

# One-pot Synthesis of Arylidene Barbituric Acid Derivatives Using $\text{Fe}_2\text{O}_3$ and $\text{Fe}_2\text{O}_3/\text{MFe}_2\text{O}_4$ ( $\text{M} = \text{Cu}$ , and $\text{Ni}$ ) Nanoparticles as Heterogeneous Catalysts in Knoevenagel Condensation Reaction

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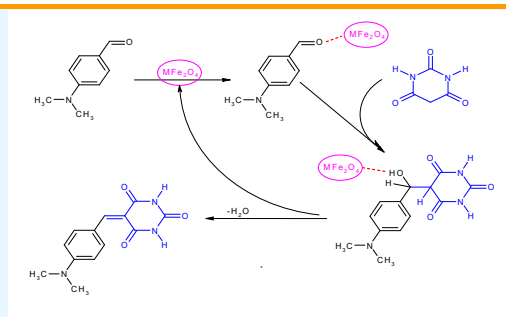
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**Abstract:** In this paper, a facile one-pot two-component synthesis of arylidene barbituric acid derivatives (Knoevenagel reaction) in the presence of heterogeneous catalyst of as-prepared  $\text{Fe}_2\text{O}_3$  and  $\text{Fe}_2\text{O}_3/\text{MFe}_2\text{O}_4$  ( $\text{M} = \text{Cu}$  and  $\text{Ni}$ ) nanoparticles under mild reaction condition is described and discussed. The as-prepared  $\text{MFe}_2\text{O}_4$  nanoparticles were characterized by FT-IR, XRD, BET and SEM. They are used as efficient heterogeneous catalysts for the one-pot two-component synthesis of arylidene barbituric acid derivatives and the effect of important parameters such as solvent and amount of catalyst was investigated on the efficiency production of arylidene barbituric acid derivatives. The results of catalytic studies confirmed high activity of as-prepared nanoparticles as heterogeneous catalysts. Finally, the arylidene barbituric acid products were obtained on high purity. The products were characterized by FT-IR,  $^1\text{H-NMR}$  and melting point. This process is simple and provides high yields of products in short reaction times.

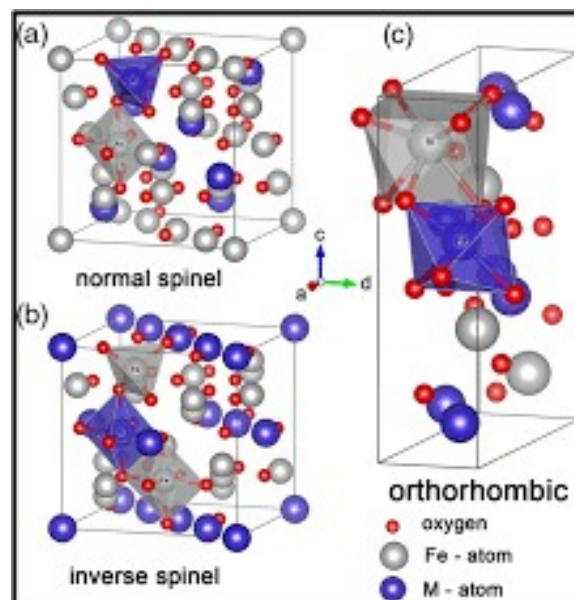
**Keywords:**  $\text{MFe}_2\text{O}_4$  nanoparticles, Arylidene barbituric acid, Heterogeneous catalyst



## 1. INTRODUCTION

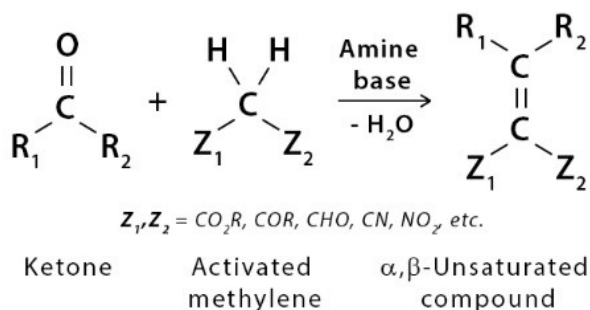
Recently, inorganic nanoparticles have attracted much attention due to their unique properties<sup>1-4</sup> and potential different applications<sup>5-10</sup> especially in the fields of catalysis for synthesis of various organic compounds such as naphthoxazinones,<sup>11</sup> pyrido[2,3-d:6,5-d'] dipyrimidines,<sup>12,13</sup> arylidene barbituric acid derivatives,<sup>14,15</sup> benzimidazole compounds,<sup>16</sup> xanthenes,<sup>17</sup> oxazepane<sup>18</sup> and coumarins.<sup>19</sup> From different inorganic nanoparticles, nanoferrites ( $\text{MFe}_2\text{O}_4$ ,  $\text{M} = \text{Co}$ ,  $\text{Ni}$ ,  $\text{Cu}$ ,  $\text{Zn}$ ) are of the most important inorganic materials, which have spinel structure (Figure 1), unique physical, chemical properties and different application.<sup>1-11</sup> The catalytic properties of inorganic nanoparticles depend on their size, surface area and shape.<sup>15,16</sup> Among the various transition metal oxide nanoparticles, magnetic nano-ferrites have been widely used as catalyst because of their low-toxicity, thermal stability, high surface area and high activity.<sup>11-14</sup> In recent years, barbituric acid has been used as row building block material in the synthesis of different organic compounds.<sup>20</sup> It has an active  $-\text{CH}_2-$  group for reactions with carbonyl group to preparation arylidene barbituric acid derivatives.<sup>14,15,21,22</sup> Barbituric acid derivatives have important biological

