A New Method for the Synthesis of New Derivatives of “1,3-diaryl-2-n-azaphenalene and n-acyl-1,3-diaryl-2-N-azephenylene” by Using Nano catalyst and Analyzing Antibacterial Activity of Structures

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ABSTRACT

In this research, synthesized well derivatives of 1,3-diaryl-2-N-azaphenalene and N-acyl-1,3-diaryl-2-N-azaphenalene as a macromolecule in the presence of nanoparticles (Fe₃O₄ coated with L-Arginine) as a magnetic Nano catalyst in a one-pot reaction of compounds 7.2-Naphthalene diol, aldehydes, ammonium derivatives (ammonium acetate or ammonium hydro phosphates) and solvent (water and alcohol) with high yield and short reaction times, economical and simple workup. In this study, apart from the innovation in the synthesis of a macromolecule, the antibacterial activity of these compounds was evaluated for the first time. The reaction was done under very moderate conditions at room temperature. The chemical structures of all synthesized compounds were determined using infrared, ¹H NMR and ¹³C NMR spectroscopies. After the production of nanoparticles, the structure of the obtained nanoparticles was characterized via Fourier transform infrared spectroscopy (IR) and field emission scanning electron microscopy (FE-SEM). The results demonstrated that the average size of the synthesized magnetite nanoparticles is about 21 nm. The heterogeneous catalyst used was easily separated magnetically and reused without any significant loss of catalytic activity and magnetism. Eventually, antibacterial activity of the synthesized compounds was investigated by Escherichia coli (ATCC: 25922) and Pseudomonas aeruginosa (ATCC: 27853) as gram negative bacteria, Staphylococcus epidermidis (ATCC: 14990) and Staphylococcus aureus (ATCC: 29213) as gram positive bacteria. Some of these products exhibit significant antibacterial activity.

Keywords: Antibacterial activity; Azaphenalene; Macromolecule; Multicomponent; Nanocatalysts; One-pot

INTRODUCTION

Multicomponent reactions (MCRs) are onestep processes in which three or more reactants react together to produce a new product without the isolation of the intermediates, where all or most of the atoms contribute to the structure of new product. These reactions are used as valuable tools for rapid and efficient synthesis of organic and drug-like compounds containing biological screening due to several aspects including minimum preparative work setup and high degree of diversity. [1-2]

Despite extensive research on this relationship, development and discovery of new MCRs is still in demand. The Biginelli, Ugi, Passerini, and Mannich reactions are some example of MCRs. [3]

The chemistry of heterocyclic compounds has attracted considerable research interest and
is considered necessary because some of these compounds are applied in anticancer, anti-inflammatory, anticonvulsant and antidiuretic treatments. [4]

In this research, the azaphenalenes derivatives have been attempted to be synthesized using the Multicomponent reactions (MCRs) method. Derivatives of azaphenalene due to the high biological activity, scarce natural supply and difficult, only small-scale, isolation from natural sources, the synthesis of this heterocyclic nucleus is currently of major importance. These compounds have very low oxidation potentials and very low negative reduction potentials and are, thus, extremely promising antioxidants in biological systems. [5–10]

Since the use of a catalyst to accelerate the reactions has always been of interest to researchers, the use of nanoparticles has been of great interest in recent years. [11-12]

Magnetic nanoparticles have led a new era of research to researchers. Magnetic nanoparticles iron oxide has expanded due to high magnetic efficiency, Surface with ratio, high volume, biocompatibility, low toxicity, and rapid response to external magnetic field, etc. in biotechnology, targeted drug delivery, chemistry, physics and industry. This method brings many economic and environmental benefits because it produces yields and effective processes of magnetic catalytic recovery.

Many investigations have focused on heterogeneous catalysts, especially magnetic nanoparticles (MNPs), for example, nanoparticles Fe₃O₄. [13-14]

Magnetic nanoparticles of iron oxide (Fe₃O₄) have been widely used as heterogeneous catalysts in organic reactions. Using merely a magnet has made them cheap, available, low toxic, recyclable and easy to separate from the reaction solution. [15–19]

We found a simple and efficient procedure for the synthesis of new 1,3-diphenyl-2-azaphenalene derivatives from the condensation of 2,7-naphthalenediol, aromatic aldehydes, and ammonia derivatives (ammonium acetate or ammonium hydrogen phosphate) in a mixture of EtOH-H₂O (3:1) in the presence Fe₃O₄@L-arginine Nano catalyst as an efficient catalyst with recycling potential and reusability. (Schemes 1 and 2).

