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ARTICLE

4-Dialkylaminopyridine modified magnetic nanoparticles: as an efficient nano-organocatalyst for one-pot synthesis of 2-amino-*4H*-chromene-3-carbonitrile derivatives in water

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A novel heterogeneous magnetic nano-organocatalyst was developed using immobilization of 4-dialkylaminopyridine moieties on Fe_3O_4 magnetic nanoparticles (MNP-DMAP). It was synthesized using the reaction of MNP-oxiran (MNPO) with *N*-methylpyridin-4-amine. The MNPO substrate was produced *via* oxidation of vinyl groups on the surface of vinyl-functionalized MNP (VMNP) using H_2O_2. To synthesis VMNP, silica-coated magnetic nanoparticles (Fe_3O_4@SiO_2) were reacted with trimethoxy(vinyl)silane. The MNP-DMAP catalyst shows remarkable activity in the synthesis of 2-amino-*4H*-chromene-3-carbonitrile derivatives using a multicomponent reaction under mild conditions in water as a green solvent. The MNP-DMAP was reusable in this process at least for 10 times without any treatments in its catalytic activity.

Introduction

Organocatalysis is an exponentially upward research field in modern organic chemistry that involves the synthesis and utilization of organocatalyst in organic transformations.[1] Recovery and reuse of organocatalysts after catalytic reactions are important factors in view point of sustainable and green chemistry.[2] Thus, organocatalysts have been immobilized or grafted onto solid supports to improve their recycling capability, leading to the appearance of *heterogeneous organocatalysis*.[3] Up to know different supports such as silica, polymer, magnetic nanoparticles (MNPs), etc. have been used and efforts on the finding new support materials for the heterogenization of organocatalysts to be continued.[4] The choice of MNPs as the substrate for the preparation of *heterogeneous organocatalysts* is very intelligently because it can cover most concerns about heterogeneous catalysts such as activity, selectivity, work up and recyclability.[5] That's the main reason for the use of magnetic support for the preparation of heterogeneous organocatalysts.[6]

MNPs have appeared as practical alternatives to other materials for use as readily available and high-surface-area solid supports in catalyst science and technology. In addition, these materials possess the main advantage which is being magnetically recoverable, thus eliminating the requirement for either solvent swelling before or catalyst separation after completion of the reaction. This advantage is resulted from this fact that MNPs can be removed from the reaction mixture using an external magnetic field. In order to immobilize organocatalysts on MNPs, they should be covalently connected to the surface through a chemical process. To prevent the aggregation of MNPs and also increase the stability of them, usually a layer of silica is coated on the surface and they have been used in silica-coated form. Silica coatings also encompass several advantages originating from their stability under aqueous conditions, simple surface modification. Furthermore, easy control of interparticle interactions of MNPs particles is possible through the variation of the shell thickness.[7] Since the silica-coated magnetic nanoparticles (Fe_3O_4@SiO_2) surface is covered with hydroxyl groups, it is possible to graft the organic groups to the MNPs surface *via* the reaction of alkoxysilane materials with silanol groups (Silanization).[8] Indeed, the organofunctional alkoxysilanes create their organic group (such as NH_2, SH, etc.) on the surface for further functionalization. Trimethoxy(vinyl)silane is an alkoxysilane which can be used for the generation of vinyl group on the surface of MNPs.[9] Conversion of vinyl group on the MNPs surface to epoxide rings opens up our hand for chemically modification through ring opening by nucleophiles. Thus, reaction of an organocatalyst containing a nucleophilic position with oxiran rings on the surface of MNPs, leading the formation of catalytic sites on its surface and producing a new *heterogeneous organocatalyst*.[10]

4-(Dimethylamino)pyridine (DMAP) is an important organocatalyst for a large variety of organic reactions.[11] Due to the importance of DMAP recovery in organic transformations (in view point of green chemistry and sustainability), many attempts have been done on its immobilization on different

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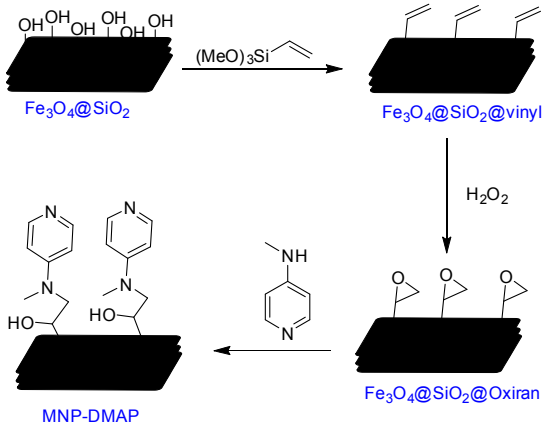
supports and synthesis of *heterogeneous DMAP-based organocatalysts*.[12]

In this study, we have introduced a new synthetic pathway to graft DMAP moiety on MNPs through the ring opening of oxiran groups on the MNPs surface with *N*-methylpyridin-4-amine. In order to show the catalytic applicability of MNP-DMAP in organic transformations it was used in a multicomponent reaction (MCR) for one-pot synthesis of a class of 2-amino-*4H*-chromene-3-carbonitrile derivatives. MCRs are attractive synthetic approaches in organic synthesis, because target molecules are produced in a single step process and diversity can be simply obtained by varying the reaction component.[13] 2-Amino-*4H*-chromene-3-carbonitriles are important due to a range of biological activities and pharmacological applications.[14] For example the following biological activities have been reported for some of the derivatives: anticoagulant, insecticidal, anticancer, antimicrobial, antibacterial, and antiviral.[15] For one-pot synthesis of a class of 2-amino-*4H*-chromene-3-carbonitrile usually malononitrile, aldehyde, and beta-diketones were reacted together in the presence of a catalyst system. In this study, the catalytic applicability of MNP-DMAP catalyst was investigated in one-pot synthesis of 2-amino-*4H*-chromene-3-carbonitrilederivatives.

Results and discussion

The synthetic pathway for the synthesis of the heterogeneous MNP-DMAP catalyst is shown in Scheme 1. Silica-coated magnetic nanoparticles (Fe_3O_4@SiO_2) were synthesized using a known procedure and reacted with trimethoxy(vinyl)silane to graft vinyl group on MNPs surface.[10a] Then, it was treated with hydrogen peroxide in order to convert vinyl groups to oxiran functionality.[10a] Ring opening of epoxy groups on the surface of MNPs with *N*-methylpyridin-4-amine resulted in the production of MNP-DMAP catalyst, successfully.



Scheme 1. Synthetic route for the preparation of MNP-DMAP catalyst.

The MNP-DMAP catalyst was characterized using some microscopic and spectroscopic techniques and the results show that it was synthesized successfully and the used procedure is efficient for chemically modification of MNPs with DMAP (see supporting information). In order to show the nano feature of the catalyst transmission electron microscopy (TEM) images of the catalyst are shown in Figure 1.

