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ORIGINAL PAPER

Synthesis of pyrazol-quinazolinones and 2,3-dihydroquinazolin-4(*1H*)-ones using $CoAl_2O_4$ nanoparticles as heterogeneous catalyst

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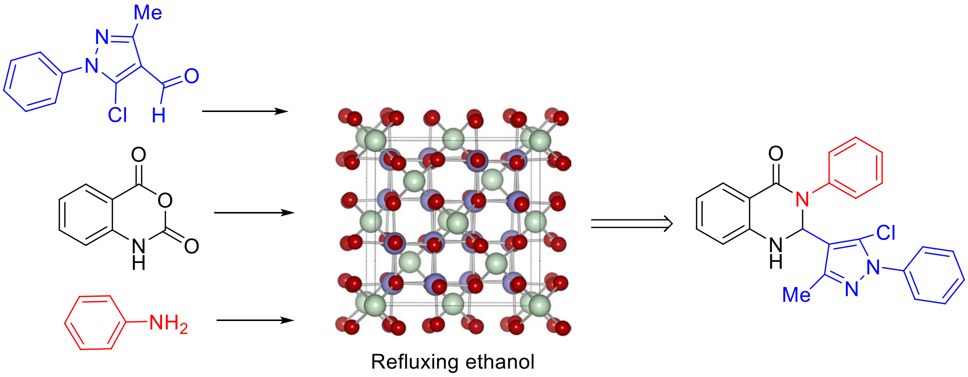
Abstract

The preparation and characterization of cobalt aluminate ($CoAl_2O_4$) magnetic nanoparticles and its application as a catalyst for the synthesis of a novel class of pyrazol-quinazolinones and 2,3-dihydroquinazolin-4(*1H*)-ones is described. The structure of the catalyst was studied by Fourier transform infrared spectroscopy, transmission electron microscopy, X-ray diffraction, and vibrating sample magnetometer analysis. The resulting cobalt aluminate ($CoAl_2O_4$) was an efficient catalyst and affords the desired products in good to excellent yields. Moreover, the catalyst could be easily recovered by magnetic separation and recycled for four times without significant loss of its catalytic activity.

Graphic abstract

2,3-Dihydroquinazolin-4(*1H*)-ones and a novel class of pyrazol-quinazolinones were synthesized through one-pot condensation reaction of isatoic anhydride, aromatic aldehydes, and amines using $CoAl_2O_4$ as nanoparticle heterogeneous catalyst in refluxing ethanol.



Keywords $CoAl_2O_4$ nanoparticles · Pyrazol-quinazolinones · Heterogeneous catalyst · Isatoic anhydride · 2,3-Dihydroquinazolinones

Introduction

Catalytic process is the key of many chemical industries. Within this subject, design of novel, highly active, and reusable catalysts has become a major area of research. Heterogeneous catalysts are favored, because of easy separation, recycling, and the use of small amount in the production

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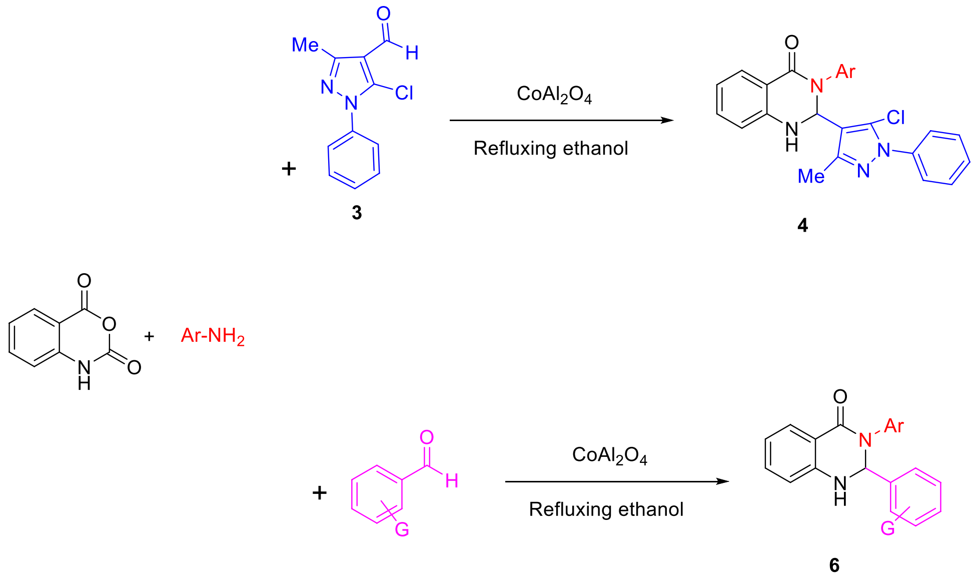
Scheme 1 Synthesis of pyrazol-quinazolinone and 2,3-dihydroquinazolin-4(*1H*)-one derivatives



[1–8]. As a matter of fact, the search for new efficient and recyclable heterogeneous catalysts has received more attention. Among them, nanoparticles (NPs) have been more desirable due to their remarkable advantages such as small size, large specific surface area, high dispersion property, good catalytic activity and selectivity, and easily modifiable surface by chemical methods [9]. In this sense, magnetic nanoparticles (MNPs) are arguably the most extensively investigated and emerged as appealing catalyst supports [8–17]. Their magnetic character makes them effective and easily separable from the reaction system by applying an external magnetic field, which eliminates the necessity of tedious filtration, centrifugation, or membrane separation steps.

Recently, cobalt aluminate spinels ($CoAl_2O_4$) were prepared and have attracted much attention due to their optical, catalytic, pigments, electrical and magnetic properties [18–28]. Also, the other applications in ceramics, color tubes, plastics, paint, rubber, and glass were reported [29, 30].