Antimicrobial agents used to treat infectious diseases and caused by various pathogenic strains (bacteria, fungi, parasites and viruses) are essential medications for humans and animals. [20]

**EXPERIMENTAL**

**General**

All chemicals were purchased from Merck or Fluka and used without any further purification. The melting points were uncorrected and measured using capillary tubes on an electro thermal digital apparatus. IR spectra were recorded by the TENSOR 27, FT-IR 5000 in KBr. 1HNMR (500 MHz), and
(mmol) was solved in 100 ml of deionized water. 

MHz spectrometers using DMSO-d$_6$ as a solvent 
electron microscope measurement was obtained 
10–80 using 0.04 as the step length. The scanning 
140$^\circ$ C. Finally, Fe$_3$O$_4$ @ L-arginine Nano catalyst is separated from the aqueous 
solution by an external magnet and washed 
6 hours at 100 °C. Finally, Fe$_3$O$_4$ @ L-arginine 

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst (mg)</th>
<th>Solvent</th>
<th>Temp. (°C)</th>
<th>Time</th>
<th>Yield A5 (%)</th>
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<td>1</td>
<td>-</td>
<td>EtOH</td>
<td>Reflux</td>
<td>7 h</td>
<td>57</td>
</tr>
<tr>
<td>2</td>
<td>-</td>
<td>1 EtOH:1 H$_2$O</td>
<td>Reflux</td>
<td>7 h</td>
<td>53</td>
</tr>
<tr>
<td>3</td>
<td>-</td>
<td>2 EtOH:1 H$_2$O</td>
<td>Reflux</td>
<td>7 h</td>
<td>60</td>
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<tr>
<td>4</td>
<td>-</td>
<td>3 EtOH:1 H$_2$O</td>
<td>Reflux</td>
<td>7 h</td>
<td>72</td>
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<tr>
<td>5</td>
<td>Fe$_3$O$_4$ @ L-arginine(50)</td>
<td>EtOH</td>
<td>r.t</td>
<td>30 min</td>
<td>81</td>
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<tr>
<td>6</td>
<td>Fe$_3$O$_4$ @ L-arginine(50)</td>
<td>1 EtOH:1 H$_2$O</td>
<td>r.t</td>
<td>30 min</td>
<td>76</td>
</tr>
<tr>
<td>7</td>
<td>Fe$_3$O$_4$ @ L-arginine(50)</td>
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<td>r.t</td>
<td>30 min</td>
<td>84</td>
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<td>8</td>
<td>Fe$_3$O$_4$ @ L-arginine(50)</td>
<td>3 EtOH:1 H$_2$O</td>
<td>r.t</td>
<td>30 min</td>
<td>90</td>
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<tr>
<td>9</td>
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<td>r.t</td>
<td>30 min</td>
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<tr>
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<td>30 min</td>
<td>90</td>
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<td>11</td>
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<tr>
<td>12</td>
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<td>r.t</td>
<td>45 min</td>
<td>90</td>
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Table 1. Optimization of reaction conditions for preparation of 1,3-diaryl-2N-azaphenalene derivatives

