ORIGINAL RESEARCH PAPER

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" Using Nano catalyst and Analyzing Antibacterial Activity of Structures

Asghar Eftekhari, Naser Foroughifar *, Malak Hekmati

Department of Organic Chemistry, Faculty of Pharmaceutical Chemistry, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran

ABSTRACT

In this research, well synthesized 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 (Fe_3O_4 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 carried out under very moderate conditions at room temperature.
The chemical structures of all synthesized compounds were determined using infrared, ^{1}H NMR and ^{13}C 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:*Multicomponent,Macromolecule,Nanocatalysts,One-pot,Azaphenalene,Antibacterial activity*

INTRODUCTION

Multicomponent reactions (MCRs) are one-step 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 examples 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 azaphenalene 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, synthesis of this heterocyclic nucleus is currently of major importance. These compounds have very low oxidation potentials and very low negative reduction potentials thus they are extremely promising antioxidants in biological systems. [5–10]

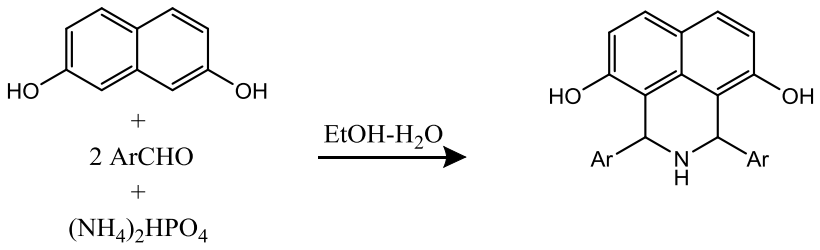
Since the use of a catalyst to accelerate the reactions has always been of interest to researchers, the use of nanoparticles has been of great interest in recent years. [11- 12]

Magnetic nanoparticles have led a new era of research to researchers. Utilization of magnetic nanoparticles, iron oxide, has expanded due to high magnetic efficiency, high ratio of surface to 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

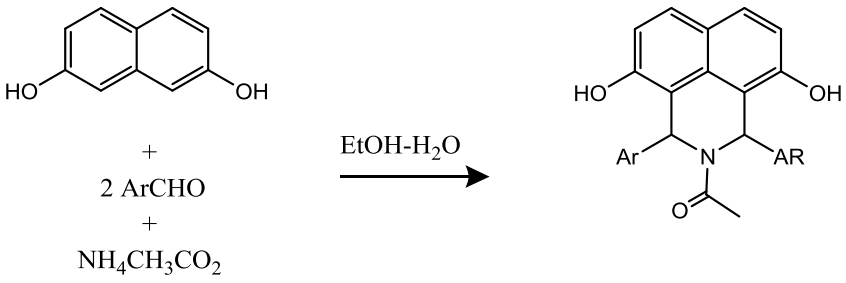
Many investigations have focused on heterogeneous catalysts, especially magnetic nanoparticles (MNPs), for example, nanoparticles of Fe_3O_4. [13-14]

Magnetic nanoparticles of iron oxide (Fe_3O_4) have been widely used as heterogeneous catalysts in organic reactions. Using merely a magnet has made them cheap, available, low toxic, recyclable and easy separation 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-H_2O (3:1) in the presence of Fe_3O_4 @ L-arginine nano catalyst as an efficient catalyst with recycling and reusability potential.(Scheme 1, 2).



Scheme1. Synthetic pathway for synthesis of 1,3-diaryl-2-N-azaphenalene



Scheme2. Synthetic pathway for synthesis of n-acyl-1, 3-diaryl -2-N-azephenylene

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]

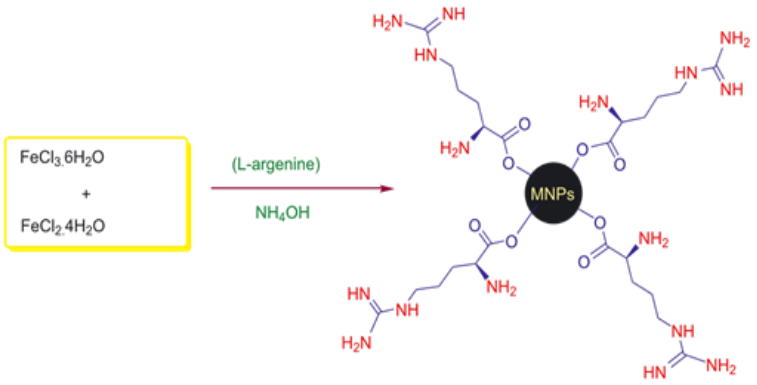
EXPERIMENTAL

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. ^{1}HNMR (500 MHz), and ^{13}C-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 eluent. Nanoparticles were characterized using an X-Pert Pro MPD XRD diffractometer (Cu-Kα, k = 0.154056 nm) over the range of 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_3O_4 @ L-arginine Nano catalyst

