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Efficient Synthesis of Nickel(II) Complex Supported on Fe_3O_4@SiO_2 Nanoparticles as a New and Facile Catalyst for Various Multicomponent Reactions

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In the present work, we have planned a new magnetically recoverable nanocatalyst. The obtained nanocatalyst designated as Fe_3O_4@SiO_2@DOPisatin-Ni(II) was characterized by FTIR, XRD, SEM, EDAX, VSM, AAS and TGA techniques. It was found that Fe_3O_4@SiO_2@DOPisatin-Ni(II) successfully catalyses the synthesis of 2,3-dihydroquinazolin-4(1H)-ones, polyhydroquinoline and 5-substituted 1H-tetrazoles in solvent free condition and PEG as a green solvent.

Keywords: Magnetically nickel(II), 2,3-Dihydroquinazolin-4(1H)-ones, Polyhydroquinoline, 5-Substituted 1H-tetrazoles

INTRODUCTION

Separation and recovering of the catalysts are fundamental steps in catalytic systems that frequently affect on process economy [1]. A heterogeneous catalyst which is often easily synthesized, easily separated from the reaction mixture and simply reused is favoured over homogeneous catalysts [2]. Although these catalysts have advantages because of the their limited surface area, the reaction rate is restricted [3]. Therefore, developing supported heterogeneous catalysts is quite essential. A possible method is use of the magnetic nano particles (MNPs) as a catalyst support which can be simply separated and recovered from the reaction mixture by applying an external magnet [1]. Also, the MNPs have attracted much attention due to their potential applications in various fields such as magnetic resonance imaging (MRI), drug delivery, supports for various catalysts [4], biomolecular sensors and magneto-thermal therapy [5].

In 1850, the first multi-component reaction (MCR) was reported by Strecker [6]. This is known as a specific synthetic strategy with some advantages including high atom economy, high selectivity [7], high bond forming efficiency [8], shorter reaction time, lower cost, energy conservation and environment friendly [9]. 2,3-Dihydroquinazolin-4(1H)-ones are important class of fused heterocycles which have applications in pharmacology such as: antibiotic, antitumor, antipyretic, antidefibrillatory, analgesic, diuretic, antihypertonic, antihistamine, antidepressant, and vasodilating behavior [10].

Polyhydroquinolines are very well-known heterocycles that have attracted great attention due to their pharmaceutical properties such as: vasodilator, calcium channel blockers, hepatoprotective, bronchodilator, antiatherosclerotic, geroprotective, antitumor and antidiabetic activity [11].

Tetrazoles are an important class of aromatic five-membered heterocycles that include four nitrogen atoms [12]. These compounds have an increasingly popular functionality due to widespread applications in biological activities such as anti-inflammatory, antibacterial, antifungal, antituberculous, antiviral, cyclo-oxygenase inhibitors, anti-nociceptive, hypoglycemic and anti-cancer activities [13].

Several methods have been reported for the synthesis of 2,3-dihydroquinazolin-4(1H)-ones [14-16], polyhydro-quinoline [11,17] and 5-substituted 1H-tetrazoles [18,19]. Some reported methods have certain disadvantages such as

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long reaction time, use of toxic solvent and low yields.

To overcome these disadvantages, we report herein the synthesis of 2,3-dihydroquinazolin-4(1H)-ones derivative by one-pot two-component condensation of anthranilamide and aldehydes catalyst by Fe_3O_4@SiO_2@DOPisatin-Ni(II) in solvent free condition at 110 ºC (Scheme 2), synthesis of polyhydroquinoline by multi-component reactions of aldehyde, dimedon, ethylacetoacetate, ammonium acetate and Fe_3O_4@SiO_2@DOPisatin-Ni(II) as catalyst in solvent free condition at 100 ºC (Scheme 4) and synthesis of 5-substituted 1H-tetrazoles by Fe_3O_4@SiO_2@DOPisatin-Ni(II) in PEG at 120 ºC (Scheme 6).

EXPERIMENTAL

Preparation of Catalyst

Preparation of the magnetic Fe_3O_4 nanoparticles (MNPs). Fe_3O_4 nanoparticles were prepared by chemical co-precipitation of Fe^{3+} and Fe^{2+} ions. Typically, a solution was prepared from $FeCl_2 \cdot 4H_2O$ (2.221 g) and $FeCl_3 \cdot 6H_2O$ (5.858 g) in deionized H_2O (100 ml) under an N_2 atmosphere and 10 ml of 30% NH_4OH. The mixture stirred about 30 min at 80 ºC under vigorous mechanical stirring to produce a black solid product. The black magnetite solid product was collected by the external magnet, washed with deionized H_2O and dried [20].

Preparation of Fe_3O_4@SiO_2. The obtained Fe_3O_4 NPs (1 g) was dispersed in 10 ml deionized water and 50 ml absolute ethanol, and solution by sonication for 30 min. Then, 5.39 g PEG, 10 ml NH_3 and 2 ml tetraethylorthosilicate (TEOS) was added to the reaction mixture. The reaction mixture was stirred at room temperature for 38 h [21]. Finally the obtained particles was separated by external magnet and sequentially washed with deionized water and ethanol and dried at room temperature.

Preparation of functionalized Fe_3O_4@SiO_2 nanoparticle with 4-(2-aminoethyl)benzene-1,2-diol (Fe_3O_4@SiO_2@DOP). Fe_3O_4@SiO_2 (1 g) was dispersed in 25 ml absolute ethanol using an ultrasonic bath for 30 min. Then 4-(2-aminoethyl)benzene-1,2-diol (dopamine) (1.5 g) was added to the reaction mixture and stirred at room temperature for 24 h. The resultant product was collected by an external magnet and washed with ethanol to remove unreacted species and dried at room temperature.

Preparation of the Fe_3O_4@SiO_2@DOPisatin. The Fe_3O_4@SiO_2@DOPisatin was obtained *via* band formation between the amino group and the active carbonyl group of isatin. In this light, initially Fe_3O_4@SiO_2@DOP (0.6 g) was dispersed in 25 ml absolute ethanol using an ultrasonic bath for 30 min. Then, 0.441 g isatin and 2-3 drops acetic acid was added to the reaction mixture. The reaction mixture was refluxed at 80 ºC for 24 h. Then the product was isolated by an external magnet, washed several times with ethanol and then finally dried.

Preparation of Fe_3O_4@SiO_2@DOPisatin-Ni(II). Fe_3O_4@SiO_2@DOPisatin (0.3g) was dispersed in 25 ml absolute ethanol using an ultrasonic bath for 30 min. In the next step 0.174 g $Ni(NO_3)_2.6H_2O$ was added to the solution and the resultant mixture was under reflux for 24 h. The obtained catalyst was separated from the crude product using an external magnet and washed with ethanol. Then, the final catalyst was dried at room temperature.

General Procedure for the Synthesis of 2,3 Dihydroquinazolin-4(1H)-ones Derivatives

A mixture of aldehyde (1 mmol), 2-aminobenzamide (1.1 mmol) and Fe_3O_4@SiO_2@DOPisatin-Ni(II) (0.03 g), was stirred at 110 ºC. After completion of the reaction as indicated by TLC, the product was dissolved in hot ethanol and then catalyst was separated from the product by an external magnet. Finally, by recrystallization from ethanol, pure products were obtained.

General Procedure for the Synthesis of Polyhydroquinoline Derivatives

A mixture of aldehyde (1 mmol), dimedon (1 mmol), ethylacetoacetate (1 mmol), ammonium acetate (1.2 mmol) and Fe_3O_4@SiO_2@DOPisatin-Ni (II) (0.03 g) was stirred on an oil bath at 100 °C until the reaction was complete (TLC). After completion of the reaction, the product was dissolved in hot ethanol. Then catalyst was separated by an external magnet. Finally, the solvent was evaporated and all products were recrystallized in ethanol, which the pure products were obtained in good to excellent yields.

General Procedure for the Synthesis of 5-Substituted 1H-tetrazoles Derivatives

A mixture of nitrile (1 mmol), sodiumazide (1.2 mmol),

Fe_3O_4@SiO_2@DOPisatin-Ni(II) (0.05 g) and PEG (3 ml) was stirred at 120 ºC. The progress of the reaction was monitored by TLC. After completion of the reaction the catalyst was separated from the reaction mixture with an external magnet and extracted with ethyl acetate (2 × 20 ml) and HCl (1 N, 20 ml). The resultant organic layer dried over Na_2SO_4 (3 g). After evaporation of ethyl acetate, corresponding 5-substituted 1H-tetrazole was obtained in good yield.

