assisted coprecipitation from an aqueous solution of Fe<sup>3+</sup> and Fe<sup>2+</sup> ions in a molar ratio of 2/1 at pH = 11 under N<sub>2</sub> atmosphere. Glycine was used to stabilize and control the growth of nanocrystals of Fe<sub>3</sub>O<sub>4</sub> by chelating carboxylate groups to Fe ions, which led to the introduction of the amine functional groups to nanocrystals. Then, the obtained magnetic nanorods underwent reaction with 2-pyridine carbaldehyde via amine groups followed by reduction in in-situ generated imine using NaBH<sub>4</sub> to give PMAA-Fe<sub>3</sub>O<sub>4</sub>.

The prepared PMAA-Fe<sub>3</sub>O<sub>4</sub> was fully characterized using FT-IR, XRD, TGA, SEM, EDX, TEM, BET, and VSM analyses. The XRD diffraction pattern of PMAA-Fe<sub>3</sub>O<sub>4</sub> is shown in Figure 1, in which seven distinct diffraction peaks are seen that are very close to the reported data and consistent with the spinal

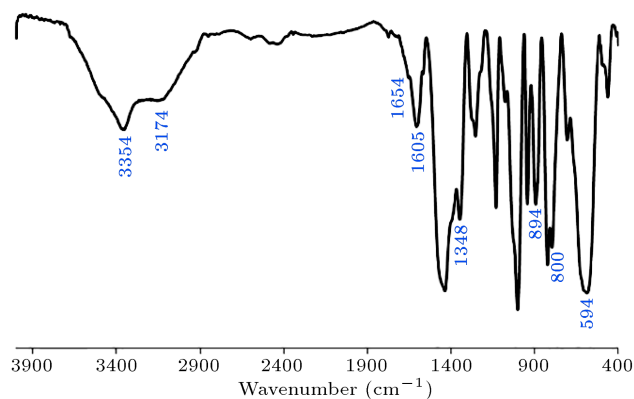


**Scheme 2.** Preparation of PMAA-Fe<sub>3</sub>O<sub>4</sub>.

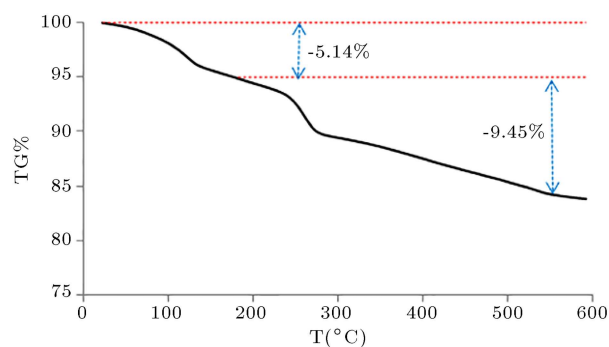


**Figure 1.** XRD pattern of PMAA-Fe<sub>3</sub>O<sub>4</sub>.

structure of Fe<sub>3</sub>O<sub>4</sub> magnetic nanoparticles [45]. FT-IR spectra were recorded in order to study the functional groups of PMAA-Fe<sub>3</sub>O<sub>4</sub>. As shown in the FT-IR spectra of PMAA-Fe<sub>3</sub>O<sub>4</sub>, N-H and O-H stretching vibrations appear at 3354 and 3174 cm<sup>-1</sup>, respectively. The bands at 1654 and 1605 cm<sup>-1</sup> are associated with stretching vibrations of C=O groups of carboxylate anions and C=C of pyridine rings, respectively, and the peak at 1348 cm<sup>-1</sup> is related to stretching modes of C-N bonds. Vibrations of Fe-O appear at 594, 800, and 894 cm<sup>-1</sup> (Figure 2). In order to investigate the thermal behavior and the percentage of organic residue on the Fe<sub>3</sub>O<sub>4</sub> magnetic nanorods, thermogravimetric analysis



**Figure 2.** FT-IR spectra of PMAA-Fe<sub>3</sub>O<sub>4</sub>.



**Figure 3.** TG of PMAA-Fe<sub>3</sub>O<sub>4</sub>.

(TGA) was performed by heating a sample under N<sub>2</sub> flow at a rate of 10°C/min, in which the first weight loss (5.14%) at 100-130°C corresponded to the removal of physically adsorbed water molecules, and the second weight loss (9.45%) was observed at around 240-275°C due to decomposition of organic residue. The obtained nanorods exhibited a good stability in the range of 275-500°C (Figure 3).