To synthesize this Nano catalyst, a mixture of salts $FeCl_3.6H_2O$ (5 mmol) and $FeCl_2.4H_2O$ (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_3O_4 @ L-arginine Nano catalyst was separated from the aqueous solution by an external magnet, washed and dried for 24 hours [21-24]. The quality of synthesized Nano catalyst has been verified by FT-IR, XRD, and SEM.



Synthesis of compounds in the presence of Fe_3O_4 @ L-arginine Nanocatalysts

At first, 100 Milligram of the synthesized nanocatalysts 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 milli liters of water-ethanol (3:1) in a balloon and was stirred for an hour without heating. Then, the mixture was held undisturbed for an hour. The reaction progression was followed 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 was observed that products were produced in less time and with better efficiency without the use of heat and reflux condition. The reaction time and efficiency values are listed in Table 2.

It should be noted that compounds were synthesized in the presence of Fe_3O_4 nanocatalysts without L-arginine, which satisfactory results were not obtained.

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

IR (KBr): $\bar{\nu}$ = 3493, 3271-2939, 1624, 1599, 1514, 1243, 1026, 832, 749 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 9.06 (s, 2H, disappeared on D2O exchange), 7.57 (d, J= 8.5, 2H), 7.14 (t, J = 7.6, 2H), 6.98 (d, J = 8.7, 2H), 6.85 (d, J = 7.5, 2H), 6.65(t, 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 D2O exchange). ^{13}C NMR (125 MHz, DMSO-d6): δ = 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-acetyle-4,9-dihydroxy-1,3-di(phenyl)-2,3-dihydro-2-azaphenalene:
IR (KBr): $\bar{\nu}$= 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): δ= 9.01 (br, 2H, disappeared on D_2O 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); ^{13}C NMR (125 MHz, DMSO-d_6): δ= 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): $\bar{\nu}$ = 3630, 3319, 3211, 3015, 2823, 2696, 1623,1604, 1543, 1511, 1429, 1309, 1246, 1174, 1130, 836, 773, 657 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ= 8.92 (br, 4H, disappeared on D2O 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); ^{13}C NMR (125 MHz, DMSO-d_6): δ= 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): $\bar{\nu}$ = 3271-2968, 1624, 1511, 1411, 1316, 1039, 840,758, 699 cm^{-1}. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 9.11 (br, 2H, disappeared on D2O exchange), 7.55 (d, J = 8.5, 2H), 7.09 (t, J = 7.6, 2H), 6.96 (d, J = 8.7, 2H), 6.91 (m, 2H), 6.84 (m, 4H), 5.15 (s, 2H), 2.20 (s, 6H), 1.91 (S, 3H). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 172.4, 150.5, 144.9, 136.99, 132.1, 128.9, 128.6, 127.6, 127.32, 125.45, 122.7, 116.3, 115.2, 53.89, 21.6, 21.5.

B10: N-acetyl-4,9-dihydroxy-1,3-di(2-chlorophenyl)-2,3-dihydro-2-azaphenalenes:
IR (KBr): $\bar{\nu}$ = 3455- 2835, 3315, 1618, 1442, 1373, 1225, 1041, 938, 835, 748 cm^{-1}; ^{1}H NMR (125 MHz, DMSOd_6): δ= 9.55 (S, 2H), 7.74 (d, J = 7.6 Hz, 2H), 7.07 (d, J = 7.6 Hz, 2H), 7.00 (d, J = 5.7 Hz, 2H), 6.80 (m, 2H), 6.58 (m, 2H), 6.15 (d, J = 7.4 Hz, 2H), 5.71 (s, 2H); 1.92 (s, 2H); ^{13}CNMR (125 MHz, DMSO-d_6): δ= 172.49, 151.35, 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 on the environments cultivated with sterilized swabs from Staphylococcus aureus, Staphylococcus epidermidis, Escherichia coli and Pseudomonas aeruginosa bacteria.