<table>
<thead>
<tr>
<th>Entry</th>
<th>Product</th>
<th>Ar</th>
<th>R</th>
<th>Time</th>
<th>Yield (%)</th>
<th>Yield (%)</th>
<th>Yield (%)</th>
<th>M.P. (°C)</th>
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<tbody>
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<td>C$_6$H$_5$</td>
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<td>5</td>
<td>76</td>
<td>92</td>
<td>207-208</td>
<td>208-209</td>
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<td>B2</td>
<td>4-ClC$_6$H$_5$</td>
<td>Me</td>
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<td>44</td>
<td>71</td>
<td>218-220</td>
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<td>B3</td>
<td>3-HOC$_6$H$_5$</td>
<td>Me</td>
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<td>83</td>
<td>212-214</td>
<td>-</td>
</tr>
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<td>Me</td>
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<td>216-217</td>
<td>216-217[5]</td>
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<td>B5</td>
<td>4-NO$_2$C$_6$H$_5$</td>
<td>Me</td>
<td>8</td>
<td>64</td>
<td>85</td>
<td>194-196</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>B6</td>
<td>N,N-Di MeC$_6$H$_5$</td>
<td>Me</td>
<td>9</td>
<td>55</td>
<td>81</td>
<td>205-207</td>
<td>-</td>
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<td>B7</td>
<td>2-NO$_2$C$_6$H$_5$</td>
<td>Me</td>
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<td>54</td>
<td>86</td>
<td>186-188</td>
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<td>Me</td>
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<td>73</td>
<td>225-227</td>
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<td>B9</td>
<td>2-MeC$_6$H$_5$</td>
<td>Me</td>
<td>6</td>
<td>73</td>
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<td>10</td>
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<td>2-CIC$_6$H$_5$</td>
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<td>B11</td>
<td>2-MeOC$_6$H$_5$</td>
<td>Me</td>
<td>7</td>
<td>73</td>
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<td>-</td>
</tr>
<tr>
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<td>A1</td>
<td>C$_6$H$_5$</td>
<td>H</td>
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<td>A2</td>
<td>4-HOC$_6$H$_5$</td>
<td>H</td>
<td>6</td>
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<td>A3</td>
<td>2-NO$_2$C$_6$H$_5$</td>
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<td>62</td>
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<td>15</td>
<td>A4</td>
<td>2-MeC$_6$H$_5$</td>
<td>H</td>
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<td>85</td>
<td>230-232</td>
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<td>2-MeOC$_6$H$_5$</td>
<td>H</td>
<td>7</td>
<td>72</td>
<td>90</td>
<td>215-216</td>
<td>215-216[24]</td>
</tr>
</tbody>
</table>

Table 2. Multicomponent one-pot synthesis of 1,3-diaryl-2N-azaphenalene derivatives

13C-NMR spectra were obtained on Brucker 125 MHz spectrometers using DMSO-d$_6$ as a solvent with TMS as an internal standard. The progress of the reaction was monitored by thin-layer chromatography (TLC) using n-hexane/EtOAc as an eluent. Nanoparticles were characterized using an X-Pert Pro MPD XRD diffractometer (Cu-Kα, λ = 0.154056 nm) over the range 2θ = 10–80 using 0.04 as the step length. The scanning electron microscope measurement was obtained using a Hitachi S-4700 field emission-scanning electron microscope (FE-SEM).

Preparation of Fe$_3$O$_4$ @ L-arginine Nano catalyst

To synthesize this Nano catalyst, a mixture of salts FeCl$_3$.6H$_2$O (5 mmol) and FeCl$_2$.4H$_2$O (2.5 mmol) was solved in d 100 ml of deionized water. Then, 2 mg of L-arginine and 30 ml of ammonia solution was added to twenty-five percent until the pH of the solution reaches 11. After that, the combination was put in reflux conditions for 6 hours at 100 ° C. Finally, Fe$_3$O$_4$ @ L-arginine Nano catalyst is separated from the aqueous solution by an external magnet and washed and dried for 24 hours [21-24]. The quality of synthesized Nano catalyst has been verified by FTIR, XRD, and SEM.
Synthesis of compounds in the presence of Fe$_3$O$_4$ @ L-arginine Nano catalysts

At first, 100 Milligram of the synthesized Nano was mixed with aldehyde (2 mmol), 2,7-Naphthalene diol (1 mmol), and ammonia derivatives (ammonium hydrogen sulfate or ammonium acetate) (2 mmol) and 4 milliliters of water-ethanol (3:1) in a balloon, and in an unheated condition, and stir it for an hour. Then, the mixture was put in an hour without moving. We followed the reaction progression with thin layer chromatography (TLC).

After completion of the reactions, 20 ml of saturated NaCl was added to the reaction mixture and stirred for 60 minutes at room temperature. The precipitate was thinned and washed with water and then dried. The product was washed with 20 ml ethyl acetate-hexane in a 4:1 ratio and dried at 100 °C under vacuum for 4 hours.

It is observed that products are produced in less time and with better efficiency without the use of heat and reflux conditions. The reaction time and efficiency values are listed in Table 2.