In order to study the morphology of the PMAA-Fe<sub>3</sub>O<sub>4</sub>, SEM images were recorded of which the aggregated rods in plate-type materials are shown (Figure 4(a)). The chemical composition of PMAA-Fe<sub>3</sub>O<sub>4</sub> was investigated using Energy Dispersive X-ray (EDX) analysis, which indicated the existence of Fe, O, and C elements, approving the functionalization of the surface of nanorods with organic molecules. However, due to high intensity of O and Fe, the intensity of nitrogen atoms peak at 0.392 keV was very low (Figure 4(b)). TEM images were obtained from fine dispersion of PMAA-Fe<sub>3</sub>O<sub>4</sub> nanoparticles in water, by spreading onto a copper grid, and then drying, in which the nanorods were shown with the lengths of 60-200 nm and the average diameter of 10 nm (Figure 4(c)).

To study the specific surface areas of the PMAA-Fe<sub>3</sub>O<sub>4</sub>, BET analysis was performed by measuring the N<sub>2</sub> adsorption-desorption isotherm (Figure 5); the measured BET surface area was 30.429 m<sup>2</sup>/g with a pore volume of 0.1748 cm<sup>3</sup>/g and average pore diameter of 22.979 nm.

Magnetic properties of the PMAA-Fe<sub>3</sub>O<sub>4</sub> were investigated by VSM analysis, which exhibited the superparamagnetic properties of the synthesized Fe<sub>3</sub>O<sub>4</sub> nanorods at room temperature with the saturation magnetization (*M<sub>s</sub>*) value of 36 emu/g and no hysteresis loop, *H<sub>c</sub>* = 0 (Figure 6).

### 3.2. Catalytic activity of the PMAA-Fe<sub>3</sub>O<sub>4</sub>

First, the catalytic activity of the prepared PMAA-Fe<sub>3</sub>O<sub>4</sub> was examined by treatment of equimolar amounts of benzaldehyde, malononitrile, and dime-done in the presence of catalytic amount of PMAA-Fe<sub>3</sub>O<sub>4</sub> in EtOH under reflux conditions for 5 h, which afforded the corresponding tetrahydro-4*H*-chromene-3-carbonitrile in 34% isolated yield. To obtain the

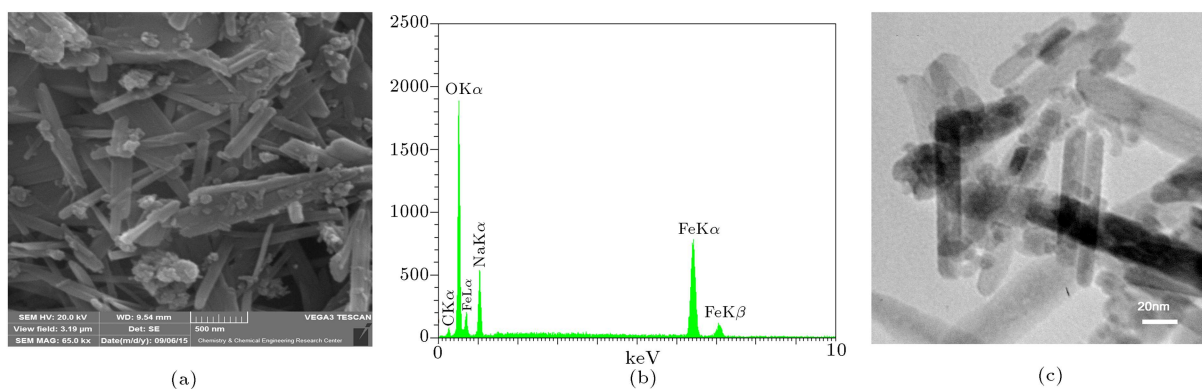


Figure 4. (a) SEM image, (b) EDX analysis and (c) TEM image of PMAA-Fe<sub>3</sub>O<sub>4</sub>.