The Concentration of bacterial suspension used a standard made of Barium sulfate equivalent to 0.5 McFarland for testing. A 0.5 McFarland standard was prepared by mixing 0.05 ml of 0.1% (w/v) $BaCl_2 \cdot 2H_2O$ 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 by 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 were 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 growth amount of the bacteria. To do this, the tubes should be held 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. Results are shown in Figure 3.

RESULTS AND DISCUSSION

Characterization of Fe_3O_4@L-arginine catalyst

Fe_3O_4@Larginine 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_3O_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 is confirmed when compared to previous reports. (Figure 1). FE-SEM images of Fe_3O_4 @ L-arginine nanoparticles are shown to determine the size of morphology (Figure 2). The crystal structure of Fe_3O_4 @L-arginine nanoparticles is evaluated using the XRD technique (Figure 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 (485), (297), (253), (210), (171), (161), and (148), respectively. According to the standard sample Fe_3O_4 (JCPDS file no. 98-007-7842), the peaks of MNPs in the XRD model are corresponded. The average crystal size of nanoparticle Fe_3O_4 @ L-arginine is assessed using Debye – Scherer's formula ($D = K \lambda/\beta \cos \theta$). The crystal size is about 21 nm in the range determined (Figure 2). By analyzing the XRD spectrum (Figure 3), which shows a pattern of counting peaks, the Fe_3O_4 synthesized sample spectrum, with standard spectrum of Fe_3O_4 (Reference No: 00.019.0629) and the Fe_3O_4 @ L-arginine synthesized sample spectrum, with the standard spectrum of Fe_3O_4 @ L-arginine (Reference No: 00.001.1111) correspond in the XRD model.