It should be noted that compounds were synthesized in the presence of Fe$_3$O$_4$ Nano catalyst without L-arginine, which satisfactory results were not obtained.

**A5: 4,9-Dihydroxy-1,3-di(2-methoxyphenyl)-2,3-dihydro-2-azaphenalene:**

IR (KBr): $\nu$ = 3493, 3271-2939, 1624, 1599, 1514, 1243, 1026, 749 cm$^{-1}$; $^1$H NMR (500 MHz, DMSO-d$_6$): $\delta$ = 9.06 (s, 2H, disappeared on D$_2$O exchange), 7.57 (d, $J = 8.5$, 2H), 7.14 (t, $J = 7.6$, 2H), 6.98 (d, $J = 8.7$, 2H), 6.65 (d, $J = 7.5$, 2H), 6.65 (d, $J = 7.6$, 2H), 6.39 (d, $J = 8.7$, 2H), 5.56 (s, 2H), 3.77 (s, 6H), 2.66 (br, 1H, disappeared on D$_2$O exchange).

$^1$C NMR (125 MHz, DMSO-d$_6$): $\delta$ = 157.4, 150.3, 132.9, 131.4, 128.5, 127.9, 122.7, 120.2, 120.3, 115.1, 114.9, 111.2, 55.8, 47.8.

**B1: N1: N-acetylene-4,9-dihydroxy-1,3-di(phenyl)-2,3-dihydro-2-azaphenalene:**

IR (KBr): = 3300-3000, 2818, 2708, 1626, 1585, 1516, 1431, 1396, 1327, 1273, 1130, 1028, 881, 736, 699, 671 cm$^{-1}$; $^1$H NMR (500 MHz, DMSO-d$_6$): $\delta$ = 9.01 (br, 2H, disappeared on D$_2$O exchange), 7.56 (d, $J = 7.7$ Hz, 2H), 7.21 (t, $J = 7.6$, 4H), 7.16 (t, $J = 7.6$, 2H), 7.08 (d, $J = 7.0$ Hz, 4H), 6.86 (d, $J = 8.7$ Hz, 2H), 5.19 (s, 2H), 1.91 (s, 3H); $^1$C NMR (125 MHz, DMSO-d$_6$): $\delta$ = 172.5, 150.5, 145.2, 132.2, 128.3, 128.1, 127.7, 126.6, 122.7, 116.2, 115.2, 53.9;

B4: N-acetyl-4,9-dihydroxy-1,3-di(4-hydroxyphenyl)-2,3-dihydro-2-azaphenalenes:

IR (KBr): $\nu$ = 3630, 3319, 3211, 2823, 2696, 1623, 1543, 1511, 1429, 1309, 1246, 1174, 1130, 836, 773, 657 cm$^{-1}$; $^1$H NMR (500 MHz, DMSO-d$_6$): $\delta$ = 8.92 (br, 4H, disappeared on D$_2$O exchange), 7.58 (d, $J = 7.4$ Hz, 2H), 7.01-6.88 (m, 6H), 6.63-6.50 (m, 4H), 5.18 (s, 2H), 1.90 (s, 3H); $^1$C NMR (125 MHz, DMSO-d$_6$): $\delta$ = 172.74, 156.72, 150.9, 132.2, 131.75, 129.59, 128.12, 122.5, 115.3, 115.1, 114.8, 53.3, 21.6.

B9: N-acetyl-4,9-Dihydroxy-1,3-di(2-methylphenyl)-2,3-dihydro-2-azaphenalene:

IR (KBr): $\nu$ = 3630, 3319, 3211, 2823, 2696, 1623, 1543, 1511, 1429, 1309, 1246, 1174, 1130, 836, 773, 657 cm$^{-1}$; $^1$H NMR (500 MHz, DMSO-d$_6$): $\delta$ = 8.92 (br, 4H, disappeared on D$_2$O exchange), 7.58 (d, $J = 7.4$ Hz, 2H), 7.01-6.88 (m, 6H), 6.63-6.50 (m, 4H), 5.18 (s, 2H), 1.90 (s, 3H); $^1$C NMR (125 MHz, DMSO-d$_6$): $\delta$ = 172.74, 156.72, 150.9, 132.2, 131.75, 129.59, 128.12, 122.5, 115.3, 115.1, 114.8, 53.3, 21.6.

