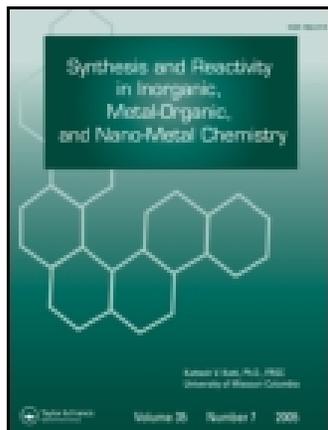


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# Synthesis of FAU Zeolite Nanoparticles as Heterogeneous Catalyst for One-Pot Synthesis of 2-Substituted Aryl (Indolyl) Kojic Acid Derivatives under Solvent-Free Condition

Bahareh Sadeghi,<sup>1</sup> Zahra Lasemi,<sup>2</sup> Fereshteh Amiri Tavasoli,<sup>1</sup> Saeedeh Hashemian,<sup>1</sup> and Hesam Zahedi<sup>1</sup>

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FAU zeolite nanoparticles have been found to be a highly efficient and versatile catalyst for preparation of 2-substituted aryl (indolyl) kojic acid derivatives through one-pot condensation of kojic acid with aryl aldehydes and indoles under solvent-free conditions. The corresponding products were obtained in very high yields and in short reaction times.

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**Keywords** aldehyde, FAU zeolite nanoparticles, heterogeneous catalyst, indole, kojic acid, solvent-free

## INTRODUCTION

The 3-substituted indoles are important classes of organic compounds of a large number of naturally occurring, as well as synthetic derivatives, and occupy a prominent position in medicinal chemistry.<sup>[1,2]</sup> A number of 3-substituted indole derivatives possess wide range of biological activities and pharmacological properties, such as anticancer, antitumor,<sup>[3]</sup> antiinflammatory, hypoglycemic, analgesic, and antipyretic activities.<sup>[4]</sup>

On the other hand, the syntheses of kojic acid derivatives have attracted great interest because of its accessibility, potential biological activity, and high reactivity.<sup>[5,6]</sup> Many kinds of kojic acids have been prepared for biological assay.<sup>[7,8]</sup> Due to the vast medicinal utility of kojic acid and 3-substituted indole derivatives, the introduction of a mild, efficient, and selective method to synthesize these compounds is still needed. There is only few articles in the literature dealing with the synthesis of 2-substituted aryl (indolyl) kojic acid derivatives.<sup>[9]</sup>

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Heterogeneous catalysts have gained much importance in recent years due to economic and environmental benefits.<sup>[10]</sup> These catalysts are generally inexpensive and easily available. They can conveniently be handled and removed from the reaction mixture, thus making the experimental procedure simple and eco-friendly. Zeolites are especially promising in their application as heterogeneous catalysts, due to their ordered structure and high porosity.<sup>[11,12]</sup> In this regard, we decided to use FAU zeolite nanoparticles as a catalyst for preparing this group of compounds.

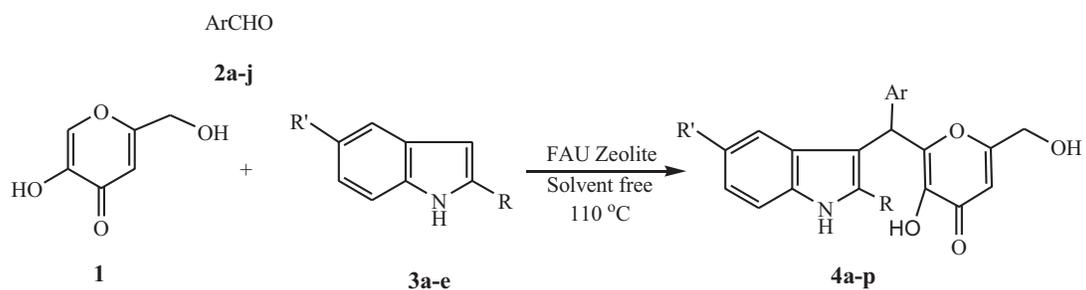
In this article, in continuation of our investigations of the application of solid acids in organic synthesis,<sup>[13–19]</sup> we prepared FAU zeolite nanoparticles and applied for the one-pot synthesis of 2-substituted aryl (indolyl) kojic acid derivatives from kojic acid, aryl aldehydes, and indole derivatives under solvent-free conditions at 110°C (Scheme 1).