Characterization Data of Selected Compounds

2-(4-Ethoxyphenyl)-2,3-dihydoquinazolin-4(1H)-one (Entry 4, Table 2). ^{1}H NMR (400 MHz, DMSO-d_6): δ_H: 7.95-7.94 (b, 1H), 7.51-7.50 (m, 2H), 7.34 (s, 1H), 7.26 (s, 1H), 6.95-6.91 (m, 3H), 6.68-6.66 (m, 1H), 5.85 (s, 1H), 5.76 (s, 1H), 4.07-4.06 (q, J = 4, 2H), 1.46-1.44 (s, 3H) ppm.

2-(2-Nitrophenyl)-2,3-dihydoquinazolin-4(1H)-one (Entry 9, Table 2). ^{1}H NMR (400 MHz, DMSO-d_6): δ_H: 8.26 (s, 1H), 8.10-8.08 (d, J = 8, 1H), 7.89-7.87 (d, J = 8, 1H), 7.83-7.80 (t, J = 0.8, 1H), 7.69-7.62 (m, 2H), 7.31-7.26 (m, 1H), 7.04 (s, 1H), 6.80 (d, J = 1.2, 1H), 6.76-6.72 (m, 1H), 6.36 (m, 1H) ppm.

Ethyl-4-(4-bromophenyl)-2,7,7-trimethyl-5-oxo-1,4,5, 6,7,8- hexahydroquinoline-3-carboxylate (Entry 4, Table 4). ^{1}H NMR (400 MHz, DMSO-d_6): δ_H: 9.14 (s, 1H), 7.40-7.38 (d, J = 8.4, 2H), 7.13-7.11 (d, J = 8.4, 2H), 4.84 (s, 1H), 4.01-3.96 (q, J = 6.8, 2H), 2.52-2.46 (d, J = 26.4, 1H), 2.31-2.27 (m, 4H), 2.20-2.16 (d, J = 16, 1H), 2.01-1.97 (d, J = 16, 1H), 1.15-1.11 (t, J = 7.2, 3H), 1.02 (s, 3H), 0.85 (s, 3H) ppm.

Ethyl-4-(4-hydroxyphenyl)-2,7,7-trimethyl-5-oxo-1,4, 5,6,7,8- hexahydroquinoline-3-carboxylate (entry 6, Table 4). ^{1}H NMR (400 MHz, DMSO-d_6): δ_H: 9.05 (s, 1H), 8.98 (s,1H), 6.95-6.93 (d, J = 8.8, 2H), 6.58-6.55 (m, 2H), 4.75 (s, 1H), 4.01-3.98 (m, 2H), 2.43-2.39 (d, J = 16, 1H), 2.31-2.26 (m, 4H), 2.19-2.15 (d, J = 16, 1H), 2.00-1.96 (d, J = 16, 1H), 1.17-1.13 (t, J = 7.2, 3H), 1.02 (s, 3H), 0.87 (s, 3H) ppm.

5-(3-Chlorophenyl)-1*H*-tetrazole (Entry 1, Table 6). ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.09-8.08 (m, 1H), 8.04-8.01 (m, 1H), 7.70-7.64 (m, 2H) ppm.

5-(4-Chlorophenyl)-1*H*-tetrazole (Entry 5, Table 6). ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 8.08-8.05 (d, *J* = 8.4, 2H), 7.73-7.69 (d, *J* = 8.4, 2H) ppm.

RESULTS AND DISCUSSION

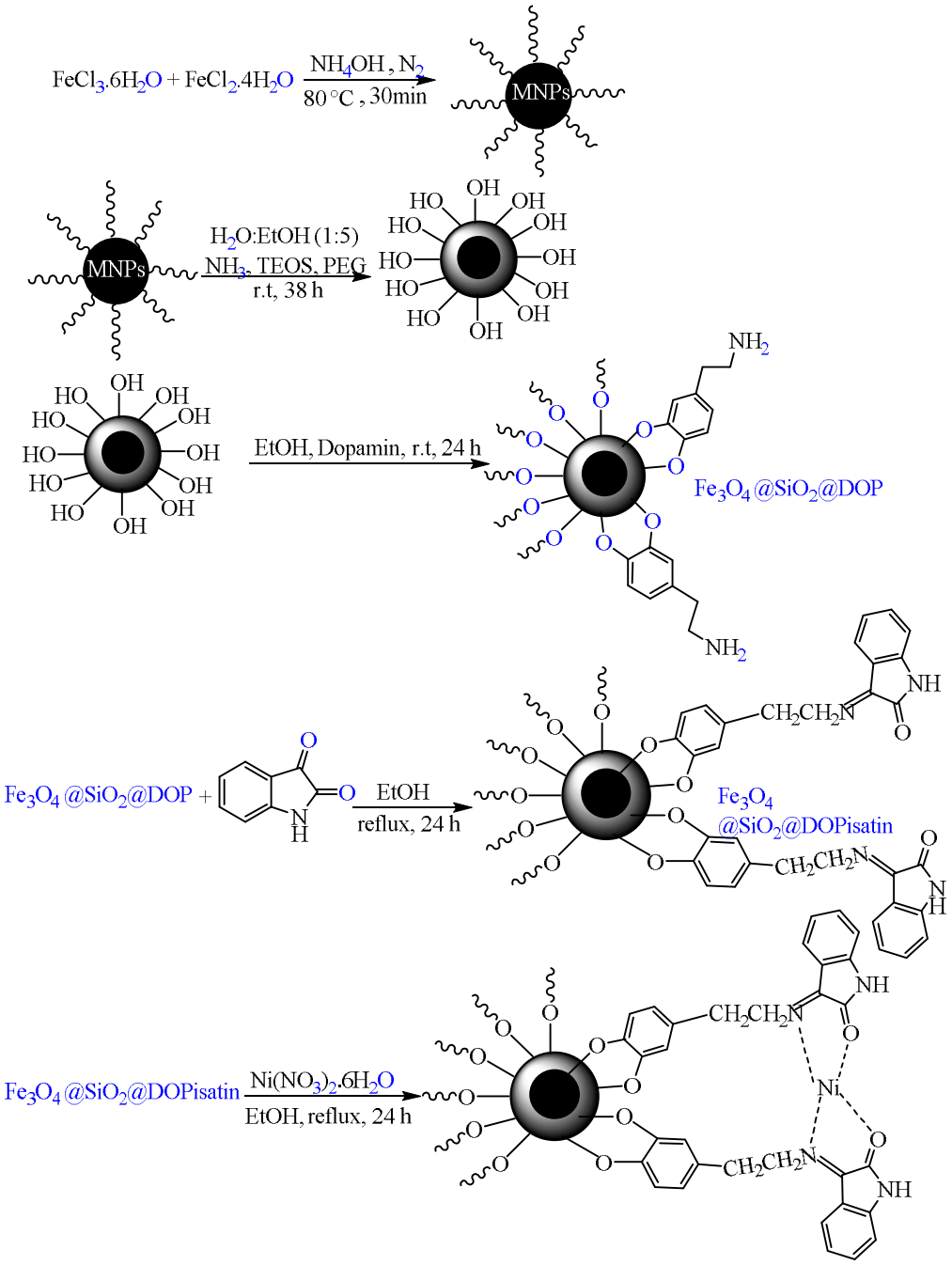
Catalyst Preparation

The details synthesis procedure of catalyst is indicated in Scheme 1. Initially the MNP of Fe_3O_4 was prepared by chemical co-precipitation of Fe^{3+} and Fe^{2+} ions with a molar ratio of 2:1, in basic solution under N_2 atmosphere at 80 °C [20]. Then, Fe_3O_4 nanoparticles were coated by tetraethylorthosilicate (TEOS). The obtained Fe_3O_4@SiO_2 was reacted with dopamine to afford Fe_3O_4@SiO_2@DOP. Then, for modification of Fe_3O_4@SiO_2@DOP, isatin was added to the Fe_3O_4@SiO_2@DOP. In the final step, $Ni(NO_3)_2.6H_2O$ was applied to obtain the final catalyst (Fe_3O_4@SiO_2@DOPisatin-Ni(II)).