activity such as anticancer, anxiolytics, sedative, and hypnotic.<sup>21</sup>



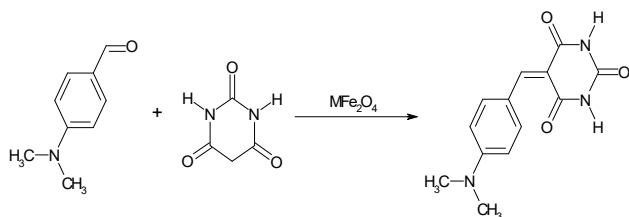
**Figure 1.** Classification of spinel ferrites as a) normal, b) inverse and c) orthorhombic

The Knoevenagel reaction<sup>23-31</sup> is a condensation reaction of carbonyl compounds and active methylene sites in the presence of a catalyst to form a carbon-carbon bond,<sup>32-43</sup> which is used to produce new intermediates for biological and pharmaceuticals active materials was discovered by Emil Knoevenagel in 1894<sup>23</sup> (Scheme 1). Recently, many researchers are trying to develop low-cost, simple and eco-friendly Knoevenagel reaction using heterogeneous and homogeneous efficient reusable catalysts.<sup>32-43</sup> For example, Anbu et al.<sup>26</sup> reported the green and sustainable processes for synthesis of  $\alpha,\beta$ -unsaturated carboxylic acids using chitosan as a reusable solid base catalyst. Roy et al.<sup>15</sup> prepared MgO nanostructure under ambient condition, which was used as active and reusable catalyst in Knoevenagel reaction between aromatic aldehydes and malononitrile and ethylcyanoacetate. Alirezvani et al.<sup>27</sup> synthesized the new covalently-modified chitosan by 1,3-dibromopropane and melamine as a heterogeneous bifunctional catalyst for the condensation of aromatic aldehyde with malononitrile. Sadjadi et al.,<sup>28</sup> developed and reported the synthesis of new metal free catalyst through decoration of chitosan with ionic liquid terminated dendritic moiety for Knoevenagel reaction. In 2023, Liandi et al.<sup>9</sup> reviewed the use of five spinel ferrite as efficient environmentally friendly catalysts in the synthesis of various organic compounds through multicomponent reactions.



Scheme 1. Knoevenagel condensation reaction

The main goal of this paper is the preparation of  $Fe_2O_3$  and  $Fe_2O_3/MFe_2O_4$  ( $M = Cu, Ni$ ) nanoparticles as a catalyst in the simple and efficient Knoevenagel reaction for the synthesis of arylidene barbituric acid derivatives (Scheme 2).



Scheme 2. Chemical reaction of 4-dimethylaminobenzaldehyde and barbituric acid

## 2. EXPERIMENTAL

### Preparation of $Fe_2O_3$ and $Fe_2O_3/MFe_2O_4$ ( $M = Cu, Ni$ ) nanoparticles

A solution of  $FeCl_3$  (0.2 mmol) and  $MCl_2 \cdot xH_2O$  (0.1 mmol) ( $M = Fe, Cu, Ni$ ) in deionized water (50 mL) was stirred for 0.5 h at 50 °C. Then, 1 g NaOH was added and the reaction mixture was stirred for 2 h at 85 °C. After that the solution was cooled to room temperature, the brown precipitates were filtered, washed with water and methanol and finally dried.

### Characterization

The crystal structure of the as-prepared  $Fe_2O_3$  and  $Fe_2O_3/MFe_2O_4$  ( $M = Cu, Ni$ ) nanoparticles was determined by a Panytical XPERTPRO X-ray diffractometer (XRD) using Cu  $K\alpha$  radiation with  $\lambda = 0.154$  nm in the  $2\theta$  range of 10-70°. Fourier transform infrared (FT-IR) spectra of  $MFe_2O_4$  nanoparticles and arylidene barbituric acid derivatives were carried out with a Perkin-Elmer spectrophotometer using KBr pellets in the range of 4000-400  $cm^{-1}$ . Morphology of the products was investigated by scanning electron microscope (SEM) using a JEOL JSM-6610LV.  $^1H$ - and  $^{13}C$ -NMR spectra of arylidene barbituric acid derivatives were recorded in  $DMSO-d_6$  solvent using a Bruker DRX-500 spectrometer with TMS as internal reference. Melting points and the elemental analysis (CHN) of arylidene barbituric acid derivatives were obtained by Yanagimoto micro melting point aperture and a Vario EA 1108 analyzer, respectively. The Brunauer-Emmett-Teller (BET) specific surface area and pore sized of  $MFe_2O_4$  nanoparticles were measured with ASAP 2460 instrument.

