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ORIGINAL PAPER

One-pot synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones by Fe_3O_4@SiO_2-imid-PMA^n nano-catalyst under ultrasonic irradiation and reflux conditions

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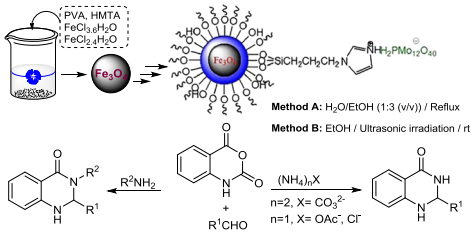
Abstract Fe_3O_4@SiO_2-imid-PMA^n efficiently catalyzes the condensation reaction of isatoic anhydride, aldehydes, and primary amines or ammonium salts to afford the corresponding 2,3-dihydroquinazolin-4(1*H*)-one derivatives under ultrasonic irradiation or reflux conditions. This method gives notable advantages such as operational simplicity, excellent yields, short reaction times, and absence of any tedious workup or purification. In addition, the excellent catalytic performance and the easy preparation, thermal stability, and separation of the catalyst make it a good heterogeneous system and a useful alternative to other heterogeneous catalysts. Also, the aforementioned nanocatalyst can be easily recovered by a magnetic field and reused for subsequent reactions for at least six times without noticeable deterioration in catalytic activity and reaction yield.

Graphical abstract



Keywords 2,3-Dihydroquinazolin-4(1*H*)-ones · Magnetic nanocatalyst · One-pot synthesis · Green synthesis · Ultrasonic irradiation

Introduction

The development of more efficient and stable catalysts has been an increasingly important goal for chemists and material scientists for both economic and environmental reasons [1]. Homogeneous catalysts show higher catalytic activities than their heterogeneous counterparts because of their solubility in reaction media, which increases the catalytic site accessibility for the substrate [2]. However, recycling homogeneous catalysts is often tedious and time consuming and there is also the issue of product contamination observed when these catalysts are used. For overcoming these drawbacks, metal and organocatalysts are immobilized on silica-coated Fe_3O_4 [2, 3]. Magnetic nanoparticles open up new avenues to introduce an amazing and efficient system for facilitating catalyst recovery in organic reactions for the goals of green chemistry [4]. Recently, a number of such functionalized Fe_3O_4

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nanoparticles have been employed in a range of organic transformations [5–8].

In recent years, Keggin-type heteropolyacids (HPAs) such as $H_3PMo_{12}O_{40}$ (PMA) have been used as efficient catalysts for a variety of organic reactions because of their superacidic and redox properties, low toxicity, ease of handling, low cost, high thermal stability, high proton mobility, water tolerance, recoverability, and reusability [9]. Although HPAs are versatile compounds in their acidic form, their main disadvantages are high solubility in polar solvents and low surface area (<10 m^2/g). Therefore, in a homogeneous reaction, the isolation of the products and the reuse of the catalyst after reaction become difficult [9]. Therefore, to overcome this problem, these materials disperse on supports (such as silica, acidic ion-exchange resins, and active carbon) which possess large surface area. The use of support allows the heteropolyacids to be dispersed over a large surface area and increases their catalytic activity [10].

Developing green procedures is an active area of research in this direction that have many advantages, such as being devoid of any carcinogenic effects, lower cost, reduced pollution, and simplicity in processing, which are valuable to the industry as well as to the environment [11]. On the other hand, the use of ultrasound irradiation represents a very powerful green chemical protocol from both the economic and synthetic point of view [12]. The use of ultrasonic irradiation accelerates an organic transformation at ambient conditions, which otherwise require harsh conditions of temperature and pressure [13]. The interaction between molecules and ultrasound is not direct, but the energy of these long wavelength can cause cavitation which makes the reaction faster [14].

One of the most frequently encountered heterocycles in medicinal chemistry is quinazolinone derivatives with wide applications including anticancer [15], antihypertensive [16], antidiuretic [17], anticonvulsant [18], antibacterial [19], antihistaminic [20], antidiabetic [21], and anti-inflammatory [22] activities.

2,3-Dihydroquinazoline derivatives are a class of heterocycles which exhibit biological and pharmaceutical activity and herbicidal agents, as well as plant growth regulators [23]. Also, these compounds can be easily oxidized to their quinazolin-4(3*H*)-one analogs [24], which are among the most important biologically active heterocyclic compounds and can be found in some natural products [25–27].

In view of these useful properties, various procedures have been reported for preparing 2,3-dihydroquinazolin-4(1*H*)-ones in literature, which include reduction of the azide functionality, the condensation reaction of anthranilamide with aldehyde or ketone, desulfurization of 2-thioxo-4(3*H*)-quinazolinones, Pd-catalyzed heterocyclization of nitroarenes, cyclization of *o*-acylaminobenzamides, preparation from isatoic anhydrides and Schiff bases, amidation of 2-aminobenzonitrile followed by oxidative ring closure, Lewis acid-surfactant combined catalysts under aqueous micellar media and the condensation of isatoic anhydride, aldehydes, and ammonium acetate or primary amine [28–34]. Also, recently a number of classical methods for the synthesis of 2,3-dihydroquinazolin-4(1*H*)-one have been reported in literature involving the use of silica sulfuric acid [33], zinc(II) perfluorooctanoate [29], silica-bonded *N*-propylsulfamic acid [35], *p*-TsOH [36], chiral phosphoric acid [37, 38], $Al(H_2PO_4)_3$ [39], Montmorillonite K-10 [40], gallium triflate [41], nano-Fe_3O_4 [42], $KAl(SO_4)_2{\cdot}12H_2O$ [34], ionic liquid/water [43], [bimm]BF_4 [44], etc. However, most of the reported methods have certain limitations such as the use of organic solvents, long reaction times, tedious processes, harsh reaction conditions and low yields of product. Thus, developing versatile approaches to synthesize quinazolinone derivatives still remains a highly desired goal in organic synthesis.