Catalyst Characterization

The prepared catalyst was characterized by Fourier transform infrared (FT-IR, Bruker, Germany) spectroscopy, X-ray diffraction (XRD, GBC-Difftech MMA), scanning electron microscopy (SEM, FESEM-TESCAN MIRA3), energy dispersive X-ray (EDX, FESEM-TESCAN MIRA3), thermogravimetric analysis (TGA, PerkinElmer Pyris Diamond, U.K), vibrating sample magnetometer (VSM, MDKFD) and atomic absorption spectroscopy (AAS, Analyticaljena novAA400p).

Figure 1 shows the FT-IR spectra of MNPs (a), Fe_3O_4@SiO_2 (b), Fe_3O_4@SiO_2@DOP (c), Fe_3O_4@SiO_2@DOPisatin (d) and Fe_3O_4@SiO_2@DOPisatin-Ni(II) (e) particles. The bands cantered around 3401 cm^{-1} and 1625 cm^{-1} are, respectively, attributed to the O-H stretching and deforming vibrations of adsorbed water. The IR spectrum of bare Fe_3O_4 (Fig. 1a) shows the peak at 579 cm^{-1} which is assigned to the Fe-O vibration. In curve (b), which is the spectrum of Fe_3O_4@SiO_2, peaks at 1094 and 954 cm^{-1} is assigned to the asymmetric and symmetric stretching vibration of Si-O-Si bond. Evidently, it confirms that the silica has been successfully coated on the surface of MNPs. Also, the absorption peaks at 586 cm^{-1} are attributed to the stretching vibration mode of Fe-O bonds in Fe_3O_4. As shown in Fig. 1c, the peaks that appeared at 579 cm^{-1}, 954-1090 cm^{-1}, 1500 cm^{-1} and 1620 cm^{-1} come from stretching vibration of Fe-O, asymmetric stretching of Si-O-Si,



Scheme 1. Preparation process of Fe_3O_4@SiO_2@DOPisatin-Ni(II)

stretching vibration of C-N and bending of NH, respectively. Also, the presence of bands in 2359 cm^{-1} and 3396 cm^{-1} regions is assigned to C-H stretching of the ethyl group and N-H stretching. The band formation between Fe_3O_4@SiO_2@DOP and isatin is confirmed by a peak at 1618 cm^{-1}. This peak is attributed to the C=N stretching.

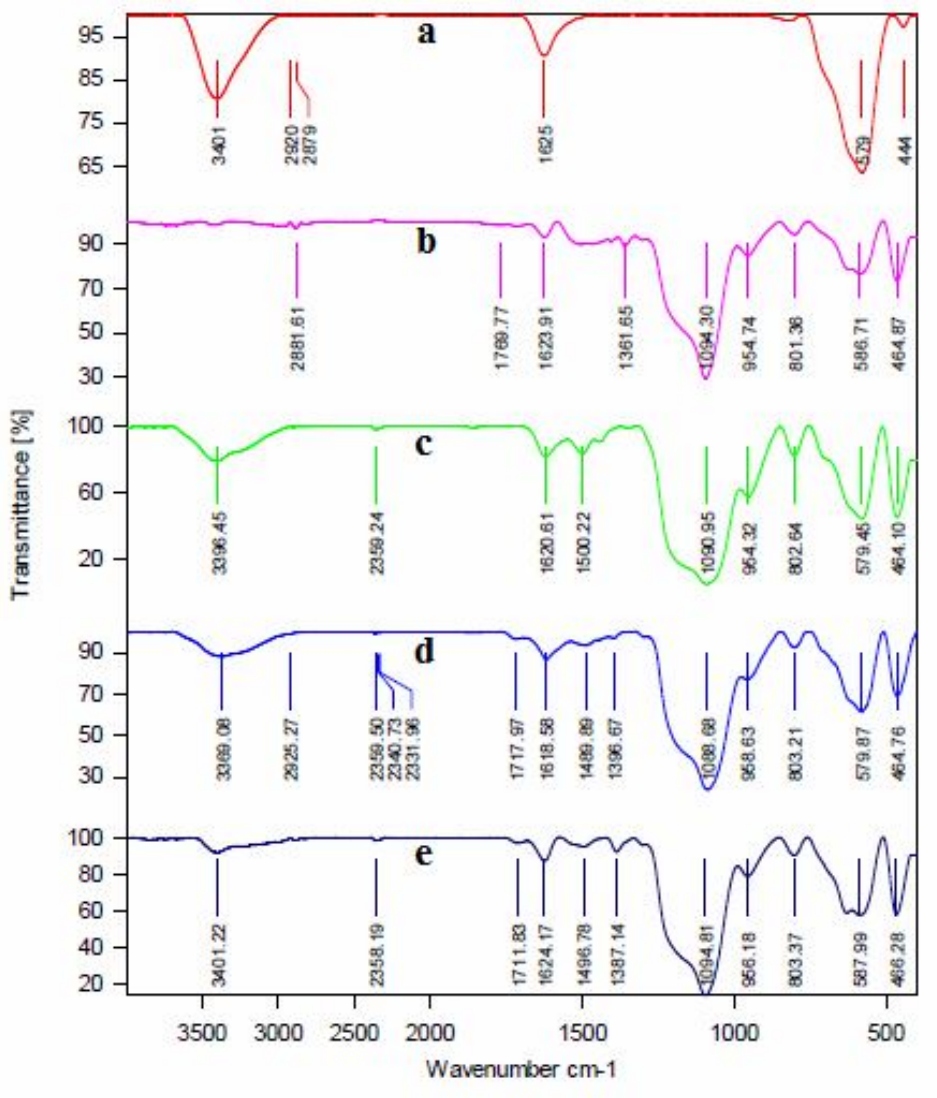


Fig. 1. FT-IR spectra for the MNPs (a), Fe_3O_4@SiO_2 (b), Fe_3O_4@SiO_2@DOP (c), Fe_3O_4@SiO_2@DOPisatin (d) and Fe_3O_4@SiO_2@DOPisatin-Ni(II) (e).

Also, another band appears around 1489 cm^{-1} which belongs to aromatic C=C stretching. The C=O stretch of the amide group appears at 1717 cm^{-1} and O-H stretching band is found at 3396 cm^{-1}. The IR spectrum of the Fe_3O_4@SiO_2@DOPisatin-Ni(II) (Fig. 1e) indicates a bond in 1624 belonging to the C=N stretching. The absorption peaks at 587 cm^{-1} are allocated to the stretching vibration mode of Fe-O bonds in Fe_3O_4. The absorption peak at 956-1094 cm^{-1} is characteristic of Si-O-Si bond stretching vibration. The presence of vibration bands in 3401 cm^{-1}, 2358 cm^{-1} and 1711 cm^{-1} demonstrated stretching of O-H, stretching CH and C=O amide, respectively. The peak at 1496 cm^{-1} concerns to C=C aromatic ring stretching. The peak of CH_2 bending appears at 1387 cm^{-1} [22].

Determination of the Ni content was carried out by atomic absorption spectroscopy (AAS). According to this analysis, the exact amount of Ni in the catalyst and recovered catalyst are found to be 0.326 mmol g^{-1} and 0.314

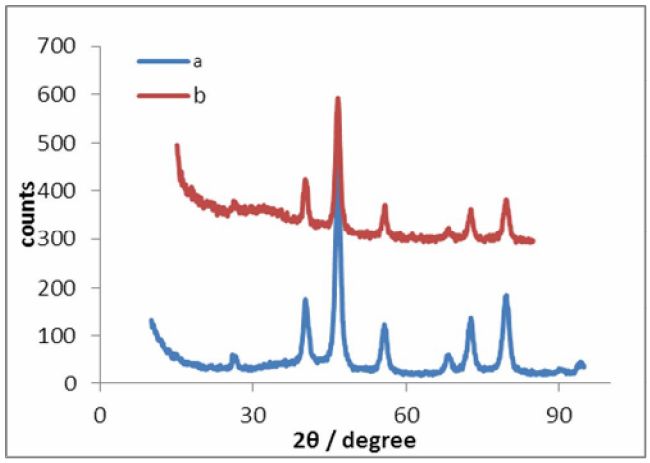


Fig. 2. The XRD pattern of Fe_3O_4 (a) and Fe_3O_4@SiO_2@DOPisatin-Ni(II) (b).