B10: N-acetyl-4,9-dihydroxy-1,3-di(2-chlorophenyl)-2,3-dihydro-2-azaphenalene:

IR (KBr): $\nu$ = 3455-2835, 3315, 1618, 1442, 1373, 1225, 1041, 938, 748 cm$^{-1}$; $^1$H NMR (125 MHz, DMSO-d$_6$): $\delta$ = 9.55 (s, 2H), 7.74 (d, $J = 7.6$ Hz, 2H), 7.07 (d, $J = 5.7$ Hz, 2H), 6.80 (m, 2H), 5.15 (s, 2H), 1.92 (s, 2H); $^1$C NMR (125 MHz, DMSO-d$_6$): $\delta$ = 172.49, 150.5, 132.15, 133.3, 130.57, 129.15, 128.63, 128.06, 126.09, 122.65, 114.94, 104.97, 51.4, 21.63.

Antibacterial activity

Primary screening

All synthesized compounds were tested for antimicrobial activity against pathogenic strains by applying the well-diffusion assay method and MIC technique.

In the first stage, the Muller Hinton Agar was prepared and divided in the thickness of 4-5 mm in the plates. Then, wells were drilled in plates with a diameter of 5 mm, and in the environments cultivated with sterilized swabs from Staphylococcus aureus, Staphylococcus epidermidis, Escherichia coli and Pseudomonas aeruginosa bacteria.

The Concentration of bacterial suspension for testing, used a standard made of Barium sulfate.
equivalent to 0.5 McFarland. A 0.5 McFarland standard was prepared by mixing 0.05 ml of 0.1% (w/v) BaCl$_2$$\cdot$2H$_2$O with 9.95 ml of 1% (v/v) sulfuric acid.

All the examined compounds and ciprofloxacin as antibacterial standard were prepared by dissolving 100 mg of each compound in 1 ml of DMSO.

An amount of 100 μl of suspension containing 0.5 McFarland standard of each examined bacterial was mixed with 20 ml of Mueller–Hinton agar, respectively, and transferred into sterilized Petri plates.

Wells of 5 mm in diameter were punched in the solidified agar plates and 100 μl of test solution was charged to individual wells and bacteria were incubated at 37 °C for 24 hours. Finally, the diameter of growth inhibition bacteria around the wells on the plate was measured with the ruler and repeated three times.

**MIC determination**

For this experiment, 9 sterile tubes were used, each of which containing 1 ml of Muller Hinton Broth culture medium. Then, 1 ml of synthesized compounds was added to the tube 1 with the intended concentration dissolved in DMSO, after mixing with the culture medium, 1 milliliter of the solution was removed and added to the second tube, and so, until the ninth tubes dilute the synthesis compounds. 1 ml was removed from the ninth tube and poured out. After that, from the microbial suspension prepared, the equivalent of the half McFarland removed, 100 μl, and added to each tube. The 10th tube contained a culture medium and synthesized compounds, which was as a negative control, the eleventh tube contained bacterial culture medium and suspension as a positive control. The concentrations of tubes of 1 to 9 are 800, 400, 200, 100, 50, 25, 12.5, 6.25, 3.125 Micrograms per milliliter. Then the tubes were heated at 37 °C for 24 hours and, to determine Mic, read the tubes’ turbidity, which indicates the amount growth of the bacteria. To do this, we should take the tubes against light, and check out how bacteria grow. The control compound, culture medium and microbes were also separately included.

Antibiotic drug (Gentamycin) was also used as positive control. The petri dishes were incubated for 18-24h 37 °C. After this period of time, results were determined by measuring inhibition zones formed around each well as millimeters (mm) diameter. The experiments were repeated three times. The results were given in Fig. 3.