## EXPERIMENTAL

Melting points were determined with an Electrothermal 9100 apparatus. The NMR spectra were recorded in (D<sub>6</sub>) DMSO and CDCl<sub>3</sub> on Bruker Avance III 400 MHz spectrometer. Elemental analyses were determined on a CHN Elemental Analyzer LECO 600. XRD patterns were recorded by a PW3719 Instrument. The morphologies of the products were observed using TEM of EM10C and SEM of a XL30 Philips microscope. Materials were purchased from Fluka and Merck companies.

### Preparation of FAU Zeolite Nanoparticles

NaOH (4.07 g) and sodium aluminate (2.09 g) were dissolved in distilled water (19.95 mL), in which meta silicate (22.07 g) was added after 30 min. The resulting mixture was stirred 10 min until a white gel was formed (solution A). Separately, sodium aluminate (13.09 g) was added to a solution of NaOH (0.14 g) in water (130.97 mL). Then meta silicate (142.43 g) was added to this solution. The resulting mixture was stirred until a white gel was formed (solution B). Mixing of solutions A and B under stirring was resulted in white gel. In order to assure the formation of white gel, the solutions were typically stirred for 24 h at room



SCH. 1. Synthesis of 2-substituted aryl (indolyl) kojic acid derivatives by the reaction of kojic acid with aryl aldehyde and indole derivatives by FAU zeolite nanoparticles

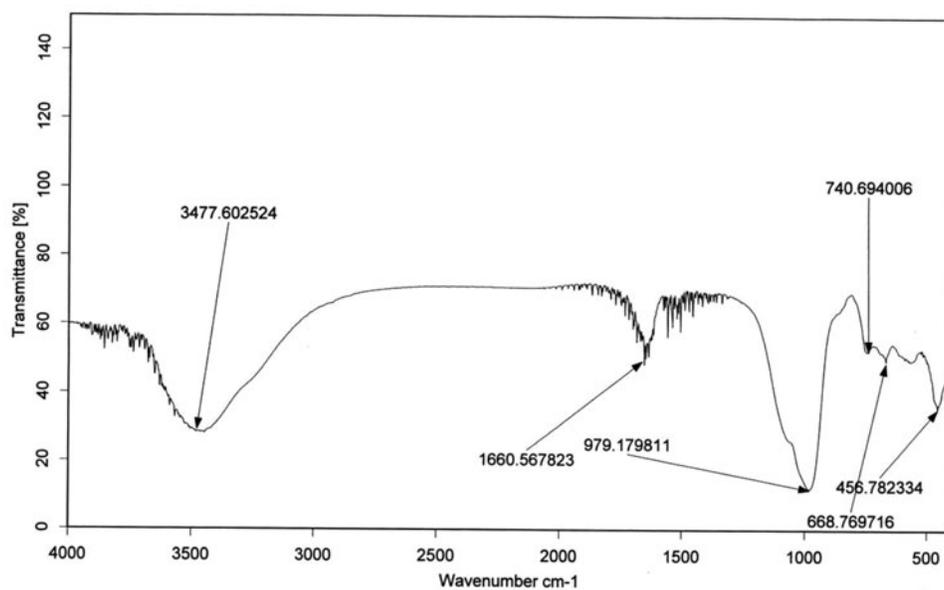


FIG. 1. FT-IR spectra of FAU zeolite nanoparticles.

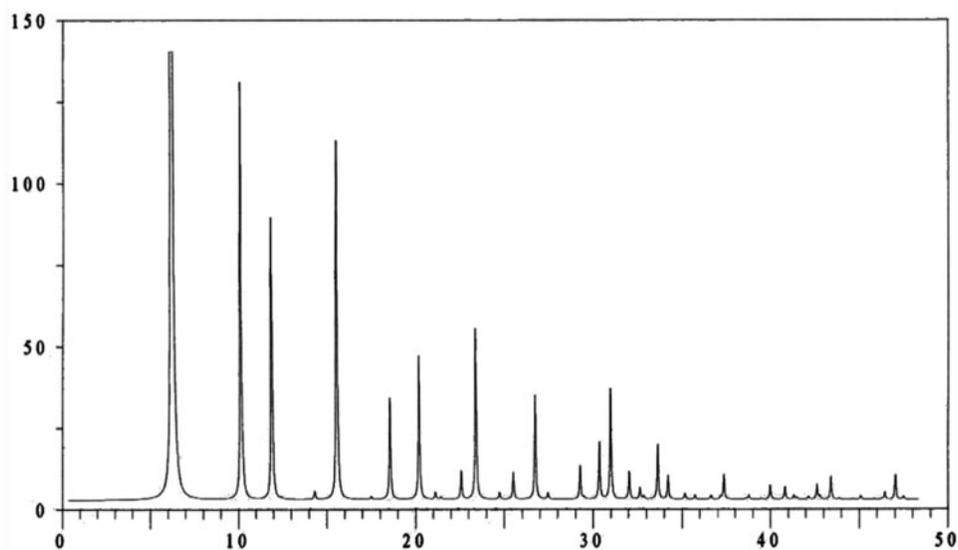


FIG. 2. XRD pattern of the FAU zeolite nanoparticles.

