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Catalytic synthesis of coumarin-linked nicotinonitrile derivatives via a cooperative vinylogous anomeric-based oxidation

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Abstract

In the presented study, we developed a new and efficient strategy for the synthesis of coumarin-linked nicotinonitrile derivatives via a cooperative vinylogous anomeric-based oxidation mechanism. Target compounds were prepared through a four component reaction between aldehyde derivatives, 2-acetyl-3*H*-benzo[*f*]chromen-3-one or 3-acetylcoumarin, malononitrile or ethyl cyanoacetate and ammonium acetate, in the presence a catalytic amount of Fe_3O_4@SiO_2@$(CH_2)_3$-urea-benzimidazole with sulfonic acid tags as a recoverable nanomagnetic catalyst. All reactions proceed smoothly with good to high yields under solvent free conditions.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s11164-020-04267-9) contains supplementary material, which is available to authorized users.

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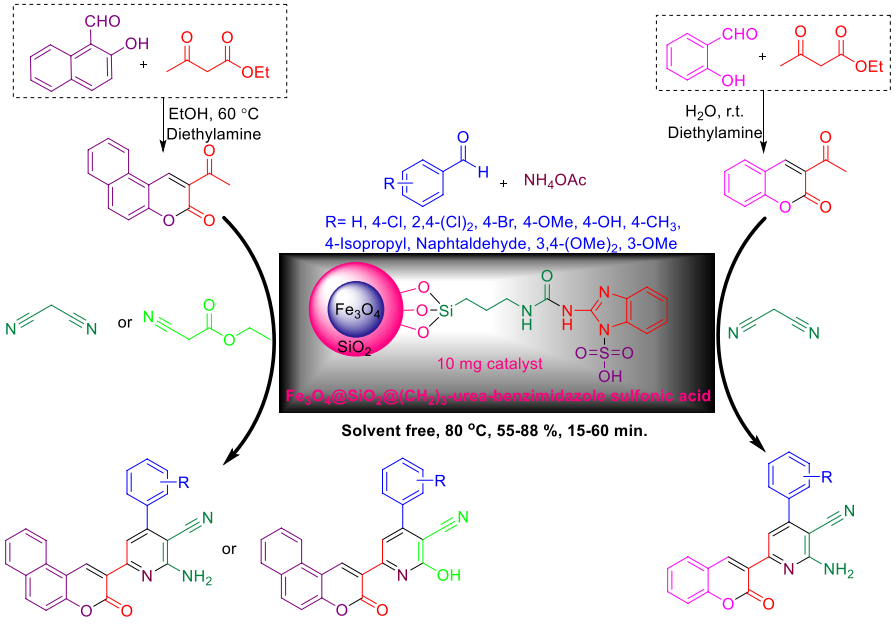
Graphic abstract

Fe3O4@SiO2@(CH2)3-urea-benzimidazole with sulfonic acid tags shows elegant catalytic activity for the preparation of coumarin linked nicotinonitrile derivateives via a cooperative vinylogous anomeric based oxidation mechanism.

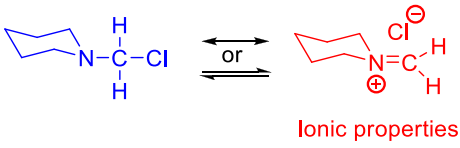


Keywords Coumarin-linked nicotinonitrile · Cooperative vinylogous anomeric-based oxidation · Multi-component reaction · Nanomagnetic catalyst

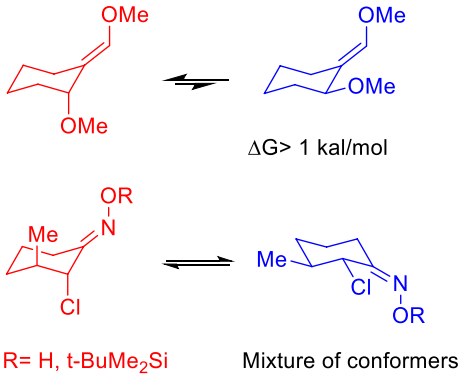
Introduction

Over the last decade, much effort has been made to achieve the concept of "ideal synthesis" by chemists. Through ideal synthesis, the target molecule, prepared via a single step and one pot manner by applying readily available starting materials without any side-product formation (100% yield). Ideal synthesis is an environmentally friendly, resource effective, simple, safe and economically acceptable protocol [1, 2]. In terms of concept, one of the closest methods to "ideal synthesis" is multi-component reactions (MCRs) strategy, which covers several aspects of it [3]. MCRs, as an important class of