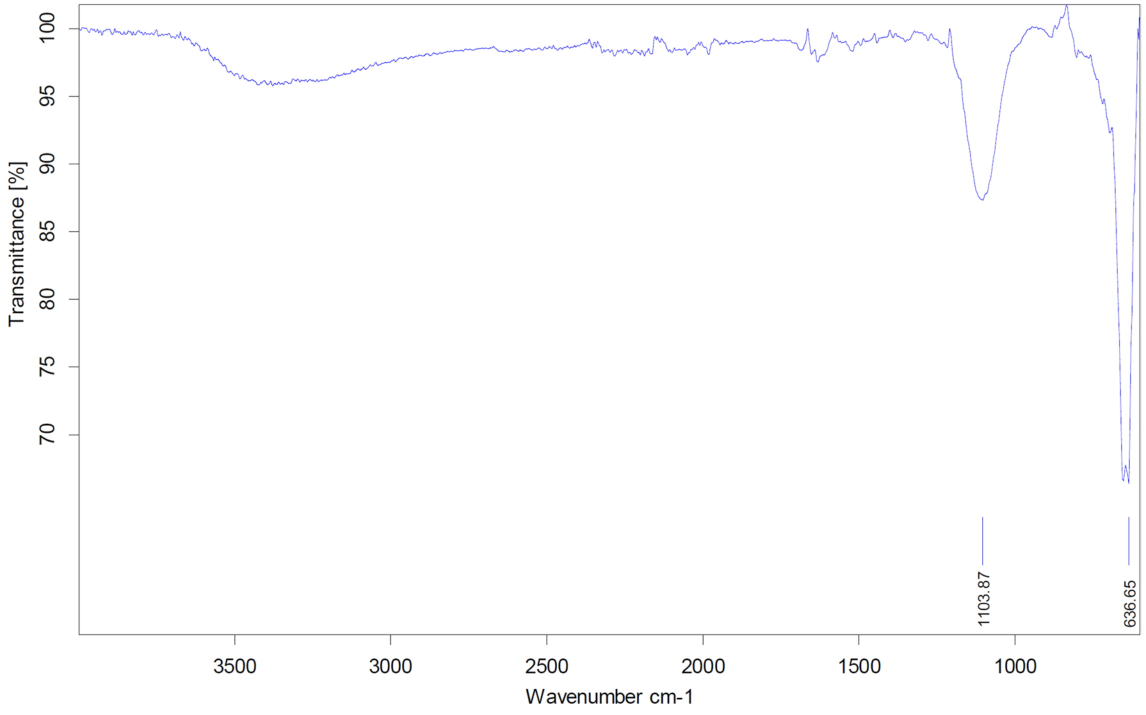


Fig. 1 FT-IR spectra of $CoAl_2O_4$ nanoparticles

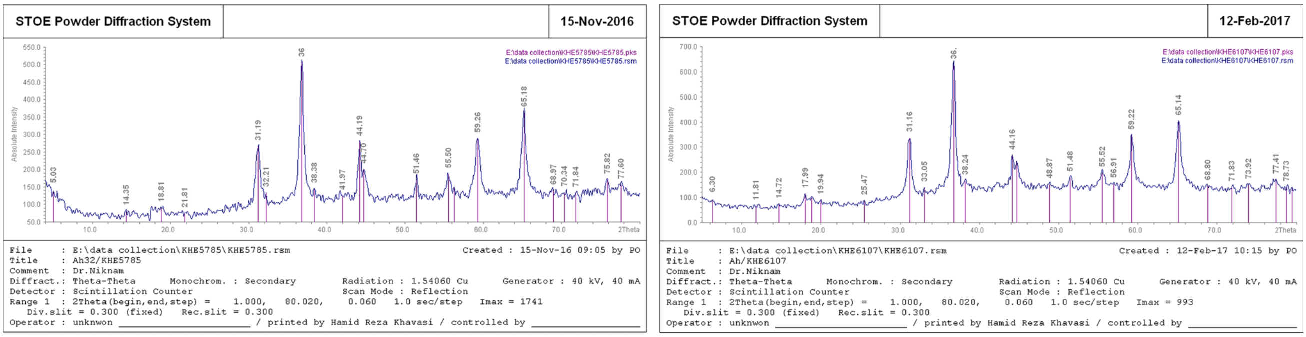


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Fig. 2 XRD of nano-$CoAl_2O_4$. Left side is fresh, and right side is after recovery

2,3-Dihydroquinazolinone derivatives are important compounds for pharmaceutical chemistry. They have shown some pharmaceutical activities such as antifertility, antibacterial, antitumor, antifungal, and monoamine oxidase inhibition [31–34]. In recent years, the synthesis of 2,3-dihydroquinazolinones was reported via a three-component condensation reaction between isatoic anhydride, and aldehydes with ammonium acetate or primary amine in the presence of different reagents or catalysts. Some of these reagents or catalysts are alum ($KAl(SO_4)_2 \cdot 12H_2O$) [35], *p*-toluenesulfonic acid [36], amberlyst-15 microwave-assisted [37], montmorillonite K-10 [38], ionic liquid [39],