Therefore, as a result of our great interest in the application of magnetic catalysts in organic reactions [45–49], herein we describe a convenient, simple, and practical procedure for the synthesis of mono- and disubstituted 2,3-dihydroquinazolin-4(1*H*)-ones by employing isatoic anhydride, aldehydes, and amines or ammonium salts in the presence of Fe_3O_4@SiO_2-Imid-PMA^n magnetic nanocatalyst in one pot under ultrasonic irradiation or reflux conditions. Figure 1 represents the procedure for the preparation of Fe_3O_4@SiO_2-imid-PMA^n step by step.

Results and discussion

In continuation of our investigations on the use of superparamagnetic catalysts for the fine chemical preparation [2, 50], here one-pot condensation of primary amines or ammonium salts and aromatic aldehydes with isatoic anhydride in the presence of Fe_3O_4@SiO_2-imid-PMA^n is reported (Scheme 1).

In a preliminary study, the reaction of benzaldehyde and aniline with isatoic anhydride was chosen as a model reaction to optimize the reaction conditions. As shown in Table 1, the model reaction was refluxed in the presence of 0.04 g of Fe_3O_4@SiO_2-imid-PMA^n and a variety of solvents such as ethanol, dichloromethane, acetonitrile, ethyl acetate, toluene, THF, water and in solvent-free conditions (Table 1, entries 1–11). The represented data in Table 1 shows that the reaction proceeded efficiently in refluxing H_2O/EtOH [1:3(v/v)] and resulted in high yields of the desired product (Table 1, entry 11).