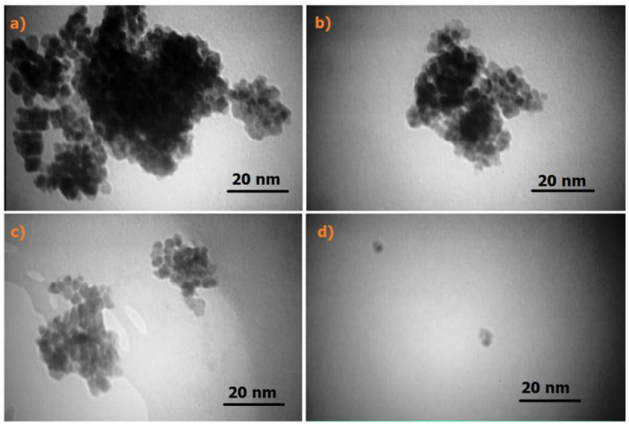


Figure 1. The TEM images of different position of the MNP-DMAP catalyst.

Catalyst particles with near spherical morphology are observable in the TEM images of the MNP-DMAP. Also the core-shell structure is clear and nanoparticles are produced in relatively good monodispersity, while the average size of nanoparticles is obtained around 5 nm which is suitable for catalysis purposes. The energy-dispersive X-ray (EDX) spectroscopy reveals that the amount of N content for the material is about 2.45%. Thus the amount of grafted DMAP on the surface of magnetic nanoparticles is estimated to be 1.8 $mmol.g^{-1}$.

After catalyst characterization, the MNP-DMAP was used as catalyst in one-pot synthesis of a class of 2-amino-*4H*-chromene-3-carbonitrile derivatives. A simple model reaction including 1,3-cyclohexanedione (**1a**), benzaldehyde (**2a**), and malononitrile (**3a**) was selected in order to optimize reaction conditions for one-pot synthesis of 2-amino-5-oxo-4-phenyl-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (**4a**) using MNP-DMAP catalyst (Table 1).

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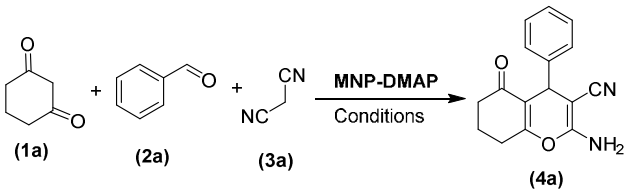
Table 1: Optimization of reaction conditions for MNP-DMAP catalyzed one-pot synthesis of 2-amino-*4H*-chromene-3-carbonitrilederivatives[a]



Entry	Catalyst (mol%)	Solvent	T (°C)	Time (h)	Yield (%)[b]
1	none	H_2O	80	12	20
2	**MNP-DMAP (5)**	**H_2O**	**80**	**0.5**	**93**
3	MNP-DMAP (5)	EtOH	80	1	85
4	MNP-DMAP (5)	DMF	100	2	90
5	MNP-DMAP (5)	MeOH	80	1	80
6	MNP-DMAP (5)	none	80	3	70
7	MNP-DMAP (2.5)	H_2O	80	5	80
8	MNP-DMAP (4)	H_2O	80	2	90
9	MNP-DMAP (5)	H_2O	95	0.5	93
10	MNP-DMAP (5)	H_2O	50	2	89
11	MNP-DMAP (5)	H_2O	rt	12	68
12	Fe_3O_4@SiO_2 (50 mg)	H_2O	80	12	55
13	DMAP (5)	H_2O	80	6	79
14	LCMNP (5)	H_2O	80	12	85
15	LPMNP (5)	H_2O	80	5	88
16	SSLP (5)	H_2O	80	5	80

[a] Reaction conditions: **1** (1 mmol), **2** (1 mmol), **3** (1 mmol) and solvent (5 mL). [b] Isolated yield.

As shown in Table 1, in the absence of catalyst and in water solvent at 80 °C, about 20% of product was obtained (entry 1). While, in the presence of about 5 mol% of catalyst the reaction yield was enhanced to 93% after 0.5 h, demonstrating high catalytic activity of the MNP-DMAP catalyst for this process (Table 1, entry 2).

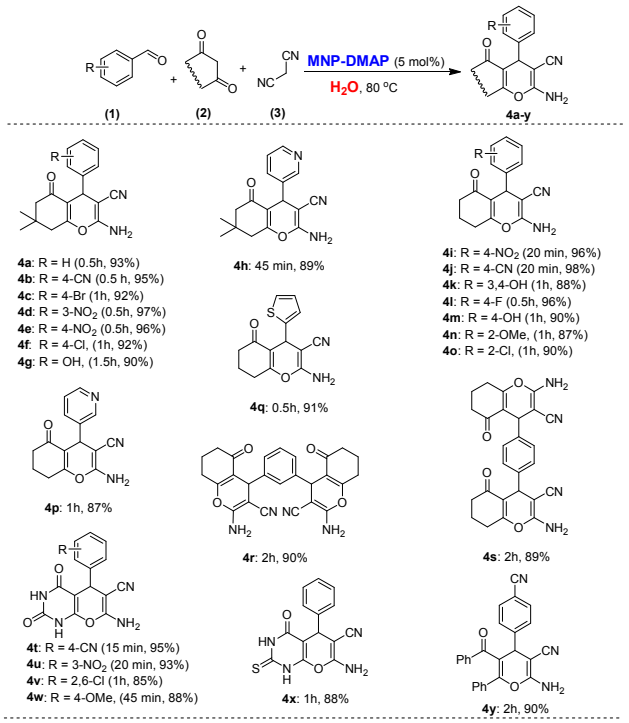
The type of solvent was changed and no superiority was observed in EtOH, DMF, MeOH related to water (Table 1, entries 3-5). Also the reaction was checked under solvent-free conditions and 70% of product was produced (Table 1, entry 6).

Then, the catalyst loading was changed and 5 mol% of catalyst was found to be optimum (Table 1, entries 7&8). The reaction temperature as another parameter was investigated and it seems that 80 °C is suitable for this transformation (Table 1, entries 9&10). At room temperature about 68% of product was isolated after 12h (Table 1, entry 11).

In order to show the high catalytic applicability of MNP-DMAP catalyst in this reaction some other catalyst was evaluated (Table 1, entries 12-16). In the presence of core-shell and DMAP as catalyst about 55% and 79% of product were obtained, demonstrating the high activity of MNP-DMAP catalyst in comparison with each of components of catalyst individually. This is a synergetic effect that observable in some of nano-organocatalyst. Indeed, the nano structure nature of the catalyst affects the activity and we have a new material with the both capability of high activity and reusability.[16]

Subsequently, some of the introduced organocatalyst in our laboratory (LCMNP,[9b] LPMNP[10a] and SSLP[10b]) were used in this reaction in order to have a comparison between the activity of MNP-DMAP and them in this reaction (Table 1, entries 14-16). Results demonstrated that MNP-DMAP catalyst is superior in activity in this reaction under optimized conditions. Thus, the MNP-DMAP is introduced as an efficient and magnetic nano-organocatalyst for one-pot synthesis of 2-amino-*4H*-chromene-3-carbonitriles (Table 1, entry 2).