**RESULTS AND DISCUSSION**

**Characterization of Fe$_3$O$_4$@L-arginine catalyst**

Fe$_3$O$_4$@L-arginine nanoparticles were characterized by Fourier transform infrared (FT-IR) spectroscopy, X-ray diffraction (XRD), Field emission scanning electron microscopy (FE-SEM). Spectrum 4a shows the FT-IR spectrum of Fe$_3$O$_4$ nanoparticles at a stretching vibration of around 3,402 and 579 cm$^{-1}$, which combines the contributions from both symmetrical and asymmetrical modes of the surface hydroxyl groups and Fe–O bonds of iron oxide, respectively. Moreover, the adsorption peaks at 1386, 1631 and 3154, 3436 cm$^{-1}$ show bending vibration of N-H and COO$^-$ respectively, which indicate the presence of band arginine on the surface of MNPs. Furthermore, the wave number separation between the COO$^-$as and COO$^-$s IR bands can be used to distinguish the type of the interaction between the carboxylate head and the metal atom. Since the wavenumber separation between the COO$^-$ as band COO$^-$s bands is 245 cm$^{-1}$(1631-1386=245 cm$^{-1}$), it can be concluded that the interaction between the COO$^-$ group and the Fe atom is covalent and bridging bidentate. It means that the amino acids were bonded on the magnetite particle surface involving bidentate chelation of amino acid groups which confirm when compared to previous reports. (Fig. 1). FE-SEM images of Fe$_3$O$_4$ @ L-arginine nanoparticles are shown to determine the size of morphology (Fig. 2). The crystal structure of Fe$_3$O$_4$ @ L-arginine nanoparticles is evaluated using the XRD technique (Fig. 3). The patterns indicate a crystallized structure at 2θ: 18.2, 30.0, 35.4, 43.08, 53.7, 57.1 and 62.7, which shows diffraction peaks, corresponding to (200), (211), and (210), (111), (110), and (200), respectively. According to the standard sample Fe$_3$O$_4$ (JCPDS file no. 98-007-7842), the peaks of MNPs in the XRD model are corresponded. The average crystal size of nanoparticle Fe$_3$O$_4$ @ L-arginine is assessed using Debye – Scherer’s formula (D = K $\lambda$/β cos θ). The crystal size is about 21 nm in the range determined (Fig. 2). By analyzing the XRD spectrum (Fig. 3), which shows a pattern of count peaks, the Fe$_3$O$_4$ synthesized sample spectrum, with standard spectrum of Fe$_3$O$_4$ (Reference No: 00.019.0629) and the Fe$_3$O$_4$ @ L-arginine synthesized sample spectrum, with the standard spectrum of Fe$_3$O$_4$ @
L-arginine (Reference No: 00.001.1111) correspond in the XRD model.

Synthesis and characterization of 1,3-diaryl-2N-azaphenalene catalyzed by Fe₃O₄ @ L-arginine

In order to optimize the reaction conditions, 9-Dihydroxy-1,3-di(2-methoxyphenyl)-2,3-dihydro-2-azaphenalene (A5) were prepared as model compounds in different amounts of catalyst, different solvents, through which the reaction of 2,7-naphthalene diol (1 mmol), aromatic benzaldehyde (2 mmol), ammonia derivatives (ammonium acetate or ammonium...
Figure 3. The XRD spectrum of Fe₃O₄ and Fe₃O₄ @ L-arginine
hydrogen phosphate (1.2 mmol) were examined. The results are given in Table 1.

First, we performed the model reaction using several solvents. Then, we examined the amount of catalyst.

It is evident from Table 1 (entry 10) that applying more than the specified quantity of catalyst did not have a positive effect on the yield of product.

As shown in Table 1, the best result was obtained using 50 mg of the Fe₃O₄ @ L-arginine catalyst in Ethanol-H₂O as a safe solvent with proportion 3:1 (Table 1, entry 8).

The conditions optimized for the production of the 1,3-diaryl-2-N-azaphenalene derivatives and n-acyl-1,3-diaryl-2-N-azephenylene derivatives were evaluated using in the absence and presence of the Fe₃O₄ @ L-arginine as a catalyst. The reaction of aromatic aldehydes carrying either electron-donating or electron withdrawing substituents with ammonia derivatives (ammonium acetate or ammonium hydrogen phosphate) is done (Table 2). Considering these results, we can see that all reactions proceeded to afford the corresponding products to good yields.

**Antibacterial study**

Pharmacological evaluation is one of the most important methods to determine the activity of the compounds. In this section, the antimicrobial activity of the compounds synthesized by well-diffusion method has been measured.

Also, the minimum inhibitory concentration (MIC) (the concentration of an antibiotic or composition that can enhance bacterial growth under laboratory conditions Inhibit) Synthesized compounds on microorganisms were measured by continuous dilution of the liquid culture medium.