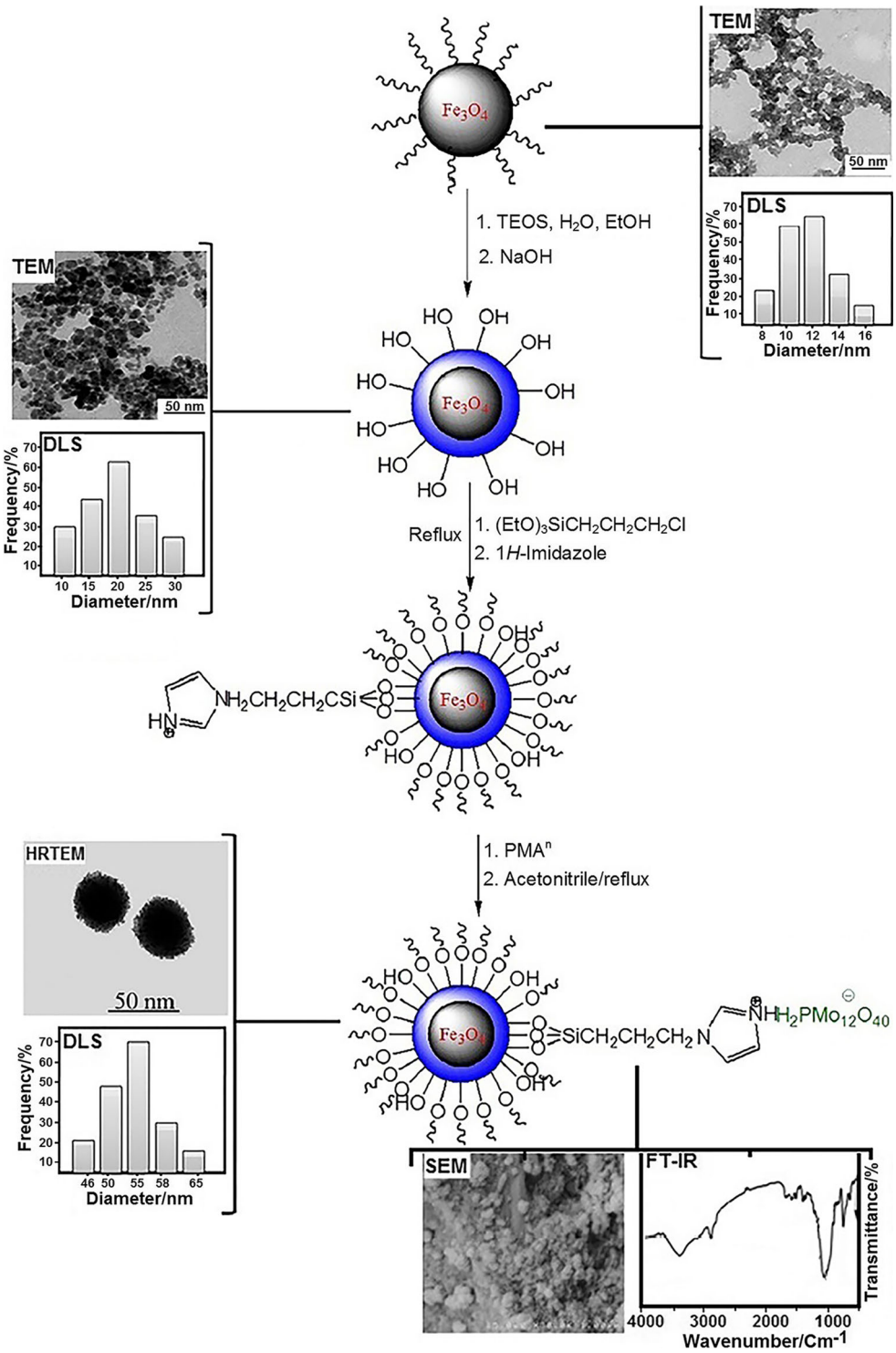


Fig. 1 Preparation and characterization of Fe_3O_4@SiO_2-imid-PMA^n

Then, we also briefly examined the effect of different temperatures and the amount of catalyst. The effect of temperature was studied by carrying out the model reaction at different temperatures in H_2O/EtOH [1:3(v/v)] in the presence of Fe_3O_4@SiO_2-imid-PMA^n (room temperature, 60 °C, and reflux; Table 1, entries 11, 17, 18) and the best result was obtained under reflux conditions (Table 1, entry 11).

To elucidate the role of the catalyst, at first, we found that in the absence of the catalyst, the yield was poor even for longer time (Table 1, entry 12). Fe_3O_4@SiO_2-imid-PMA^n proved to be a superior catalyst among all the catalysts screened in this transformation. It should be noted that 0.04 g of catalyst was efficient enough to catalyze the reaction under reflux conditions in H_2O/EtOH [1:3 (v/v)]

Scheme 1

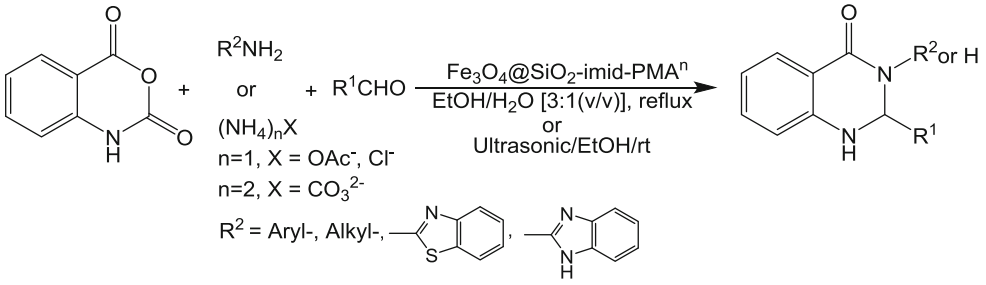


Table 1 Optimization of different proportions of Fe_3O_4@SiO_2-imid-PMA^n and also the effect of solvents and temperature on the reaction of isatoic anhydride, benzaldehyde, and aniline

Entry	Solvent	Catalyst amount/g	Condition	Time/h	Yield/%[a]
1	Solvent-free	0.04	90 °C	2	77
2	EtOH	0.04	Reflux	2	85
3	CH_2Cl_2	0.04	Reflux	2	51
4	CH_3CN	0.04	Reflux	2	67
5	EtOAc	0.04	Reflux	2	57
6	Toluene	0.04	Reflux	2	79
7	THF	0.04	Reflux	2	43
8	H_2O	0.04	Reflux	2	63
9	H_2O/EtOH = [1:1(v/v)]	0.04	Reflux	2	78
10	H_2O/EtOH = [3:1(v/v)]	0.04	Reflux	2	68
11	H_2O/EtOH = [1:3(v/v)]	0.04	Reflux	2	89
12	H_2O/EtOH = [1:3(v/v)]	None	Reflux	24	18
13	H_2O/EtOH = [1:3(v/v)]	0.01	Reflux	3	38
14	H_2O/EtOH = [1:3(v/v)]	0.02	Reflux	3	72
15	H_2O/EtOH = [1:3(v/v)]	0.03	Reflux	2	83
16	H_2O/EtOH = [1:3(v/v)]	0.05	Reflux	2	88
17	H_2O/EtOH = [1:3(v/v)]	0.04	R.T	12	41
18	H_2O/EtOH = [1:3(v/v)]	0.04	60 °C	3	62
19	H_2O/EtOH = [1:3(v/v)]	0.03	Sonication (40 kHz)/r.t	0.42	89
20	H_2O/EtOH = [1:1(v/v)]	0.03	Sonication (40 kHz)/r.t	0.50	82
21	H_2O/EtOH = [3:1(v/v)]	0.03	Sonication (40 kHz)/r.t	0.50	74
22	EtOH	0.03	Sonication (40 kHz)/r.t	0.17	92
23	H_2O	0.03	Sonication (40 kHz)/r.t	0.50	73
24	EtOH	None	Sonication (40 kHz)/r.t	1	12
25	EtOH	0.01	Sonication (40 kHz)/r.t	0.50	55
26	EtOH	0.02	Sonication (40 kHz)/r.t	0.33	68
27	EtOH	0.025	Sonication (40 kHz)/r.t	0.33	90
28	EtOH	0.035	Sonication (40 kHz)/r.t	0.17	88

Reaction conditions: isatoic anhydride (1 mmol), benzaldehyde (1 mmol), aniline (1.2 mmol), 4 cm^3 solvent

[a] Isolated yield

(Table 1, entry 11), and increasing the amount of catalyst did not improve the yield significantly (Table 1, entry 16). On the other hand, decreasing the catalyst concentration resulted in lower yields under the same conditions (Table 1, entries 13–15). Also, to improve the yields, we performed reactions using different quantities of reagents.