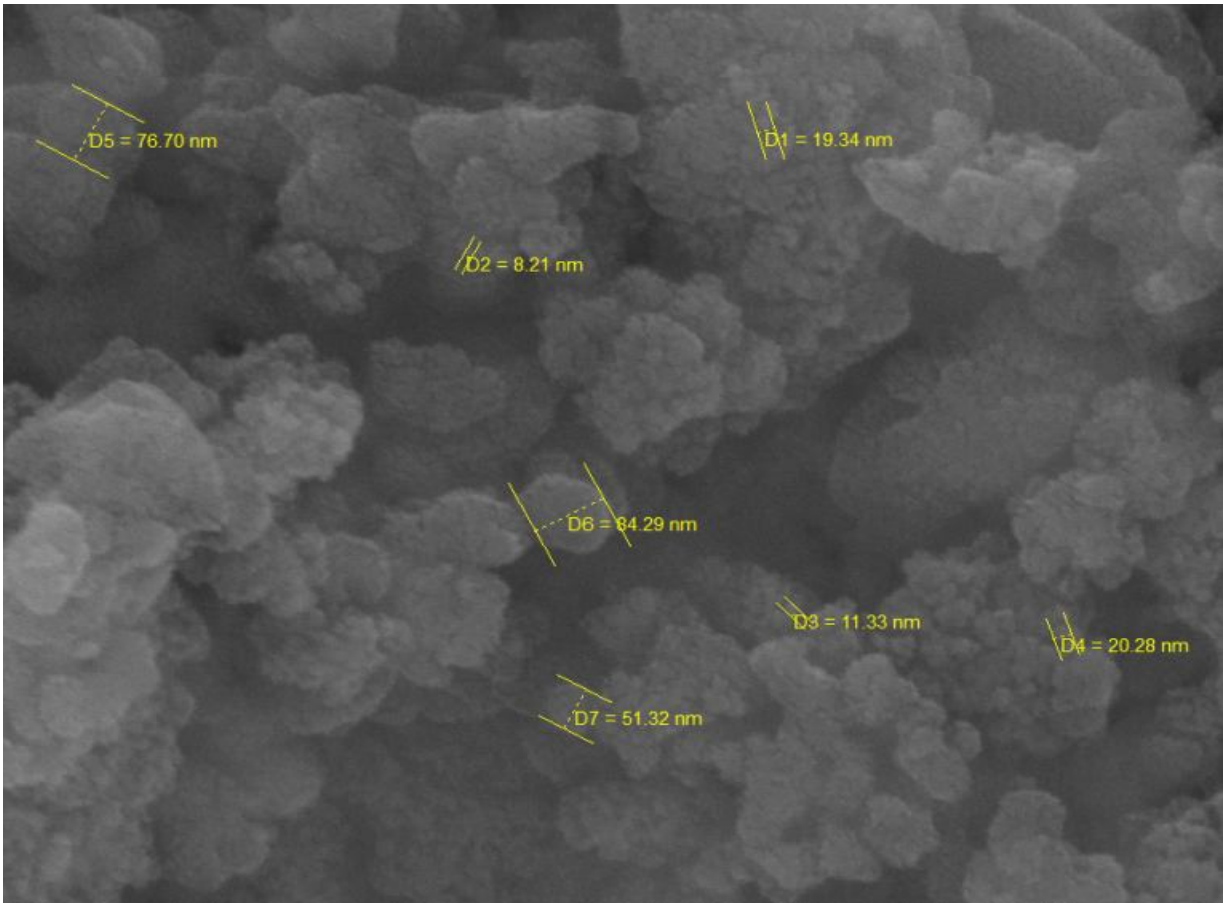


Fig. 3. SEM images of the Fe_3O_4@SiO_2@DOPisatin-Ni(II).

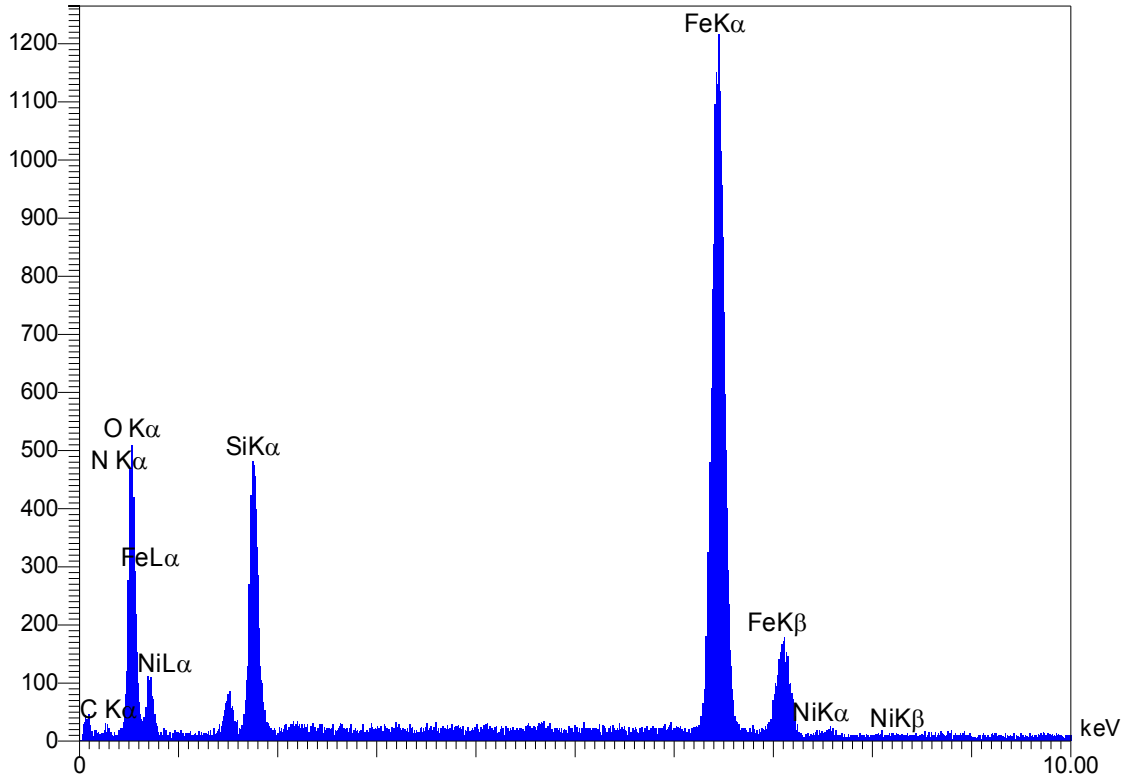


Fig. 4. EDX spectrum for Fe_3O_4@SiO_2@DOPisatin-Ni(II).

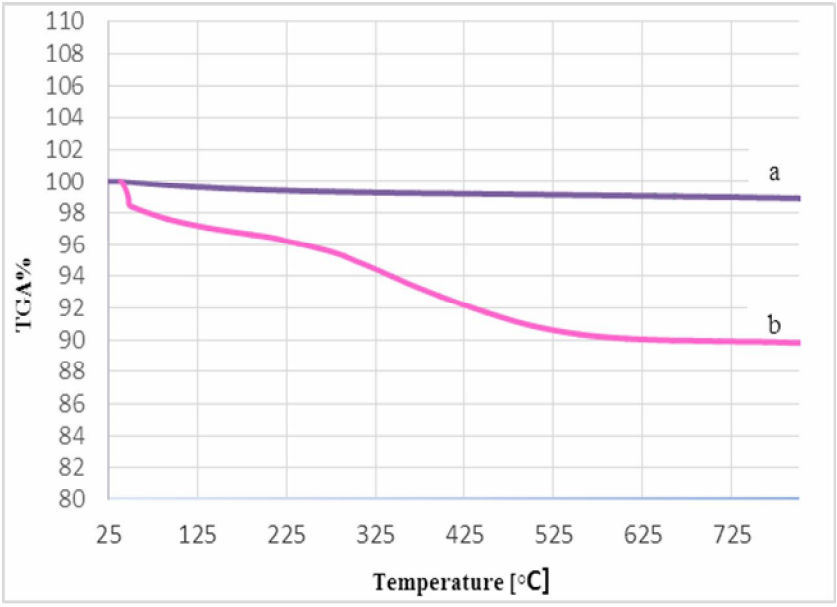


Fig. 5. TGA profile of Fe_3O_4 (a) and Fe_3O_4@SiO_2@DOPisatin-Ni(II) (b).

mmol g^{-1} respectively.