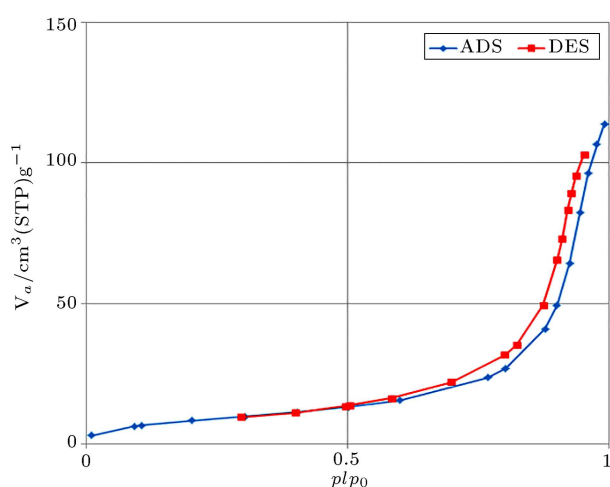


Figure 5. The N<sub>2</sub> adsorption-desorption isotherm of the PMAA-Fe<sub>3</sub>O<sub>4</sub>.

optimal conditions for the reaction of benzaldehyde, malononitrile, and dimedone, we carried out experiments 1-10, as illustrated in Table 1. Entries 1-3 show the solvent effects on the reaction, which were investigated with regards to the green chemistry considerations, water, EtOH, and solvent-free conditions. When water was used, the major isolated product was benzylidene malononitrile, intermediate of the reaction,

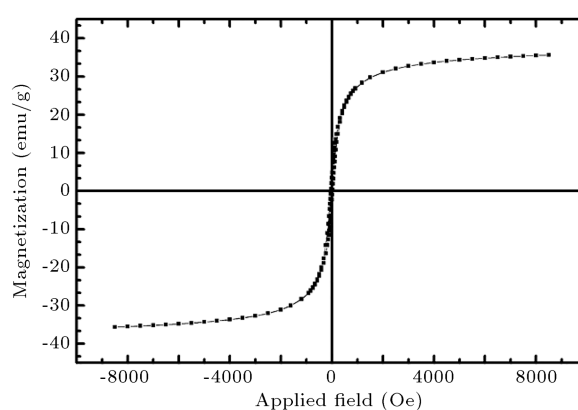


Figure 6. VSM analysis of PMAA-Fe<sub>3</sub>O<sub>4</sub>.

and the corresponding 4*H*-chromene-3-carbonitrile was obtained only in 28% yield after 12 h of reaction time. The solvent-free condition was chosen for acceptable yield (51%). To achieve an optimal temperature, reaction was conducted at various temperatures (entries 3-7) and 110°C was selected as reaction temperature, leading to corresponding product in 51% yield in very short reaction time (10 min). Then, the catalyst loading was investigated, and due to the high yield of the product (70%) within a short reaction time, 0.02 g of catalyst was selected as the optimum amount for the

Table 1. Optimization of the reaction conditions<sup>a</sup>.

Entry	Solvent	PMAA-Fe <sub>3</sub> O <sub>4</sub> (g)	Temperature (°C)	Time (min)	Yield (%) <sup>b</sup>
1	Water	0.015	Reflux	720	28
2	EtOH	0.015	Reflux	300	34
3	Solvent-Free	0.015	110	10	51
4	Solvent-Free	0.015	100	20	47
5	Solvent-Free	0.015	80	25	38
6	Solvent-Free	0.015	70	60	16
7	Solvent-Free	0.015	rt	360	NR <sup>c</sup>
8	Solvent-Free	0.010	110	10	42
9	Solvent-Free	0.020	110	10	70
10	Solvent-Free	0.025	110	10	71

<sup>a</sup>Reactions were conducted by treatment of 0.5 mmol of dimedone with equimolar amounts of benzaldehyde and malononitrile.