Scheme 1 Hidden ionicity in *N*-(chloromethyl)piperidine due to anomeric effect

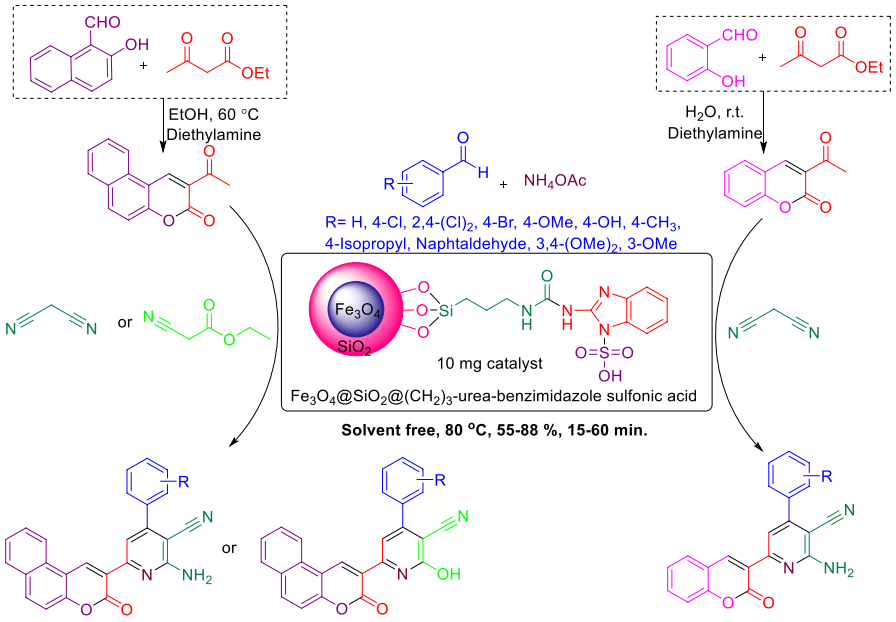


Scheme 2 Vinylogous anomeric effect operates in the exocyclic π-systems



chemical transformations, incorporate three or more starting materials for the synthesis of complex molecule through a low synthetic cost and high atom economy procedure [4]. The concept of MCRs is well reviewed [5–12].

Construction of catalytic systems which displays high activity and selectivity (such as homogeneous catalysts) and possesses the easy separation and reusability (such as heterogeneous catalysts) has become a hot research topic in the domain of modern organic synthesis [13]. By applying magnetic nanoparticles in the preparation of catalytic systems, both of the superior characteristics of homogeneous and heterogeneous catalysts can be simultaneously achieved. Catalytic systems are based on magnetic



Scheme 3 Catalytic synthesis of coumarin-linked nicotinonitrile derivatives in the presence a catalytic amount of $Fe_3O_4@SiO_2@(CH_2)_3$-urea-benzimidazole sulfonic acid

nanoparticles holding various admirable features including high surface area to bulk ratios, easy surface modification, high activity, selectivity, thermal and chemical stability. By these characteristic technics, applying heterogeneous magnetic nanoparticles as catalysts can bring chemists closer to "ideal synthesis" [14–20].

Due to the diverse capabilities of pyridine systems in different chemical domains of applications including natural products, bioactive compounds and market drugs, agrochemicals, material science and catalysis, researchers' interest in these versatile molecules have been extensively intensified [21–25]. On the other hands, coumarin-containing heterocyclic molecules are widespread in natural products and represent varied pharmacological usages such as anti-inflammatory, antioxidant, antitumor and antimicrobial activities. One the shining example of commercially available drugs bearing coumarin moiety is Novobiocin which applied as antimicrobial agent [26–30]. Therefore, it can be expected that the existence of two biological active sites within the structure of a single molecule gives unique pharmaceutical features to that molecule. Despite the unique characteristics of coumarin-linked pyridine systems, a few methods have been reported for their synthesis [31–41]. Therefore, presenting a powerful and efficient method for their preparation is highly desirable.

After the discovery of the concept of anomeric effect, it is widely applied for explanation of several unusual phenomena [42–60]. For example, the hidden ionicity of *N*-(chloromethyl)piperidine can be explained by the anomeric interactions between nitrogen lone pairs with C–Cl anti-bonding orbital ($n_N \rightarrow \sigma^*_{C-Cl}$). In this compound, due to salt-like reactivity, the chlorine atom is quantitatively precipitated by $AgNO_3$ and can be exchanged to a perchlorate anion (Scheme 1) [61].

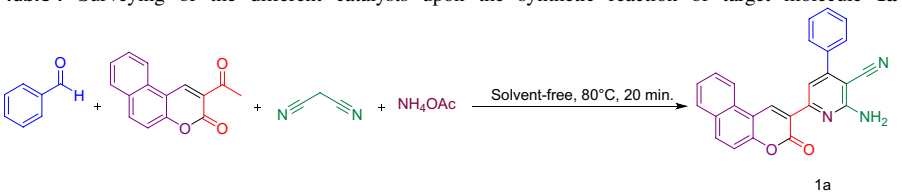
In vinylogous anomeric effect, the anomeric interactions are transmitted through double bonds. For example, vinylogous anomeric effect can operate with exocyclic π-systems such as alkenes and ketoximes (Scheme 2) [44, 62–71].

In this paper, in order to expand the concepts of anomeric-based oxidation and cooperative vinylogous anomeric-based oxidation [72, 73], and reported new protocols for the synthesis of pyridine derivatives [74–78], we investigated the catalytic performance of Fe_3O_4@SiO_2@$(CH_2)_3$-urea-benzimidazole sulfonic acid at the synthesis of coumarin-linked nicotinonitrile derivatives under gentle reaction conditions (Scheme 3).

Results and discussion

Cooperativity of stereoelectronic effects has been observed when more than one donor working together. We have recently introduced "cooperative vinylogous anomeric-based oxidations" based on the use of the vinylogous anomeric effect for the removal of hydride, a major stage which is needed to support the final oxidation/aromatization in the synthesis of susceptible molecules [73]. Since that the development of anomeric-based oxidation (ABO) is our main interest [72], herein the multi-component synthesis of coumarin-linked nicotinonitrile derivatives, which are able to take advantage of the cooperative vinylogous anomeric interactions between nitrogen lone pairs (n_N) and the allylic σ^*_{C-H} orbital ($n_N \rightarrow \sigma^*_{C-H}$) and aromatization of the *N*-hetero cycle ring under acidic conditions, is reported.