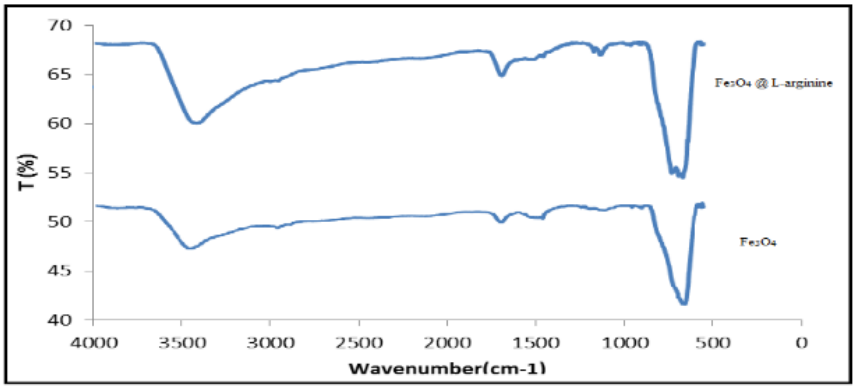
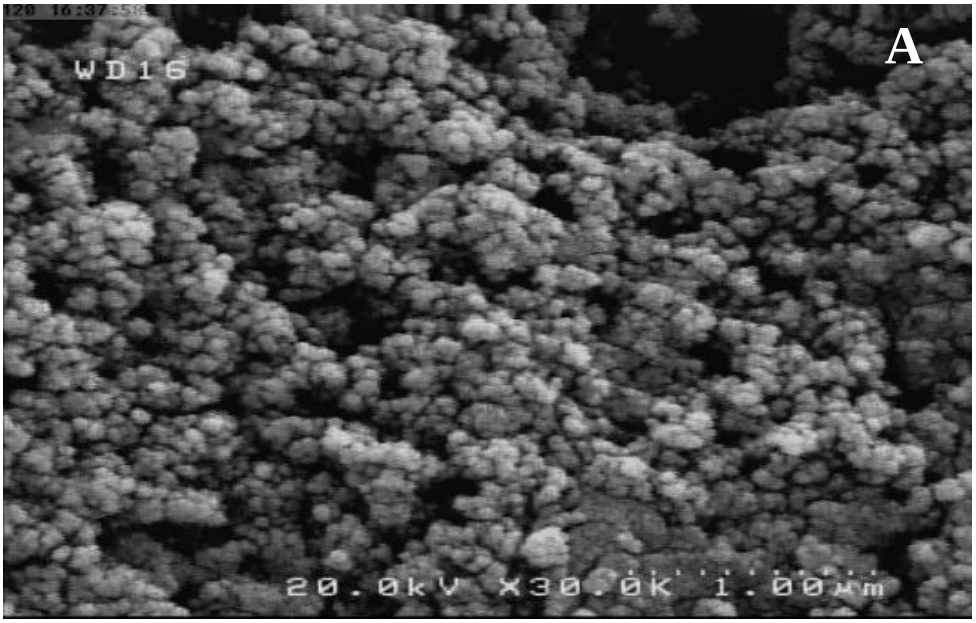
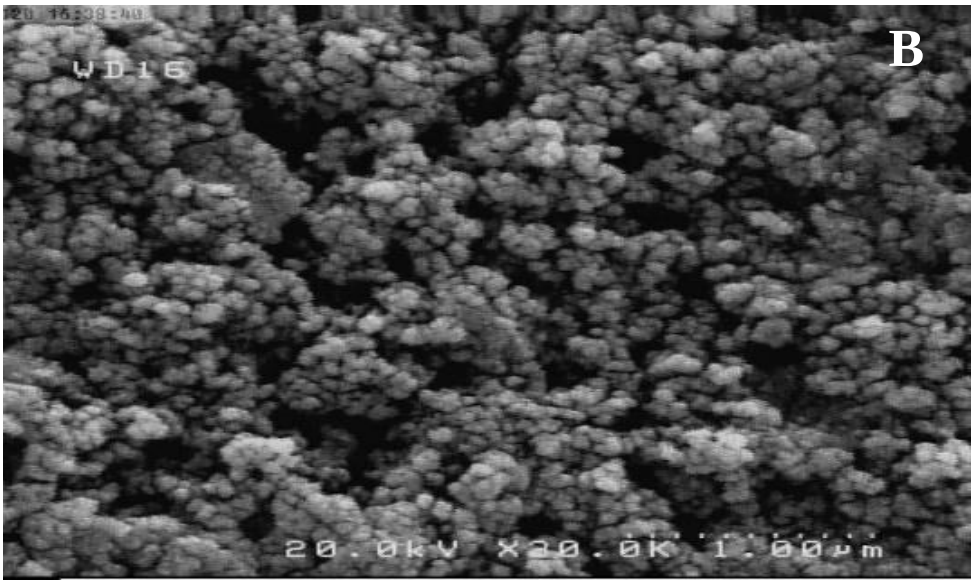


Figure 1. Comparison of FT-IR spectra for Fe_3O_4 and Fe_3O_4 @ L-arginine



(a)



(b)

Figure 2. The SEM. image of Fe_3O_4 (a) and Fe_3O_4 @ L-arginine(b)