Table 2 Fe_3O_4@SiO_2-imid-PMA^n catalyzed the synthesis of mono- and disubstituted derivatives of 2,3-dihydroquinazolin-4(1*H*)-one

Entry	R^1	R^2NH_2 or $(NH_4)^+X^-$	Method A[a]		Method B[b]		Product	M.p./°C
			Time/h	Yield/%[c]	Time/min	Yield/%[c]		
1	C_6H_5	CH_3CH_2	1.5	88	5	94	**1a**	135–137 (134–137 [37])
2	*p*-ClC_6H_4	CH_3CH_2	2	87	10	88	**1b**	134–136 (132–135 [37])
3	*p*-$O_2NC_6H_4$	CH_3CH_2	1	91	5	89	**1c**	158–160 (160–161 [37])
4	*m*-$O_2NC_6H_4$	CH_3CH_2	1.5	92	8	94	**1d**	175–177 (176–178 [37])
5	*p*-HOC_6H_4	CH_3CH_2	2.5	81	25	86	**1e**	178–180 (180–182 [54])
6	*p*-$CH_3OC_6H_4$	CH_3CH_2	2.5	84	20	90	**1f**	123–125 (124–126 [37])
7	C_6H_5	C_6H_5	2	89	10	92	**1g**	203–205 (205–206 [29])
8	*p*-ClC_6H_4	C_6H_5	2.5	85	15	91	**1h**	213–215 (214–217 [54])
9	*m*-$O_2NC_6H_4$	C_6H_5	2	86	18	87	**1i**	184–186 (186–188 [54])
10	*p*-$O_2NC_6H_4$	C_6H_5	3	81	25	84	**1j**	194–196 (195–196 [29])
11	*m*-$CH_3C_6H_4$	C_6H_5	2.5	80	15	82	**1k**	193–195 (194–196 [29])
12	*p*-$CH_3OC_6H_4$	C_6H_5	3	88	12	88	**1l**	202–204 (204–205 [29])
13	C_6H_5	CH_3	1.5	90	15	93	**1m**	163 (164–165 [37])
14	*p*-ClC_6H_4	CH_3	1.5	88	10	90	**1n**	187–188 (188–190 [37])
15	*p*-$CH_3OC_6H_4$	CH_3	1.5	91	18	89	**1o**	145–147 (145–146 [37])
16	*p*-$CH_3OC_6H_4$	Benzothiazolyl	2.0	91	30	92	**1p**	185–187 (184–186 [55])
17	*o*-$CH_3OC_6H_4$	Benzothiazolyl	2.5	89	35	93	**1q**	227–229 (225–230 [55])
18	2,5-$(CH_3O)_2C_6H_3$	Benzothiazolyl	3.0	92	30	87	**1r**	226–227 (225–226 [56])
19	$CH_3(CH_2)_5$	Benzothiazolyl	4	87	24	91	**1s**	150–152 (148–151 [29])
20	2,3-$(Cl)_2C_6H_3$	Benzothiazolyl	1.5	93	10	95	**1t**	247–249 (246–248 [56])
21	*o*-$CH_3OC_6H_4$	Benzoimidazolyl	2.5	90	18	88	**1u**	273–275 (275 [56])
22	2,5-$(CH_3O)_2C_6H_3$	Benzoimidazolyl	3.0	93	20	94	**1v**	234–236 (235 [56])
23	*p*-$O_2NC_6H_4$	Benzoimidazolyl	2.5	95	8	93	**1w**	>300 (>300 [56])
24	C_6H_5	CO_3^{2-}	2	92	16	91	**2a**	219–221 (218–220 [57])
25	*p*-ClC_6H_4	CO_3^{2-}	2	93	12	94	**2b**	196–197 (198–200 [57])
26	*p*-$CH_3C_6H_4$	CO_3^{2-}	3	87	30	87	**2c**	232–233 (233–234 [40])
27	*o*-$CH_3OC_6H_4$	CO_3^{2-}	2	85	40	83	**2d**	163–165 (165–167 [40])
28	*p*-$CH_3OC_6H_4$	CO_3^{2-}	4	90	25	94	**2e**	180–181 (178–180 [57])
29	2-Furanyl	CO_3^{2-}	2.5	88	16	91	**2f**	167–168 (165–167 [40])
30	C_6H_5	AcO^-	2	82	12	90	**2g**	218–219 (218–220 [57])
31	*p*-ClC_6H_4	AcO^-	3	84	10	84	**2h**	197–198 (198–200 [57])
32	*p*-$CH_3C_6H_4$	AcO^-	4	80	30	86	**2i**	231–233 (233–234 [40])
33	*o*-$CH_3OC_6H_4$	AcO^-	2.5	78	30	83	**2j**	165–166 (165–167 [40])
34	*p*-$CH_3OC_6H_4$	AcO^-	3.5	81	14	89	**2k**	179 (178–180 [58])
35	2-Furanyl	AcO^-	2.5	86	26	92	**2l**	166–167 (165–167 [40])
36	C_6H_5	Cl^-	2	83	18	85	**2m**	217–218 (218–220 [57])
37	*p*-ClC_6H_4	Cl^-	3	79	10	78	**2n**	198 (198–200 [57])
38	*p*-$CH_3C_6H_4$	Cl^-	3.5	76	30	81	**2o**	232–234 (233–234 [40])
39	*o*-$CH_3OC_6H_4$	Cl^-	2.5	80	25	87	**2p**	164–165 (165–167 [40])
40	*p*-$CH_3OC_6H_4$	Cl^-	4	77	50	80	**2q**	179–181 (178–180 [57])
41	2-Furanyl	Cl^-	2.5	85	28	92	**2r**	167–169 (165–167 [40])