Table 1 Surveying of the different catalysts upon the synthetic reaction of target molecule **1a**[a]



1a

Entry	Utilized catalyst	Load of catalyst	Yield (%)[b]
1	Silica sulfuric acid (SSA)	10 mg	82
2	Fe_3O_4	10 mg	42
3	Fe_3O_4@SiO_2	10 mg	40
4	Fe_3O_4@SiO_2@$(CH_2)_3$-urea-benzimidazole	10 mg	63
5	Fe_3O_4@SiO_2@$(CH_2)_3$-urea-benzimidazole sulfonic acid	10 mg	80
6	$FeCl_3$	10 mol%	38
7	$AlCl_3$	10 mol%	36
8	H_2SO_4	10 mol%	62
9	HCl	10 mol%	88
10	NH_2SO_3H	10 mol%	58
11	$Al(HSO_4)_3$	10 mol%	42
13	$Fe(HSO_4)_3$	10 mol%	48
14	$Ca(HSO_4)_2$	10 mol%	46
15	CAN	10 mol%	78
16	$NaHCO_3$	10 mol%	36
17	Oxalic acid	10 mol%	72
18	*p*-Toluenesulfonic acid (PTSA)	10 mol%	85

[a]Reaction condition: benzaldehyde (1 mmol, 0.106 g), malononitrile (1 mmol, 0.066 g), 2-acetyl-3*H*-benzo[*f*]chromen-3-one (1 mmol, 0.238 g) and ammonium acetate (1 mmol, 0.077 g), solvent free, 80 °C, 20 min

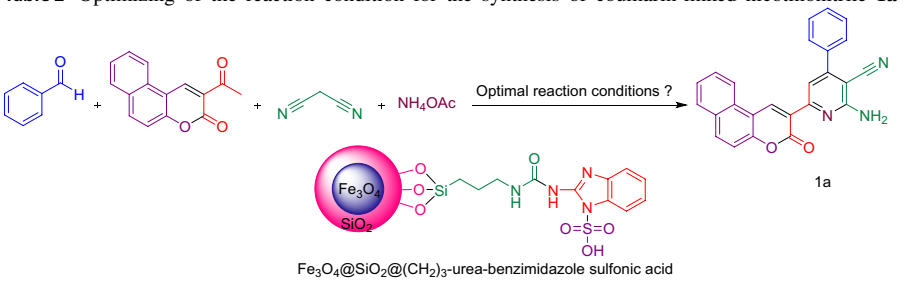
[b]Isolated yields

Application of Fe_3O_4@SiO_2@$(CH_2)_3$-urea-benzimidazole sulfonic acid in the synthesis of coumarin-linked nicotinonitrile derivatives

At first, to find the best catalyst for the synthesis of coumarin-linked nicotinonitrile derivatives, several catalysts were explored upon the reaction of benzaldehyde, 2-acetyl-3*H*-benzo[*f*]chromen-3-one, malononirtile and ammonium acetate as a model reaction under solvent-free conditions at 80 °C at 20 min and the achieved data are embedded in Table 1.

From the obtained experimental data as inserted in Table 1, it can be inferred that in addition to the Fe_3O_4@SiO_2@$(CH_2)_3$-urea-benzimidazole sulfonic acid (entry 5), the model reaction performed well in the presence of SSA (entry 1), HCl (entry 9)

Table 2 Optimizing of the reaction condition for the synthesis of coumarin-linked nicotinonitrile **1a**[a]



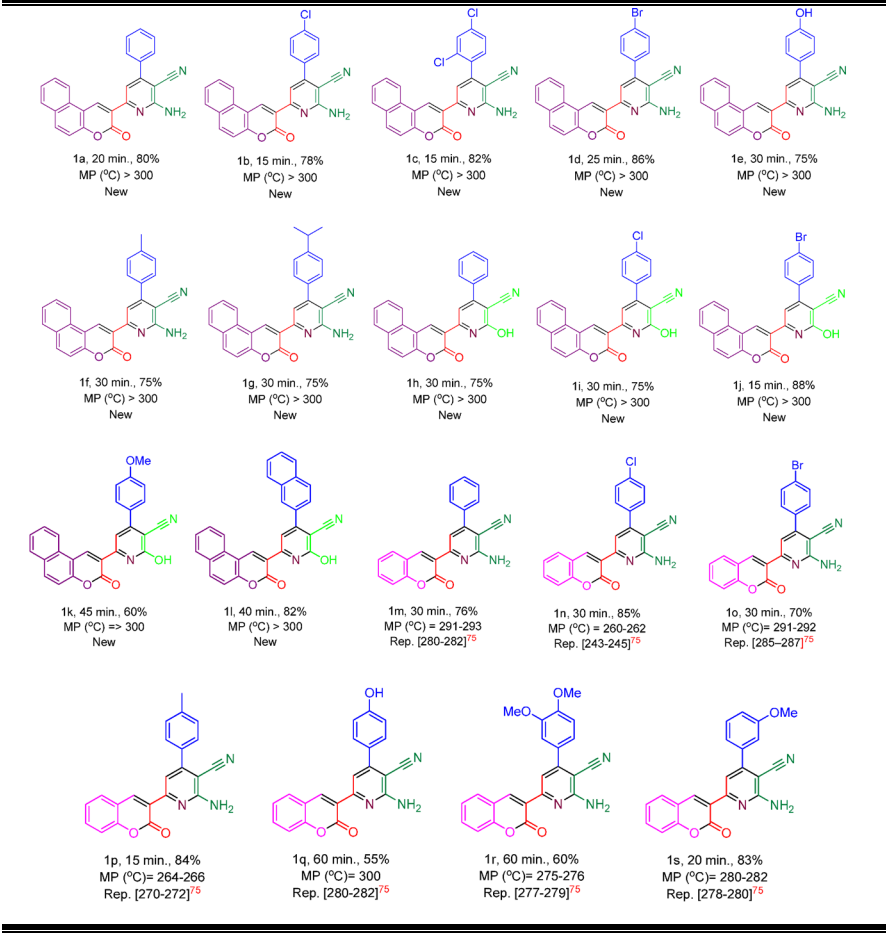
Entry	Solvent	Temperature (°C)	Load of catalyst (mg)	Time (min.)	Yield (%)[b]
1	–	90	10	15	78
2	–	80	20	20	82
3[c]	–	80	10	20	80
4		80	5	30	67
5	–	80	–	20	35
6	–	80	–	120	60
7	–	70	10	20	70
8	–	60	10	35	62
9	–	r.t.	10	20	Trace
10	–	r.t.	10	120	30
11	H_2O	Reflux	10	120	-
12	EtOH	Reflux	10	120	65
13	*n*-Hexane	Reflux	10	240	61
14	EtOAc	Reflux	10	120	78
15	CH_2Cl_2	Reflux	10	240	–
16	PEG	120	10	240	83