### General procedure for the Knoevenagel reaction

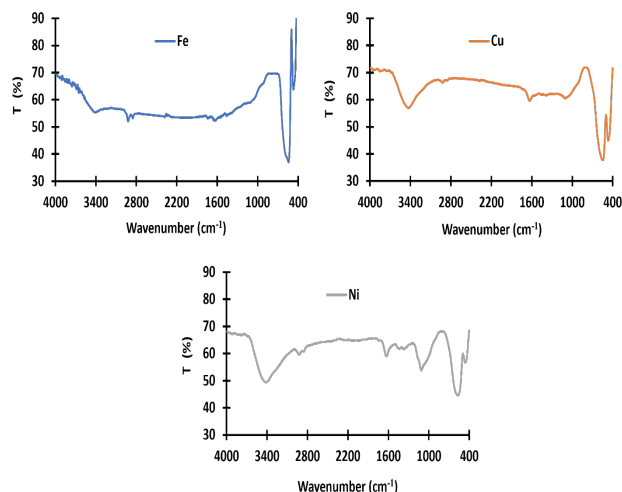
1 mmol of aldehyde, 1 mmol of barbituric acid, 20 mg of  $Fe_2O_3$  and  $Fe_2O_3/MFe_2O_4$  ( $M = Cu, Ni$ ) nanoparticles and suitable solvent (20 mL) were added to flask. The resulting mixture was stirred at room temperature and after completion of the reaction as monitored by thin layer chromatography (TLC), the arylidene barbituric acid precipitates were filtered, washed with cold methanol and dried. The pure arylidene barbituric acid derivatives were obtained after recrystallization in  $EtOH/CHCl_3$  (1:1 v/v).

## 3. RESULTS AND DISCUSSION

### Characterization of $MFe_2O_4$ nanoparticles

To investigate the functional groups of the as-prepared  $Fe_2O_3$  and  $Fe_2O_3/MFe_2O_4$  ( $M = Cu, Ni$ ) nanoparticles, they were characterized using FT-IR spectroscopy. The FT-IR spectra are given in Figure 1. The peaks appeared at about 3420  $cm^{-1}$  and 1630  $cm^{-1}$  corresponds to the O-H stretching of  $H_2O$  molecules adsorbed on the surface of nanoparticles.<sup>1,4,8</sup> There are two strong bands at about 470  $cm^{-1}$  and 550  $cm^{-1}$  which correspond to M-O stretching vibrations of tetrahedral site of the spinel structure and O-M-O bending vibrations of octahedral site of the spinel structure of  $MFe_2O_4$  nanoparticles.<sup>1,8</sup>

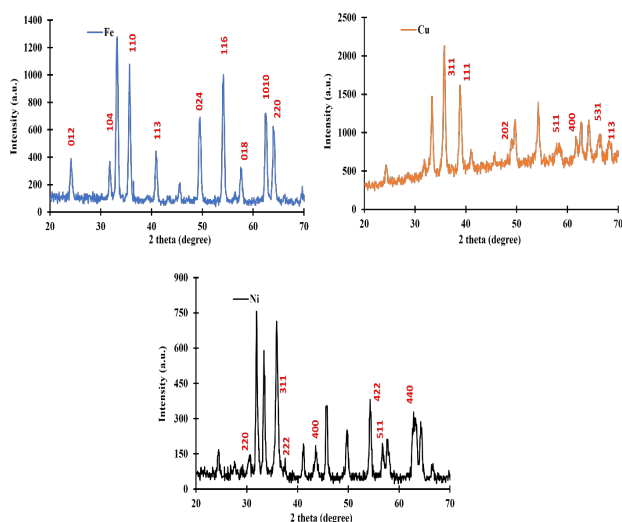
The XRD patterns of the as-prepared  $Fe_2O_3$  and  $Fe_2O_3/MFe_2O_4$  ( $M = Cu, Ni$ ) nanoparticles are shown in Figure 2. All the diffraction peaks appeared at different  $2\theta$  values match the JCPDS cards numbers of 033-0664, 34-0425, and 10-0325 very well and revealed that the  $Fe_2O_3$



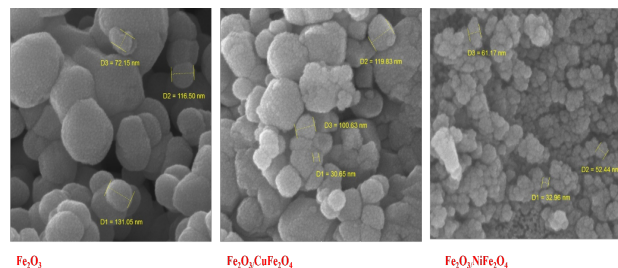
**Figure 1.** FT-IR spectra of as-prepared  $\text{Fe}_2\text{O}_3$  and  $\text{Fe}_2\text{O}_3/\text{MFe}_2\text{O}_4$  (M = Cu, Ni) nanoparticles.

is cubic structure,<sup>44</sup>  $\text{CuFe}_2\text{O}_4$  is tetragonal structure<sup>2,3</sup> and  $\text{NiFe}_2\text{O}_4$  is cubic structure.<sup>45</sup> The peak broadening indicates that the  $\text{MFe}_2\text{O}_4$  compounds have nanocrystalline nature. The average size of  $\text{MFe}_2\text{O}_4$  nanoparticles was calculated by Scherer equation ( $d = 0.94 \lambda / \beta \cos \theta$ ) and was found to be 95 nm for  $\text{Fe}_3\text{O}_4$ , 88 nm for  $\text{CuFe}_2\text{O}_4$  and 59 nm for  $\text{NiFe}_2\text{O}_4$ , which is in agreement with the size obtained from the SEM images (Figure 3).