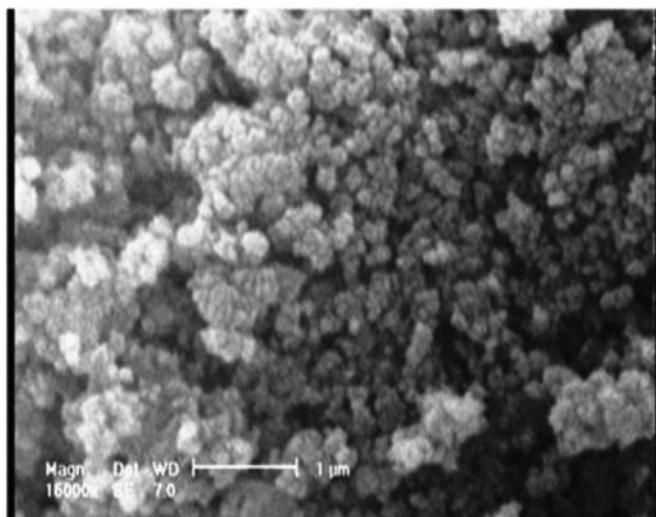


FIG. 3. SEM image of the FAU zeolite nanoparticles.

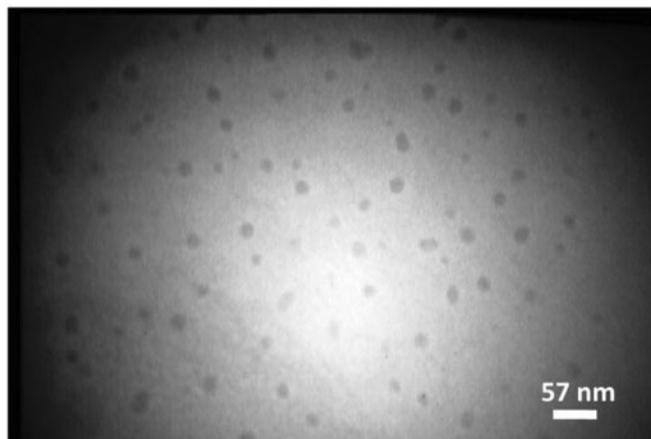


FIG. 4. TEM image of the FAU zeolite nanoparticles.

temperature. Then, resulting gel transferred into an autoclave, where the hydrothermal crystallization was carried out at 100°C for 8 h. Finally, FAU zeolites were filtered and washed with distilled water. This procedure was repeated until the pH of the supernatant decreased to lower than 8. Then the powder was dried at 110°C over night. The as-synthesized zeolitic powders were calcined in oven at 230°C for 4 h.

#### General Procedure for the Preparation of 2-Substituted Aryl (Indolyl) Kojic Acid Derivatives (4)

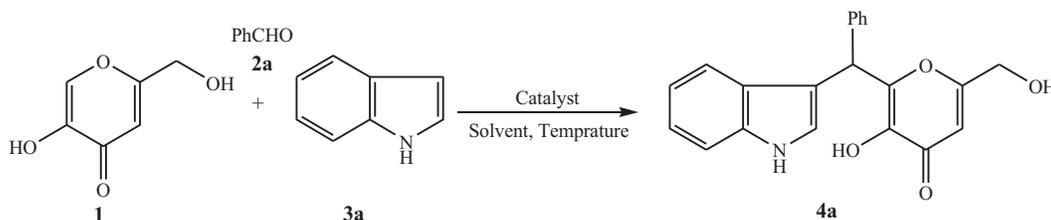
A mixture of kojic acid **1** (1 mmol), aryl aldehyde **2** (1 mmol), and FAU zeolite nanoparticles (0.008 g) was stirred at 110°C. After 10 min, indole **3** (1 mmol) was added and the reaction was continued for appropriate time. After the completion of the reaction (as monitored by TLC), water was added with reaction mixture (15 mL) and extracted with ethyl acetate (3 × 10 mL). The organic layer was dried over sodium sulfate and concentrated under vacuum. The crude product was chromatographed in silica gel (70:30 *n*-hexane/ethyl acetate) and appropriate isolated yield is shown in Table 5. The new products were known compounds and characterized by <sup>1</sup>H NMR, <sup>13</sup>C NMR spectra and known compounds were identified by comparing melting point and <sup>1</sup>H NMR spectra with does reported in the literature.