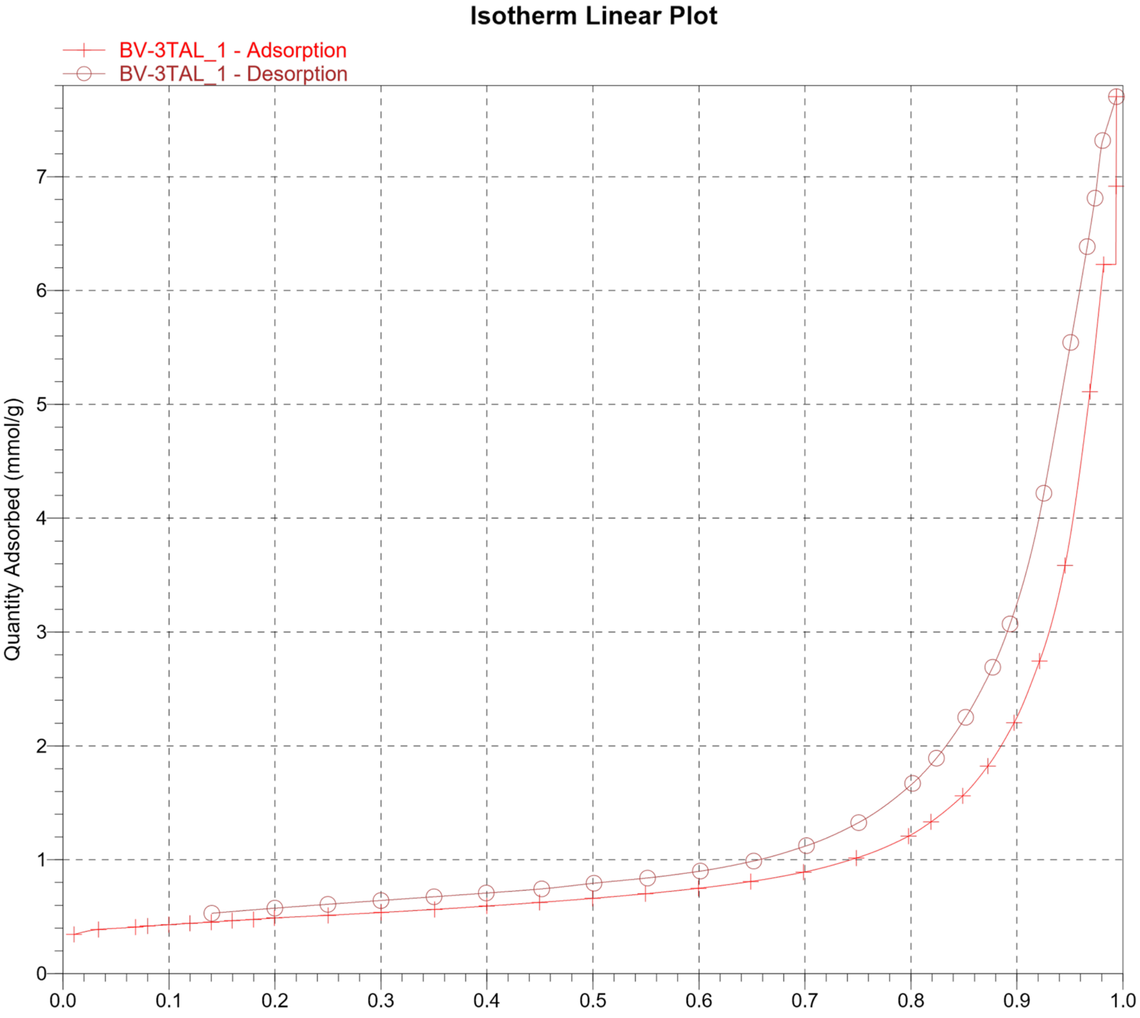


Fig. 3 Adsorbtion–desorption of $CoAl_2O_4$ nanoparticles

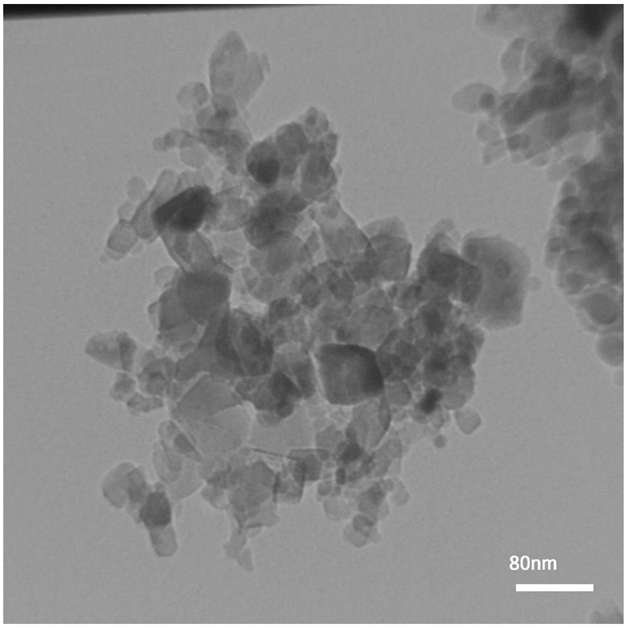


Fig. 4 Transmission electron microscopic (TEM) image of $CoAl_2O_4$ nanoparticles

silica sulfuric acid [40], $Ga(OTf)_3$ [41], $Zn(PFO)_2$ [42], MCM-41-SO_3H [43], $Al(H_2PO_4)_3$ [44], Al/Al_2O_3 [45], Fe_3O_4 nanoparticles [46], SiO_2-$FeCl_3$ [47], silica-bonded *S*-sulfonic acid [48], silica-bonded *N*-propylsulfamic acid [49], ethylenediamine diacetate [50], deep eutectic solvent [51], SiO_2-$ZnCl_2$ [52], nano-copper [53], Cu-CNTs nanocomposite [54], metal complexes with multi-walled carbon nanotubes [55], TiO_2 nanoparticles [56], glycerosulfonic acid [57], and carbon-SO_3H [58].

The synthesis of new and important types of heterocyclic compounds in green and eco-friendly conditions continues to attract wide attention among synthetic chemists. Herein, we describe a facile three-component condensation reaction consisting of isatoic anhydride, aromatic aldehyde, and amine in refluxing ethanol to synthesize the 2,3-dihydroquinazolin-4(*1H*)-ones and also a novel class of pyrazolquinazolinones derivatives (Scheme 1).

Experimental

Chemicals and reagents

Chemicals were purchased from Merck and Aldrich Chemical Companies. The products were characterized by comparison of their spectral and physical data with those reported in the literature. For recording ^1H NMR spectra we use Bruker (500, 400, or 300 MHz) Avance Ultrashield in pure deuterated DMSO-d_6 and $CDCl_3$ solvents with tetramethylsilane (TMS) as internal standard. Mass spectra were recorded on a FINNIGAN-MAT 8430 mass spectrometer operating at 70 eV. FT-IR spectroscopy (Shimadzu FT-IR 8300 spectrophotometer) was employed for characterization of the products. Melting points determined in open capillary tubes in a Barnstead Electrothermal 9100 BZ circulating oil melting point apparatus. The reaction monitoring was accomplished by TLC on silica gel PolyGram SILG/UV254 plates. Column chromatography was carried out on columns of silica gel 60 (70–230 mesh).

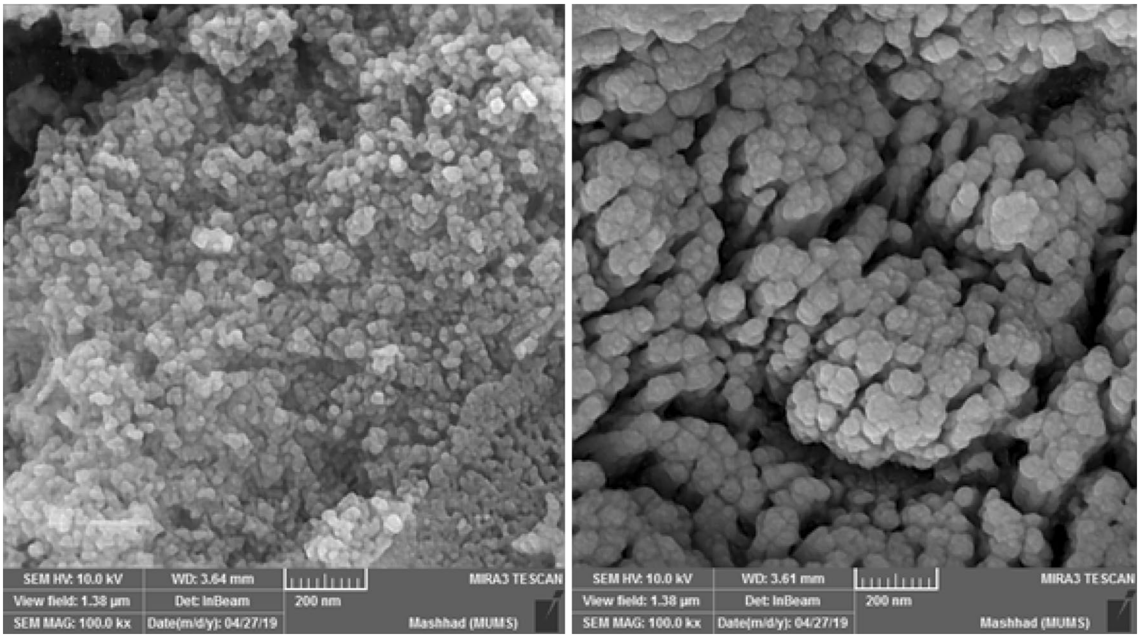


Fig. 5 SEM image of $CoAl_2O_4$ nanoparticles. Left side is fresh, and right side is after recovery