The FE-SEM images of as-prepared  $\text{Fe}_2\text{O}_3$  and  $\text{Fe}_2\text{O}_3/\text{MFe}_2\text{O}_4$  (M = Cu, Ni) nanoparticles were gathered and were represented in Fig. 3. The images confirmed that the particles in the as-prepared  $\text{Fe}_2\text{O}_3$  and  $\text{Fe}_2\text{O}_3/\text{MFe}_2\text{O}_4$  (M = Cu, Ni) have quasi-spherical shapes with different sizes. However, the crystal sizes of  $\text{Fe}_2\text{O}_3/\text{NiFe}_2\text{O}_4$  composite are lower than  $\text{Fe}_2\text{O}_3/\text{CuFe}_2\text{O}_4$  and  $\text{Fe}_2\text{O}_3$ .



**Figure 2.** XRD patterns of as-prepared  $\text{Fe}_2\text{O}_3$  and  $\text{Fe}_2\text{O}_3/\text{MFe}_2\text{O}_4$  (M = Cu, Ni) nanoparticles.

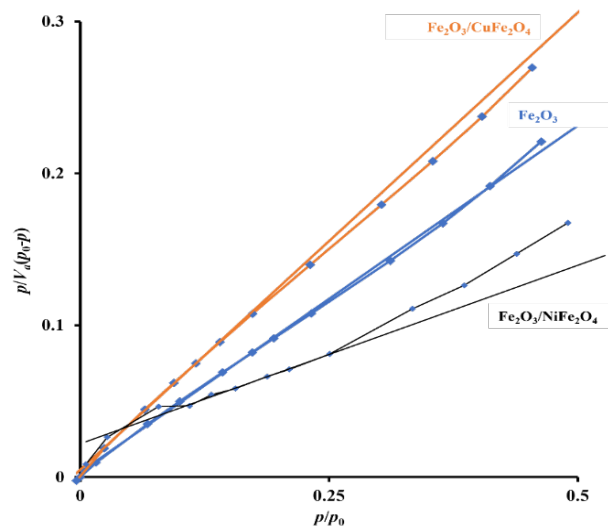


**Figure 3.** FE-SEM images of as-prepared  $\text{Fe}_2\text{O}_3$  and  $\text{Fe}_2\text{O}_3/\text{MFe}_2\text{O}_4$  (M = Cu, Ni) nanoparticles.

The  $\text{N}_2$  adsorption/desorption isotherms and pore size distribution of as-prepared  $\text{Fe}_2\text{O}_3$  and  $\text{Fe}_2\text{O}_3/\text{MFe}_2\text{O}_4$  (M = Cu, Ni) nanoparticles were represented in Figures 4 and 5, respectively. Also, data were shown in Table 1. According to Table 1, the  $\text{Fe}_2\text{O}_3/\text{CuFe}_2\text{O}_4$  nanoparticles exhibited higher surface area and pore volume compared to the  $\text{Fe}_2\text{O}_3$  and  $\text{Fe}_2\text{O}_3/\text{NiFe}_2\text{O}_4$ .

**Table 1.** The BET analysis of as-prepared  $\text{Fe}_2\text{O}_3$  and  $\text{Fe}_2\text{O}_3/\text{MFe}_2\text{O}_4$  (M = Cu, Ni) nanoparticles

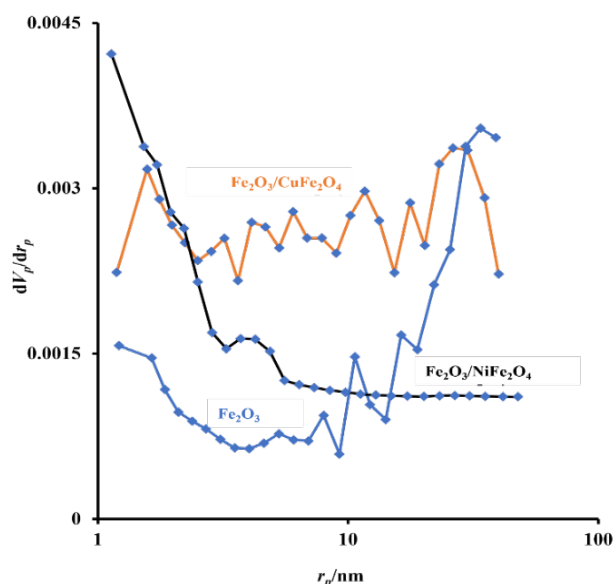
	$\text{Fe}_2\text{O}_3$	$\text{Fe}_2\text{O}_3/\text{CuFe}_2\text{O}_4$	$\text{Fe}_2\text{O}_3/\text{NiFe}_2\text{O}_4$
$V_m$ [ $\text{cm}^3(\text{STP}) \text{g}^{-1}$ ]	2.1765	3.162	0.4395
$a_{\text{BET}}$ [ $\text{m}^2 \text{g}^{-1}$ ]	9.4733	13.763	3.913
Total pore volume ( $p/p_0 = 0.979$ ) [ $\text{cm}^3 \text{g}^{-1}$ ]	0.1116	0.138	0.0015466
Average pore diameter [nm]	47.127	40.113	3.2339



**Figure 4.**  $\text{N}_2$  adsorption/desorption isotherms of as-prepared  $\text{Fe}_2\text{O}_3$  and  $\text{Fe}_2\text{O}_3/\text{MFe}_2\text{O}_4$  (M = Cu, Ni).

### Investigation of catalytic activity

Due to the unique properties of arylidene barbituric acid derivatives,<sup>21</sup> we are interested in the preparation of  $\text{Fe}_2\text{O}_3$  and  $\text{Fe}_2\text{O}_3/\text{MFe}_2\text{O}_4$  (M = Cu, Ni) nanoparticles as a catalyst in Knoevenagel reaction<sup>23-31</sup> for simple and low-cost synthesis of them. In this reaction, to find best condition, we should examine the important parameters such as the effect of solvent and the amount of catalyst.