#### Spectral Data of New Products

2-((1H-Indol-3-yl)(4-methylphenyl)methyl)-3-hydroxy-6-(hydroxymethyl)-4H-pyran-4-one (**4c**): <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub> + CDCl<sub>3</sub>, 1:4): δ 2.32 (s, 3H), 4.21 (dd, 2H), 5.65 (s, 1H), 6.29 (s, 1H), 6.63 (s, 1H), 6.70–7.35 (m, 8H), 7.43 (s, 1H), 10.19 (s, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 21.7, 38.5, 59.1, 111.3, 119.1, 119.4, 119.7, 122.1, 123.6, 126.2, 129.8, 131.4, 133.6, 134.9, 136.6, 138.7, 145.5, 150.1, 167.2, 173.3. Anal. Calc. for C<sub>22</sub>H<sub>19</sub>O<sub>4</sub>N: C, 73.12; H, 5.30; N, 3.87. Found: C, 73.08; H, 5.32; N, 3.80.

2-((1H-Indol-3-yl)(4-bromophenyl)methyl)-3-hydroxy-6-(hydroxymethyl)-4H-pyran-4-one (**4d**): <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub> + CDCl<sub>3</sub>, 1:4): δ 4.25 (dd, 2H), 5.57 (s, 1H), 6.19 (s, 1H), 6.67 (s, 1H), 7.03 (t, *J* = 8 Hz, 1H), 7.18–7.26 (m, 2H), 7.37–7.43 (m, 3H), 7.54–7.58 (m, 2H), 7.98 (s, 1H), 10.14 (s, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 39.6, 59.2, 111.1, 119.1, 119.4, 119.8, 122.1, 123.6, 126.8, 130.5, 131.3, 133.7, 135.2, 136.7, 138.8, 143.1, 150.2, 167.1, 173.4. Anal. Calc. for C<sub>21</sub>H<sub>16</sub>O<sub>4</sub>NBr: C, 59.17; H, 3.78; N, 3.28. Found: C, 59.20; H, 3.75; N, 3.24.

2-((1H-Indol-3-yl)(2-nitrophenyl)methyl)-3-hydroxy-6-(hydroxymethyl)-4H-pyran-4-one (**4e**): <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub> + CDCl<sub>3</sub>, 1:4): δ 4.24 (dd, 2H), 5.50 (s, 1H), 6.09 (s, 1H), 6.61 (s, 1H), 7.02–7.21 (m, 3H), 7.37–7.43 (m, 3H), 7.54–7.56 (m, 1H), 7.71–7.74 (m, 1H), 8.09 (d, 1H, *J* = 8.2), 10.41 (s, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 38.7, 60.1,



SCH. 2. Model reaction for optimization reaction conditions.

TABLE 1  
Study of BET tests of FAU zeolite nanoparticles

Entry	Type of measurement	FAU zeolite
1	Sample weight (g)	9.11
2	Temperature (°C)	110
3	Saturated vapor pressure (KPa)	89.121
4	Mean pore diameter (nm)	50.239
5	Total pore volume (cm <sup>3</sup> .g <sup>-1</sup> )	0.41
6	As, BET (m <sup>2</sup> .g <sup>-1</sup> )	3.27

111.1, 119.5, 119.7, 122.2, 123.8, 124.0, 124.4, 127.2, 128.8, 130.9, 132.3, 135.2, 138.8, 141.4, 150.4, 167.8, 176.3. Anal. Calc. for C<sub>21</sub>H<sub>16</sub>O<sub>6</sub>N<sub>2</sub>: C, 64.28; H, 4.11; N, 7.14. Found: C, 64.24; H, 4.15; N, 7.16.