[a]Reaction condition: benzaldehyde (1 mmol, 0.106 g), malononitrile (1 mmol, 0.066 g), 2-acetyl-3*H*-benzo[*f*]chromen-3-one (1 mmol, 0.238 g) and ammonium acetate (1 mmol, 0.077 g), [b]Isolated yields, [c]Data for the model reaction under air, nitrogen and argon atmosphere are similar

and PTSA (entry 18) and shows comparative results. But from the recovering and reusing viewpoint, the Fe_3O_4@SiO_2@$(CH_2)_3$-urea-benzimidazole sulfonic acid is the best choice.

In the next step, for evaluation the optimal operational reaction conditions, we tested the model reaction in the presence of different amounts of Fe_3O_4@SiO_2@$(CH_2)_3$-urea-benzimidazole sulfonic acid, varied solvents and also solvent free conditions under various operational temperatures. Afterward, by collecting and investigating the resulting data as summarized in Table 2, we found that solvent-free conditions, 80 °C and using 10 mg of Fe_3O_4@SiO_2@$(CH_2)_3$-urea-benzimidazole sulfonic acid, provide the best results for the model reaction (Table 2, Entry 3).

Table 3 Catalytic synthesis of coumarin-linked nicotinonitrile derivatives under mild reaction conditions[a]



[a]Reaction condition: aryl aldehyde (1 mmol), malononitrile or ethyl cyanoacetate (1 mmol), 2-acetyl-3*H*-benzo[*f*]chromen-3-one or 3-acetylcoumarin (1 mmol) and ammonium acetate (1 mmol, 0.077 g), solvent free, 80 °C, catalyst = 10 mg, reported yields are referred to isolated yields

In the next step, in another set of reactions, by the optimal reaction parameters in hands, this multi-component reaction pathway, applied for the synthesis of coumarin-linked nicotinonitriles. In this step, the scope and generality of the reaction expanded by applying different arylaldehydes, 2-acetyl-3*H*-benzo[*f*]chromen-3-one or 3-acetylcoumarin, malononitrile or ethyl cyanoacetate and ammonium acetate. The obtained data as inserted in Table 3 show that the presented protocol is a powerful and efficient method for the synthesis of varied coumarin-linked nicotinonitrile derivatives.

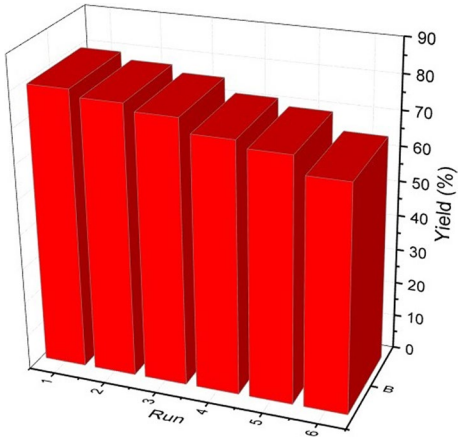
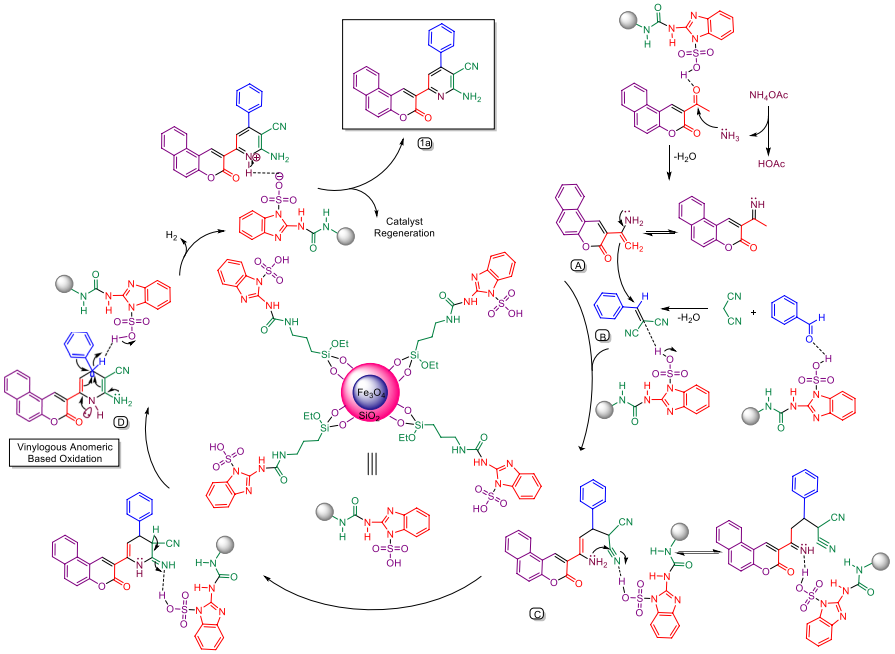