The generality and scope of the reaction was investigated using the synthesis of divers 2-amino-*4H*-chromene-3-carbonitrile derivatives (Scheme2).



Scheme 2. Products of one-pot synthesis of 2-amino-*4H*-chromene-3-carbonitrile derivatives using MNP-DMAP catalyst. Reaction conditions: **1** (1 mmol), **2** (1 mmol), **3** (1 mmol) and H_2O (5 mL). All yields are isolated products.

As shown in Scheme 2, different 2-amino-*4H*-chromene-3-carbonitrile derivatives can be synthesized in high yields and relatively short reaction time using MNP-DMAP catalyst. Different beta-diketones including dimedone, 1,3-cyclohexadione, barbituric acid, thiobarbituric acid and 1,3-diphenylpropane-1,3-dione were successfully used and corresponding products were obtained in high yields. Both aldehydes including electron donating and electron withdrawing groups were used and the reaction yields for all of them were high. Nitro, cyano, methoxy, halogen, and

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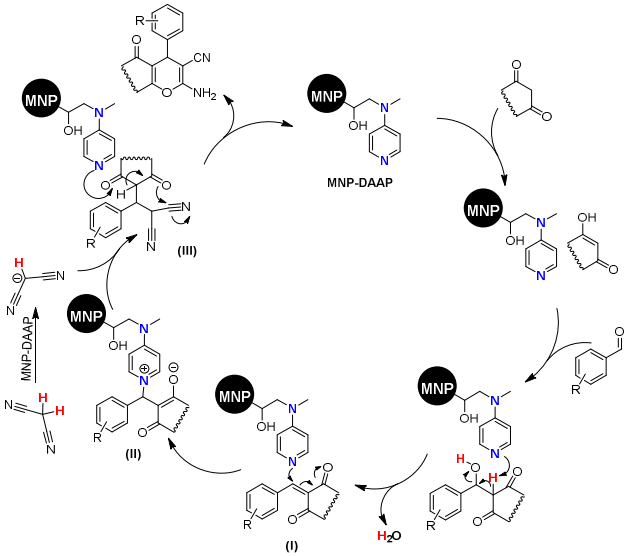
hydroxy functional groups on aldehydes tolerated the reaction conditions well. Also for heterocyclic aldehydes good yields of products were obtained. Bis-functionalized aldehydes were also tested and compound **4r** and **4s** were isolated in 90 and 89% isolated yields, respectively. Overall, this catalyst system and optimized conditions are useful for synthesis of diverse 2-amino-*4H*-chromene-3-carbonitrile derivative.

It should be mentioned that the separation of the catalyst from the reaction mixture is possible using a magnetic field and work up process is very simple. The 2-amino-*4H*-chromene-3-carbonitrile products were obtained in high yield with less impurity. The pure products were obtained via recrystallization in hot ethanol.

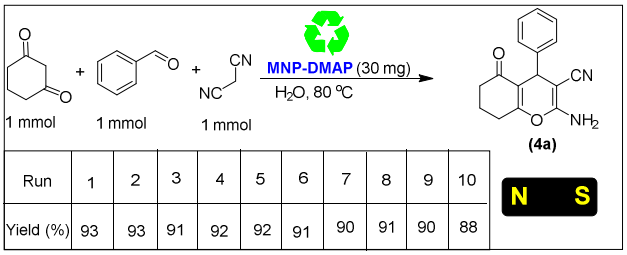
The reaction mechanism for this process is suggested based on the previous reports in the literature (Scheme 3).[9b] The role of catalyst is attributed to the 4-dialkylaminopyridine part which is a basic organocatalyst with remarkable nucleophilic power on pyridine nitrogen atom.



Scheme 3. The proposed reaction mechanism for MNP-DMAP-catalyzed one-pot synthesis of 2-amino-*4H*-chromene-3-carbonitrile using MCR of malononitrile, aldehydes, and beta-diketones.

It seems that, the reaction is started by deprotonation of beta dicarbonyl compound (it is more acidic than malononitrile) and its conversion to enol/enolate form. The nitrogen atom of the MNP-DMAP acts as base in this step. The condensation of aldehydes and beta dicarbonyl compound in enol form resulted in the production of knoevenagel intermediate (**I**). The Michael addition of DMAP nitrogen to intermediate **I** forms intermediated **II** which is more reactive for nucleophilic attack of malononitrile. This leads to the formation of a highly intermediate (**III**). This complex intermediate is subject to next intermolecular reactions with help of MNP-DMAP catalyst, leading to the formation of product. Deprotonation of catalyst completes the catalytic cycle by releasing the catalyst.

The level of recyclability of the MNP-DMAP catalyst for this reaction was also investigated by use of model reaction. When the reaction was complete, the catalyst was separated from the reaction mixture using an external magnetic field and was then washed with hot ethanol. The recycled catalyst was dried in oven and used for the next run. The recycled catalyst could be reused 10 times without a significant decrease in its catalytic activity (Fig. 2).



Run	1	2	3	4	5	6	7	8	9	10
Yield (%)	93	93	91	92	92	91	90	91	90	88

Figure 2. The reusable capability of MNP-DMAP catalyst in synthesis of 2-amino-*4H*-chromene-3-carbonitrile.

In order to show that the catalyst activity of the MNP-DMAP catalyst did not change significantly during the reaction process, the nitrogen content of recycled catalyst after 10 cycles of reusability was investigated using the elemental analysis method and the results show that only about 0.2% of nitrogen was lost. These results are in good agreement with the reactivity of MNP-DMAP catalyst after recovery.

Conclusions

In conclusion, we have introduced an efficient and simple method for chemical stabilization of DMAP on magnetic nanoparticles. The ring opening reaction of exist oxiran rings on the MNP surface using *N*-methylpyridin-4-amine resulting in the production of MNP-DMAP catalyst. This is an efficient strategy for chemical modification of magnetic nanoparticles with DMAP. The MNP-DMAP was used as an efficient heterogeneous organocatalyst in a three-component coupling reaction of aldehydes, beta diketones and malononitrile for one-pot synthesis of 2-amino-*4H*-chromene-3-carbonitrile under mild and green conditions. This organocatalyst system was reused 10 times in the designed protocol without any change in its catalytic activity. The MNP-DMAP provides great promise toward further useful applications in other organic transformations.

Experimental Section

General

Chemicals were purchased from Fluka and Aldrich chemical companies and used without further purification. The known products were characterized by comparison of their spectral and physical data with those reported in the literature. ^{1}H (250 MHz) and ^{13}C NMR (62.5 MHz) spectra were recorded on a Bruker Avance spectrometer in $CDCl_3$ solution with

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tetramethylsilane (TMS) as an internal standard. Transmission electron microscopy (TEM) analyses were performed on a Philips model CM 10 instrument. Melting points were determined in open capillary tubes in a Barnstead Electro-thermal 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).