<sup>b</sup>Yields refer to isolated products.

<sup>c</sup>NR: No Reaction.

reaction of 0.5 mmol of each substrate (entries 3 and 8-10).

With the optimum conditions in hand, the scope of the reaction was investigated by heating a mixture of dimedone (0.5 mmol) with equimolar amounts of malononitrile and various substitute benzaldehydes in the presence of 0.020 g of PMAA-Fe<sub>3</sub>O<sub>4</sub> under solvent-free conditions at 110°C for 10-20 min, leading to corresponding tetrahydro-4*H*-chromene-3-carbonitriles in 59-78% yields. The results are summarized in Table 2. Not only electron withdrawing substituted (2-Cl, 4-Cl, 2-NO<sub>2</sub> and 3-NO<sub>2</sub>) benzaldehydes, but

**Table 2.** PMAA-Fe<sub>3</sub>O<sub>4</sub> catalyzed synthesis of compounds 1.

Entry	Ar	Yield (%)	mp (°C)	
			Measured	Reported
1	C <sub>6</sub> H <sub>5</sub>	70	224-226	226-228 [37]
2	2-ClC <sub>6</sub> H <sub>4</sub>	63	210-211	217-218 [46]
3	4-ClC <sub>6</sub> H <sub>4</sub>	68	210-212	208-210 [46]
4	4-MeC <sub>6</sub> H <sub>4</sub>	65	217-219	214-216 [46]
5	2-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	70	220-222	224-226 [46]
6	3-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	69	208-210	208-211 [46]
7	4-MeOC <sub>6</sub> H <sub>4</sub>	59	201-203	199-201 [46]
8	2-naphthyl	78	259-261	258-260 [47]
9	2-thienyl	70	218-221	220-222 [47]

also electron donating substituted (4-Me and 4-MeO) benzaldehydes worked well in the reaction.

Also, the catalytic efficiency of PMAA-Fe<sub>3</sub>O<sub>4</sub> in the reaction of a variety of aromatic aldehydes with malononitrile and β-naphthol or α-naphthol was studied under the similar reaction conditions, in which corresponding 4*H*-benzo[*h*]chromene-3-carbonitrile 2 or 1*H*-benzo[*f*]chromene-2-carbonitrile 3 was obtained in 61-90% yields within 10-30 min (Table 3).

The results encouraged us to synthesize 2-amino-4-aryl-6-(hydroxymethyl)-8-oxo-4,8-dihydropyrano [3,2-*b*]pyran-3-carbonitriles 4 via PMAA-Fe<sub>3</sub>O<sub>4</sub>-catalyzed three-component reaction of aromatic aldehydes, malononitrile, and kojic acid. When reaction was conducted under solvent-free conditions, the yield was moderate; therefore, the solvent effect was investigated by subjecting the starting materials to the catalytic amount of PMAA-Fe<sub>3</sub>O<sub>4</sub>, in which reaction in EtOH under reflux conditions led to acceptable yield. As shown in Table 4, the scope of the reaction was studied by heating a variety of aromatic aldehydes with malononitrile and kojic acid in the presence of 0.020 g of PMAA-Fe<sub>3</sub>O<sub>4</sub> in EtOH under reflux conditions, leading to corresponding pyrano[3,2-*b*]pyran-3-carbonitrile derivatives 4 in 64-98% yields. Also, ethyl cyanoacetate worked well in the similar reaction.