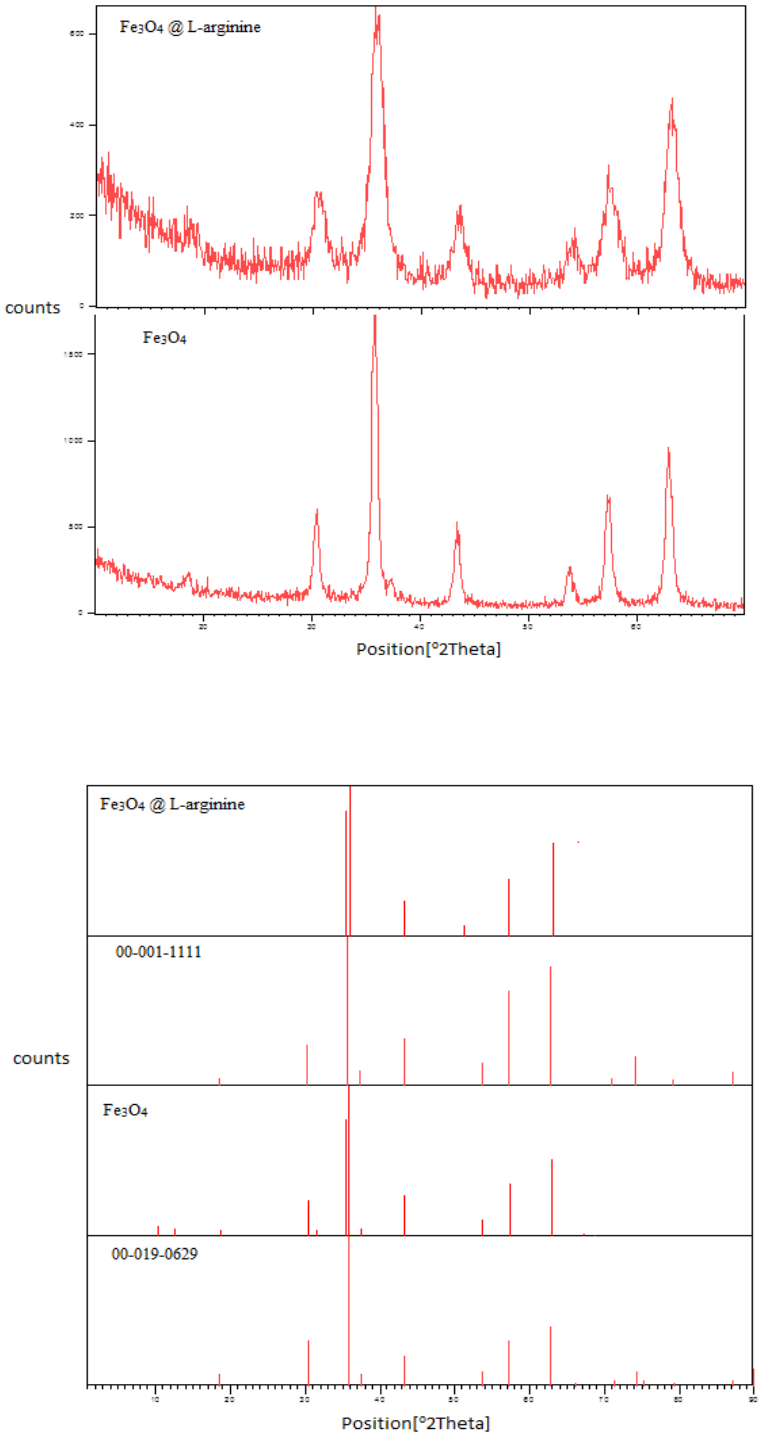


Figure 3. The XRD spectrum of Fe_3O_4 and Fe_3O_4 @ L-arginine

Synthesis and characterization of 1,3-diaryl-2N-azaphenalene catalyzed by Fe_3O_4@L-arginine

In order to optimize the reaction conditions, 9-Dihydroxy-1,3- di (2-methoxyphenyl) -2,3 -dihydro-2-zaphenalene (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 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 Fe_3O_4 @ L-arginine catalyst in Ethanol-H_2O as a safe solvent with proportion 3:1 (Table 1, entry 8).

Table 1. Optimization of reaction conditions for preparation of 1،3-diaryl-2N-azaphenalene derivatives

Entry	Catalyst (mg)	Solvent	Temp. (^oC)	Time	Yield A5 (%)
1	-	EtOH	Reflux	7 h	57
2	-	1 EtOH:1 H_2O	Reflux	7 h	53
3	-	2 EtOH:1 H_2O	Reflux	7 h	60
4	-	3 EtOH:1 H_2O	Reflux	7 h	72
5	Fe_3O_4 @ L-arginine(50)	EtOH	r.t	30 min	81
6	Fe_3O_4 @ L-arginine(50)	1 EtOH:1 H_2O	r.t	30 min	76
7	Fe_3O_4 @ L-arginine(50)	2 EtOH:1 H_2O	r.t	30 min	84
8	Fe_3O_4 @ L-arginine(50)	3 EtOH:1 H_2O	r.t	30 min	90
9	Fe_3O_4 @ L-arginine(25)	3 EtOH:1 H_2O	r.t	30 min	79
10	Fe_3O_4 @ L-arginine(75)	3 EtOH:1 H_2O	r.t	30 min	90
11	Fe_3O_4 @ L-arginine(50)	3 EtOH:1 H_2O	r.t	15 min	86
12	Fe_3O_4 @ L-arginine(50)	3 EtOH:1 H_2O	r.t	45 min	90

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 Fe_3O_4 @ 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) was done (Table 2). Considering these results, we can see that all reactions proceeded to afford the corresponding products to good yields.