Preparation of Fe_3O_4 nanoparticles

Magnetic nanoparticles were prepared *via* co-precipitation of Fe (III) and Fe (II) ions in the presence of sodium hydroxide.[10a,c] In a canonical flask, a mixture of $FeCl_2.4H_2O$ (15 mmol, 2.9g) and $FeCl_3.6H_2O$ (30 mmol, 8.1 g) was dissolved in 100 mL of deionized water and put under nitrogen atmosphere for 10 minutes. Then, the pH of this solution was increased to 11 by adding a 1M solution of NaOH immediately at 40 °C. Subsequently, the temperature of mixture was enhanced to 60 °C and the solution was stirred for 20 minute in this temperature. The magnetic nanoparticles as a dark solid were isolated from the solution by magnetic separation and washed with deionized water until pH 7 reached.

Preparation of Fe_3O_4@SiO_2 nanoparticles

Fe_3O_4@SiO_2 nanoparticles were prepared based on the literature:[10a,c] to a mixture of 125 mL of heptanes, 25 mL of *i*-PrOH, 20 mL of PEG-300, and 10 mL of water, 2 g of Fe_3O_4 was added. Then the mixture was stirred by mechanical stirrer under N_2 gas for 30 minutes. 20 mL of tetraethyl ortho silicate (TEOS) was added to the mixture next and then the solution was stirred for 12 h at 30 °C. After the specified time, 10 mL of ammonia was added and the solution was stirred continuously for another 12 h. The precipitation was washed with ethanol (3 ×10) and collected by external magnetic field. The desired product was dried under vacuum overnight.

Synthesis of vinyl magnetic nanoparticle (VMNP)[10a,c]

In a three-necked flask (100 mL) containing 70 mL of dry chloroform, 10 g of Fe_3O_4 was charged. Then trimethoxy(vinyl)silane (3.54 g, 0.02 mol) was added to the reaction mixture drop-wise over a period of 5 min at room temperature. When the addition was completed, the mixture was stirred for 12 h at the refluxing temperature of chloroform. Then, the reaction mixture was filtered and the obtained solid was dried in a vacuum at 50 °C to obtain a vinyl MNP (VMNP) substrate. The amount of vinyl group on the surface of MNPs was estimated to be 3.42 mmol/g according to the elemental analysis.

Synthesis of MNP-oxiran (MNPO)[10a,c]

A solution of 5g vinyl MNP (VMNP), and H_2O_2 30% (20 mL) were stirred at 50 °C for 12 h. The resulting precipitate was filtered through a celite pad, washed with water, dried in vacuum to afford the MNPO substrate (5.52 g). The presence of ethylene oxide group on the silica substrate was detected by the bright pink color of the phenolphthalein (as indicator) when air passed through an aqueous solution of NaCl. The quantitative amount of oxiran group on the substrate was identified to be 2.8 mmol/g using elemental analysis, which it showed that a remarkable amount of vinyl groups is converted to oxiran under applied conditions.

Synthesis of 4-dialkylaminopyridinemagnetic nanoparticles (MNP-DMAP) catalyst[10c]

For the synthesis of MNP-DMAP catalyst, 1.5 g of *N*-methylpyridin-4-amine was added in to a prepared solution containing 5.0 g of VMNP in 30 mL chloroform. Subsequently, the mixture was stirred for 12h at refluxing temperature of chloroform. The resulting precipitate was filtered through a celite pad, washed with water, dried in vacuum to afford the MNP-DMAP catalyst (1.8 mmol/g of supported DMAP).

General Procedure for the synthesis of 2-amino-*4H*-chromene-3-carbonitrile compounds

A mixture of aldehyde (1 mmol), 1,3-*beta*-dicarbonyl (1 mmol), malononitrile (1 mmol)and MNP-DMAP (30 mg, 5 mol %) in H_2O (4 mL) was stirred at room temperature for appropriate time. The progress of the reaction was monitored by TLC. After completion of the reaction, as showed by TLC, The catalyst was recovered magnetically by attaching a general magnet to the external of the reactor vessel and the reaction mixture was filtered and the residual washed with ethanol (3 × 5 mL).

2-Amino-7,7-dimethyl-5-oxo-4-phenyl-5,6,7,8-tetrahydro-*4H*-chromene-3-carbonitrile (4a)

White crystal (Yield: 93%, 0.24 g); Mp: 231-232 °C [Lit. 230-232 °C].[17a] IR (KBr): 3394, 3325, 3209, 2885, 2198, 1681, 1666, 1604, 1450, 1373, 1249, 1211, 1157, 1033, 1002, 840, 740, 694, 655 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 7.20-7.27 (m, 2H, Ar), 7.12-7.15 (m, 3H, Ar), 6.97 (s, 2H, NH_2), 4.15 (s, 1H, CH), 2.48 (s, 2H, CH_2), 2.08-2.21 (m, 2H, CH_2), 1.00 (s, 3H, CH_3), 0.92 (s, 3H, CH_3). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 183.7, 162.4, 157.6, 152.5, 149.6, 149.4, 132.2, 128.5, 118.8, 118.7, 109.4, 87.3, 57.5, 35.7. Anal. Calcd. for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.41; H, 6.03; N, 9.48.

2-Amino-4-(4-cyanophenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-*4H*-chromene-3-carbonitrile (4b)

White crystal (Yield: 95%, 0.27 g); Mp: 230-232°C [Lit. 227-229°C].[17b] IR (KBr): 3471, 3355, 3193, 2962, 2877, 2229, 2191, 1689, 1666, 1604, 1504, 1465, 1411, 1365, 1249, 1211, 1157, 1141, 1041, 856, 632, 563 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 7.74 (d, *J* = 8.2 Hz, 2H, Ar), 7.33 (d, *J* = 8.0 Hz, 2H, Ar), 4.27 (s, 1H, CH), 2.50 (s, 2H, CH_2), 2.05-2.26 (m, 2H, CH_2), 1.01 (s, 3H, CH_3), 0.93 (s, 3H, CH_3). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 195.7, 163.0, 158.4, 150.1, 132.3, 128.2, 119.3, 118.7, 111.6, 109.3, 57.0, 49.7, 35.7, 31.7, 28.1, 26.8. Anal. Calcd. for $C_{19}H_{17}N_3O_2$: C, 71.46; H, 5.37; N, 13.16. Found: C, 71.39; H, 5.30; N,13.20.

2-Amino-4-(4-bromophenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-*4H*-chromene-3-carbonitrile (4c)

White crystal (Yield: 92%, 0.30 g); Mp: 208-210 °C [Lit. 207-209 °C].[17c] IR (KBr): 3394, 3317, 3209, 2873, 2191, 1681, 1654, 1604, 1485, 1407, 1369, 1253, 1215, 1161, 1141, 1072, 1037,

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1010, 844, 771, 563 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 7.45 (d, *J* = 7.7 Hz, 2H,Ar), 7.08 (d, *J* = 8.2 Hz, 2H,Ar),7.04 (s, 2H, NH_2),4.15 (s, 1H, CH), 2.48 (s, 2H, CH_2), 2.04-2.25 (m, 2H, CH_2), 1.00 (s, 3H, CH_3), 0.92 (s, 3H, CH_3). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 195.6, 162.5, 158.4, 144.1, 131.1, 129.4, 119.6, 119.5, 112.1, 57.6, 55.9, 49.8, 35.1, 31.7, 28.2, 26.7, 18.4. Anal. Calcd. for $C_{18}H_{17}BrN_2O_2$: C, 57.92; H, 4.59; N, 7.51. Found: C, 57.88; H, 4.53; N, 7.46.