Fig. 1 The reusing test of the described nanomagnetic catalyst



Scheme 4 Plausible mechanistic process for the synthesis of target molecule **1a** via a cooperative vinylogous anomeric-based oxidation

Recovery and reusing test

The reusability is one of the valuable advantages of any catalytic systems. In a separate study, the recyclability of $Fe_3O_4@SiO_2@(CH_2)_3$-urea-benzimidazole sulfonic acid was also investigated upon the condensation reaction between

benzaldehyde, malononitrile, 2-acetyl-3*H*-benzo[*f*]chromen-3-one and ammonium acetate in 20 min. After completion of each run, hot $CHCl_3$ was added to the reaction mixture. The desired product and unreacted starting materials dissolve in hot $CHCl_3$, but the nanomagnetic catalyst is not soluble. Afterward, using an external magnet, the nanomagnetic catalyst was separated from the reaction mixture and thoroughly washed with $CHCl_3$ and preserved for the next run. The reuse test was successful over five continuous runs with only a marginal decreasing in its catalytic activity (Fig. 1).

In a suggested plausible reaction mechanism as portrayed in the Scheme 4, in the presence of $Fe_3O_4@SiO_2@(CH_2)_3$-urea-benzimidazole sulfonic acid, the enamine intermediate A (generated from the reaction of ammonium acetate and related methylketone), attacked as a nucleophile to Knoevenagel intermediate B which is converted to the intermediate C. In the next step, through intramolecular nucleophilic attack, intermediate C converted to intermediate D. In the last step, via a cooperative vinylogous anomeric-based oxidation ($n_N \rightarrow \sigma^*_{C-H}$) (CVABO) pathway, target molecule **1a** is produced.

Conclusions

In summary, the catalytic application of $Fe_3O_4@SiO_2@(CH_2)_3$-urea-benzimidazole sulfonic acid as a recoverable nanomagnetic catalyst was investigated in the construction of coumarin-linked nicotinonitrile derivatives through a four component reaction between aldehyde derivatives, 2-acetyl-3*H*-benzo[*f*]chromen-3-one or 3-acetylcoumarin, malononitrile or ethyl cyanoacetate and ammonium acetate under mild and solvent-free reaction conditions with good to high yields. The final step of the mechanistic route for the synthesis of target molecules has proceeded via a cooperative vinylogous anomeric-based oxidation mechanism. In an extension of the classic anomeric effect, this research presented vinyl heteroatoms are able to donate electron density from their lone pairs into the accepting σ^* orbital through an intervening π orbitals. Also, the applied nanomagnetic catalyst has excellent reusability in the investigated multi-component reactions.

Experimental

The commercially available chemicals were obtained from Sigma-Aldrich and Merck chemical companies and used as received without further purification. The reaction progress and purity of the prepared structures were monitored by TLC performed with silica gel SIL G/UV 254 plates. FT-IR spectra were recorded on a PerkinElmer Spectrum Version 10.02.00 using KBr pellets. The ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Bruker spectrometer (δ in ppm) using DMSO-d_6 as solvent with chemical shifts measured relative to $Si(CH_3)_4$ as internal standard. Melting points were determined with a Buchi B-545 melting point apparatus in open capillary tubes.

General procedure for construction of Fe_3O_4@SiO_2@$(CH_2)_3$-urea-benzimidazole sulfonic acid

The reusable biological urea-based nanomagnetic catalyst namely Fe_3O_4@SiO_2@$(CH_2)_3$-urea-benzimidazole sulfonic acid was prepared based on our recently reported protocol [76].

General procedure for the synthesis of 2-acetyl-3*H*-benzo[*f*]chromen-3-one

In a round bottom flask, a mixture of 2-hydroxy-1-naphtaldehyde (20 mmol, 3.4 g) and ethyl acetoacetate (20 mmol, 2.6 g) and dimethylamine (0.5 mL) in 10 mL EtOH was stirred at 60 °C for 12 h. After that, the yellow precipitate filtered off and washed with ethanol to obtain pure product.

General procedure for the synthesis of 3-acetylcoumarin

According to the previously reported procedures [35, 38–41, 75], a mixture of 2-hydroxy benzaldehyde (20 mmol, 2.4 g), ethyl acetoacetate (20 mmol, 2.6 g) and dimethylamine (0.5 mL) in 10 mL distilled water was stirred at room temperature until a yellow precipitate was formed. After that, the precipitate filtered off, washed several times with ethanol to give pure 3-acetylcoumarin.