2-((1H-Indol-3-yl)(3-nitrophenyl)methyl)-3-hydroxy-6-(hydroxymethyl)-4H-pyran-4-one (**4f**): <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub> + CDCl<sub>3</sub>, 1:4): δ 4.22 (dd, 2H), 5.54 (s, 1H), 6.03 (s, 1H), 6.71 (s, 1H), 7.02–7.55 (m, 7H), 8.10 (s, 1H), 8.23 (s, 1H), 10.21 (s, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 39.7, 59.7, 111.1, 118.1, 119.5, 120.1, 120.6, 122.2, 122.9, 124.3, 127.5, 129.0 (2C), 131.1 (2C), 136.5, 139.5, 148.3, 151.2, 167.3, 174.2. Anal. Calc. for C<sub>21</sub>H<sub>16</sub>O<sub>6</sub>N<sub>2</sub>: C, 64.28; H, 4.11; N, 7.14. Found: C, 64.30; H, 4.09; N, 7.15.

2-((1H-Indol-3-yl)(4-nitrophenyl)methyl)-3-hydroxy-6-(hydroxymethyl)-4H-pyran-4-one (**4g**): <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub> + CDCl<sub>3</sub>, 1:4): δ 4.32 (dd, 2H), 5.60 (s, 1H), 6.07 (s, 1H), 6.70 (s, 1H), 7.05 (t, *J* = 7.4 Hz, 1H), 7.22 (t, *J* = 7.4 Hz, 1H), 7.35–7.54 (m, 6H), 8.17 (d, 1H, *J* = 8.3 Hz), 10.15 (s, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 40.2, 59.4, 111.3, 118.1, 119.6 (2C), 122.3 (2C), 123.6 (2C), 126.6, 128.8, 129.5, 130.9, 136.7, 146.5, 151.8, 167.1, 173.5. Anal. Calc. for C<sub>21</sub>H<sub>16</sub>O<sub>6</sub>N<sub>2</sub>: C, 64.28; H, 4.11; N, 7.14. Found: C, 64.26; H, 4.13; N, 7.10.

2-((1H-Indol-3-yl)(4-chloro-2-nitrophenyl)methyl)-3-hydroxy-6-(hydroxymethyl)-4H-pyran-4-one (**4h**): <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub> + CDCl<sub>3</sub>, 1:4): δ 4.25 (dd, 2H), 5.75 (s, 1H), 6.01 (s, 1H), 6.67 (s, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 7.23 (t, *J* = 7.5 Hz, 1H), 7.36–7.55 (m, 5H), 7.86 (s, 1H), 8.05 (s,

TABLE 2  
Effect of different catalysts on the yield of **4a**<sup>a</sup>

Entry	Catalyst (g)	Yield (%)
1	KAl(SO <sub>4</sub> ) <sub>2</sub> .12H <sub>2</sub> O (0.01 g)	60
2	ZnO-NPs (0.01 g)	70
3	CuCl <sub>2</sub> .2H <sub>2</sub> O (0.01 g)	40
4	SbCl <sub>5</sub> -SiO <sub>2</sub> (0.01 g)	40
5	SnCl <sub>2</sub> .2H <sub>2</sub> O (0.01 g)	35
6	ZnSO <sub>4</sub> .H <sub>2</sub> O (0.01 g)	50
7	FAU zeolite NPs (0.01 g)	97

<sup>a</sup>Reaction conditions: 60 min at 110°C in solvent-free conditions.

TABLE 3  
Effect of different solvents on the yield of **4a**

Entry	Solvent	Yield (%)
1	EtOH <sup>a</sup>	60
2	THF <sup>b</sup>	20
3	DMF <sup>a</sup>	60
4	H <sub>2</sub> O <sup>a</sup>	45
5	<i>n</i> -Hexane <sup>a</sup>	10
6	Toluene <sup>a</sup>	50
7	Solvent-free <sup>b</sup>	97

<sup>a</sup>60 min at reflux temperature in 10 mL solvent in the presence of 0.008 g of FAU zeolite nanoparticles.

<sup>b</sup>60 min at 110°C in the presence of 0.008 g of FAU zeolite nanoparticles.

1H), 10.23 (s, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 39.6, 60.2, 111.2, 119.5, 120.3, 122.2, 122.9, 123.9, 124.1, 127.5, 128.8, 130.9, 131.4, 132.2, 134.9, 136.5, 137.4, 145.6, 150.5, 167.6, 176.1. Anal. Calc. for C<sub>21</sub>H<sub>15</sub>O<sub>6</sub>N<sub>2</sub>Cl: C, 59.09; H, 3.54; N, 6.56. Found: C, 59.12; H, 3.51; N, 6.53.