2-Amino-7,7-dimethyl-4-(3-nitrophenyl)-5-oxo-5,6,7,8-tetrahydro-*4H*-chromene-3-carbonitrile (4d)

White crystal (Yield: 97%, 0.29 g); Mp: 212-214 °C [Lit. 213-214 °C].[17d] IR (KBr): 3433, 3332, 3201, 2869, 2183, 1681, 1596, 1527, 1350, 1249, 1211, 1157, 1134, 1041, 902, 825, 686 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 8.02-8.07 (m, 1H, Ar), 7.94-7.95 (m, 1H, Ar),7.55-7.62 (m, 2H, Ar), 7.15 (s, 2H, NH_2), 4.39 (s, 1H, CH), 2.52 (s, 2H, CH_2), 2.06-2.27 (m, 2H, CH_2), 1.01 (s, 3H, CH_3), 0.93 (s, 3H, CH_3). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 195.7, 163.1, 158.5, 147.7, 146.9, 134.1, 129.9, 121.7, 121.5, 119.3, 111.7, 57.1, 49,7, 35.3, 31.7, 28.2, 26.6. Anal. Calcd. for $C_{18}H_{17}N_3O_4$: C, 63.71; H, 5.05; N, 12.38. Found: C, 63.59; H, 4.89; N, 12.20.

2-Amino-7,7-dimethyl-4-(4-nitrophenyl)-5-oxo-5,6,7,8-tetrahydro-*4H*-chromene-3-carbonitrile (4e)

White crystal (yield: 96%, 0.28 g); Mp: 174-176 °C [Lit. 177-178 °C].[17d] IR (KBr): 3386, 3325, 3209, 2962, 2191, 1651, 1604, 1519, 1365, 1211, 1041, 864, 825 cm^{-1}. ^{1}H NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 8.14 (d, *J* = 8.7 Hz, 2H, Ar), 7.41 (d, *J* = 8.7 Hz, 2H, Ar), 7.16 (s, 2H, NH_2), 4.34 (s, 1H, CH), 2.47 (s, 2H, CH_2), 2.04-2.20 (m, 2H, CH_2), 1.01 (s, 3H, CH_3), 0.93 (s, 3H, CH_3). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 195.6, 163.0, 158.5, 152.2, 146.1, 128.5, 123.6, 119.2, 111.6, 56.9, 55.9, 49.7, 35.5, 31.7, 28.1, 26.8, 18.4. Anal. Calcd. for $C_{18}H_{17}N_3O_4$: C, 63.71; H, 5.05; N, 12.38. Found: C, 63.62; H, 5.12; N, 12.29.

2-Amino-4-(4-chlorophenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-*4H*-chromene-3-carbonitrile (4f)

White crystal (Yield: 92%, 0.26 g); Mp: 210-212 °C [Lit. 209–210 °C].[17d] IR (KBr): 3379, 3178, 2962, 2191, 1674, 1635, 1488, 1365, 1218, 1033, 771 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 7.31 (d, *J* = 8.2 Hz, 2H, Ar), 7.14 (d, *J* = 8.5 Hz, 2H, Ar),7.03 (s, 2H, NH_2), 4.16 (s, 1H, CH), 2.47 (s, 2H, CH_2), 2.03-2.25 (m, 2H, CH_2), 0.99 (s, 3H, CH_3), 0.91 (s, 3H, CH_3). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 195.6, 162.5, 158.4, 143.6, 131.0, 129.0, 128.2, 119.5, 112.2, 57.6, 55.9, 49.8, 35.0, 31.7, 28.2, 26.7, 18.4. Anal. Calcd. for $C_{18}H_{17}ClN_2O_2$: C, 65.75; H, 5.21; N, 8.52. Found: C, 65.62; H, 5.28; N, 8.46.

2-Amino-4-(4-hydroxyphenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-*4H*-chromene-3-carbonitrile(4g)

White crystal (yield: 90%, 0.24 g); Mp: 200-203 °C [Lit. 205-206 °C].[17e] IR (KBr): 3436, 3271, 3193, 2950, 2931, 2349, 2202, 1612, 1558, 1508, 1373, 1257, 1222, 1172, 1137, 837 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 9.25 (s, 1H, OH), 6.89-6.92 (m, 4H), 6.63 (d, *J* = 8.2 Hz, 2H, Ar), 4.04 (s, 1H, CH), 2.46 (s, 2H, CH_2), 2.03-2.25 (m, 2H, CH_2), 1.00 (s, 3H, CH_3), 0.92 (s, 3H, CH_3). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 195.7, 163.1, 158.5, 147.7, 146.9, 134.1, 129.9, 121.7, 121.6, 119.3, 111.7, 57.1, 49.7, 35.3, 31.7, 28.2, 26.6. Anal. Calcd. for $C_{18}H_{18}N_2O_3$: C, 69.66; H, 5.85; N, 9.03. Found: C, 69.59; H, 5.91; N, 8.90.

2-Amino-7,7-dimethyl-5-oxo-4-(pyridin-3-yl)-5,6,7,8-tetrahydro-*4H*-chromene-3-carbonitrile (4h)

White crystal (yield: 89%, 0.23 g); Mp: 227-229°C [Lit. 225-226 °C].[17f] IR (KBr): 3317, 3178, 2962, 2183, 1651, 1604, 1427, 1373, 1249, 1218, 1141, 1033, 840, 709, 563 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 8.36 (s, 2H, Ar), 7.49-7.52 (m, 1H, Ar), 7.27-7.31 (m, 1H, Ar),7.09 (s, 2H, NH_2), 4.21 (s, 1H, CH), 2.49 (s, 2H, CH_2), 2.05-2.25 (m, 2H, CH_2), 1.00 (s, 3H, CH_3), 0.91 (s, 3H, CH_3). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 195.6, 162.9, 158.5, 148.6, 147.7, 139.9, 134.6, 123.5, 119.4, 111.6, 57.2, 49.8, 33.3, 31.7, 28.1, 26.8. Anal. Calcd. for $C_{17}H_{17}N_3O_2$: C, 69.14; H, 5.80; N, 14.23. Found: C, 68.95; H, 5.67; N, 14.35.

2-Amino-4-(4-nitrophenyl)-5-oxo-5,6,7,8-tetrahydro-*4H*-chromene-3-carbonitrile (4i)

Yellow crystal (yield: 96%, 0.25 g); Mp: 236-239 °C [Lit. 235-236 °C].[17g] IR (KBr): 3417, 3332, 3217, 2862, 2198, 1651, 1596, 1519, 1419, 1342, 1257, 1211, 1172, 1134, 1072, 1002, 910, 817, 732, 694, 732, 694cm^{-1}. ^{1}H-NMR(250 MHz, DMSO-d_6): δ (ppm): δ (ppm): 8.13 (d, *J* = 7.2 Hz, 2H, Ar), 7.44 (d, *J* = 7.5 Hz, 2H, Ar),7.15 (s, 2H, NH_2), 4.34 (s, 1H, CH), 2.61 (s, 2H, CH_2), 2.24 (s, 2H, CH_2), 1.91-1.92 (m, 2H, CH_2). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 195.8, 165.0, 158.4, 152.2, 146.1, 128.5, 123.5, 119.3, 112.6, 56.8, 36.1, 35.4, 26.4, 19.6. Anal. Calcd. for $C_{16}H_{13}N_3O_4$: C, 61.73; H, 4.21; N, 13.50. Found: 61.68; H, 4.16; N, 13.43.