General procedure for the synthesis of coumarin-linked nicotinonitrile derivatives

To a mixture of aromatic aldehydes (1 mmol), 2-acetyl-3*H*-benzo[*f*]chromen-3-one (1 mmol, 0.238 g) or 3-acetylcoumarin (1 mmol, 0.188 g), malononitrile (1 mmol, 0.066 g) or ethyl cyanoacetate (1 mmol, 0.113 g) and ammonium acetate (1.5 mmol, 0.116 g), 10 mg of Fe_3O_4@SiO_2@$(CH_2)_3$-urea-benzimidazole sulfonic acid were added as a catalyst. The obtained reaction mixture was stirred under solvent-free conditions at 80 °C according to the appropriate times (Table 3). The reaction progress was monitored by TLC using *n*-hexane: EtOAc (1:1) as eluent. After the reaction was completed, in order to separate the catalyst, hot $CHCl_3$ was added to the reaction mixture and the desired products and unreacted starting materials were dissolved. Afterward, undissolved nanomagnetic catalyst was easily separated from the reaction mixture by utilizing an external magnet, washed with $CHCl_3$ and recovered for subsequent reaction. After evaporation of solvent, the crude solid was obtained by adding methanol and finally was purified using CH_2Cl_2. The desired products were obtained in good to excellent isolated yields as presented in Table 3.

Selected spectral data

2-Acetyl-3*H*-benzo[*f*]chromen-3-one

M.p. = 184–186 °C, FT-IR (KBr, ν, cm^{-1}): 3065, 2932, 1734, 1674, 1557, 1221, 1207.

^{1}H NMR (301 MHz, DMSO-d_6) δ_{ppm}: 9.28(s, 1H, Chromene ring), 8.63 (d, 1H, J = 9 Hz, Aromatic), 8.34 (d, 1H, J = 9 Hz, Aromatic), 8.10 (d, 1H, J = 9 Hz, Aromatic), 7.83–7.77(m, 1H, Aromatic), 7.71–7.65 (m, 1H, Aromatic), 7.64 (d, 1H, J = 9 Hz, Aromatic), 2.67 (S, 3H, Me).

^{13}C NMR (76 MHz, DMSO-d_6) δ_{ppm}: 195.6, 158.9, 155.8, 142.9, 136.7, 130.4, 129.9, 129.6, 127.0, 123.6, 122.8, 116.9, 112.8.

2-Amino-6-(3-oxo-3*H*-benzo[*f*]chromen-2-yl)-4-phenylnicotinonitrile (1a)

M.p. > 300 °C, FT-IR (KBr, ν, cm^{-1}): 3498, 3376, 2213, 1727, 1623, 1568, 1214.

^{1}H NMR (301 MHz, DMSO-d_6) δ_{ppm}: 9.72 (s, 1H, Chromene ring), 8.57 (d, 1H, J = 6 Hz, Aromatic), 8.31 (d, 1H, J = 6 Hz, Aromatic), 8.13 (d, 1H, J = 6 Hz, Aromatic), 7.85–7.80 (m, 2H, Aromatic), 7.66–7.61 (m, 7H, Aromatic and Pyridine ring), 7.17 (br, 2H, NH_2).

^{13}C NMR (76 MHz, DMSO-d_6) δ_{ppm}: 160.7, 159.5, 155.4, 154.3, 153.7, 140.0, 137.5, 135.2, 130.5, 130.2, 129.7, 129.5, 129.4, 129.3, 129.1, 128.6, 126.9, 122.6, 122.3, 117.2, 116.9, 113.5, 112.8, 88.6.

MS (EI, 70 eV), m/z (%): 389.

2-Amino-4-(4-chlorophenyl)-6-(3-oxo-3*H*-benzo[*f*]chromen-2-yl)nicotinonitrile (1b)

M.p. > 300 °C, FT-IR (KBr, ν, cm^{-1}): 3490, 3350, 3056, 2208, 1724, 1609, 1567, 1209.

^{1}H NMR (301 MHz, DMSO-d_6) δ_{ppm}: 9.72 (s, 1H, Chromene ring), 8.56 (br, 1H, Aromatic), 8.31 (br, 1H, Aromatic), 8.14 (br, 1H, Aromatic), 7.86–7.68 (m, 8H, Aromatic and Pyridine ring), 7.25 (br, 2H, NH_2).

^{13}C NMR (76 MHz, DMSO-d_6) δ_{ppm}: 160.6, 159.5, 154.3, 154.0, 153.8, 140.0, 136.2, 135.2, 135.1, 130.5, 130.5, 129.7, 129.5, 129.2, 126.9, 122.4, 122.3, 119.0, 117.0, 116.9, 113.4, 112.5, 88.4.

MS (EI, 70 eV), m/z (%): 423.

2-Amino-4-(2,4-dichlorophenyl)-6-(3-oxo-3*H*-benzo[*f*]chromen-2-yl) nicotinonitrile (1c)

M.p. > 300 °C, FT-IR (KBr, ν, cm^{-1}): 3473, 3354, 3061, 2210, 1722, 1628, 1570, 1553, 1517, 1277.

^{1}H NMR (301 MHz, DMSO-d_6) δ_{ppm}: 9.72 (s, 1H, Chromene ring), 8.55 (d, 1H, J = 9 Hz, Aromatic), 8.30 (d, 1H, J = 9 Hz, Aromatic), 8.12 (d, 1H, J = 9 Hz,

Aromatic), 7.89 (br, 1H, Aromatic), 7.89 (br, 1H, Aromatic), 7.71–7.56 (m, 5H, Aromatic and Pyridine ring), 7.30 (br, 2H, NH_2).

^{13}C NMR (76 MHz, DMSO-d_6) δ_{ppm}: 160.0, 159.4, 154.4, 153.8, 152.4, 140.2, 135.5, 135.4, 135.3, 132.9, 132.3, 130.5, 129.9, 129.7, 129.5, 129.3, 128.4, 126.89, 122.3, 122.2, 116.9, 116.2, 113.5, 112.9, 90.2.