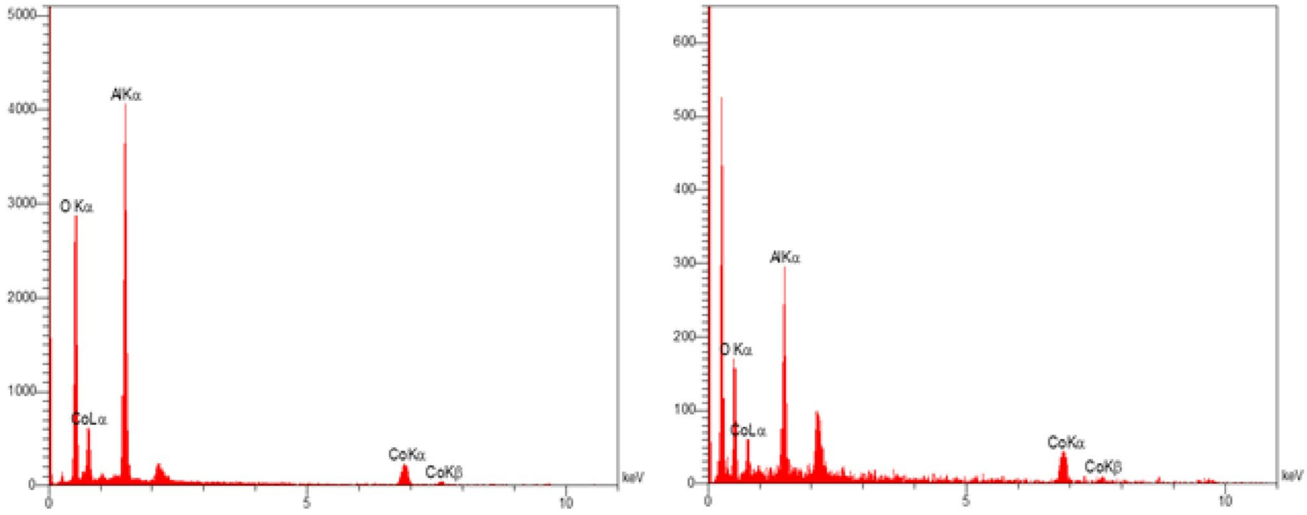
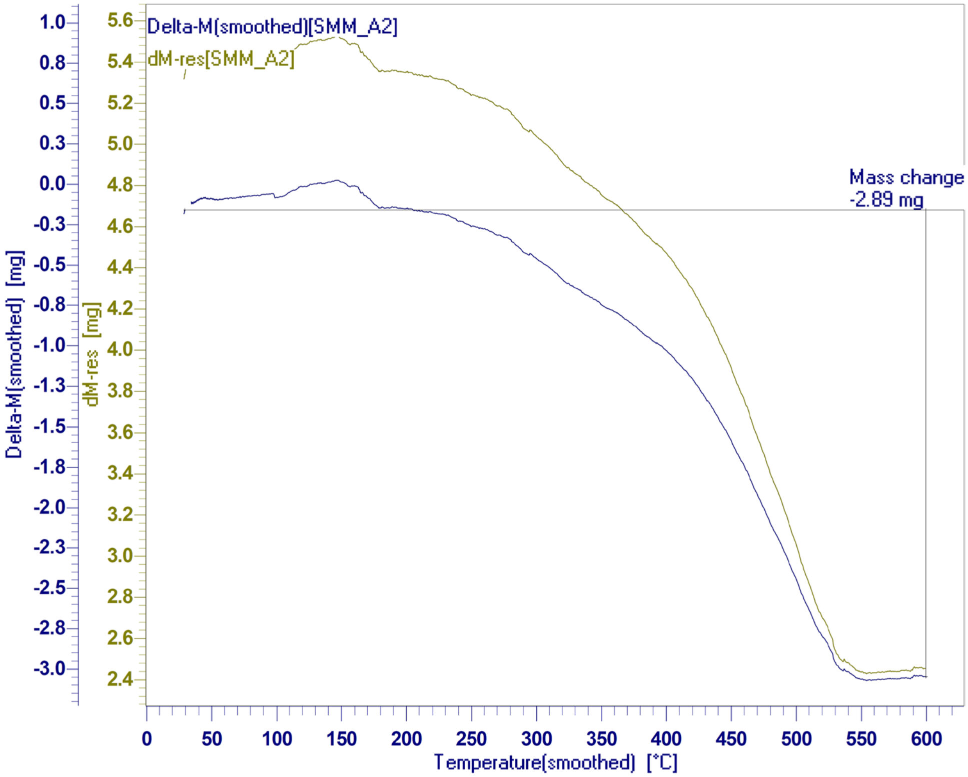


Fig. 6 EDX of $CoAl_2O_4$ nanoparticles. Left side is fresh, and right side is after recovery

Fig. 7 TGA of $CoAl_2O_4$ nanoparticles



Procedure for preparation of $CoAl_2O_4$ catalyst

Stoichiometric amounts of cobalt nitrate hexahydrate (1 eq, 1.45 g) and aluminum nitrate nonahydrate (1 eq, 3.75 g) were separately dissolved in deionized water (5 mL). Then, polyethylene glycol 4000 (0.2 g) was added to the cobalt nitrate solution under vigorous stirring. The aluminum nitrate solution was then added slowly and kept at a temperature close to 0 °C in a bath room. Then, aqueous solution of potassium hydroxide (5 eq) was added dropwise under vigorous stirring. Meanwhile, a transparent green color to dark blue colloidal solution was produced. The resulting colloidal solution was filtered and calcined at 700 °C for 2 h and then kept in an autoclave for 24 h.

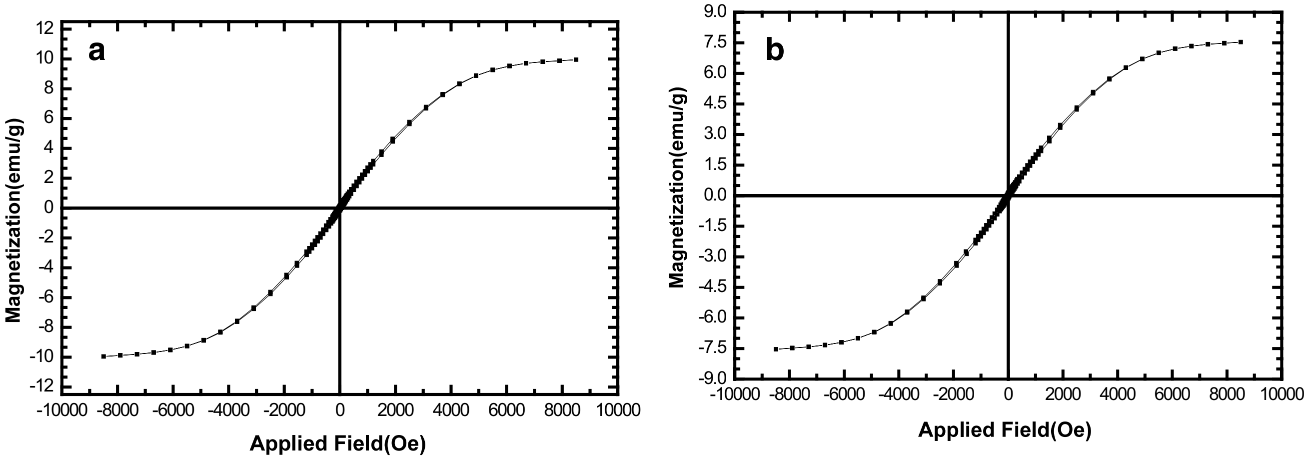


Fig. 8 Vibrating sample magnetometer curve of synthesized $CoAl_2O_4$ nanoparticles. **a** Fresh $CoAl_2O_4$ and **b** after recovery

Table 1 Reaction of isatoic anhydride and benzaldehyde with aniline in the presence of different amounts of catalysts