2-Amino-4-(4-cyanophenyl)-5-oxo-5,6,7,8-tetrahydro-*4H*-chromene-3-carbonitrile (4j)

White crystal (yield: 98%, 0.26 g); Mp: 230-232°C. IR (KBr): 3425, 3332, 3217, 2862, 2221, 2198, 1651, 1604, 1496, 1411, 1365, 1257, 1211, 1164, 1126, 1064, 1002, 910, 840 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 7.73 (d, *J* = 8.2 Hz, 2H, Ar), 7.35 (d, *J* = 8.0 Hz, 2H, Ar),7.11 (s, 2H, NH_2), 4.26 (s, 1H, CH), 2.60 (s, 2H, CH_2), 2.24-2.29 (m, 2H, CH_2), 1.90-1.92 (m, 2H, CH_2). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 195.8, 165.0, 158.4, 150.2, 132.3, 128.2, 119.3, 118.7, 112.6, 109.3, 56.9, 36.1, 35.6, 26.4, 19.6. Anal. Calcd. for $C_{17}H_{13}N_3O_2$: C, 70.09; H, 4.50; N, 14.42. Found: C, 70.18; H, 4.39; N, 14.35.

2-Amino-4-(3,4-dihydroxyphenyl)-5-oxo-5,6,7,8-tetrahydro-*4H*-chromene-3-carbonitrile(4k)

Yellow crystal (yield: 88%, 0.22 g); Mp: 267-269 °C. IR (KBr): 3456, 3186, 2920, 2850, 2192, 1617, 1593, 1473, 1365, 1238, 1180, 1137, 1110, 964 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 9.32 (s, 1H), 8.66-8.78 (m, 1H), 8.55 (s, 1H), 8.39 (s, 1H), 6.54-6.56 (m, 1H), 6.44-6.45 (m, 1H), 6.31-6.35 (m, 1H), 4.72 (s, 1H, CH), 2.46-2.48 (m, 2H, CH_2), 2.17 (s, 2H, CH_2), 1.86-1.87 (m, 2H, CH_2). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 194.7, 150.7, 144.2, 142.9, 138.5, 117.9, 115.1, 114.8, 112.8, 56.9, 36.8, 30.7, 26.2, 20.7. Anal. Calcd. for $C_{16}H_{14}N_2O_4$: C, 64.42; H, 4.73; N, 9.39. Found: C, 64.34; H, 4.80; N, 9.28.

2-Amino-4-(4-fluorophenyl)-5-oxo-5,6,7,8-tetrahydro-*4H*-chromene-3-carbonitrile (4l)

White crystal (yield: 96%, 0.24 g); Mp: 215-217 °C [Lit.213-215 °C].[17h] IR (KBr): 3417, 3332, 3217, 2931, 2360, 2191, 1651, 1604, 1504, 1419, 1365, 1211, 1157, 1072, 1002, 840, 532 cm^{-}

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[1]. ^{1}H NMR (250 MHz, DMSO-d_6/TMS) δ (ppm):7.17 (d, *J* = 2.7 Hz, 2H, Ar), 7.07 (d, *J* = 2.7 Hz, 2H, Ar), 7.00 (s, 2H, NH_2), 4.19 (s, 1H, CH), 2.57 (s, 2H, CH_2), 2.23 (s, 2H, CH_2), 1.87-1.90 (m, 2H, CH_2). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 195.8, 164.4, 162.7, 158.9, 158.3, 140.9, 129.0, 119.6, 115.1, 113.5, 57.9, 36.2, 34.7, 26.4, 19.7. Anal. Calcd. for $C_{16}H_{13}FN_2O_2$: C, 67.60; H, 4.61; N, 9.85. Found: C, 67.53; H, 4.50; N, 9.69.

2-Amino-4-(4-hydroxyphenyl)-5-oxo-5,6,7,8-tetrahydro-*4H*-chromene-3-carbonitrile (4m)

White crystal (yield: 90%, 0.22 g); Mp: 237-238 °C [Lit. 234-236°C].[17h] IR (KBr): 3379, 3321, 3193, 3012, 2815, 2198, 1674, 1647, 1604, 1539, 1512, 1454, 1419, 1377, 1253, 1199, 1168, 1141, 1068, 1010, 914, 894, 837, 783, 624, 536 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 9.22 (s, 1H, OH), 6.89 (s, 4H), 6.62 (d, *J* = 8.0 Hz, 2H, Ar), 4.05 (s, 1H, CH), 2.47- 2.56 (m, 2H, CH_2), 2.23 (s, 2H, CH_2), 1.86- 1.90 (m, 2H, CH_2). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 195.8, 163.9, 158.3, 155.9, 135.1, 128.0, 119.8, 114.9, 114.1, 58.5, 36.3, 34.4, 26.3, 19.7. Anal. Calcd. for $C_{16}H_{14}N_2O_3$: C, 68.08; H, 5.00; N, 9.92. Found: C, 67.93; H, 4.80; N, 9.82.

2-Amino-4-(2-methoxyphenyl)-5-oxo-5,6,7,8-tetrahydro-*4H*-chromene-3-carbonitrile (4n)

White crystal (yield: 87%, 0.22 g); Mp: 215-217 °C. IR (KBr): 3379, 3313, 3159, 2962, 2835, 2187, 1681, 1651, 1577, 1542, 1488, 1458, 1369, 1253, 1211, 1164, 1134, 1068, 1049, 999, 829, 752, 702, 609, 536 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 7.11-7.13 (m, 1H), 6.92-6.95 (m, 2H), 6.80-6.82 (m, 3H), 4.53 (s, 1H, CH), 3.75 (s, 3H, CH_3), 2.57-2.58 (m, 2H, CH_2), 2.22-2.28 (m, 2H, CH_2), 1.90-1.94 (m, 2H, CH_2). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 195.7, 165.0, 158.8, 156.7, 132.4, 128.0, 127.6, 120.4, 119.7, 113.0, 111.5, 57.5, 55.6, 36.3, 29.5, 26.4, 19.8. Anal.Calcd.for $C_{17}H_{16}N_2O_3$: C, 68.91; H, 5.44; N, 9.45. Found: C, 68.80; H, 5.49; N, 9.32.