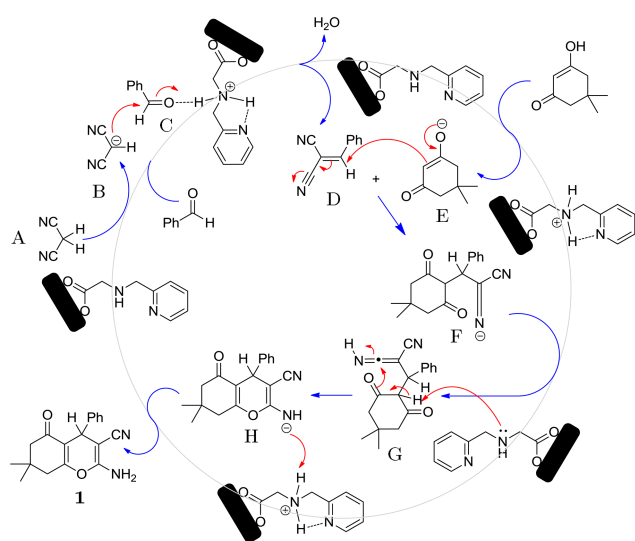
The proposed catalytic cycle of PMAA-Fe<sub>3</sub>O<sub>4</sub>

**Table 3.** PMAA-Fe<sub>3</sub>O<sub>4</sub>-catalyzed synthesis of compounds 2 and 3.

Entry	Ar	α- or β-Naphthol	Yield (%)	mp (°C)	
				Measured	Reported
1	2-ClC <sub>6</sub> H <sub>4</sub>	β	68	267-268	259-261 [32]
2	2-ClC <sub>6</sub> H <sub>4</sub>	α	61	245-248	236-237 [32]
3	3-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	β	73	235-236	233-235 [48]
4	3-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	α	63	212-213	214-216 [49]
5	4-MeC <sub>6</sub> H <sub>4</sub>	β	90	265-266	265-267 [50]
6	4-MeC <sub>6</sub> H <sub>4</sub>	α	65	203-205	204-205 [51]

**Table 4.** PMAA-Fe<sub>3</sub>O<sub>4</sub>-catalyzed synthesis of compounds 4.

Entry	Ar	X	Yield (%)	mp (°C)	
				Measured	Reported
1	C <sub>6</sub> H <sub>5</sub>	CN	96	222-225	220-222 [52]
2	2-ClC <sub>6</sub> H <sub>4</sub>	CN	88	212-216	210-213 [52]
3	4-ClC <sub>6</sub> H <sub>4</sub>	CN	64	194-196	195-197 [53]
4	4-BrC <sub>6</sub> H <sub>4</sub>	CN	81	230-231	228-230 [54]
5	3-NO <sub>2</sub> C <sub>6</sub> H <sub>4</sub>	CN	68	246-248	236-238 [54]
6	4-MeC <sub>6</sub> H <sub>4</sub>	CN	95	223-225	224-226 [54]
7	2-thienyl	CN	88	230-232	235-237 [52]
8	3,4-(OCH <sub>2</sub> O)C <sub>6</sub> H <sub>3</sub>	CN	92	219-220	New
9	2-naphthyl	CN	82	258-259	New
10	C <sub>6</sub> H <sub>5</sub>	CO <sub>2</sub> Et	77	193-195	193-194 [55]
11	4-ClC <sub>6</sub> H <sub>4</sub>	CO <sub>2</sub> Et	89	194-197	196-198 [55]



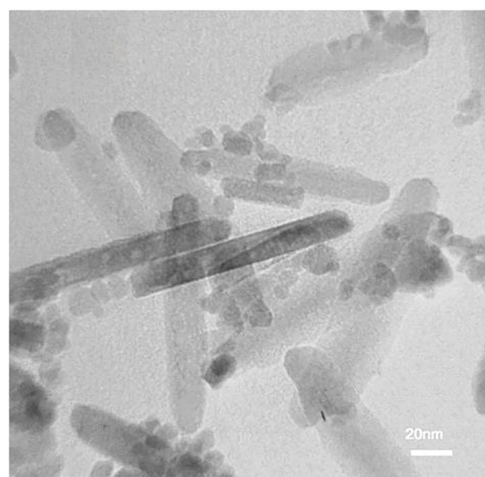
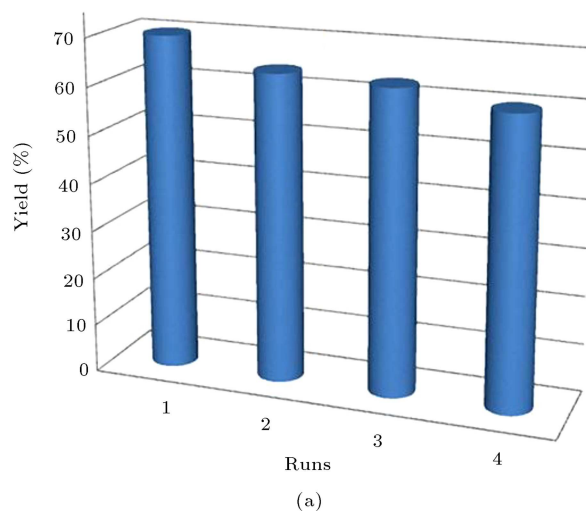
**Scheme 3.** Proposed catalytic cycle of the PMAA-Fe<sub>3</sub>O<sub>4</sub>.