[a] Reaction conditions: isatoic anhydride (1 mmol), primary amine (1.2 mmol), or ammonium salts (ammonium acetate 1.2 mmol, ammonium carbonate 0.6 mmol, or ammonium chloride 1.2 mmol), aldehyde (1 mmol), 0.04 g Fe_3O_4@SiO_2-imid-PMA^n, 4 cm^3 H_2O/EtOH [1:3 (v/v)], reflux

[b] Reaction conditions: isatoic anhydride (1 mmol), primary amine (1.2 mmol) or ammonium salts (ammonium acetate 1.2 mmol, ammonium carbonate 0.6 mmol, or ammonium chloride 1.2 mmol), aldehyde (1 mmol), 0.03 g Fe_3O_4@SiO_2-imid-PMA^n, 4 cm^3 EtOH, ultrasonic irradiation, rt

[c] Isolated yields

The best result was obtained with 1:1:1.2 ratios of benzaldehyde, isatoic anhydride, and aniline in the presence of 0.04 g of magnetic catalyst. Therefore, we employed the optimized conditions for the preparation of mono- and disubstituted 2,3-dihydroquinazolin-4(1*H*)-ones.

Considering the ability of ultrasonic irradiation for the acceleration of organic reactions, we examined the model reaction under ultrasonic irradiation at room temperature in the presence of various solvents and various amounts of catalyst. As it is clear from Table 1, the best results were obtained in the presence of 0.03 g of catalyst in EtOH (Table 1, entry 22). Compared with conventional heating, the reaction catalyzed by Fe_3O_4@SiO_2-imid-PMA^n under ultrasonic irradiation showed a more effective catalytic activity. Obviously, ultrasound irradiation could accelerate the reaction and the chemical effects of ultrasounds resulted from implosive collapse of the cavitation period of the sound waves [51–53].

Following the obtained results, other derivatives of 2,3-dihydroquinazolin-4(1*H*)-one were synthesised using different types of amines or ammonium salts and aldehydes under the optimized conditions. The results are summarized in Table 2. As expected, disubstituted derivatives of 2,3-dihydroquinazolin-4(1*H*)-one were also afforded in good to excellent yields under both refluxing H_2O/EtOH [1:3 (v/v)] and ultrasonic irradiation in EtOH. A series of aromatic aldehydes carrying either electron-releasing or electron-withdrawing substituents afforded high yields of products (Table 2). The substitution groups on the aromatic ring had no obvious effect on the yield. Several aliphatic and aromatic amines were used for this reaction. Aliphatic amines afforded the products in shorter time compared to aromatic analogs (Table 2, entries 1–15).

We also have introduced an efficient and environmentally friendly approach for the synthesis of heterocyclic compounds via the three-component condensation reaction of isatoic anhydride and aromatic aldehydes with 2-aminobenzothiazole or 2-aminobenzimidazole under optimized conditions in good yields (Table 2, entries 16–23).

To compare the efficiency of ammonium salts in the synthesis of 2,3-dihydroquinazolin-4(1*H*)-ones, the reactions were carried out using ammonium carbonate, acetate, and chloride under the same reaction conditions. In all cases, monosubstituted 2,3-dihydroquinazolin-4(1*H*)-ones were produced in good yields (Table 2, entries 24–41). Moreover, it is clear that, under the same reaction conditions, reactions under ultrasonic irradiation led to shorter reaction times.

Table 3 Reaction of isatoic anhydride, aniline, and benzaldehyde using different acid catalysts