Entry	Catalyst (g)	Solvent	Conditions	Time (min)	Yield (%)[a]
1	–	Ethanol	Reflux	600	–
2	$CoAl_2O_4$ (0.01)	Ethanol	Reflux	120	45
3	$CoAl_2O_4$ (0.02)	Ethanol	Reflux	120	89
4	$CoAl_2O_4$ (0.03)	Ethanol	Reflux	120	89
5	$CoAl_2O_4$ (0.02)	Dichloromethane	Reflux	120	20
6	$CoAl_2O_4$ (0.02)	Acetonitrile	Reflux	120	70
7	$CoAl_2O_4$ (0.02)	Methanol	Reflux	120	85
8	$CoAl_2O_4$ (0.02)	Toluene	80 °C	120	< 20
9	$CoAl_2O_4$ (0.02)	Tetrahydrofuran	Reflux	120	< 20
10	$CoAl_2O_4$ (0.02)	Ethanol	R.T.	480	Trace
11	$CoAl_2O_4$ (0.02)	Ethanol	50 °C	120	30
12	$CoAl_2O_4$ (0.02)	Ethanol	65 °C	120	50
13	$Co(NO_3)_2{\cdot}6H_2O$ (0.02)	Ethanol	Reflux	240	50
14	$CoCl_2{\cdot}6H_2O$ (0.02)	Ethanol	Reflux	240	55
15	Acidic Al_2O_3 (0.02)	Ethanol	Reflux	240	60

The molar ratio of isatoic anhydride:benzaldehyde:aniline was 1:1:1 mmol, respectively, in solvent (5 mL) at reflux conditions

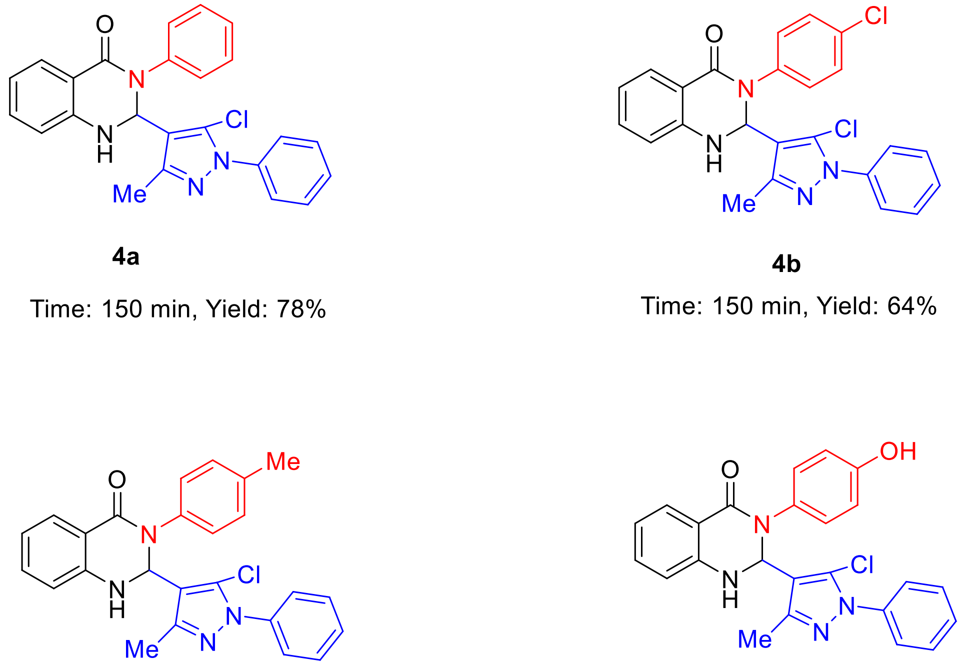
[b] Isolated yield

General procedure for the synthesis of pyrazol-quinazolinones (4)

To a mixture of isatoic anhydride (1 mmol), 5-chloro-3-methyl-1-phenyl-*1H*-pyrazole-4-carbaldehyde (**3**) (1 mmol), and aniline derivatives (1 mmol) in 5 mL ethanol was added 0.02 g nano-$CoAl_2O_4$, and the resulting mixture was heated under reflux conditions. After completion of the reaction, as indicated by TLC, the nano-$CoAl_2O_4$ was removed by an external magnet while the mixture was hot and the remaining was washed with warm ethanol (2 × 3 mL). The mixture was cooled to precipitate the corresponding pyrazol-quinazolinone products which were finally purified by column chromatography on silica gel. The recovered catalyst was reused for subsequent runs.

2-(5-chloro-3-methyl-1-phenyl-*1H*-pyrazol-4-yl)-3-phenyl-2,3-dihydroquinazolin-4(*1H*)-one (4a)

m.p. 216-218 °C. IR (KBr): 1684 (N–C = O) cm^{-1}. ^1H NMR (500 MHz, DMSO-d_6) δ (ppm): 2.23 (s,1H), 6.47 (s, 1H), 6.75–6.81 (m, 2H), 7.19–7.22 (m, 3H), 7.28–7.35 (m, 6H), 7.45 (t, $J = 7.4$ Hz, 1H), 7.50 (t, $J = 7.8$ Hz, 2H), 7.72 (d, $J = 7.8$ Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ (ppm): 13.8, 66.6, 114.8, 115.2, 115.6, 118.1, 125.2, 126.8, 127.5,



Scheme 2 Synthesis of pyrazol-quinazolinone derivatives

4a

Time: 150 min, Yield: 78%

4b

Time: 150 min, Yield: 64%

4c

Time: 160 min, Yield: 80%

4d

Time: 150 min, Yield: 79%

128.3, 128.5, 128.9, 129.0, 129.8, 134.2, 137.8, 140.3, 148.4, 149.0, 163.9. Anal. Calcd. for $C_{24}H_{19}ClN_4O$; C, 69.48; H, 4.62; Cl, 8.54; N, 13.50%. Found C, 69.17; H, 4.73; N, 13.21%. MS (*m/z*): 414 (M^+), 323 (base peak).

2-(5-chloro-3-methyl-1-phenyl-*1H*-pyrazol-4-yl)-3-(4-chlorophenyl)-2,3-dihydroquinazolin-4(*1H*)-one (4b)

m.p. 219–221 °C. IR (KBr): 3270 (N–H), 1613 (N–C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.38 (s, 3H), 6.43 (s, 1H), 6.76 (d, $J=8.1$ Hz, 1H), 6.98 (t, $J=7.5$ Hz, 1H), 7.12–7.16 (m, 1H), 7.22–7.29 (m, 4H), 7.36–7.52 (m, 6H), 8.05 (dd, $J_1=7.0$ Hz, $J_2=1.2$ Hz, 1H),; ^{13}C NMR (125 MHz, DMSO-d_6) δ (ppm): 13.3, 66.1, 114.4, 114.7, 115.1, 117.7, 124.7, 126.4, 127.0, 127.8, 128.1, 128.4, 128.5, 129.3, 133.8, 137.3, 139.8, 147.9, 148.5, 163.4. Anal. Calcd. for $C_{24}H_{18}Cl_2N_4O$; C, 64.15; H, 4.04; Cl, 15.78 N, 12.47%. Found C, 63.79; H, 4.13; N, 12.11%. MS (*m/z*): 449 (M^+, base peak), 450 (M^++1), 451 (M^+ +2).