As presented in Fig. 2 the catalyst was characterized by peak positions at 2θ values of 23.58, 40.02, 46.46, 55.58, 66.58, 72.3 and 79.26 in the XRD pattern. The position of all peaks in the XRD pattern Fe_3O_4@SiO_2@DOPisatin-Ni(II) with the corresponding reflections of (111), (220), (311), (400), (422), (511) and (440) conforms to the standard XRD pattern of Fe_3O_4 [23]. The characteristic diffraction peaks reflections of crystalline inverse cubic spinel structures of MNPs. The XRD pattern of catalyst indicated the stability of the crystalline phase of Fe_3O_4 nanoparticles during functionalization of MNPs.

One of the electron microscopes employed to show the images of a sample and recognition its morphology is scanning electron microscope (SEM). Figure 3 displays the SEM image of Fe_3O_4@SiO_2@DOPisatin-Ni(II). It shows spherical morphology of catalyst with an average diameter less than 84 nm.

The energy dispersive X-ray (EDX) of Fe_3O_4@SiO_2@DOPisatin-Ni(II) indicated the presence of C, N, O, Si, Fe and Ni in the catalyst. Weight percentages of elements obtained were 0.61, 0.22, 3.71, 1.88, 92.63 and 0.95 respectively (Fig. 4).

The amount of the catalyst loading and stability of the materials can be inferred from the thermo gravimetric analysis (TGA). Figure 5 shows the TGA curves of the Fe_3O_4@SiO_2@DOPisatin-Ni(II) and bare Fe_3O_4 nanoparticles. The weight loss at temperatures below 200 °C is due to loss of adsorbed water or the water formed from the condensation of hydroxyl groups. The weight loss of 6% between 225-625 °C was assigned to the thermal decomposition of organic groups grafted to Fe_3O_4.

To investigate the magnetic properties of the catalyst, the technical of vibrating sampling magnetometry (VSM) was used. Obviously, the lower magnetic value of catalyst in comparison with MNPs is due to the coating of silica and the attached layer on the catalyst.

Catalytic Studies

Herein, after characterizing Fe_3O_4@SiO_2@DOPisatin-Ni(II), we examined its catalytic activity in some multi-component reaction such as synthesis of 2,3-dihydroquinazolin-4(1H)-one, polyhydroquinolines and 5-substituted 1H-tetrazoles, respectively.

Initially we selected the one-pot synthesis of 2,3-dihydroquinazolin-4(1H)-one using condensation of aldehyde, 2-aminobenzamide and catalyst in solvent free condition at 110 °C.

First, to optimize the reaction conditions for the synthesis of 2,3-dihydroquinazolin-4(1H)-ones derivative (Scheme 1), we investigated the reaction of benzaldehyde (1 mmol) with 2-aminobenzamide (1.1 mmol) and Fe_3O_4@SiO_2@DOPisatin-Ni(II) as catalyst in various solvents. The results showed that the highest product yield is obtained in solvent free condition. Then, the effect of the amount of catalyst on the conversion rate of the reaction was studied by varying the amount of Fe_3O_4@SiO_2@DOPisatin-Ni(II). As shown in Table 1, entry 4, the best results are observed using 0.03 g of catalyst. As the synthesis of 2,3-dihydroquinazolin-4(1H)-one yields is dependent to temperature, the effect of temperature was studied and temperature of 110 °C was found to be ideal temperature for this reaction (Table 1, entry 4 and 11-14).

The reaction of the various benzaldehyde derivatives, including electron-donating and electron-withdrawing groups on aromatic ring was then investigated to confirm the generality of the present method. The results of this study are summarized in Table 2.

As shown in Scheme 3, the proposed mechanism of synthesis 2-aryl-2,3-dihydroquinazolinone-4(1H)-one was indicated. The anthranilamide reacted with the carbonyl group in aldehyde activated, and the intermediate I formed. The imine intermediate II was prepared *via* dehydration of intermediate I. Finally, in final step, the intramolecular cyclization of imine intermediate II generated the final product [30].

In the second part of our work, we tested the catalytic activity of Fe_3O_4@SiO_2@DOPisatin-Ni(II) in the one-pot synthesis of polyhydroquinoline derivatives (Scheme 4).

To achieve more efficient synthesis of polyhydroquinoline, reaction of 4-methylbenzaldehyde (1 mmol), dimedon (1 mmol), ethylacetoacetate (1 mmol), ammonium acetate and Fe_3O_4@SiO_2@DOPisatin-Ni(II) as catalyst was selected as model system, to find the optimum conditions. Firstly, the effect of different solvents, various amounts of catalyst, various amounts of ammonium acetate,

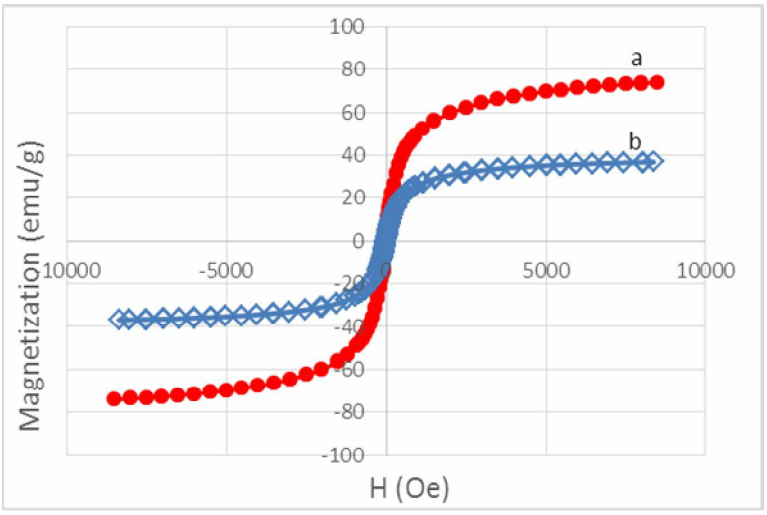
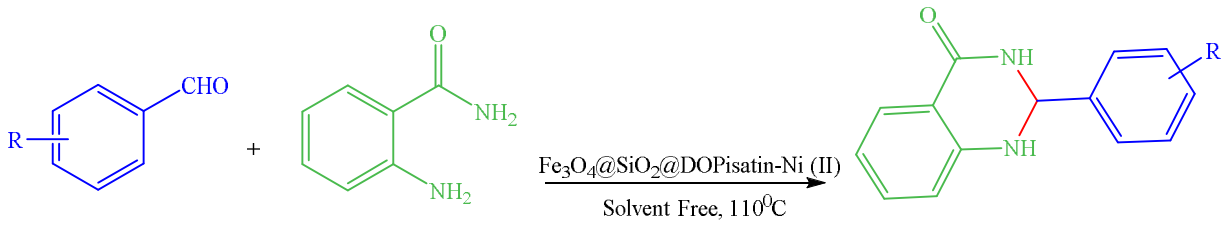


Fig. 6. VSM analysis of Fe_3O_4 (a) and Fe_3O_4@SiO_2@DOPisatin-Ni(II) (b).



Scheme 2. Synthesis of 2,3-dihydroquinazolin-4(1H)-one derivatives catalyzed by Fe_3O_4@SiO_2@DOPisatin-Ni(II).

and temperature was studied on the model reaction. According to data given in Table 3, entry 1, solvent free was the most efficient condition for this reaction. The amounts of catalyst were another essential factor favoring the yield of the reaction. Use of 0.03 g of catalyst achieved maximum product yield of 97% (Table 3, entry 1). A further increase in the amount of catalyst did not indicate any considerable improvement in the yield. The effect of temperature was investigated by carrying out the model reaction at different temperatures under solvent-free condition (60 °C, 80 °C, 90 °C, 100 °C, 110 °C and 120 °C) and the best results were obtained at 100 °C (Table 3, entries1).

As shown in entry 1 of Table 3, the best results are obtained with 4-methylbenzaldehyde (1 mmol), dimedone (1 mmol), ammonium acetate (1.2 mmol), ethylacetoacetate (1 mmol) in the presence of Fe_3O_4@SiO_2@DOPisatin-Ni(II) (0.03 g) and solvent free condition at 100 ºC. As shown in Table 4, under optimized conditions, the scope of synthesis of polyhydroquinoline derivatives with other aldehydes was found to be quite good.

Proposed mechanism for the formation of polyhydroquinoline is shown in Scheme 5. The condensation of aldehydes with the active methylene compounds (Knoevenagel Condensation) formed the α,β-unsaturated compound. Then, the Michael-type addition of the resultant intermediates produced polyhydroquinoline [31].