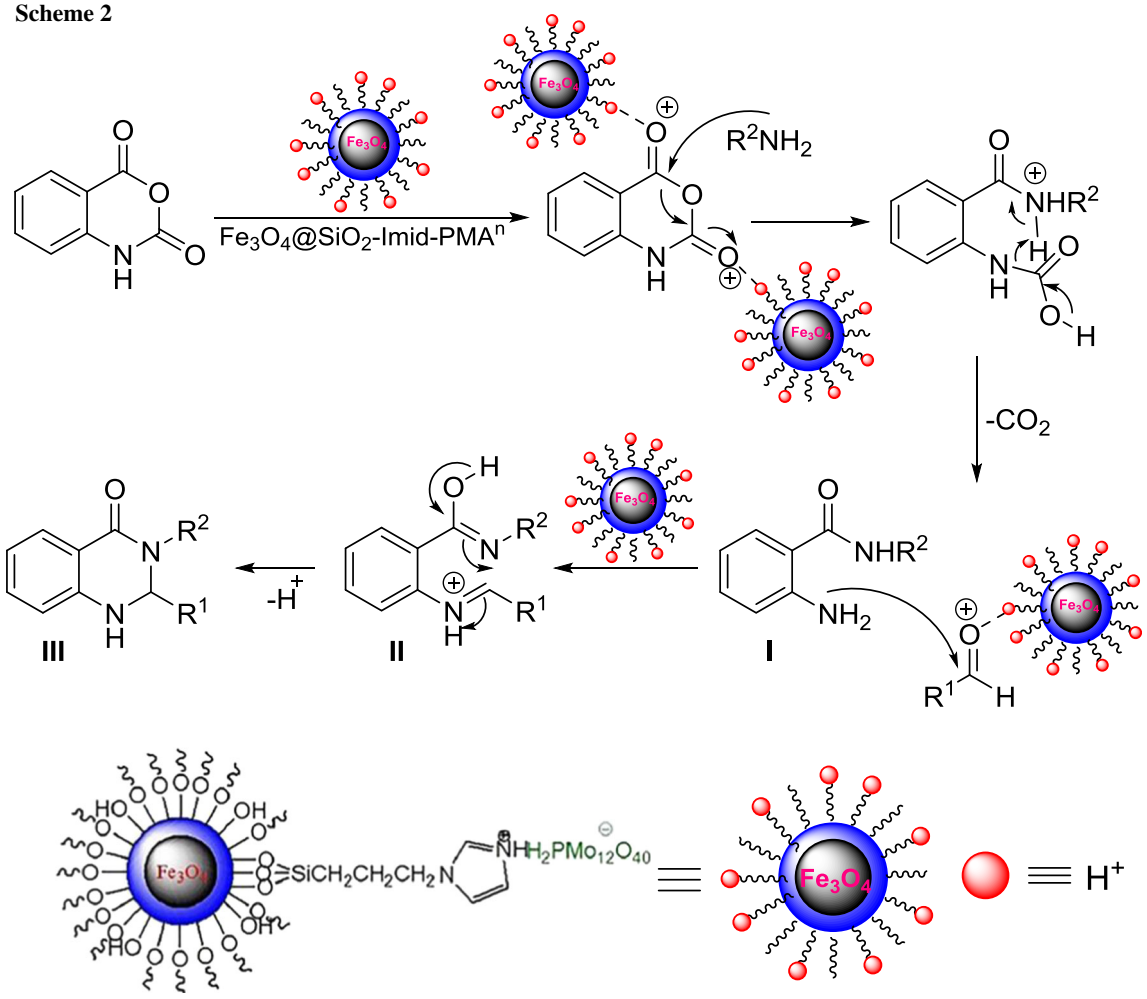
Entry	Catalyst	Conditions	Time/h	Yield/%[a]	References
1	Montmorillonite K-10	EtOH/reflux	6.5	80	[40]
2	$Zn(PFO)_2$	H_2O/EtOH [1/3 (v/v)]/reflux	6	82	[29]
3	Silica sulfuric acid	EtOH/reflux	6.5	80	[30]
4	$KAl(SO_4)_2.12H_2O$	EtOH/reflux	4	78	[34]
		H_2O/reflux	1	65	
5	$Ga(OTf)_3$	EtOH/reflux	1	79	[41]
6	*β*-Cyclodextrin	H_2O/reflux	3	84	[58]
7	[bmim]BF_4	Solvent-free/70 °C	1.5	80	[45]
8	Copolymer-PTSA	EtOH/reflux	6.5	82	[28]
9	SSA	H_2O/80 °C	4.5	85	[59]
		Solvent-free/80 °C	5	80	
10	*p*-TsOH	H_2O/reflux	2.5	79	[23]
		EtOH/reflux	6.5	65	
11	Dodecylbenzenesulfonic acid	Ultrasound irradiation/H_2O/rt	1.5	83	[60]
12	Silicasulfuric acid	Ultrasound irradiation/H_2O/rt	2	25	[60]
13	Fe_3O_4@SiO_2 (0.04 g)	EtOH/reflux	8	36	This work
14	Fe_3O_4@SiO_2-imid-PMA^b (0.04 g)	H_2O/EtOH [1:3(v/v)]/reflux	3	82	This work
15	Fe_3O_4@SiO_2-imid-PMA^n (0.04 g)	H_2O/EtOH [1:3(v/v)]/reflux	2	89	This work
16	Fe_3O_4@SiO_2-imid-PMA^b (0.03 g)	Ultrasound irradiation/EtOH/rt	0.17	81	This work
17	Fe_3O_4@SiO_2-imid-PMA^n (0.03 g)	Ultrasound irradiation/EtOH/rt	0.17	92	This work

Reaction of isatoic anhydride, benzaldehyde, and aniline using different catalysts

b bulk, *n* nano

[a] Yields refer to isolated pure product

Scheme 2



To compare the reactivity of the Fe_3O_4@SiO_2-imid-PMA^n with the previously reported catalysts, a comparative chart is presented in Table 3. In comparison with the other reported catalysts in literature, we observed that the Fe_3O_4@SiO_2-imid-PMA^n gives better yield in shorter reaction time than another catalyst (Table 3). Also, analyzing the reactions on catalysts such as Fe_3O_4@SiO_2 and Fe_3O_4@SiO_2-imid-PMA^b under both refluxing H_2O/EtOH [1:3(v/v)] and ultrasonic irradiation lead to lower yields and long times to produce the desired products (Table 3, entries 13, 14, 16).

The plausible general mechanistic pathway is shown in Scheme 2. First, the isatoic anhydride is activated with Fe_3O_4@SiO_2-imid-PMA^n by the formation of hydrogen bonding with the carbonyl group followed by nucleophilic attack of amine on the carbonyl group, and then anthranilamide **I** could be produced with the liberation of carbon dioxide.

Fe_3O_4@SiO_2-Imid-PMA^n act as Bronsted acid and play a significant role in increasing the electrophilic character of the aldehydes. Subsequently, the reaction of activated aldehyde with **I** proceeds to afford intermediate **II** that is converted to product **III** via an intramolecular cyclization.

A series of catalytic cycles were run to investigate the stability of the catalyst. In each case, the catalyst was recovered by an external magnetic field, followed by rinsing with hot ethanol, dried at 70 °C for 2 h and reused for subsequent reactions. In each cycle, the reaction was performed under the optimized conditions.