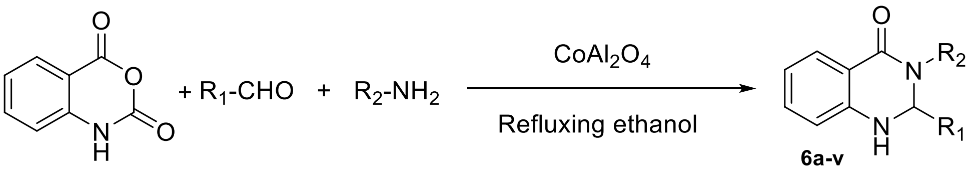
2-(5-chloro-3-methyl-1-phenyl-*1H*-pyrazol-4-yl)-3-(*p*-tolyl)-2,3-dihydroquinazolin-4(*1H*)-one (4c)

m.p. 190–192 °C. IR (KBr): 3289 (N–H), 1630 (N–C=O) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 2.32 (s, 3H), 2.39 (s, 3H), 6.40 (s, 1H), 6.73 (d, $J=7.8$ Hz, 1H), 6.92 (t, $J=7.4$ Hz, 1H), 7.08–7.14 (m, 4H), 7.30–7.50 (m, 7H), 8.05 (d, $J=7.8$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 13.9, 21.1, 67.0, 114.4, 114.7, 116.6, 119.7, 124.9, 127.1, 128.5, 129.1, 129.3, 129.5, 129.6, 133.8, 136.7, 137.2, 137.7, 146.7, 149.0, 164.3. Anal. Calcd. for $C_{25}H_{21}ClN_4O$; C, 70.01; H, 4.94; Cl, 8.26; N, 13.06%. Found C, 69.68; H, 4.90; N, 12.72%. MS (*m/z*): 428 (M^+), 429 (M^++1, base peak).

2-(5-chloro-3-methyl-1-phenyl-*1H*-pyrazol-4-yl)-3-(4-hydroxyphenyl)-2,3-dihydroquinazolin-4(*1H*)-one (4d)

m.p. 236–238 °C. IR (KBr): 3300–3000 (OH & N–H), 1615 (N–C=O) cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6) δ (ppm): 2.24 (s, 3H), 6.73 (s, 1H), 6.65–6.82 (m, 4H), 7.00 (d, $J=8.4$ Hz, 2H), 7.30–7.37 (m, 4H), 7.44–7.56 (m, 3H), 7.74 (d, $J=6.9$ Hz, 1H), 9.50 (brs, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ (ppm): 13.8, 66.8, 114.7, 115.2, 115.5, 115.8, 117.9, 125.1, 126.8, 128.5, 128.9, 129.3, 129.8, 131.4, 134.0, 137.8, 148.4, 149.0, 156.6, 164.0. Anal. Calcd. for $C_{24}H_{19}ClN_4O_2$; C, 66.90; H, 4.44; Cl, 8.23; N, 13.00%. Found C, 66.56; H, 4.49; N, 12.74%. MS (*m/z*): 430 (M^+), 431 (M^++1, base peak).

Table 2 Preparation of 2,3-dihydroquinazolinones catalyzed by $CoAl_2O_4$ in refluxing ethanol



Entry	R_1	R_2	Product	Time (min)	Yield (%)[a]	M. P. °C	M. P. °C (Lit.)
1	C_6H_5–	C_6H_5–	**6a**	120	89	207–209	205–206 [46]
2	4-F–C_6H_4–	C_6H_5–	**6b**	130	83	235–237	235–237 [55]
3	4-Br–C_6H_4–	C_6H_5–	**6c**	130	80	221–223	223–225 [46]
4	4-Cl–C_6H_4–	C_6H_5–	**6d**	130	82	216–218	219–220 [41]
5	4-MeO–C_6H_4–	C_6H_5–	**6e**	150	80	205–207	204–205 [42]
6	4-Me–C_6H_4–	C_6H_5–	**6f**	130	82	223–225	215–216 [46]
7	2-Thionyl-	C_6H_5–	**6 g**	200	78	197–199	197–200 [48]
8	C_6H_5-	4-Me–C_6H_4–	**6 h**	130	92	198–200	197–198 [46]
9	4-Me–C_6H_4–	4-Me–C_6H_4–	**6i**	80	80	243–247	244–246 [55]
10	4-MeO–C_6H_4–	4-Me–C_6H_4–	**6j**	130	90	246–248	241–243 [54]
11	4-MeO–C_6H_4–	4-MeO–C_6H_4–	**6 k**	130	92	225–227	227–228 [50]
12	4-Me–C_6H_4–	C_6H_5–CH_2CH_2–	**6 l**	90	87	151–153	151–154 [48]
13	4-Cl–C_6H_4–	C_6H_5–CH_2CH_2–	**6 m**	90	89	156–158	156–158 [48]
14	4-Me–C_6H_4–	4-HO–C_6H_4–	**6n**	200	75	249–251	248–250 [55]
15	4-Cl–C_6H_4–	2-HO–5–ClC_6H_3–	**6o**	120	70	235–237	235–236 [55]
16	4-Me–C_6H_4–	H	**6p**	120	88	227–228	223–225 [53]
17	4-MeO–C_6H_4–	H	**6q**	100	87	179–180	178–180 [35]
18	4-Cl–C_6H_4–	H	**6r**	130	82	203–205	198–200 [35]
19	4-Br–C_6H_4–	H	**6 s**	120	85	201–203	195–197 [45]
20	4-F–C_6H_4–	H	**6t**	120	80	195–197	194–196 [57]
21	2-Thionyl–	H	**6u**	160	75	216–218	216–219 [48]
22	2-HO–C_6H_4-	H	**6v**	130	75	250–252	252–254 [43]
23	Me–CH_2CH_2–	C_6H_5-	**–**	360	–	–	–

[a] Isolated yield

General procedure for the synthesis of 2,3-dihydro-dihydroquinazolinone derivatives (6)

To a mixture of isatoic anhydride (1 mmol), aromatic aldehyde (1 mmol), and ammonium acetate or primary amine (1 mmol) in 5 mL ethanol was added 0.02 g nano-$CoAl_2O_4$, and the resulting mixture was heated under reflux conditions. After completion of the reaction, as indicated by TLC, the nano-$CoAl_2O_4$ was removed by an external magnet. The mixture was cooled to precipitate the corresponding 2,3-dihydroquinazolinone products which were finally purified by recrystallization using hot ethanol. The recovered catalyst was reused for subsequent runs.

Results and discussion

Initially, cobalt aluminate with a spinel-type structure was synthesized using a colloidal method, with slight differences from the method reported by Blanco et al. [26], and Ragupathi and co-workers [27]. The preparation of $CoAl_2O_4$ was carried out by adding the polyethylene glycol 4000 (0.2 g) to the aqueous solutions of cobalt nitrate hexahydrate and aluminum nitrate nonahydrate with stirring. Then, the potassium hydroxide solution was added at temperature close to 0 °C. The resulting dark blue colloidal solution was filtered and calcined at 700 °C for 2 h. Then, it was kept in an autoclave for 24 h (see supplementary information Figure S1).