**Figure 5.** The por size distribution of as-prepared  $\text{Fe}_2\text{O}_3$  and  $\text{Fe}_2\text{O}_3/\text{MFe}_2\text{O}_4$  ( $\text{M} = \text{Cu}, \text{Ni}$ )

Initially, the Knoevenagel condensation reaction of barbituric acid (0.64 g, 0.01 mol) and aldehyde with 1:1 molar ratio at the presence of 0.01 g catalyst was examined in different solvent such as acetonitrile, acetic acid, dichloromethane, water, ethanol, methanol and 1:1 v/v water/ethanol and water/methanol at room temperature to provide the best solvent.

The effect of various solvent at the presence of 0.01 catalyst was considered for the Knoevenagel condensation of 4-dimethylaminobenzaldehyde and barbituric acid and the results are shown in Table 2. It was observed that the 1:1 v/v of ethanol/water was required to achieve maximum yield of the desired product. The maximum yield of desired product was obtained in ethanol/water (1:1 v/v) mixture, due to these polar solvents can be better solvated the transition state of the substrates and the yield and rate reaction were increased. Similar result was reported by Rajput and Kaur using  $\text{CoFe}_2\text{O}_4$  nanoparticles as catalyst.<sup>4</sup>

After that, we investigated the effect of catalyst dose on the yield and rate reaction. The results are shown in Table 3. It can be seen that, when the reaction was studied in the presence of 0.03 g of the catalyst, the desired product was obtained in high yields, because of the increases of active sites on the surface of catalyst. Low yield of the desired product was obtained in the absence of the catalyst under similar condition even in longer times.<sup>4,17</sup>

After the optimized solvent and catalyst dose, the Knoevenagel reaction was examined using different aldehydes with electron-withdrawing and electron-donating substituents and the results are shown in Table 4. All aldehydes gave the desired products in high yields.

**Table 2.** The effect of solvent on the yield and time reaction of Knoevenagel condensation of 4-dimethylaminobenzaldehyde and barbituric acid at r.t. at the presence of 0.01 catalyst

Catalyst	Solvent	Time (min)	Yield (%)
$\text{Fe}_2\text{O}_3$	$\text{CH}_3\text{CN}$	11	40
$\text{Fe}_2\text{O}_3/\text{CuFe}_2\text{O}_4$		14	37
$\text{Fe}_2\text{O}_3/\text{NiFe}_2\text{O}_4$		15	36
$\text{Fe}_2\text{O}_3$	$\text{CH}_3\text{COOH}$	10	42
$\text{Fe}_2\text{O}_3/\text{CuFe}_2\text{O}_4$		11	38
$\text{Fe}_2\text{O}_3/\text{NiFe}_2\text{O}_4$		11	36
$\text{Fe}_2\text{O}_3$	$\text{CHCl}_3$	9	51
$\text{Fe}_2\text{O}_3/\text{CuFe}_2\text{O}_4$		10	49
$\text{Fe}_2\text{O}_3/\text{NiFe}_2\text{O}_4$		11	48
$\text{Fe}_2\text{O}_3$	$\text{CH}_3\text{OH}$	8	62
$\text{Fe}_2\text{O}_3/\text{CuFe}_2\text{O}_4$		8	59
$\text{Fe}_2\text{O}_3/\text{NiFe}_2\text{O}_4$		9	55
$\text{Fe}_2\text{O}_3$	$\text{C}_2\text{H}_5\text{OH}$	7	74
$\text{Fe}_2\text{O}_3/\text{CuFe}_2\text{O}_4$		8	70
$\text{Fe}_2\text{O}_3/\text{NiFe}_2\text{O}_4$		8	68
$\text{Fe}_2\text{O}_3$	$\text{H}_2\text{O}$	7	71
$\text{Fe}_2\text{O}_3/\text{CuFe}_2\text{O}_4$		7	68
$\text{Fe}_2\text{O}_3/\text{NiFe}_2\text{O}_4$		8	66
$\text{Fe}_2\text{O}_3$	$\text{C}_2\text{H}_5\text{OH}/\text{H}_2\text{O}$ (1:1 v/v)	5	82
$\text{Fe}_2\text{O}_3/\text{CuFe}_2\text{O}_4$		8	80
$\text{Fe}_2\text{O}_3/\text{NiFe}_2\text{O}_4$		9	80

**Table 3.** The effect of catalyst dose on the yield and time reaction of Knoevenagel condensation of 4-dimethylaminobenzaldehyde and barbituric acid at room temperature

Catalyst	Catalyst amount (g)	Time (min)	Yield (%)
$\text{Fe}_2\text{O}_3$	0.01	4	82
$\text{Fe}_2\text{O}_3/\text{CuFe}_2\text{O}_4$	0.01	7	80
$\text{Fe}_2\text{O}_3/\text{NiFe}_2\text{O}_4$	0.01	9	80
$\text{Fe}_2\text{O}_3$	0.02	4	86
$\text{Fe}_2\text{O}_3/\text{CuFe}_2\text{O}_4$	0.02	5	84
$\text{Fe}_2\text{O}_3/\text{NiFe}_2\text{O}_4$	0.02	7	81
$\text{Fe}_2\text{O}_3$	0.03	3	93
$\text{Fe}_2\text{O}_3/\text{CuFe}_2\text{O}_4$	0.03	4	90
$\text{Fe}_2\text{O}_3/\text{NiFe}_2\text{O}_4$	0.03	5	87