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

Entry	Product	Ar	R	Without catalyst		With catalyst		M.P. (°C)	
				Time (h)	Yield (%)	Time (min)	Yield (%)	Found	Reported [Ref]
1	B1	C_6H_5	Me	5	76	30	92	207-208	208-209 [5]
2	B2	4-ClC_6H_4	Me	7	44	30	71	218-220	- [3]
3	B3	3-HOC_6H_4	Me	6	36	30	83	212-214	-
4	B4	4-HOC_6H_4	Me	6	47	30	72	216-217	216-217[5]
5	B5	4-$NO_2C_6H_4$	Me	8	64	30	85	194-196	-
6	B6	N,N-Di MeC_6H_4	Me	9	55	30	81	205-207	-
7	B7	2-$NO_2C_6H_4$	Me	8	54	30	86	186-188	-
8	B8	2-BrC_6H_4	Me	9	29	30	73	225-227	-
9	B9	2-MeC_6H_4	Me	6	73	30	91	258-259	-
10	B10	2-ClC_6H_4	Me	8	42	30	71	214-216	- [3]
11	B11	2-$MeOC_6H_4$	Me	7	73	30	85	204-206	-
12	A1	C_6H_5	H	5	70	30	87	202-203	202-203[24]
13	A2	4-HOC_6H_4	H	6	35	30	68	204-206	204-206[22]
14	A3	2-$NO_2C_6H_4$	H	8	62	30	93	191-193	-
15	A4	2-MeC_6H_4	H	6	72	30	85	230-232	-
16	A5	2-$MeOC_6H_4$	H	7	72	30	90	215-216	215-216[24]

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, two gram-positive bacteria were used, Staphylococcus aureus (ATCC 29213) and Staphylococcus epidermidis (ATCC 14990), and two gram-negative bacteria, Escherichia coli (ATCC 25922) and Pseudomonas aeruginosa (ATCC 27853) were used.

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 did not have antimicrobial properties and samples 7 and 12 had the most antimicrobial activity. Table 3 indicates antimicrobial activity.

Table 3. Antimicrobial activity of Product

Entry	Product	S. aureus ATCC 29213	S. epidermidis ATCC 14990	E. coli ATCC 25922	P. aeruginosa ATCC 27853
1	B1	NA	NA	NA	NA
2	B2	10	12	14	13
3	B3	NA	NA	NA	NA
4	B4	NA	NA	NA	NA
5	B5	16	15	18	15
6	B6	13	15	15	17
7	B7	18	20	22	19
8	B8	16	18	20	17
9	B9	13	15	18	15
10	B10	NA	NA	NA	NA
11	B11	14	17	18	16
12	A1	19	18	23	20
13	A2	17	20	19	17
14	A3	19	18	15	17
15	A4	18	19	18	17
16	A5	12	13	15	11
Ciproflo xacin	-	28	27	30	29

NA: It means no effect of anti-microbial properties.

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 was not 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 4. The minimum inhibitory concentration (MIC) of Product

Entry	Product	S. aureus ATCC 29213	S.epidermidis ATCC 14990	E. coli ATCC 25922	P.aeruginosa ATCC 27853
1	B1	NA	NA	NA	NA
2	B2	400 µg/ml	200 µg/ml	100 µg/ml	50 µg/ml
3	B3	NA	NA	NA	NA
4	B4	NA	NA	NA	NA
5	B5	100 µg/ml	50 µg/ml	25 µg/ml	25 µg/ml
6	B6	200 µg/ml	100 µg/ml	50 µg/ml	50 µg/ml
7	B7	100 µg/ml	50 µg/ml	12.5 µg/ml	6.25 µg/ml
8	B8	100 µg/ml	50 µg/ml	12.5 µg/ml	12.5 µg/ml
9	B9	100 µg/ml	100 µg/ml	50 µg/ml	50 µg/ml
10	B10	NA	NA	NA	NA
11	B11	100 µg/ml	100 µg/ml	50 µg/ml	25 µg/ml
12	A1	100 µg/ml	25 µg/ml	6.25 µg/ml	12.5 µg/ml
13	A2	100 µg/ml	25 µg/ml	12.5 µg/ml	6.25 µg/ml
14	A3	100 µg/ml	50 µg/ml	25 µg/ml	12.5 µg/ml
15	A4	50 µg/ml	50 µg/ml	12.5 µg/ml	25 µg/ml
16	A5	100 µg/ml	100 µg/ml	25 µg/ml	50 µg/ml
Ciproflo xacin	-	12.5 µg/ml	12.5 µg/ml	50 µg/ml	50 µg/ml

CONCLUSION

To put it briefly, we managed to produce an efficient reaction, single-dish, low-time and high-efficiency without the use of heat and reflux 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 Fe_3O_4 @ L-arginine nanocatalysts.