for the reaction of malononitrile, benzaldehyde, and dimedone is depicted in Scheme 3. Due to its high basicity ( $pK_a = 10-11.5$ ), secondary amine acts as base to take a proton from active methylene compounds **A**, leading to secondary ammonium, which is stabilized via intramolecular H-bonding with lone pair of pyridine; this could be a reason for high catalytic activity of the prepared PMAA-Fe<sub>3</sub>O<sub>4</sub>. In-situ generated anion **B** attacks benzaldehyde, activated by H-bonding between carbonyl of benzaldehyde and ammonium (**C**), to give benzylidene malononitrile **D**, which undergoes Michael addition by enolate anion of dimedone **E**, generated by deprotonating dimedone with amine moiety of PMAA-Fe<sub>3</sub>O<sub>4</sub>. By protonation of ethanimine **F**, followed by intramolecular cyclization (**G** to **H**) and then proton transfer reaction, final product **1** is produced along with the regeneration of the catalyst.

Recoverability and reusability of the catalyst were investigated; the catalyst was separated using an external magnetic field, washed with acetone three times, and then dried in an oven at 60°C. Then, fresh reagents (malononitrile, benzaldehyde, and dimedone) were treated with remaining catalyst under the reaction conditions for four runs, in which no considerable decrease in the yield was observed, indicating that PMAA-Fe<sub>3</sub>O<sub>4</sub> could be recycled as a catalyst (Figure 7(a)). In order to investigate the stability of the catalyst during the separation and reusing process, TEM images were recorded after four runs, in which no considerable changes in the shape and size were observed (Figure 7(b)).

#### 4. Conclusions

We synthesized 2-[(2-pyridinylmethyl)amino] acetic acid functionalized Fe<sub>3</sub>O<sub>4</sub> magnetic nanorods. Functionalization of the organic molecules on the nanorods



(b)

**Figure 7.** (a) Reusability of the PMAA-Fe<sub>3</sub>O<sub>4</sub> catalyst. (b) TEM image of the catalyst after four runs.

was confirmed by FT-IR, EDX, and TGA techniques, showing that 9.45 wt% of the nanorods were organic molecules. The crystalline phase of the nanorods was determined as Fe<sub>3</sub>O<sub>4</sub> by XRD. SEM and TEM images exhibited the formation of nanorods with the lengths of 60-200 nm and the average diameter of 10 nm. Also, the surface area of 30.429 m<sup>2</sup>/g with a pore volume of 0.1748 cm<sup>3</sup>/g and average pore diameter of 22.979 nm was determined by BET and the saturation magnetization ( $M_s$ ) value of 36 emu/g, with no hysteresis loop,  $H_c = 0$ , was investigated by VSM analysis, showing the superparamagnetic properties of the synthesized Fe<sub>3</sub>O<sub>4</sub> nanorods. The catalytic activity of the synthesized PMAA-functionalized magnetic nanorods was investigated in three-component reactions of malononitrile with substitute benzaldehydes and a variety of enolic or phenolic components, leading to various chromene and pyran derivatives in good to high yields within a short reaction time. Simple preparation of catalyst, simple reaction procedure and workup, and easy separation

and recoverability of catalyst are some advantages of our methodology.

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