MS (EI, 70 eV), m/z (%): 458.

2-Amino-4-(4-bromophenyl)-6-(3-oxo-3*H*-benzo[*f*]chromen-2-yl)nicotinonitrile (1d)

M.p. > 300 °C, FT-IR (KBr, ν, cm^{-1}): 3486, 3387, 3064, 2926, 2212, 1728, 1626, 1564, 1218, 819.

^{1}H NMR (301 MHz, DMSO-d_6) δ_{ppm}: 9.68 (s, 1H, Chromene ring), 8.53 (d, 1H, J = 9 Hz, Aromatic), 8.28 (d, 1H, J = 6 Hz, Aromatic), 8.10 (d, 1H, J = 6 Hz, Aromatic), 7.82–7.79 (m, 2H, Aromatic), 7.76 (s, 1H, Pyridine ring), 7.70–7.63 (m, 3H, Aromatic), 77.59 (d, 2H, J = 9 Hz, Aromatic), 7.20 (br, 2H, NH_2).

^{13}C NMR (76 MHz, DMSO-d_6) δ_{ppm}: 158.9, 154.1, 153.9, 149.1, 144.6, 141.1, 137.0, 135.0, 132.4, 132.3, 131.2, 130.8, 130.5, 129.5, 129.1, 126.9, 124.4, 123.7, 123.1, 119.9, 117.0, 116.2, 113.4, 112.5, 96.4, 95.4, 79.9.

MS (EI, 70 eV), m/z (%): 468.

2-Amino-4-(4-hydroxyphenyl)-6-(3-oxo-3*H*-benzo[*f*]chromen-2-yl)nicotinonitrile (1e)

M.p. > 300 °C, FT-IR (KBr, ν, cm^{-1}): 3496, 3380, 2955, 2210, 1731, 1612, 1567.

^{1}H NMR (301 MHz, DMSO-d_6) δ_{ppm}: 10.03 (s, 1H, OH), 9.65 (s, 1H, Chromene ring), 8.51 (d, 1H, J = 6 Hz, Aromatic), 8.26 (d, 1H, J = 9 Hz, Aromatic), 8.08 (d, 1H, J = 9 Hz, Aromatic), 7.84–7.79 (m, 1H, Aromatic), 7.75 (s, 1H, Pyridine ring), 7.68–7.61 (m, 2H, Aromatic), 7.51 (d, 2H, J = 9 Hz, Aromatic), 7.03 (br, 2H, NH_2), 6.97 (d, 2H, J = 9 Hz, Aromatic).

^{13}C NMR (76 MHz, DMSO-d_6) δ_{ppm}: 160.8, 159.5, 155.2, 154.2, 153.3, 139.8, 135.1, 130.5, 130.4, 130.2, 129.6, 129.5, 129.2, 127.9, 126.8, 122.7, 122.3, 117.6, 116.9, 116.2, 113.5, 112.5, 88.1.

MS (EI, 70 eV), m/z (%): 405.

2-Amino-6-(3-oxo-3*H*-benzo[*f*]chromen-2-yl)-4-*p*-tolylnicotinonitrile (1f)

M.p. > 300 °C, FT-IR (KBr, ν, cm^{-1}): 3494, 3354, 3056, 2923, 2219, 1738, 1628, 1567, 1211, 818.

^{1}H NMR (301 MHz, DMSO-d_6) δ_{ppm}: 9.64 (s, 1H, Chromene ring), 8.50 (d, 1H, J = 9 Hz, Aromatic), 8.25 (d, 1H, J = 9 Hz, Aromatic), 8.06 (d, 1H, J = 6 Hz, Aromatic), 7.81 (t, 1H, J = 6 Hz, Aromatic), 7.75 (s, 1H, Pyridine ring), 7.67–7.59 (m, 2H, Aromatic), 7.52 (d, 2H, J = 6Hz, Aromatic), 7.39 (d, 2H, J = 9 Hz Aromatic), 7.10 (br, 2H, NH_2), 2.41 (s, 3H, CH_3).

^{13}C NMR (76 MHz, DMSO-d_6) δ_{ppm}: 160.7, 159.4, 155.2, 154.2, 153.4, 140.0, 139.8, 135.1, 134.5, 130.4, 129.9, 129.6, 129.4, 129.2, 128.5, 126.8, 122.4, 122.2, 117.3, 116.9, 113.4, 112.6, 88.4, 21.4.

MS (EI, 70 eV), m/z (%): 403.

2-Amino-4-(4-isopropylphenyl)-6-(3-oxo-3*H*-benzo[*f*]chromen-2-yl)nicotinonitrile (1g)

M.p. > 300 °C, FT-IR (KBr, ν, cm^{-1}): 3498, 3360, 3064, 2961, 2216, 1731, 1618, 1568.

^{1}H NMR (301 MHz, DMSO-d_6) δ_{ppm}: 9.72 (s, 1H, Chromene ring), 8.57 (d, 1H, J = 6 Hz, Aromatic), 8.33–8.30 (m, 1H, Aromatic), 8.13 (d, 1H, J = 6 Hz, Aromatic), 7.88–7.83 (m, 1H, Aromatic), 7.80 (s, 1H, Pyridine ring), 7.72–7.66 (m, 2H, Aromatic), 7.60 (d, 2H, J = 6 Hz, Aromatic), 7.48 (d, 2H, J = 6 Hz, Aromatic), 7.14 (br, 2H, NH_2), 3.02 (septet, 1H, J = 6 Hz, CH). 1.31 (d, 6H, J = 3 Hz, CH_3).