2-((1H-Indol-3-yl)(naphthalene-3-yl)methyl)-3-hydroxy-6-(hydroxymethyl)-4H-pyran-4-one (**4i**): <sup>1</sup>H NMR (400 MHz, DMSO-d<sub>6</sub> + CDCl<sub>3</sub>, 1:4): δ 4.20 (dd, 2H), 5.01 (s, 1H), 5.98 (s, 1H), 6.32 (s, 1H), 6.71 (t, *J* = 7.2 Hz, 1H), 6.85 (t, *J* = 7.2 Hz, 1H), 7.14–7.67 (m, 9H), 7.85 (s, 1H), 10.19 (s, 1H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 38.7, 59.4, 108.2, 109.1, 111.5, 118.1, 118.7, 119.4 (2C), 121.5, 123.5, 125.0, 125.9, 126.4, 126.7, 129.6, 130.8, 131.8, 134.1, 134.6, 137.9, 143.5, 152.9, 164.2, 173.3. Anal. Calc. for C<sub>25</sub>H<sub>19</sub>O<sub>4</sub>N: C, 75.55; H, 4.82; N, 3.52. Found: C, 75.50; H, 4.85; N, 3.56.

## RESULTS AND DISCUSSION

FAU zeolite nanoparticles were prepared via hydrothermal method according to experimental section. The synthesized FAU zeolite nanoparticles were characterized using Fourier Transform Infrared (FT-IR), X-ray diffraction (XRD), scanning

TABLE 4  
Effect of catalyst loading on the yield of **4a**<sup>a</sup>

Entry	Amount of catalyst (g)	Temperature (°C)	Yield (%)
1	—	110	—
2	0.001	110	50
3	0.005	110	70
4	0.008	110	97
5	0.008	100	85
6	0.008	80	80
7	0.008	60	75
8	0.008	120	97

<sup>a</sup>Reaction conditions: 60 min at 110°C in solvent-free conditions.

TABLE 5  
 Synthesis of 2-substituted aryl (indolyl) kojic acid derivatives by the reaction of kojic acid with aryl aldehyde and indole derivatives catalyzed by FAU zeolite nanoparticles

Entry	Aldehyde	Indole	Product <sup>a</sup>	Time (min)	Yield (%) <sup>b</sup>	M.p (°C) <sup>[Ref]</sup>
1	 <b>2a</b> 2a	 <b>3a</b> 3a	<b>4a</b>	55	97	79–81 <sup>[9]</sup>
2	 <b>2b</b> 2b	 <b>3a</b> 3a	<b>4b</b>	45	93	93–94 <sup>[9]</sup>
3	 <b>2c</b> 2c	 <b>3a</b> 3a	<b>4c</b>	60	87	96–98 <sup>[9]</sup>
4	 <b>2d</b> 2d	 <b>3a</b> 3a	<b>4d</b>	60	93	Oil
5	 <b>2e</b> 2e	 <b>3a</b> 3a	<b>4e</b>	70	83	87–89
6	 <b>2f</b> 2f	 <b>3a</b> 3a	<b>4f</b>	85	82	169–171
7	 <b>2g</b> 2g	 <b>3a</b> 3a	<b>4g</b>	75	82	170–173
8	 <b>2h</b> 2h	 <b>3a</b> 3a	<b>4h</b>	80	85	167–168
9	 <b>2i</b> 2i	 <b>3a</b> 3a	<b>4i</b>	85	87	169–171
10	 <b>2j</b> 2j	 <b>3a</b> 3a	<b>4j</b>	55	92	79–80
11	 <b>2b</b> 2b	 <b>3b</b> 3b	<b>4k</b>	45	90	84–85 <sup>[9]</sup>
11	 <b>2c</b> 2c	 <b>3b</b> 3b	<b>4l</b>	50	89	89–90 <sup>[9]</sup>

(Continued on next page)

TABLE 5  
 Synthesis of 2-substituted aryl (indolyl) kojic acid derivatives by the reaction of kojic acid with aryl aldehyde and indole derivatives catalyzed by FAU zeolite nanoparticles (*Continued*)

Entry	Aldehyde	Indole	Product <sup>a</sup>	Time (min)	Yield (%) <sup>b</sup>	M.p (°C) <sup>[Ref]</sup>
12	 <b>2j</b> <b>2j</b>	 <b>3b</b> <b>3b</b>	<b>4m</b>	55	94	86–88 <sup>[9]</sup>
14	 <b>2c</b> <b>2c</b>	 <b>3c</b> <b>3c</b>	<b>4n</b>	70	82	97–98 <sup>[9]</sup>
15	 <b>2c</b> <b>2c</b>	 <b>3d</b> <b>3d</b>	<b>4o</b>	65	89	Oil <sup>[9]</sup>
16	 <b>2c</b> <b>2c</b>	 <b>3e</b> <b>3e</b>	<b>4p</b>	65	93	Oil <sup>[9]</sup>

<sup>a</sup>All the products were identified by <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra and also by comparing of melting point and <sup>1</sup>H NMR spectra with those of authentic samples reported in the literature.