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

Also, Fe_3O_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 Fe_3O_4 @ L-arginine nanocatalysts were characterized using FT-IR spectroscopy, XRD, FE-SEM.

Also, by analyzing the antibacterial and antimicrobial effects products by measuring the diameter of growth inhibition, products No. 1, 3, 4, and 10 did not have antimicrobial features and samples 7 and 12 had 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 were lower than the standard limits.

REFERENCES

1. (a) Mont, N.; Teixido, J.; Borrell, J.; Kappe, C. O.´ Tetrahedron Lett. 2003; 44: 5385-5387; (b) Chetia, A.; Saikia, C. J.; Lekhok, K. C.; Boruah, R. C. Tetrahedron Lett. 2004; 45: 26492651; (c) Weber, L. Drug Discovery Today. 2002; 7: 143-147.
2. Dehbalaei MG, Foroughifar N, and Pasdar H. Biointerface Research in Applied Chemistry. 2018; 8: 3016-3022.
3. Foroughifar N, Mobinikhaledi A, Moghanian H, Chemistry letters. 2010; 39: 1-180.
4. Domling A. Chem Rev. 2006; 106: 17-89.
5. Mobinikhaledi A, Foroughifar N, Moghanian H, Mozaffari, Research on Chemical Intermediates. 2015; 41: 6523-6532.
6. Haddon R.C, Nature.1975; 256: 394-396.
7. Itkis M.E, Chi X, Cordes A.W, Haddon R.C, Science. 2002; 296: 1443-1445.
8. Shimizu S, Zhu H, Kobayashi N, Chemistry.2010; 16: 11151-11159.
9. Hodgson J.L, Namazian M, Bottle S.E,Coote M.L, Phys J. Chem. A. 2007;111:13595-13605.
10. Daloze D, Braekman J.C, Pasteels J, Chemoecology.1994; 5:173-183.
11. Karami S, Foroughifar N, Khajeh-Amiri A, Pasdar H,Biointerface Research in Applied Chemistry.2016;6: 1833 – 1836.
12. Foroughifar N, Khajeh-Amiri A, Pasdar H, Foroughifar N, Dehbalaei MG, Hoghoghi A.Biointerface Research in Applied Chemistry.2016; 6:1502 -1510 .
13. Gholami Dehbalaei M, Foroughifar N, Khajeh-Amiri A, Pasdar H, Journal of the Chinese Chemical Society. 2018; 65: 1356-1369.
14. Dehbalaei MG, Foroughifar N, Pasdar H, Khajeh-Amiri,New Journal of Chemistry. 2018; 421:327-335.
15. Hu JT, Odom TW, Lieber CM. Chem. Res.1999; 32: 435-445
16. Tamoradi, T., Ghorbani-Choghamarani, A., & Ghadermazi, M. New Journal of Chemistry, 2017; 41: 11714-11721.
17. Hashmi, A. S. K., and G. J. Hutchings. Angew. Chem. Int. Ed. 2006; 45: 7896-7936.
18. Gawande M, Rathi A, Branco P and Varma R. Applied Sciences. 2013; 3:656-74.
19. B Baig RN, Varma RS.Chemical Communications. 2013; 49:752-770
20. Mady, M. F., Awad, G. E., & Jørgensen, K. B. European journal of medicinal chemistry, 2014;84: 433-443
21. Siabi, S., Pasdar, H., Foroughifar, N., Davallo, M., & Fazaeli, R. Biointerface Research in Applied Chemistry.2018; 8: 3418-3421.
22. Khadivi, R., Pasdar, H., Foroughifar, N., & Davallo, M. Biointerface Research in Applied Chemistry .2017; 7.6: 2238-2242.
23. Saghavaz, B. H., Pasdar, H., & Foroughifar, N. Biointerface Research in Applied Chemistry2016; 6.6:49-52
24. Foroughifar N, Mobinikhaledi A, Moghanian H. Synthetic Communications. 2010; 40:1812-1821