2-Amino-4-(2-chlorophenyl)-5-oxo-5,6,7,8-tetrahydro-*4H*-chromene-3-carbonitrile (4o)

White crystal (yield: 90%, 0.23 g); Mp: 213-215 °C. IR (KBr): 3328, 3182, 2935, 2191, 1681, 1647, 1600, 1365, 1261, 1245, 1211, 1164, 1137, 1068, 1002, 910, 748, 536 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 7.31-7.34 (m, 1H, Ar), 7.14-7.24 (m, 3H, Ar), 6.99 (s, 2H, NH_2), 4.68 (s, 1H, CH), 2.60 (s, 2H, CH_2), 2.21-2.24 (m, 2H, CH_2), 1.90-1.94 (m, 2H, CH_2). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 195.6, 165.0, 158.4, 141.6, 132.0, 128.8, 128.0, 127.4, 119.2, 112.8, 109.8, 56.7, 36.2, 32.6, 26.4, 19.7. Anal. Calcd. for $C_{16}H_{13}ClN_2O_2$: C, 63.90; H, 4.36; N, 9.31. Found: C, 63.65; H, 4.19; N, 9.20.

2-Amino-5-oxo-4-(pyridin-3-yl)-5,6,7,8-tetrahydro-*4H*-chromene-3-carbonitrile (4p)

White crystal (yield: 87%, 0.20 g); Mp: 183-184 °C. IR (KBr): 3363, 3305, 3035, 2970, 2881, 2191, 2360, 1662, 1612, 1589, 1477, 1431, 1365, 1261, 1242, 1215, 1176, 1134, 1068, 1045, 1029, 1002, 894, 840, 713, 632, 540 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 8.36-8.39 (m, 2H, Ar), 7.51- 7.55 (m, 1H, Ar), 7.27-7.32 (m, 1H, Ar), 7.10 (s, 2H, NH_2), 4.23 (s, 1H, CH), 2.57- 2.60 (m, 2H, CH_2), 2.22- 2.30 (m, 2H, CH_2), 1.90-1.94 (m, 2H, CH_2). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 195.8, 164.9, 158.4, 148.6, 147.7, 140.0, 134.6, 123.5, 119.4, 57.1, 36.1, 33.2, 26.4, 19.6. Anal. Calcd for $C_{15}H_{13}N_3O_2$: C, 67.40; H, 4.90; N, 15.72. Found: C, 67.15; H, 4.86; N, 15.68.

2-Amino-5-oxo-4-(thiophen-2-yl)-5,6,7,8-tetrahydro-*4H*-chromene-3-carbonitrile (4q)

White crystal (yield: 91%, 0.22 g); Mp: 205-207 °C [Lit. 205–206 °C].[17i] IR (KBr): 3321, 3174, 2866, 2191, 1681, 1651, 1608, 1361, 1245, 1211, 1161, 1134, 1114, 1064, 1002, 852, 709, 536 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 7.26-7.28 (m, 1H, Ar), 7.09 (s, 2H, NH_2), 6.80-6.87 (m, 2H, Ar), 4.49 (s, 1H, CH), 2.46-2.48 (m, 2H, CH_2), 2.28 (s, 2H, CH_2), 1.83-1.93 (m, 2H, CH_2). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 195.7, 164.2, 158.9, 149.1, 126.7, 124.3, 123.9, 119.6, 113.9, 57.7, 36.1, 30.2, 26.3, 19.6. Anal. Calcd. for $C_{14}H_{12}N_2O_2S$: C, 61.75; H, 4.44; N, 10.29. Found: C, 61.60; H, 4.36; N, 10.18.

4,4'-(1,3-phenylene)bis(2-amino-5-oxo-5,6,7,8-tetrahydro-*4H*-chromene-3-carbonitrile) (4r)

White crystal (yield: 90%, 0.37 g); Mp: 315-317 °C. IR (KBr): 3394, 3325, 3209, 2931, 2191, 1651, 1596, 1365, 1242, 1203, 1164, 1134, 1002, 910, 709, 540 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 7.13-7.16 (m, 1H), 6.92-6.97 (m, 7H), 4.13 (s, 2H, CH), 2.57 (s, 4H, CH_2), 2.23-2.25 (m, 4H, CH_2), 1.92-1.93 (m, 4H, CH_2). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 195.7, 195.6, 164.7, 164.3, 158.8, 158.2, 144.6, 128.1, 125.5, 125.1, 124.8, 119.7, 114.1, 113.4, 58.2, 57.6, 36.2, 34.9, 34.7, 26.4, 19.7. Anal. Calcd. for $C_{26}H_{22}N_4O_4$: C, 68.71; H, 4.88; N, 12.33. Found: C, 68.80; H, 4.76; N, 12.26.

2-Amino-4-(4-(2-amino-3-cyano-5-oxo-5,6,7,8-tetrahydro-*4H*-chromen-4-yl)phenyl)-8-oxo-5,6,7,8-tetrahydro-*4H*-chromene-3-carbonitril (4s)

White crystal (yield: 89%, 0.36 g); Mp: >320 °C [Lit. >300 °C].[17j] IR (KBr): 3452, 3328, 3201, 2896, 2191, 1681, 1600, 1558, 1365, 1245, 1203, 1137, 1068, 999, 810 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS)δ (ppm): 7.03 (s, 4H), 6.95 (s, 4H), 4.12 (s, 2H, CH), 2.58 (s, 4H, CH_2), 2.25-2.27 (m, 4H, CH_2), 1.90-1.92 (m, 4H, CH_2). ^{13}C-NMR (62.5 MHz, DMSO/TMS) δ (ppm): 195.9, 164.6, 158.6, 157.4, 154.5, 142.8, 126.9, 124.4, 119.8, 113.7, 108.7, 58.9, 58.1, 36.2, 34.8, 34.7, 28.6, 21.5. Anal. Calcd. for $C_{26}H_{22}N_4O_4$: C, 68.71; H, 4.88; N, 12.33. Found: C, 68.64; H, 4.78; N, 12.26.

7-Amino-5-(4-cyanophenyl)-2,4-dioxo-1,3,4,5-tetrahydro-*2H*-pyrano[2,3-d]pyrimidine-6-carbonitrile (4t)

White crystal (yield: 95%, 0.26g); Mp: 254-257 °C [Lit.254-256°C].[17k] IR (KBr): 3379, 3178, 3101, 2854, 2198, 1720, 1674, 1635, 1527, 1404, 1342, 1280, 1188, 1103, 987, 609 cm^{-1}. ^{1}H NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 12.11 (s, 1H, NH), 11.07 (s, 1H, NH), 7.74 (d, *J* = 7.7 Hz, 2H, Ar), 7.41 (d, *J* = 8.0 Hz, 2H, Ar),7.21 (s, 2H, NH_2), 4.32 (s, 1H, CH). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 171.0, 162.5, 158.4, 143.6, 131.0, 129.0, 128.2, 119.4, 112.2, 92.0, 57.6, 35.0. Anal. Calcd. for $C_{15}H_9N_5O_3$: C, 58.63; H, 2.95; N, 22.79. Found: C, 58.70; H, 2.89; N, 22.71.