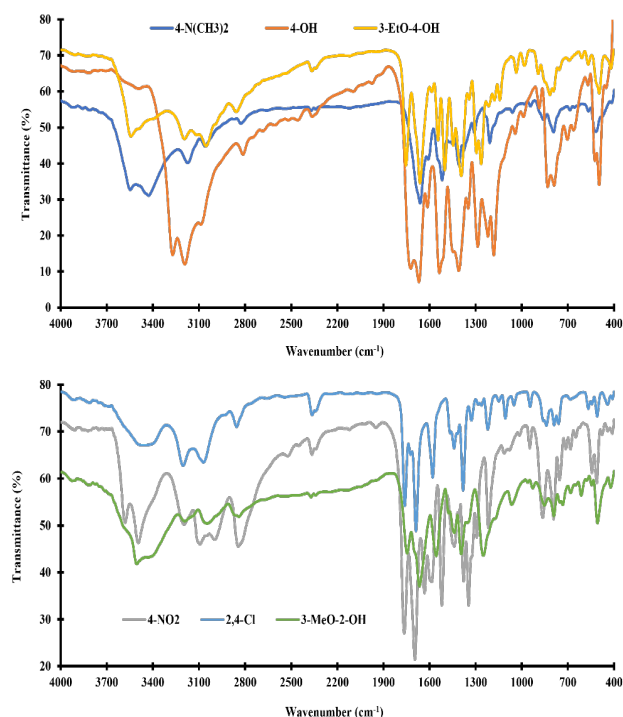
### Characterization of arylidene barbituric acid derivatives

The arylidene barbituric acid products were purified by recrystallization form  $\text{EtOH}/\text{CHCl}_3$  (1:1 v/v) and characterized by  $^1\text{H-NMR}$ , FT-IR spectroscopies and melting point (Table 5). The FT-IR spectra of them are shown in Figure 6. The characteristic peaks between 3200- and 3600  $\text{cm}^{-1}$  are assigned to the existence of different functional groups such as  $-\text{NH}_2$  and  $-\text{OH}$  groups.<sup>46</sup> The peaks are appeared from 1400-1700  $\text{cm}^{-1}$  are assigned to the existence of aromatic rings and carbonyl groups.<sup>24</sup> The  $^1\text{H-NMR}$  spectra of 5-(3-ethoxy-4-hydroxybenzylidene)barbituric acid and 5-(4-dimethylaminobenzylidene)barbituric acid are shown in Figure 7.

The FT-IR and  $^1\text{H-NMR}$  results of desired arylidene barbituric acid compounds confirmed that the products were produced with good selectivity without any by-products formation.<sup>14</sup> According to the literatures,<sup>14,21,38</sup> it seems that the Lewis basic sites on the surface of catalysts are responsible for preparation of desire products due to the interaction of them with carbonyl group of aldehydes or hydroxy group of intermediate compounds. A proposed mechanism for the preparation of 5-(4-dimethylamino-benzylidene)barbituric acid is given in Scheme 3.

**Table 4.** Synthesis of arylidene barbituric acid derivatives in the presence of as-prepared catalysts

Catalyst	Aldehyde	Time (min)	Yield (%)
Fe <sub>2</sub> O <sub>3</sub>	4-Dimethylaminobenzaldehyde	3	93
Fe <sub>2</sub> O <sub>3</sub> /CuFe <sub>2</sub> O <sub>4</sub>		4	90
Fe <sub>2</sub> O <sub>3</sub> /NiFe <sub>2</sub> O <sub>4</sub>		5	87
Fe <sub>2</sub> O <sub>3</sub>	4-Nitrobenzaldehyde	8	72
Fe <sub>2</sub> O <sub>3</sub> /CuFe <sub>2</sub> O <sub>4</sub>		17	68
Fe <sub>2</sub> O <sub>3</sub> /NiFe <sub>2</sub> O <sub>4</sub>		20	69
Fe <sub>2</sub> O <sub>3</sub>	4-Hydroxybenzaldehyde	6	88
Fe <sub>2</sub> O <sub>3</sub> /CuFe <sub>2</sub> O <sub>4</sub>		7	84
Fe <sub>2</sub> O <sub>3</sub> /NiFe <sub>2</sub> O <sub>4</sub>		7	96
Fe <sub>2</sub> O <sub>3</sub>	3-Methoxy-2-hydroxybenzaldehyde	2	96
Fe <sub>2</sub> O <sub>3</sub> /CuFe <sub>2</sub> O <sub>4</sub>		3	95
Fe <sub>2</sub> O <sub>3</sub> /NiFe <sub>2</sub> O <sub>4</sub>		3	93
Fe <sub>2</sub> O <sub>3</sub>	3-Ethoxy-4-hydroxybenzaldehyde	2	98
Fe <sub>2</sub> O <sub>3</sub> /CuFe <sub>2</sub> O <sub>4</sub>		2	97
Fe <sub>2</sub> O <sub>3</sub> /NiFe <sub>2</sub> O <sub>4</sub>		3	93
Fe <sub>2</sub> O <sub>3</sub>	2,4-Dichlorobenzaldehyde	8	89
Fe <sub>2</sub> O <sub>3</sub> /CuFe <sub>2</sub> O <sub>4</sub>		9	86
Fe <sub>2</sub> O <sub>3</sub> /NiFe <sub>2</sub> O <sub>4</sub>		9.12	83.40