In continuation of this work, we report the synthesis of 5-substituted 1H-tetrazoles by the Nickel-catalyzed [3+2] cycloaddition between the corresponding nitriles and sodium azide in PEG at 120 ºC (Scheme 6).

In the cycloaddition reaction between phenyl cyanide

Table 1. Optimization Condition for the Condensation of Benzaldehyde (1mmol) and 2-Aminobenzamide (1.1 mmol)[a]

Entry	Catalyst (g)	Solvent	Temperature (ºC)	Yield (%)[b]
1	0	-[c]	110	38
2	0.01	-[c]	110	40
3	0.02	-[c]	110	65
4	0.03	-[c]	110	95
5	0.04	-[c]	110	92
6	0.05	-[c]	110	94
7	0.03	EtOH	Reflux	70
8	0.03	H_2O	Reflux	80
9	0.03	PEG	110	45
10	0.03	EtOAc	Reflux	Trace
11	0.03	-[c]	60	Trace
12	0.03	-[c]	80	43
13	0.03	-[c]	100	80
14	0.03	-[c]	120	95

[a]60 min. [b]Isolated yield. [c]Solvent free.

and NaN_3, we investigated the effect of solvents, amount of catalyst and temperature on the formation of tetrazole. To study the effect of catalyst, phenyl cyanide (1 mmol) was treated with sodium azide (1.2 mmol) in the presence of different amounts of Fe_3O_4@SiO_2@DOPisatin-Ni(II) and the obtained results are shown in Table 5. As shown in Table 5, entry 2, when the reaction is carried out in the presence of 0.05 g of the catalyst, the corresponding product will be in a high yield of 91%. Among the solvents tested PEG gave a high yield of the product. Next, we examined the effect of the temperature on the synthesis of 5-substituted 1H-tetrazoles. We applied room temperature, 70 °C, 100 °C and 120 °C. Therefore, the best result was obtained in 120 °C.

The optimization of the reaction for the synthesis of 5-substituted 1H-tetrazoles with respect to the amounts of the starting materials and the catalyst led to nitrile (1 mmol), sodium azide (1.2 mmol), PEG (3 mL), and catalyst (0.05 g) at 120 ºC. We investigated the substrate scope and generality of the protocol by employing structurally various nitriles, including electron-donating and electron-withdrawing groups on aromatic ring. The results of the [3+2] cycloaddition reaction of various nitriles with NaN_3 are summarized in Table 6.

A plausible mechanism for the formation of 5-substituted1H-tetrazol is shown in Scheme 7. Initially, the

Table 2. Synthesis of 2,3-Dihydroquinazolin-4(1H)-ones Catalyzed by Fe_3O_4@SiO_2@DOPisatin-Ni(II) in Solvent Free Condition and at 110 ºC

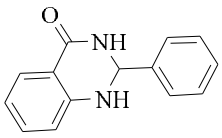
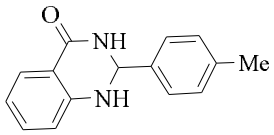
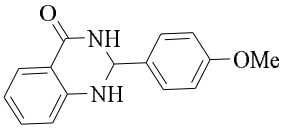
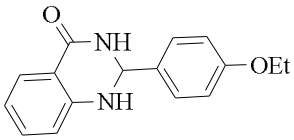
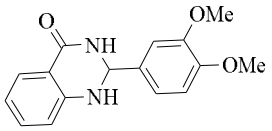
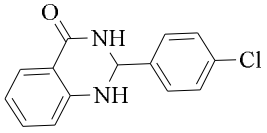
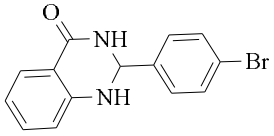
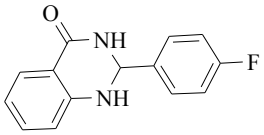
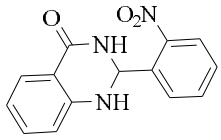
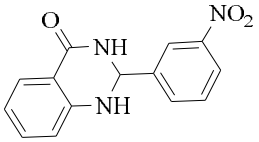
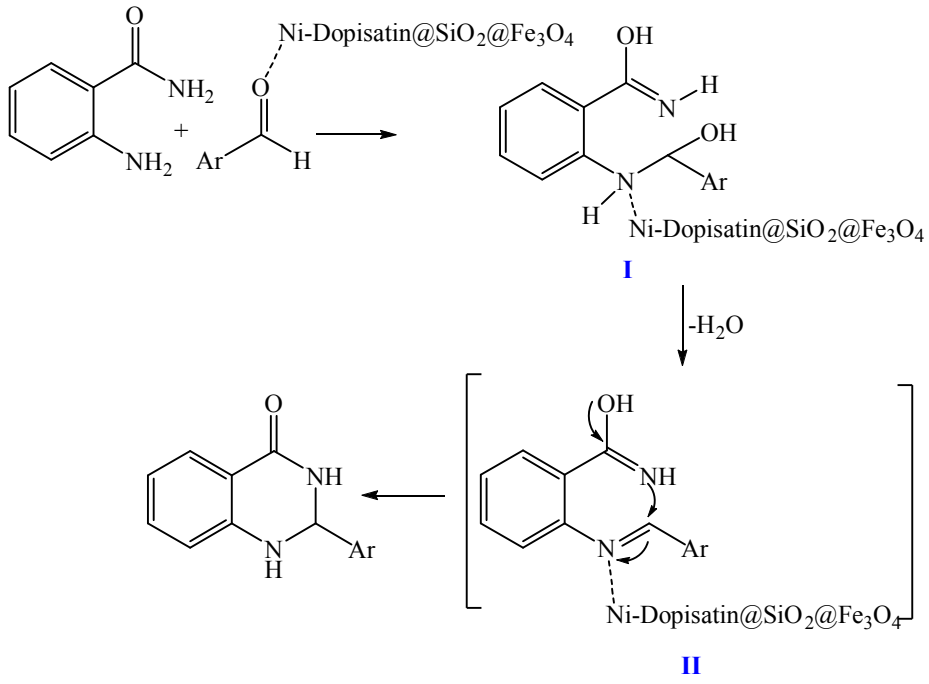
Entry	Product	Time (min)	Yield (%)[a]	M. P. (ºC)	Ref.
1		60	95	223-226	[15]
2		75	98	230-232	[24]
3		60	95	176-178	[15]
4		65	94	170-173	[25]
5		70	97	210-213	[26]
6		85	93	196-198	[26]
7		90	91	197-199	[27]
8		120	90	194-197	[28]

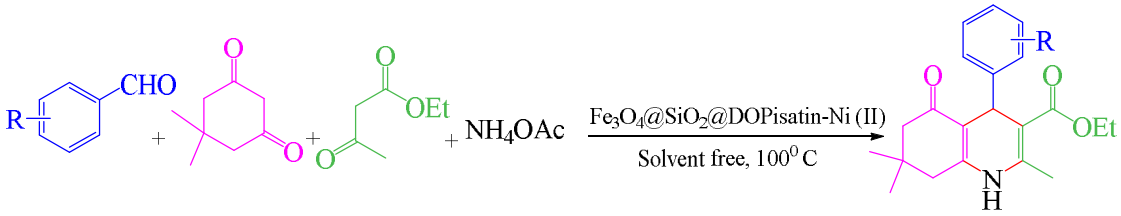
Table 2. Continued

9		180	90	189-193	[27]
10		160	92	192-195	[29]

[a]Isolated yield.



Scheme 3. Proposed mechanism for the synthesis of 2-aryl-2,3-dihydroquinazolinone-4(1H)-one



Scheme 4. Synthesis of polyhydroquinoline derivatives using Fe_3O_4@SiO_2@DOPisatin-Ni(II)

Table 3. Optimization Condition for the Synthesis of Polyhydroquinoline Using 4-Methyl-benzaldehyde, Dimedone, Ammonium Acetate, Ethylacetoacetate and Catalyst as a Model Reaction in 110 min

Entry	Catalyst (g)	Ammonium acetate (mmol)	Solvent	Temperature (ºC)	Yield (%)[a]
1	0.03	1.2	-[b]	100	97
2	0.03	1.2	H_2O	Reflux	Trace
3	0.03	1.2	EtOH	Reflux	80
4	0.03	1.2	PEG	100	75
5	0.03	1.2	DMSO	100	20
6	0	1.2	-[b]	100	0
7	0.01	1.2	-[b]	100	60
8	0.02	1.2	-[b]	100	82
9	0.05	1.2	-[b]	100	97
10	0.03	1.1	-[b]	100	85
11	0.03	1	-[b]	100	71
12	0.03	1.2	-[b]	60	20
13	0.03	1.2	-[b]	80	45
14	0.03	1.2	-[b]	90	70
15	0.03	1.2	-[b]	110	97
16	0.03	1.2	-[b]	120	96

[a]Isolated yield. [b]Solvent free.

nanocatalyst reacts with azide to afford the $[Fe_3O_4@SiO_2@Dopisatin\text{-}Ni(II)]\text{-}N_3$(I) catalytic species. Then, the [3+2] cycloaddition takes place between the CN bond of nitrile and (I) to afford the intermediate(II) and (III). Due to formation of complex(II) from precoordination of the nitrogen atom of the CN group of nitrile with (I), the cyclization step accelerates. This procedure leads to the produce of final heterocycle [22].