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

electron microscope (SEM), transmission electron microscope (TEM), and BET.

The FT-IR spectra of the zeolite is shown in Figure 1. The spectra shows a broad and strong band at region 3200–3600 cm<sup>-1</sup>. This broad band is due to silanol OH groups (Si-OH). The predominant absorbance peak at 979 cm<sup>-1</sup> was due to Si-O-Al group. The bands between 456 and 740 cm<sup>-1</sup> were due to Si-O, Al-O, Si-Al, and Si-O-Si. The absorption band at 668 cm<sup>-1</sup> was due to Si-O-Na group.

The dimensions of nanoparticles were observed with XRD and SEM. The size of FAU zeolite nanoparticles are about 50–60 nm. SEM images of FAU zeolite nanoparticles also confirmed that the nanoparticles were homogeneously dispersed in cubic structure (Figures 2 and 3). It is clearly seen on the TEM images of FAU zeolite nanoparticles that the crystals size are 50–60 nm (Figure 4).

BET results are given in the Table 1. This information includes the measurement of surface area, total pore volume, and the average pore diameter of FAU zeolite nanoparticles. According to the obtained data, the ideal surface area was obtained approximately 3.27 m<sup>2</sup>/g and the average pore diameter was obtained 50.2 nm.

To obtain optimal conditions, the reaction between benzaldehyde with indole and kojic acid was regarded as model reaction (Scheme 2).

To emphasize the effect of the catalyst, a series of different catalysts were applied for the model reaction. All reactions were

run under the same conditions, and similar amounts of catalysts (0.01 g) were used. As it is clear in the Table 2, FAU zeolite nanoparticles resulted in highest conversion to the desired product.

Model reaction was examined in different solvents such as EtOH, THF, DMF, H<sub>2</sub>O, *n*-hexane, and toluene, in the presence of FAU zeolite nanoparticles (0.008 g) at their reflux temperature (Table 3). The results in Table 3 show the efficiency of solvent-free conditions which gives the desired product in excellent yield. This reaction in protic and aprotic solvents did not afford reasonable yield of the product (Table 3, entries 1–6).

Increasing the catalyst loading from 0.001 to 0.008 g, increased the yield of the reaction significantly (Table 4, entries 2–4). The best catalyst loading was found in 0.008 g, which gave an excellent yield of 4a only after 60 min.

The above model reaction was carried out at different temperatures with 0.008 g of FAU zeolite nanoparticles. It was found that the desired compound 4a was obtained in excellent yield at 110°C (Table 4, entries 4–7). Further increase of the temperature (120°C) neither increased the yield nor shortened the reaction time (Table 4, entry 8).

A series of aromatic aldehydes **2** were treated with kojic acid **1** and indole derivatives **3** in the presence of FAU zeolite nanoparticles (0.008 g) under solvent-free conditions at 110°C (Table 5). Benzaldehyde and 2-naphthaldehyde were treated with kojic acid and indole, and the corresponding 2-substituted aryl (indolyl) kojic acid derivatives were produced in excellent

yields (Table 5, entries 1 and 10). When kojic acid and indole reacted with aldehydes such as 3-phenoxy, 4-methoxy, and 4-methyl benzaldehyde, the corresponding product was formed with 87 to 93% yields (Table 5, entries 2–4). Aromatic aldehydes including halogen group and electron-withdrawing group on phenyl such as 2-nitro, 3-nitro, and 4-nitro benzaldehyde, reacted well with kojic acid and indole to afford desired products in good yields (Table 5, entries 5–9).

Interestingly, substituted indoles were also effective for this three-component reaction. When 2-methyl indole were reacted with kojic acid and aldehydes such as 3-phenoxy, 4-methoxy benzaldehyde, and 2-naphthaldehyde under the same reaction conditions, a higher yield of the 2-substituted aryl (indolyl) kojic acid product was obtained in shorter times (Table 5, entries 11–13). Similarly, when 2-phenyl, 5-chloro, and 5-bromo indole reacted with 4-methoxy benzaldehyde and kojic acid in the presence of FAU zeolite nanoparticles (0.008 g) at 110°C, a good yield of the corresponding products was obtained (Table 5, entries 14–16).