The FT-IR spectrum of cobalt aluminate is shown in Fig. 1. The absorption band at 480–590 cm^{-1} indicates the presence of Co–O stretching frequencies, and the band at 640–760 cm^{-1} range belongs to Al–O vibrations. Also,

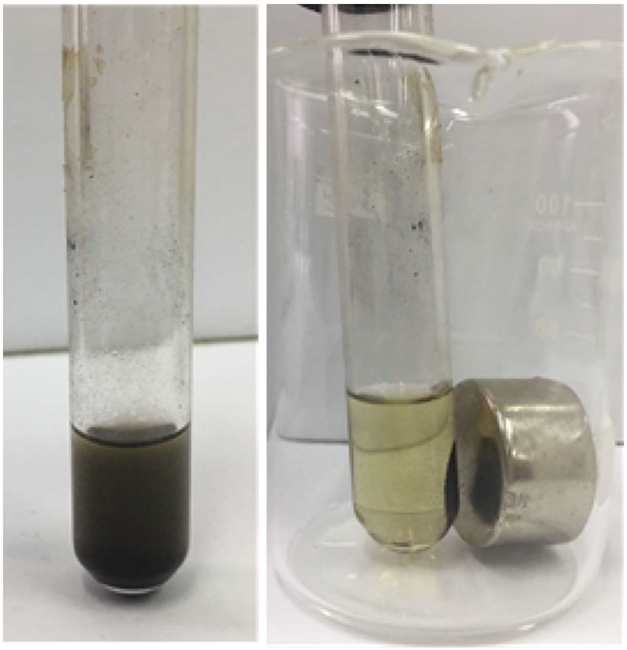


Fig. 9 Separation of the catalyst with external magnet

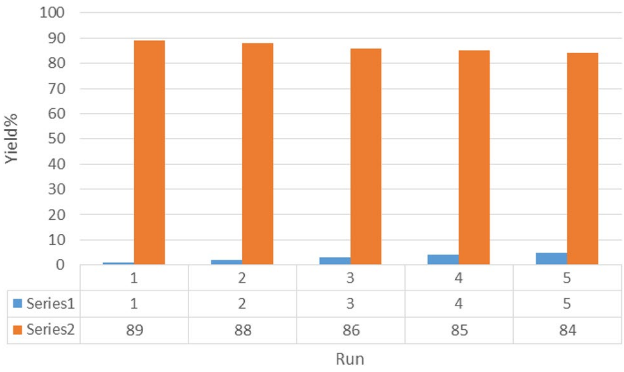


Fig. 10 Recyclability of nano-$CoAl_2O_4$ in the reaction of isatoic anhydride and benzaldehyde with aniline. Reaction time = 120 min

the Al–O–Co interactions have frequencies in the range of 450–800 cm^{-1} [25, 28].

The XRD. X-ray powder diffraction for nano-$CoAl_2O_4$ is shown in Fig. 2. The figure indicates peaks at 31, 36, 55, 59, 65, and 77° 2θ that the spinel phase was obtained with high crystallinity. However, small peaks at 44, 51, and 75° 2θ that belong to CoO impurities were also detected, indicating the precursor solution was slightly off-stoichiometry, which is in agreement with the result previously reported by Granados et al. [25]. The average crystal sizes, which were calculated using Scherrer's formula, were ~ 26 and 28 nm for $CoAl_2O_4$ and CoO, respectively.

Also, the cobalt and aluminum contents in $CoAl_2O_4$ were measured by XRF instrument. The XRF results showed 64.4% present for CoO and 29.3% present for Al_2O_3 (see supplementary information). The increased active site of $CoAl_2O_4$ nanoparticles was studied by the nitrogen adsorption–desorption isotherms from the BET analysis (Fig. 3).

The specific surface area and pore volume of cobalt aluminate spinel catalyst were obtained as 38.569 $m^2\ g^{-1}$ and 0.177 $cm^3\ g^{-1}$, respectively (see supporting information).

Figure 4 shows TEM images of nano-$CoAl_2O_4$. The particle sizes were in the range of 10–80 nm. The TEM images and XRD revealed the nanosized particles.

The morphology of nano-$CoAl_2O_4$ was investigated by SEM methods. The SEM images demonstrate that the obtained cobalt aluminate has a uniform structure and aggregate sheets are detected (Fig. 5).

The EDX pattern of $CoAl_2O_4$ is shown in Fig. 6. This analysis indicated the presence of constituent elements Al, O, and Co in the cobalt aluminate.

TGA curve for the catalyst ($CoAl_2O_4$) is shown in Fig. 7. The decrease in gravity began at about 170 °C, which indicated the decomposition of the catalyst. The mass changes were scanned for the ranges between − 5 and + 5 mg which it has shown 2.89 mg and approximately 28.9% weight loss mass.

The magnetization curve for $CoAl_2O_4$ nanoparticles was run. It is of great importance that a catalyst should possess sufficient magnetic and super-paramagnetic properties for its practical application (Fig. 8).

The catalytic activity of $CoAl_2O_4$ nanoparticles was investigated in the synthesis of 2,3-dihydroquinazolinones via a one-pot three-component condensation reaction between isatoic anhydride and aromatic aldehydes with aniline derivatives. In a preliminary study, the reaction of isatoic anhydride and benzaldehyde with aniline was chosen as a model reaction in refluxing ethanol (Table 1). To illustrate the need of $CoAl_2O_4$ for this condensation we examined the model reaction in the absence of $CoAl_2O_4$ in refluxing ethanol (Table 1, entry 1). The results show clearly that $CoAl_2O_4$ is an effective catalyst for this transformation and in the absence of $CoAl_2O_4$ the reaction did not take place, even after 10 h. As indicated in Table 1, the best results have been obtained with 0.02 g of $CoAl_2O_4$ in refluxing ethanol. By increasing the amount of $CoAl_2O_4$ to 0.03 g the yield of corresponding product was not changed.

The model reaction was also examined in various solvents in the presence of 0.02 g of $CoAl_2O_4$ (Table 1). As shown in Table 1, condensation reaction in ethanol and methanol gave the best results in the case of yield, and we chose ethanol for environmental sustainability. Also, the model reaction was converted into corresponding product in ethanol at lower temperature in longer reaction times and lower yields (Table 1, entries 10–12). In order to show the efficiency of the catalyst in comparison with its components the model reaction was examined in the presence of cobalt

Scheme 3 Plausible mechanism for the synthesis of 2,3-dihydroquinazolin-4(*1H*)-ones