Recyclability of the Catalyst

Significance of heterogeneous catalyst over the homogeneous counterpart is its ease of separation from the reaction mixture by an external magnet and its recyclability without any significant decrease in activity. In this light, to investigate this issue, the recyclability of the catalyst was examined using a model reaction between 4-methyl-benzaldehyde (1 mmol), dimedone (1 mmol), ammonium acetate (1.2 mmol), ethylacetoacetate (1 mmol) in the presence of $Fe_3O_4@SiO_2@DOPisatin\text{-}Ni(II)$ (0.03 g) and solvent free condition at 100 ºC. After the completion of the reaction, the catalyst was easily and rapidly separated from the reaction mixture using an external magnet and washed with ethanol and dried at room temperature. Then, the recovered catalyst was applied to the next step. As shown in

Table 4. Synthesis of Polyhydroquinoline Catalyzed by Fe_3O_4@SiO_2@DOPisatin-Ni(II) in Solvent Free Conditions at 100 ºC

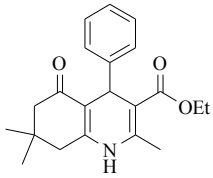
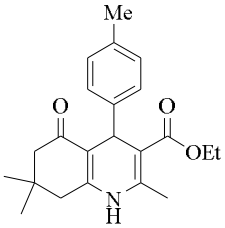
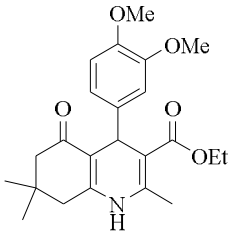
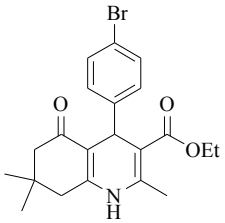
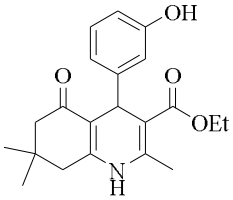
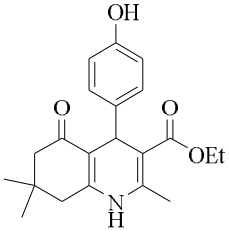
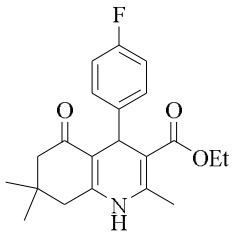
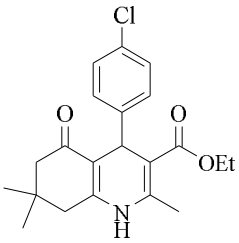
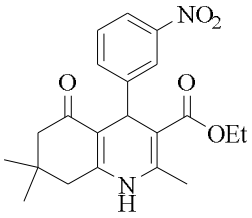
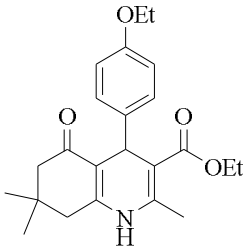
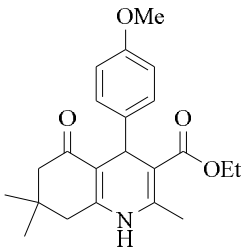
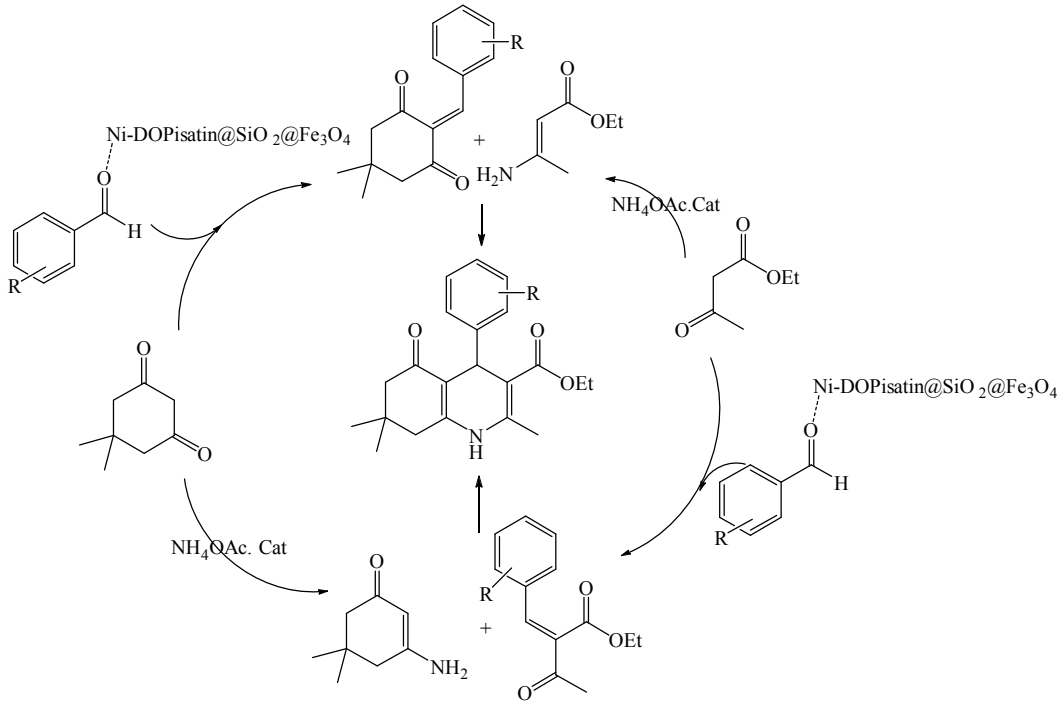
Entry	Product	Time (min)	Yield (%)[a]	M. P. (ºC)	Ref.
1		120	98	216-217	[31]
2		110	97	259-260	[32]
3		100	96	203-206	[31]
4		120	94	248-250	[31]
5		120	91	222-228	[33]
6		160	97	233-234	[34]

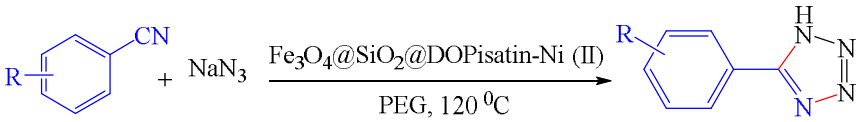
Table 4. Continued

7		120	90	182-185	[31]
8		120	97	236-240	[31]
9		180	98	177-179	[35]
10		120	95	174-180	[31]
11		120	95	248-250	[31]

[a]Isolated yield.



Scheme 5. Proposed mechanism for the synthesis of polyhydroquinoline derivatives



Scheme 6. Synthesis of 5-substituted 1H-tetrazoles by using of Fe_3O_4@SiO_2@DOPisatin-Ni(II)

Fig. 8, the catalyst can be reused over 7 times without any significant loss of its catalytic activity.

In order to show the efficiency of this procedure, we compared the results of the preparation of polyhydroquinoline from 4-methylbenzaldehyde, dimedone, ammonium acetate and ethylacetoacetate with the results in the literature (Table 7, entry 1-5). Also, we checked the merit of Fe_3O_4@SiO_2@DOPisatin-Ni(II) for the synthesis of 2-(phenyl)-2,3-dihydoquinazolin-4(1H)-one ((Table 7, entry 7,8) and 5-(4-Chlorophenyl)-1H-tetrazole (Table 7, entry 10, 11). As shown in Table 7, the catalyst showed a good reaction time and high yield.