^{13}C NMR (76 MHz, DMSO-d_6) δ_{ppm}: 160.7, 159.5, 155.2, 154.3, 153.5, 150.7, 139.9, 135.1, 134.9, 130.5, 129.7, 129.5, 129.2, 128.6, 127.4, 126.9, 122.5, 122.3, 117.4, 116.9, 113.4, 112.8, 88.4, 33.8, 24.2.

MS (EI, 70 eV), m/z (%): 431.

2-Hydroxy-6-(3-oxo-3*H*-benzo[*f*]chromen-2-yl)-4-phenylnicotinonitrile (1h)

M.p. > 300 °C, FT-IR (KBr, ν, cm^{-1}): 3415, 3054, 2228, 1725, 1651, 1605, 1582.

^{1}H NMR (400 MHz, DMSO-d_6) δ_{ppm}: 12.75 (br, 1H, OH), 9.51 (s, 1H, Chromene ring), 8.75 (br, 1H, Aromatic), 8.37 (br, 1H, Aromatic), 8.17 (br, 1H, Aromatic), 7.82–7.27 (m, 9H, Aromatic and Pyridine ring).

MS (EI, 70 eV), m/z (%): 309.

4-(4-Chlorophenyl)-2-hydroxy-6-(3-oxo-3*H*-benzo[*f*]chromen-2-yl)nicotinonitrile (1i)

M.p. > 300 °C, FT-IR (KBr, ν, cm^{-1}): 3429, 3055, 2922, 2854, 2229, 1738, 1648, 1561, 815.

^{1}H NMR (400 MHz, DMSO-d_6) δ_{ppm}: 12.85 (br, 1H, OH), 9.50 (s, 1H, Chromene ring), 8.73 (br, 1H, Aromatic), 8.37 (br, 1H, Aromatic), 8.15 (br, 1H, Aromatic), 7.79–7.72 (m, 7H, Aromatic and Pyridine ring), 7.27 (br, 1H, Aromatic).

^{13}C NMR (76 MHz, DMSO-d_6) δ_{ppm}: 161.5, 158.7, 154.5, 154.4, 146.5, 141.5, 136.1, 136.0, 136, 135.2, 130.6, 130.5, 129.6, 129.5, 129.3, 127.1, 123.3, 118.3, 116.9, 116.5, 113.3, 108.8, 101.8.

MS (EI, 70 eV), m/z (%): 424.

4-(4-Bromophenyl)-2-hydroxy-6-(3-oxo-3*H*-benzo[*f*]chromen-2-yl)nicotinonitrile (1j)

M.p. > 300 °C, FT-IR (KBr, ν, cm^{-1}): 3454, 3061, 2955, 2208, 1727, 1605, 1568.

^{1}H NMR (301 MHz, DMSO-d_6) δ_{ppm}: 12.75 (br, 1H, OH), 9.50 (s, 1H, Chromene ring), 8.75 (d, 1H, $J=9$ Hz, Aromatic), 8.37 (d, 1H, $J=9$ Hz, Aromatic), 8.15 (d, 1H, $J=9$ Hz, Aromatic), 7.87–7.85 (m, 3H, Aromatic), 7.74–7.69 (m, 4H, Aromatic and Pyridine ring), 7.27 (br, 1H, Aromatic).

MS (EI, 70 eV), m/z (%): 469.

2-Hydroxy-4-(4-methoxyphenyl)-6-(3-oxo-3*H*-benzo[*f*]chromen-2-yl) nicotinonitrile (1k)

M.p. > 300 °C, FT-IR (KBr, ν, cm^{-1}): 3317, 3145, 3053, 2229, 1735, 1647, 1560, 1096, 821.

^{1}H NMR (301 MHz, DMSO-d_6) δ_{ppm}: 12.05 (s, 1H, OH), 9.48 (s, 1H, Chromene ring), 8.75 (d, 1H, $J=9$ Hz, Aromatic), 8.36 (d, 1H, $J=9$ Hz, Aromatic), 8.14 (d, 1H, $J=9$ Hz, Aromatic), 7.84–7.68 (m, 5H, Aromatic and Pyridine ring), 7.25–7.17 (m, 3H, Aromatic), 3.88 (s, 3H, OCH_3).

^{13}C NMR (76 MHz, DMSO-d_6) δ_{ppm}: 161.7, 159.6, 158.7, 154.3, 145.8, 141.3, 136.0, 130.5, 130.4, 129.6, 129.5, 129.3, 128.4, 127.1, 123.3, 118.4, 117.1, 116.9, 114.9, 113.3, 108.7, 108.0, 99.4, 56.0.

MS (EI, 70 eV), m/z (%): 420.

2-Hydroxy-4-(naphthalen-2-yl)-6-(3-oxo-3*H*-benzo[*f*]chromen-2-yl)nicotinonitrile (1l)

M.p. > 300 °C, FT-IR (KBr, ν, cm^{-1}): 3320, 3058, 2211, 1729, 1715, 1562, 1030, 816.

^{1}H NMR (301 MHz, DMSO-d_6) δ_{ppm}: 12.70 (br, 1H, OH), 9.53 (s, 1H, Chromene ring), 8.76 (d, 1H, $J=6$ Hz Aromatic), 8.39–8.36 (m, 2H, Aromatic, 8.19–8.06 (m, 4H, Aromatic), 7.87–7.82(m, 2H, Aromatic), 7.73–7.65 (m, 4H, Aromatic and Pyridine ring), 7.40 (br, 1H, Aromatic).

MS (EI, 70 eV), m/z (%): 440.

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