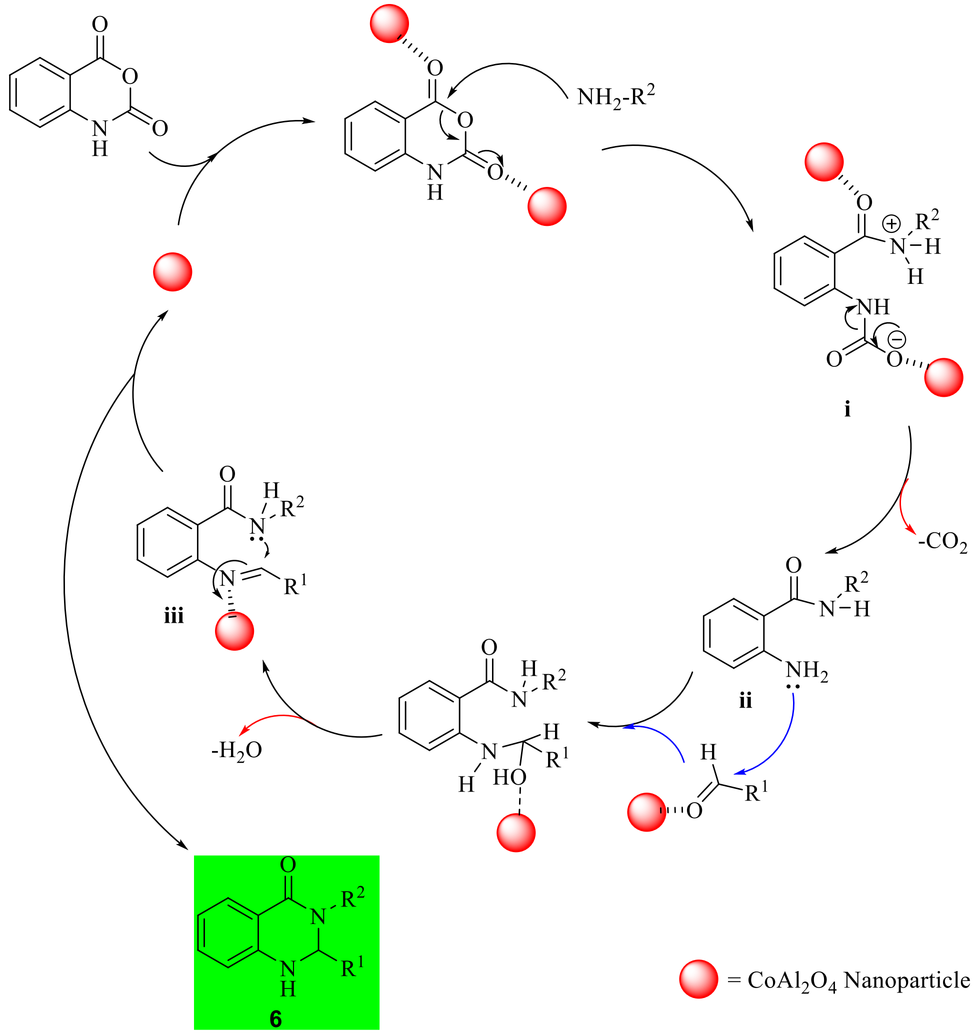


Table 3 Reaction of isatoic anhydride and benzaldehyde with aniline in the presence of different amounts of catalysts

Catalyst	Catalyst load (g)	Time (min)	Yield (%)[a]	Refs.
p-Ts-OH	0.5 mol	2.5 h (3.5 h)	79 (60)	[35]
Montmorillonite K-10	0.3	6.5 h (5 h)	80 (73)	[37]
Silica sulfuric acid	0.11	6.5 h (3.5 h)	80 (90)	[39]
Ga(OTf)$_3$	0.05 mmol	(50)	(86)	[40]
Zn(PFO)$_2$	0.027	6 h	82	[41]
MCM-41-SO$_3$H	0.005	(15)	(90)	[43]
Al/Al$_2$O$_3$	0.036	(15)	(92)	[45]
Fe$_3$O$_4$ nanoparticles	0.15	120 (120)	80 (85)	[46]
SiO$_2$-FeCl$_3$	0.005	(10)	(87)	[47]
SBSSA	0.005	(90)	(87)	[48]
SBNPSA	0.1	(150)	(86)	[49]
SiO$_2$-ZnCl$_2$	0.025	(14)	(89)	[51]
Nano-copper	0.1 mmol	30	85	[52]
Cu-CNTs nanocomposite	0.04	5	99	[53]
CoAl$_2$O$_4$	0.005	120 (120)	89 (88)	present work

[a] Isolated yield

nitrate, cobalt chloride, and acidic alumina. The model reaction was converted in the presence of cobalt nitrate and cobalt chloride as catalysts into the corresponding product after 240 min in 50% and 55% yields, respectively (Table 1, entries 13 and 14). Also, acidic alumina converted the model reaction after 240 min in 60% yield (Table 1, entry 15).

In order to synthesize the novel class of pyrazol-quinazolinones the reaction between 5-chloro-3-methyl-1-phenyl-*1H*-pyrazole-4-carbaldehyde (**3**) and isatoic anhydride with aniline derivatives was investigated under optimized conditions. As shown in Scheme 2, the aniline derivatives such as 3-chloro-aniline, 4-methyl-aniline, and 4-hydroxy-aniline treated with isatoic anhydride and aldehyde **3** and corresponding products **4a–d** were obtained in good to high yields.

The generality of this process was applied for the synthesis of 2,3-dihydroquinazolinones via the reaction between isatoic anhydride and the wide range of substituted and structurally diverse aromatic aldehydes with anilines or ammonium salt under optimized conditions (Table 2).

Aniline bearing electron-donating groups such as methyl or methoxy, and electron-withdrawing groups such as halogen substituted (F, Cl, and Br) was employed, and all 2,3-dihydroquinazolinones were obtained in high to excellent yields. Also, 2-phenylethyl amine as an aliphatic amine gave corresponding product in high yield (Table 2, entries 12 and 13). 2-Hydroxybenzaldehyde reacted with isatoic anhydride and ammonium acetate gave corresponding product after 130 min in 75% yield (Table 2, entry 22). Heterocyclic aldehydes such as 2-thionyl were converted into corresponding products in high yield (Table 2, entries 7 and 21). Moreover, the reaction between isatoic anhydride and other aromatic aldehydes with ammonium acetate gave corresponding products in high yields (Table 2). Aliphatic aldehydes such as butanal failed to give the corresponding product under optimized reaction conditions (Table 2, entry 23).

The possibility of recycling the catalyst was examined using the reaction of isatoic anhydride and benzaldehyde with aniline under optimized conditions. Upon completion, the catalyst was removed by external magnet (Fig. 9).

The recycled catalyst could be reused four times without any treatment (Fig. 10). Also, for the recovered catalyst the XRD (Fig. 2, right side), SEM (Fig. 5, right side), EXD (Fig. 6, right side), and VSM (Fig. 8, right side) were performed and they have shown that slight changes occurred in the morphology and magnetism of the recovered catalyst.

The recommended mechanism to provide 2,3-dihydroquinazolin-(*1H*)-4-ones by $CoAl_2O_4$ as the catalyst is shown in Scheme 3 [46–49, 53–56]. Initially, the catalyst activated the carbonyl isatoic anhydride group to get the compound ready for amine group attack. This causes the C–O bond breaking in carbonyl group and forming of the intermediate (1). Subsequently, a CO_2 molecule left the compound and intermediate (2) was attained. Then, the catalytic-activated aldehyde group was attacked by an ammonium nitrogen lone pair and intermediate (3) was obtained. Finally, the product (**6**) was obtained by ring formation and hydrogen displacement.

Finally, a comparative study of $CoAl_2O_4$ with other recently reported catalysts for the synthesis of 2,3-diphenyl-2,3-dihydroquinazolin-*1H*-4-one (**6a**) as a model compound was made, which revealed that $CoAl_2O_4$ is an equally efficient and reusable catalyst (Table 3).

Conclusions

In conclusion, $CoAl_2O_4$ nanoparticles were prepared in the presence of polyethylene glycol 4000 as a green and eco-friendly medium. Introducing a novel class of pyrazol-quinazolinones and also, using magnetic heterogeneous catalyst which easily removable by external magnet, easy and clean work-up, high yields and recovery of the catalyst makes this method practical for multi-component condensation reaction of quinazolinone synthesis.

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