The key feature of the magnetically separable catalysis is the reusability of the catalyst. The recyclability of the catalyst was investigated using a model reaction between isatoic anhydride, benzaldehyde, and aniline in the presence of the Fe_3O_4@SiO_2-imid-PMA^n catalyst under refluxing H_2O/EtOH [1:3 (v/v)] and ultrasonic irradiation in ethanol. As shown in Fig. 2a, limited decline in the catalytic activity of the catalyst was observed after six cycles.

The amounts of the nano heteropolyacid leaching for the reactions under the optimized conditions were detected.

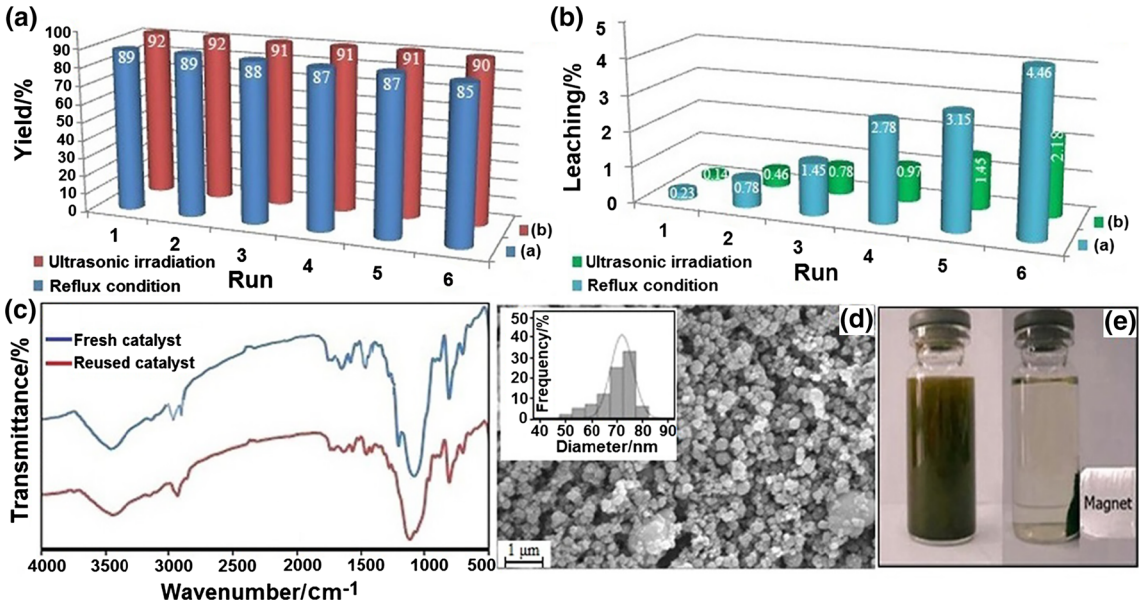


Fig. 2 **a** Recyclability of Fe_3O_4@SiO_2-imid-PMA^n in the synthesis of **1g** under the optimized conditions. **b** PMA^n leaching in each reaction cycle. **c** The FT-IR spectrum of the fresh and reused catalyst. **d** SEM and DLS images of Fe_3O_4@SiO_2-imid-PMA^n nanoparticles after six reaction cycles. **e** Photo images of magnetic field response of Fe_3O_4@SiO_2-imid-PMA^n nanoparticles

The molybdenum (Mo) amount in the reaction medium after each reaction cycle was measured through ICP and the details are shown in Table 2b. The analysis of the reaction mixture by the ICP technique showed that the leaching of $H_3PMo_{12}O_{40}$ was negligible.

Figure 2c shows the FT-IR spectra of the fresh and reused catalyst. The presence of vibration bands at 556, 794, 864, 956, 1055, 1095, 1454, and 2790–2985 cm^{-1}, which is due to the Fe–O, Mo–O_e–MO, Mo–O_c–MO, Mo–O_t, P–O, Si–O–Si, C=N, and CH, respectively, demonstrates the existence of Fe_3O_4@SiO_2-imid-PMA^n in the spectrum (Fig. 2c). This clearly indicated the presence of nano $H_3PMo_{12}O_{40}$ on the silica support even after the reaction.

SEM and DLS images of the catalyst after the six recycle have been represented in Fig. 2d. As shown in Fig. 2d, Fe_3O_4@SiO_2-imid-PMA^n nanospheres had an average diameter of 80 nm, were of uniform size, and showed good dispersity. Additionally, the hydrodynamic diameter of the catalyst was investigated by the DLS technique (Fig. 2d). This size distribution is centered at a value of 75 nm. Generally, the size of the catalysts will be increased after each cycle and leaching of $H_3PMo_{12}O_{40}$ and increasing of catalyst size lead to decreases in the yield. The theoretical curve of standard distribution from our studies was calculated by means of Microsoft Excel.

Besides its high catalytic capacity and stability, a noticeable feature of the catalyst was that it could be easily separated from the solution with a magnet and showed no tendency to self-aggregation, thus forming a stable suspension. As shown in Fig. 2e, by applying an external magnet to the side wall of a sealed vessel, the catalyst was magnetically separated from the solution (Fig. 2e).

Conclusion

In conclusion, we have reported an efficient catalyst for the synthesis of quinazolinone derivatives by the three-component one-pot condensation of isatoic anhydride with amines or ammonium salt and aldehydes under ultrasonic irradiation or reflux conditions. The present method offers several advantages including easy recovery and reuse of catalyst by magnetic field, short reaction time, high yields, ease of workup, and use of cheap and commercially available starting materials. We believe that many biologically active derivatives could be synthesised by this multicomponent reaction with high atomic economy. Moreover, the catalyst used is easily recovered by the external magnetic field and reused without any noticeable loss of activity after at least six times.