Accordingly, to investigate the antimicrobial activity of compounds, was used the two gram-positive bacteria, Staphylococcus aureus (ATCC 29213) and Staphylococcus epidermidis (ATCC 14990), and the two gram-negative bacteria, Escherichia coli (ATCC 25922) and Pseudomonas aeruginosa (ATCC 27853).

These results are compared with the antibacterial drug Ciprofloxacin as a standard.

By analyzing the antibacterial and antimicrobial effects and measuring the diameter of growth inhibition, products No. 1, 3, 4, and 10 won’t have antimicrobial properties and samples 7 and 12 have the most antimicrobial activity. Table 3 indicates antimicrobial activity.

In the second step, quantitative testing was performed to determine the minimum inhibitory concentration (MIC) of the compounds. In fact, Mic is the minimum concentration of samples in which growth isn’t visible. Table 4 shows the MIC products.

Tested compounds exhibited a variety of MICs, ranging from 0 to 400 μg ml⁻¹ against Gram-positive and Gram-negative bacterial strains, compared to the standard drug ciprofloxacin with MIC value of 12.5 and 50 μg ml⁻¹.

### Table 3. Antimicrobial activity of Product

<table>
<thead>
<tr>
<th>Entry</th>
<th>Product</th>
<th>S. aureus ATCC 29213</th>
<th>S. epidermidis ATCC 14990</th>
<th>E. coli ATCC 25922</th>
<th>P. aeruginosa ATCC 27853</th>
</tr>
</thead>
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<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
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<td>14</td>
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<td>NA</td>
<td>NA</td>
</tr>
<tr>
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<td>B4</td>
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<td>NA</td>
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<td>NA</td>
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<td>15</td>
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<td>15</td>
<td>17</td>
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<td>20</td>
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<td>19</td>
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<tr>
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<td>23</td>
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</tr>
<tr>
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<td>A2</td>
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</tr>
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<td>A5</td>
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<td>28</td>
<td>27</td>
<td>30</td>
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NA: It means no effect of anti-microbial properties.
Conclusions

To put it briefly, we managed to produce an efficient reaction, single-dish, low-time and high-efficiency without the use of heat and reflex for the production of derivatives of 1,3-diaryl-2-n-azaphenalene and n-acyl-1,3-diaryl-2-n-azaphenalene from a mixture of five compounds of 2,7-naphthalene diol, aldehydes, ammonia derivatives (ammonium acetate or ammonium hydrogen phosphate), and solvent (water and alcohol) in the presence of \( \text{Fe}_3\text{O}_4 \) @ L-arginine Nano catalysts.

As shown in Table 1, when using a nanoscale, the reaction time is, on average, one-fifth of the time when the catalyst is not used, while the efficiency of the reactions is improved by 20 to 50%. It also saves energy due to non-use of heat.

Also, \( \text{Fe}_3\text{O}_4 \) has been considered as a Nano-catalyst because of the availability, low toxicity, recyclability and easy separation of the reaction solution. The catalyst can be used 5 times without losing its function. The \( \text{Fe}_3\text{O}_4 \) @ L-arginine Nano catalysts was characterized using FT-IR spectroscopy, XRD, FESEM.

Also, by analyzing the antibacterial and antimicrobial effects Products by measuring the diameter of growth inhibition, products No. 1, 3, 4, and 10 don't have antimicrobial features and samples 7 and 12 have the most antimicrobial activity.

In the second step, quantitative testing was performed to determine the minimum inhibitory concentration (MIC) of the compounds. In conclusion, the results showed that the activity of the samples was not evaluated as well as the standard sample in the gram-positive bacteria. However, the results obtained in the gram-negative bacteria, were satisfactory. For example, samples 2, 6, 9, 11 and 16 are similar to the standard, and samples 5, 7, 8, 12, 13, 14, and 15 are lower than the standard limits.

Conflict of Interest

The authors declare that there is no conflict of interests regarding the publication of this manuscript.

References


Table 4. The minimum inhibitory concentration (MIC) of Product

<table>
<thead>
<tr>
<th>Entry</th>
<th>Product</th>
<th>S. aureus ATCC 29213</th>
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