**Figure 6.** FT-IR spectra of as-prepared arylidene barbituric acid derivatives.

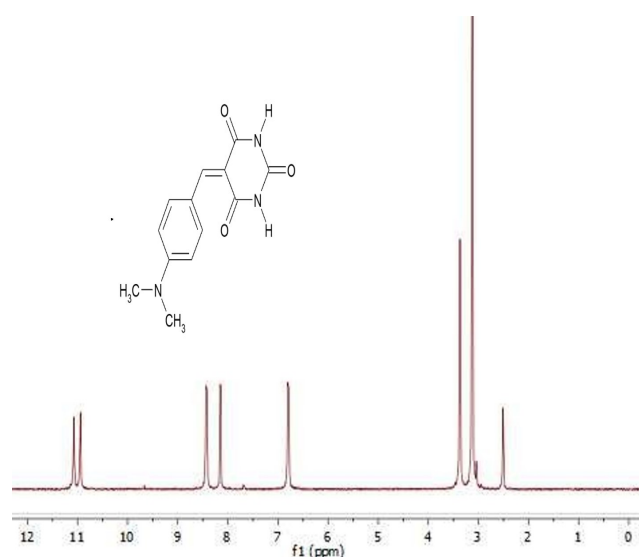
### Recovery and reusability of catalysts

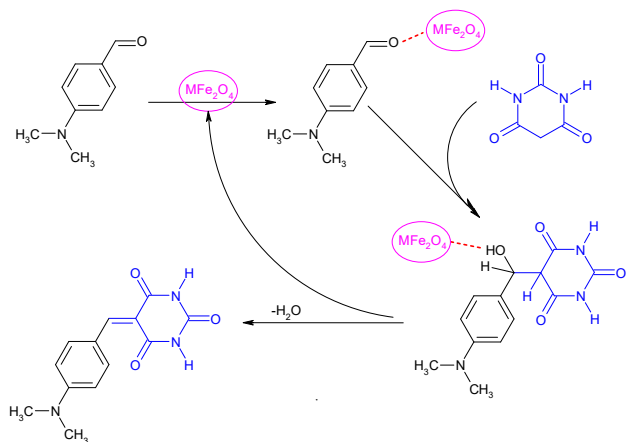
As an advantage of heterogeneous catalysts is their simple recovery and reusability. In this study, after each reaction between aldehyde and barbituric acid, the catalyst was separated from the reaction mixture, washed twice with methanol:chloroform (1:1 v/v), and finally followed by drying at 80 °C for 3 h. The recycled catalysts were used five times in the reaction of 4-dimethylamino benzaldehyde and barbituric acid for the preparation of 5-(4-dimethylaminobenzylidene)barbituric acid as model at optimum condensation conditions.

The results predicted no appreciable loss in the catalytic activity (Figure 9), revealing their good stability and reusability.<sup>36</sup> In Figure 10, the XRD patterns and SEM image of the as-prepared Fe<sub>2</sub>O<sub>3</sub> nanoparticle after 5 recycled used was shown. The position and intensities of all peaks were agreed as well as Fe<sub>2</sub>O<sub>3</sub> (JCPDS card no. 033-0664)<sup>44</sup> and SEM image confirmed that the size and shape of Fe<sub>2</sub>O<sub>3</sub> catalyst after the reaction is agreement with the size and shape before the reaction.

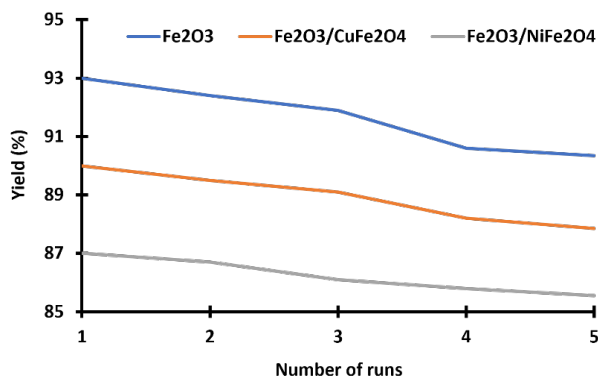
**Table 5.** <sup>1</sup>H-NMR and FT-IR spectral data and melting point of desired compounds

R substituents	FT-IR	<sup>1</sup> H-NMR	M.P. (°C)
4-NO <sub>2</sub>	3581, 3495, 3197, 3094, 2844, 1764, 1695, 1632, 1586, 1520, 1438, 1378, 1346, 1292, 1217, 792, 755, 543, 512	11.48 (s), 11.30 (s), 8.31 (s), 8.23 (d), 8.02 (d),	245
4-OH	3271, 3192, 3045, 2813, 1722, 1669, 1613, 1535, 1409, 1348, 1286, 1219, 1181, 1042, 831, 789, 703, 524, 496	11.3 (s), 11.15 (s), 10.85 (s), 8.25 (d), 8.15 (s), 6.9 (s)	> 320
3-MeO-2-OH	3505, 3192, 3046, 2840, 1745, 1665, 1556, 1439, 1393, 1250, 1066, 928, 852, 791, 733, 682, 613, 545, 507, 421	11.35 (s), 11.15 (s), 9.88 (s), 8.68 (s), 7.78 (s), 7.16 (s), 6.81 (s), 3.92 (s)	> 320
2,4-Cl	3445, 3203, 3070, 2853, 1760, 1722, 1688, 1578, 1466, 1440, 1381, 1221, 1106, 1050, 945, 759, 687, 566, 543	11.65 (s), 11.35 (s), 8.22 (s), 7.85 (s), 7.66 (s)	268
4-N(CH <sub>3</sub> ) <sub>2</sub>	3549, 3425, 3169, 3060, 2828, 1661, 1605, 1517, 1408, 1377, 1208, 860, 793, 514	11.08 (s), 10.96 (s), 8.54 (d), 8.16 (s), 6.83 (d), 3.11 (s)	275
3-EtO-4-OH	3542, 3194, 3053, 2857, 1752, 1662, 1588, 1544, 1500, 1446, 1393, 1295, 1264, 1177, 1143, 1035, 982, 892, 916, 567, 496, 419	11.24 (s), 11.12 (s), 10.54 (s), 8.46 (s), 8.21 (s), 7.78 (s), 6.89 (d), 3.14 (s), 1.36 (s)	> 320