Experimental

All chemicals were commercially available and used without further purification. The NMR spectra were recorded on a Bruker Avance DPX 500 MHz spectrometer in chloroform ($CDCl_3$) using tetramethylsilane (TMS) as

an internal reference. Fourier transform infrared (FT-IR) spectra were obtained using a Shimadzu FT-IR 8300 spectrophotometer. Dynamic light scatterings (DLS) were recorded on a HORIBA-LB550. Scanning electron microscopy (SEM) image was obtained on Philips XL-30ESEM. Melting points were obtained in open capillary tubes and measured on an electrothermal 9200 apparatus. Mass spectra were obtained at 70 eV. The C, H, N, and S elemental analyses were carried out by using a Thermofinigan Flash EA-1112 CHNSO rapid elemental analyzer. Sonication was performed using an ultrasound cleaning bath (KQ-250B, China) with a frequency of 40 Hz and voltage of 220 V. All yields refer to the isolated products. Therefore, all of the products were characterized by FT-IR, ^{1}H NMR and ^{13}C NMR, and also by comparison with authentic samples.

Preparation of Fe_3O_4@SiO_2-imid-PMA^n

The catalyst (Fe_3O_4@SiO_2-Imid-PMA^n) was synthesized by the reported procedure [50]. Briefly, firstly Fe_3O_4@SiO_2 core–shell was prepared by the coprecipitation method. The mixture of 1.3 g $FeCl_3{\cdot}6H_2O$ (4.8 mmol) in 15 cm^3 water was added to the solution of polyvinyl alcohol (PVA 15000), as a surfactant, and 0.9 g $FeCl_2{\cdot}4H_2O$ (4.5 mmol) in 15 cm^3 water, which was prepared by completely dissolving PVA in water followed by the addition of $FeCl_2{\cdot}4H_2O$. The resultant solution was left to be stirred for 30 min at 80 °C. Then, hexamethylenetetramine (1.0 mol/dm^3) was added dropwise with vigorous stirring to produce a black solid product when the reaction media reached pH 10. The resultant mixture was heated on a water bath for 2 h at 60 °C and the black magnetite solid product was separated and washed with ethanol three times and then dried at 80 °C for 10 h. Then, 0.50 g Fe_3O_4 nanoparticle (2.1 mmol) was dispersed in the mixture of 50 cm^3 ethanol, 5 cm^3 deionized water, and 0.20 cm^3 tetraethoxysilane, followed by the addition of 5.0 cm^3 of NaOH (10 wt%). This solution was stirred mechanically for 30 min at room temperature. Then the product, Fe_3O_4@SiO_2, was separated by an external magnet and was washed with deionized water and ethanol three times and dried at 80 °C for 10 h.

In the second step, Fe_3O_4@SiO_2-imid was synthesized. Fe_3O_4@SiO_2 (1 g) was added to the solution of 0.241 g 3-chlorotriethoxypropylsilane (1 mmol) and 0.0680 g imidazole (1 mmol) in 20 cm^3 *p*-xylene and the resultant mixture was under reflux for 24 h under a nitrogen atmosphere. After refluxing for about 24 h, the mixture was cooled to room temperature, filtered by an external magnet, and the product was washed with xylene to remove any reacted species and dried at 70 °C for 6 h.

PMA^n nanoparticles were prepared in the tertiary step. In a typical procedure, 5 mmol of bulk $H_3PMo_{12}O_{40}$ (PMA^b) was dispersed in 50 cm^3 *n*-octane and the resulting dispersion was stirred vigorously for 30 min at room temperature to form a homogeneous dispersion. This dispersion was transferred into a Teflon-lined stainless autoclave filling 80 % of the total volume. The autoclave was sealed and maintained at 150 °C for 12 h. The autoclave was then cooled to room temperature. Finally, the resulting powder was filtered and washed for several times by octane and dried in a vacuum at 80 °C for 12 h.

In the last step, 1.0 g Fe_3O_4@SiO_2-Imid was added to a solution of PMA^n (1.0 mmol) in 20 cm^3 was taken in a round-bottom flask. The mixture was refluxed for 24 h under a nitrogen atmosphere. After 24 h, the mixture was filtered by an external magnet, washed with acetonitrile and dichloromethane, and dried at 70 °C for 6 h. FT-IR spectrum of the catalyst showed the expected bands, including distinctive bands due to anchoring of PMA^n onto Fe_3O_4@SiO_2-imid.

General procedure for the synthesis of mono- and disubstituted derivatives of 2,3-dihydroquinazolin-4(1H)-one

A mixture of isatoic anhydride (1 mmol), ammonium salt (ammonium acetate 1.2 mmol, ammonium carbonate 0.6 mmol, or ammonium chloride 1.2 mmol) or primary amine (1.2 mmol), aldehyde (1 mmol) and 0.04 g (reflux) or 0.03 g (ultrasonic) Fe_3O_4@SiO_2-imid-PMA^n catalyst in 4 cm^3 H_2O/EtOH [1:3 (v/v)] was refluxed in an oil bath or sonicated at room temperature in 4 cm^3 ethanol for an appropriate time as mentioned in Table 2. After the completion of the reaction, as monitored by TLC [eluent: petroleum ether:ethyl acetate: 4:1 (v/v)], the catalyst was separated using a magnetic field and the residue was concentrated to afford the crude product. Finally, the crude product was recrystallized from ethanol.

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