7-Amino-5-(3-nitrophenyl)-2,4-dioxo-1,3,4,5-tetrahydro-*2H*-pyrano[2,3-d]pyrimidine-6-carbonitrile (4u)

Orange crystal (yield: 93%, 0.28 g); Mp: 264-265 °C [Lit. 265 °C].[17l] IR (KBr): 3417, 3317, 3201, 3101, 3024, 2854, 2191, 1666, 1535, 1404, 1350, 1280, 1218, 1103, 987, 794, 717, 678 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 12.15 (s, 1H,

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NH), 11.08 (s, 1H, NH), 8.04 (s, 2H, Ar), 7.70 (s, 1H, Ar), 7.55-7.61 (m, 1H, Ar), 7.25 (s, 2H, NH_2), 4.45 (s, 1H, CH). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 162.4, 157.7, 152.5, 149.4, 147.6, 146.3, 134.4, 129.8, 122.0, 121.8, 118.8, 87.4, 57.5, 35.3. Anal. Calcd. for $C_{14}H_9N_5O_5$: C, 51.38; H, 2.77; N, 21.40. Found: C, 51.28; H, 2.85; N, 21.34.

7-Amino-5-(2,6-dichlorophenyl)-2,4-dioxo-1,3,4,5-tetrahydro-2H-pyrano[2,3-d]pyrimidine-6-carbonitrile(4v)

White crystal (yield: 85%, 0.26 g); Mp: 250-252 °C. IR (KBr): 3463, 3352, 3163, 3001, 2584, 2198, 1701, 1635, 1608, 1577, 1508, 1400, 1280, 1199, 1107, 1049, 983, 771, 605, 559 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 10.96 (s, 2H, NH), 7.30-7.42 (m, 3H, Ar), 7.21 (s, 2H, NH_2), 3.89 (s, 1H, CH). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 170.7, 162.1, 158.6, 153.3, 149.7, 135.8, 135.7, 130.2, 129.1, 128.4, 118.4, 85.8, 59.7, 32.0. Anal. Calcd. for $C_{14}H_8Cl_2N_4O_3$: C, 47.89; H, 2.30; N, 15.96. Found: C, 47.97; H, 2.19; N, 15.85.

7-Amino-5-(4-methoxyphenyl)-2,4-dioxo-1,3,4,5-tetrahydro-2H-pyrano[2,3-d]pyrimidine-6-carbonitrile (4w)

Yellow crystal (yield: 88%, 0.24 g); Mp: 282-285°C [Lit. 280–284°C].[17m] IR (KBr): 3398, 3186, 3008, 2835, 2194, 1716, 1678, 1635, 1508, 1396, 1342, 1276, 1245, 1172, 1099, 1037, 987, 848, 655, 605, 543 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 11.09 (s, 2H, NH), 7.03-7.09 (m, 4H), 6.81 (d, *J* = 8.2 Hz, 2H, Ar), 4.13 (s, 1H, CH), 3.68 (s, 3H, CH_3). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 167.7, 162.3, 157.4, 151.6, 149.4, 136.1, 128.2, 119.2, 113.5, 88.6, 59.0, 54.9, 34.8. Anal. Calcd. for $C_{15}H_{12}N_4O_4$: C, 57.69; H, 3.87; N, 17.94. Found: C, 57.58; H, 3.71; N, 17.86.

7-Amino-4-oxo-5-phenyl-2-thioxo-1,3,4,5-tetrahydro-*2H*-pyrano[2,3-d]pyrimidine-6-carbonitrile (4x)

Yellow crystal (yield: 88%, 0.23 g); Mp: >330 °C. IR (KBr): 3070, 2889, 2192, 1647, 1596, 1558, 1454, 1400, 1299, 1191, 1014, 991, 891, 794, 532 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 10.33 (s, 2H, NH), 7.22-7.27 (m, 2H), 7.12-7.15 (m, 3H), 6.97-6.99 (m, 2H), 3.96(s, 1H, CH). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 174.1, 173.2, 163.7, 162.5, 140.3, 130.3, 127.0, 124.6, 120.6, 79.1, 60.7, 34.0. Anal. Calcd for $C_{14}H_{10}N_4O_2S$: C, 56.37; H, 3.38; N, 18.78. Found: C, 56.29; H, 3.31; N, 18.64.

2-Amino-5-benzoyl-4-(4-cyanophenyl)-6-phenyl-*4H*-pyran-3-carbonitrile (4y)

Yellow crystal (yield: 90%, 0.34 g); Mp: 270-272°C. IR (KBr): 3328, 3190, 2866, 2198, 1685, 1647, 1604, 1577, 1496, 1446, 1415, 1326, 1261, 1222, 1149, 1114, 1029, 902, 852, 810, 767, 698 cm^{-1}. ^{1}H-NMR (250 MHz, DMSO-d_6/TMS) δ (ppm): 7.44-7.54 (m, 7H), 7.27-7.29 (m, 2H), 7.13-7.20 (m, 6H), 6.81 (s, 1H), 4.67 (s, 1H, CH). ^{13}C-NMR (62.5 MHz, DMSO-d_6/TMS) δ (ppm): 194.8, 159.7, 151.5, 149.0, 136.5, 132.7, 132.5, 131.8, 128.8, 128.6, 128.5, 128.1, 128.0, 127.7, 119.4, 109.8, 55.7, 41.3. Anal. Calcd. for $C_{26}H_{17}N_3O_2$: C, 77.41; H, 4.25; N, 10.42. Found: C, 77.34; H, 4.48; N, 10.32.

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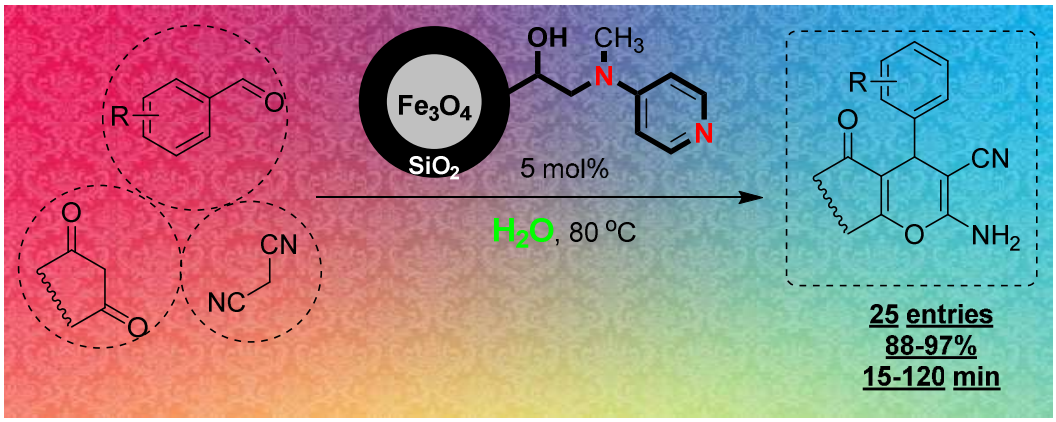

A new DMAP-based magnetic nano-organocatalyst was developed for efficient one-pot synthesis of 2-amino-*4H*-chromene-3-carbonitrile derivatives in water as a green solvent.