## CONCLUSION

In summary, we have reported an efficient procedure for one-pot synthesis of 2-substituted aryl (indolyl) kojic acid derivatives through three-component reactions of kojic acid with indoles and aryl aldehydes using a catalytic amount of FAU zeolite nanoparticles under solvent-free conditions. By incorporating two biologically potential moiety in a single molecule, the biological activity of these compounds may be enhanced. The main advantages of this procedure include high yields, simple experimental procedure, short-reaction times, use of various substrates, ease of the work-up, nonuse of hazardous organic solvents, and use of heterogeneous and environmentally friendly

catalyst, which make it a useful, attractive, and green strategy for formation of a wide range of 2-substituted aryl (indolyl) kojic acid derivatives.

## REFERENCES

1. Gribble, G.W. *J. Chem. Soc. Perkin Trans 1*. **2000**, 1045.
2. Xiong, W.N.; Yang, C.G.; Jiang, B. *Bioorg. Med. Chem.* **2001**, *9*, 1773.
3. Zhu, S.; Ji, S.; Su, X.; Sun, C.; Liu, Y. *Tetrahedron Lett.* **2008**, *49*, 1777.
4. Farghaly, A.M.; Habib, N.S.; Khalil, M.A.; Sayed, O.A.; Alexandria, E. *J. Pharm. Sci.* **1989**, *3*, 90.
5. Zhu, M.P.; Kimiaki, I. *Tetrahedron Lett.* **1997**, *38*, 5301.
6. Xiong, X.; Pirrung, M. C. *Org. Lett.* **2008**, *10*, 1151.
7. (a) Sefkow, M.; Kaatz, H. *Tetrahedron Lett.* **1999**, *40*, 6561. (b) Barham, H.N.; Reed, G.N. *J. Am. Chem. Soc.* **1938**, *60*, 1541.
8. (a) Kobayashi, Y.; Kayahara, H.; Tadasa, K.; Tanaka, H. *Bioorg. Med. Chem. Lett.* **1996**, *6*, 1303. (b) Fox, R.C.; Taylor, P.D. *Synth. Commun.* **1998**, *28*, 1575. (c) Shestopalov, A.A.; Rodinovskaya, L.A.; Shestopalov, A.M.; Litvinov, V.P. *Russian. Chem. Bulletin.* **2004**, *53*, 724.
9. Reddy, B.V.S.; Reddy, M.R.; Madan, Ch.; Kumar, K.P.; Rao, M.S. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 7507.
10. (a) Ramesh, C.; Ravindranath, N.; Das, B. *J. Org. Chem.* **2003**, *68*, 7101. (b) Ramesh, C.; Mahender, G.; Ravindranath, N.; Das, B. *Tetrahedron Lett.* **2003**, *44*, 1465. (c) Das, B.; Banerjee, J.; Ravindranath, N. *Tetrahedron*. **2004**, *60*, 8357. (d) Das, B.; Ravinder Reddy, K.; Thirupathi, P. *Tetrahedron Lett.* **2006**, *47*, 5855. (e) Das, B.; Venkateswarlu, K.; Krishnaiah, M.; Holla, H. *Tetrahedron Lett.* **2006**, *47*, 7551.
11. McMorn, P.; Hutchings, G. *J. Chem. Soc. Rev.* **2004**, *33*, 108.
12. Hutchings, G. *J. Annu. Rev. Mater. Res.* **2005**, *35*, 143.
13. Sadeghi, B.; Mirjalili, B.F.; Hashemi, M.M. *Tetrahedron Lett.* **2008**, *49*, 2575.
14. Mirjalili, B.F.; Hashemi, M.M.; Sadeghi, B.; Emtiazi, H. *J. Chin. Chem. Soc.* **2009**, *56*, 386.
15. Sadeghi, B.; Hassanabadi, A.; Bidaki, S. *J. Chem. Res.* **2011**, *35*, 666.
16. Sadeghi, B.; Hassanabadi, A.; Kamali, M. *J. Chem. Res.* **2012**, *36*, 9.
17. Sadeghi, B.; Zavar, S.; Hassanabadi, A. *J. Chem. Res.* **2012**, *36*, 343.
18. Sadeghi, B.; Nasirian, Z.; Hassanabadi, A. *J. Chem. Res.* **2012**, *36*, 391.
19. Sadeghi, B.; Farahzadi, E.; Hassanabadi, A. *J. Chem. Res.* **2012**, *36*, 539.