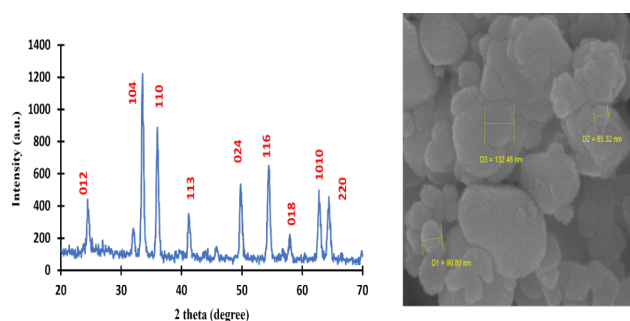
**Figure 7.** <sup>1</sup>H-NMR spectra of 5-(4-dimethylaminobenzylidene)barbituric acid.



**Figure 8.** Proposed mechanism for synthesis of 5-(4-dimethylaminobenzylidene)barbituric acid.



**Figure 9.** Recyclability study of catalysts on the synthesis of 5-(4-dimethylaminobenzylidene)barbituric acid.



**Figure 10.** The XRD pattern and SEM image of Fe<sub>2</sub>O<sub>3</sub> catalyst recycled after the Knoevenagel reaction.

### Comparison with other catalysts

Until now, numerous catalysts were synthesized and used in the Knoevenagel condensation reaction involving aromatic aldehydes and barbituric acid.<sup>14,20-22,47-62</sup> The results were compared with those reported in the previous works (Table 6). It can be seen that the efficiency of the as-prepared catalysts is similar to the previous results. However, the results not show the disadvantages such as using expensive raw materials, and hazardous organic

solvents. This method is simple, eco-friendly and efficient for the preparation of arylidene barbituric acid.

**Table 6.** Comparison of our results with previous results

Catalyst	Condition	Time (min)	Yield (%)	Ref.
Bentonite	H <sub>2</sub> O/90 °C	5-25	90-98	55
PVC/NiFe <sub>2</sub> O <sub>3</sub> /Fe <sub>2</sub> O <sub>3</sub>	Hot water	0.5-22	75-95	54
CoFe <sub>2</sub> O <sub>4</sub>	H <sub>2</sub> O:Ethanol	2-6	70-95	14
PVP Ni nanoparticles	Ethylene glycol, 50 °C	10-15	91	57
Nanoporous MMT-HClO <sub>4</sub>	H <sub>2</sub> O, 70 °C	4	94	61
Taurine	H <sub>2</sub> O, 90 °C	9	96	60
CMZO	Ethanol, 60-70 °C	60	85	59
BF <sub>3</sub> , nano-γ-Al <sub>2</sub> O <sub>3</sub>	Ethanol, r.t.	30	84	58
(H <sub>2</sub> -pip)(H <sub>2</sub> PO <sub>4</sub> )	H <sub>2</sub> O, Ethanol, 80°C	20	96	6
Fe <sub>2</sub> O <sub>3</sub>	H <sub>2</sub> O:Ethanol, r.t.	3-8	72-96	This work
Fe <sub>2</sub> O <sub>3</sub> /CuFe <sub>2</sub> O <sub>4</sub>	H <sub>2</sub> O:Ethanol, r.t.	4-17	68-95	This work
Fe <sub>2</sub> O <sub>3</sub> /NiFe <sub>2</sub> O <sub>4</sub>	H <sub>2</sub> O:Ethanol, r.t.	5-20	69-93	This work

## 4. CONCLUSIONS

In this paper, we synthesized Fe<sub>2</sub>O<sub>3</sub> and Fe<sub>2</sub>O<sub>3</sub>/MFe<sub>2</sub>O<sub>4</sub> (M = Cu, Ni) and used them as new simple, eco-friendly, efficient, non-toxic, recoverable, and inexpensive catalyst in Knoevenagel condensation reaction for the preparation of different arylidene barbituric acid derivatives. Simple process, an aqueous medium, low catalyst loading, non-toxic reagent, high yields of the desire products and short reaction time are the attractive features of this work. Also, the catalysts showed recyclability up to five runs without any notable reduction in their activity. Therefore, the as-prepared Fe<sub>2</sub>O<sub>3</sub> and Fe<sub>2</sub>O<sub>3</sub>/MFe<sub>2</sub>O<sub>4</sub> (M = Cu, Ni) nanoparticles was proposed as novel catalysts in the multicomponent reactions for synthesis various organic compounds.

## CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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