CONCLUSIONS

In an effort to develop an innovative and efficient heterogeneous catalytic system for multi-component reaction, we have synthesized Fe_3O_4@SiO_2@DOPisatin-Ni(II) as an efficient, new and reusable catalyst for the synthesis of 2,3-dihydroquinazolin-4(1H)-ones, polyhydroquinoline and 5-substituted 1H-tetrazoles. The advantages of the catalyst are the novelty, easy separation by an external magnet, easy preparation, functionalization without tedious condition, easy recovery and low toxicity and price. To follow the principles of green chemistry, these multi-

Table 5. Optimization the Reaction Condition for the Synthesis of 5-Substituted 1H-tetrazoles Using Phenyl Cyanide, NaN_3 and Catalyst as a Model Reaction[a]

Entry	Catalyst (g)	Solvent	Temperature (ºC)	Yield (%)[b]
1	0.05	DMSO	120	20
2	0.05	PEG	120	91
3	0.05	EtOH	Reflux	Trace
4	0.05	PEG	100	72
5	0.05	PEG	70	20
6	0.05	PEG	r.t.	N.R
7	0	PEG	120	Trace
8	0.01	PEG	120	30
9	0.03	PEG	120	50

[a]40 min. [b]Isolated yield.

Table 6. Synthesis of 5-Substituted 1H-tetrazoles Catalyzed by Fe_3O_4@SiO_2@DOPisatin-Ni(II) in PEG at 120 ºC

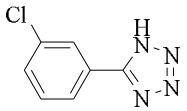
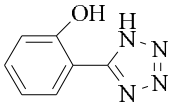
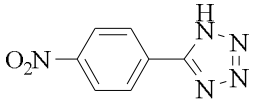
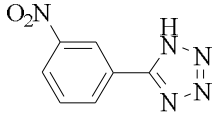
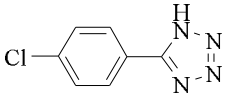
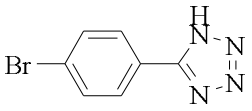
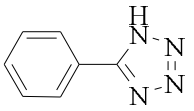
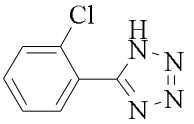
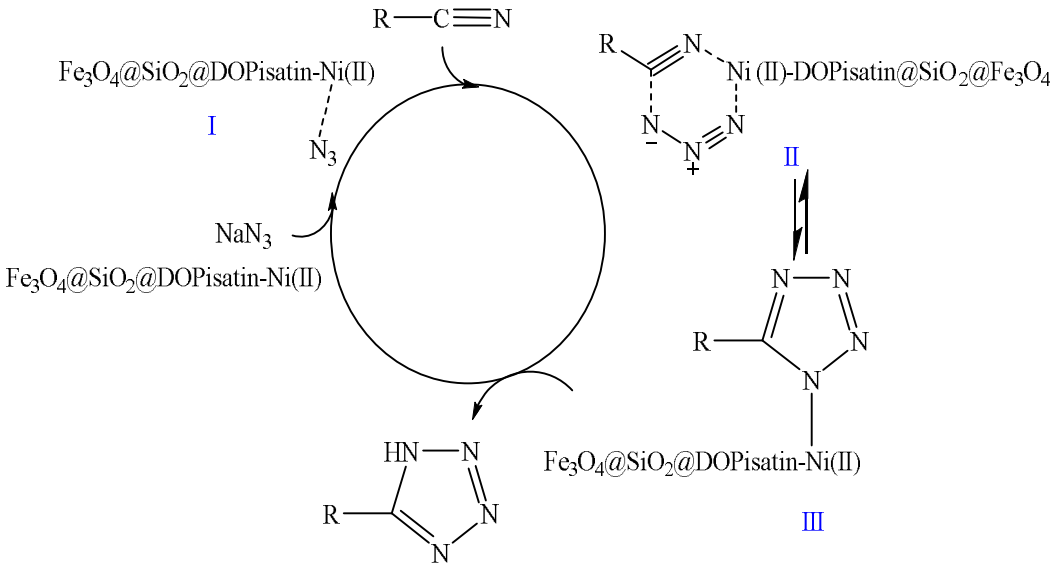
Entry	Product	Time (h)	Yield (%)[a]	M. P. (ºC)	Ref.
1		0.83	90	127-130	[36]
2		1	92	220-225	[36]
3		12	73	217-220	[22]
4		10	84	148-150	[36]
5		1.67	85	259-260	[37]

Table 6. Continued

6		5	79	261-266	[36]
7		0.67	91	210-215	[36]
8		1	88	176-180	[36]

[a]Isolated yield.



Scheme 7. Proposed mechanism for the synthesis of 5-substituted 1H-tetrazoles

component reactions were also performed in solvent free condition or PEG. Two major novelties of this work are that, first, for the first time, Fe_3O_4@SiO_2@DOPisatin-Ni(II) as a new, efficient and reusable nanocatalyst is used for the synthesis of three important heterocyclic compounds; 2,3-dihydroquinazolin-4(1H)-ones, polyhydroquinoline and 5-substituted 1H-tetrazoles, and second, a green solvent of PEG or solvent free condition is used.

ACKNOWLEDGEMENTS

This work was supported by the research facilities of Ilam University, Ilam, Iran.

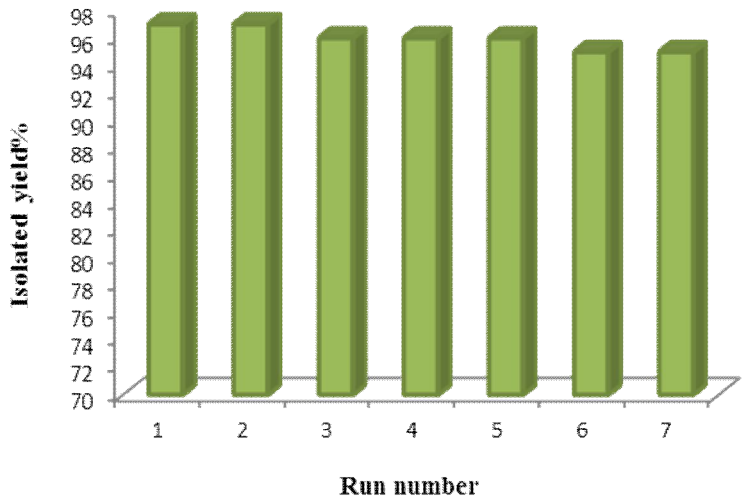


Fig. 7. Recovery of the catalyst in the synthesis of polyhydroquinoline.

Table 7. Comparison the Results of Fe_3O_4@SiO_2@DOPisatin-Ni(II) with other Catalysts

Entry	Condition	Time (min)	Yield (%)	Ref.
1	Bakers' yeast (200 mg), D-glucose (300 mg), phosphate buffer (pH 7.0, 5 ml), r.t	24 h	82[a]	[17]
2	$PdCl_2$, Na_2CO_3, TBAB, THF, Reflux	4.3 h	86[a]	[11]
3	GSA@MNPs (0.05 g), EtOH, Reflux	260	89[a]	[31]
4	Boehmite-SSA (0.03 g), EtOH, Reflux	250	96[a]	[38]
5	Fe_3O_4-SA-PPCA (10 mg), ethanol, 50 °C	110	91[a]	[39]
6	Fe_3O_4@SiO_2@DOPisatin-Ni(II) (0.03 g), 100 °C, solvent free	110	97[a]	This work
7	$Sc(OTf)_3$ (1 mol%), 5 mol% of L6 and powdered 4A˚ molecular sieves, r.t., CH_2Cl_2	48 h	84[b]	[14]
8	GSA@MNPs (0.05 g), EtOH, Reflux	55	90[b]	[31]
9	Fe_3O_4@SiO_2@DOPisatin-Ni(II) (0.03g), 110 °C, solvent free	60	95[b]	This work
10	[AMWCNTs-O-Cu(II)-PhTPY (4 mol%), NH_4OAc, DMF,70 °C	150	90[c]	[40]
11	$BaWO_4$ (0.104 mmol), DMF, 120 °C	24 h	90[c]	[18]
12	Fe_3O_4@SiO_2@DOPisatin-Ni(II) (0.05 g), 120 °C, PEG	100	85[c]	This work

[a]Synthesis of ethyl-4-(4-methylphenyl)-2,7,7-trimethyl-5-oxo-1,4,5,6,7,8- hexahydroquinoline-3-carboxylate. [b]Synthesis of 2-(phenyl)-2,3-dihydoquinazolin-4(1H)-one. [c]Synthesis of 5-(4-Chlorophenyl)-1H-tetrazole.

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