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An eco-friendly catalytic route for one-pot synthesis of 2-amino-6-(2-oxo-2*H*chromen-3-yl)-4-arylnicotinonitrile derivatives by silica-supported perchloric acid ($HClO_4$–SiO_2) under solvent-free conditions

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Abstract A facile and environmentally benign synthesis of some 2-amino-6-(2-oxo-2*H*-chromen-3-yl)-4-arylnicotinonitrile derivatives from the reaction of 3-acetylcoumarin, aromatic aldehydes, and malononitrile under solvent-free condition in the presence of silica-supported perchloric acid ($HClO_4$–SiO_2) is described. The ability to reuse the catalyst, the high yields, and ease of purification are the important features of this process.

Keywords 2-amino-6-(2-oxo-2*H*-chromen-3-yl)-4-arylnicotinonitrile · Coumarin · $HClO_4$–SiO_2 · Solid support reagent · 3-acetylcoumarin

Introduction

Over the years, coumarin (2-oxo-2*H*-chromene) derivatives have been established as well-known naturally occurring oxygen-heterocyclic compounds isolated from various plants which occupy a special role in nature [1]. The plant extracts containing coumarin-related heterocycles are employed as herbal remedies in traditional systems of medicine. They belong to the flavonoid class of plant secondary metabolites. Coumarin derivatives constitute an important class of heterocyclic compounds that have attracted significant attention in recent years [2, 3]. They have attracted intense interest because of their diverse pharmacological

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properties like anti-HIV [4], anticoagulant [5], antibacterial [6], antioxidant [7], dyslipidemic [8], and anticancer agents [9], and antimicrobial activity [10].

In view of the pharmaceutical importance of heterocyclic compounds, various methods have been developed for the synthesis of coumarin scaffolds [11, 12]. Of these, the three-component coupling of 3-acetylcoumarin, an aromatic aldehyde, and ammonium acetate is of great interest and was done by using acetic acid under microwave irradiation [13, 14]. Although these procedures have some advantages such as good yields, in the field of modern organic chemistry the discovery of new synthetic methodologies to facilitate the preparation of organic compounds is a demand point of research activity. Thus, the development of efficient synthetic methods for coumarins of this type has become important in synthetic and medicinal chemistry.

Therefore, considering the above and as a part of our ongoing programmed synthesis of biologically active heterocyclic molecules [15–19], an efficient and convenient synthesis of 2-amino-6-(2-oxo-2*H*-chromen-3-yl)-4-arylnicotinonitrile derivatives has been accomplished by the multi-component reaction of 3-acetylcoumarin, aromatic aldehydes, and malononitrile using silica-supported perchloric acid ($HClO_4$–SiO_2) [20] as an efficient catalyst in good yields under solvent-free condition (Scheme 1).

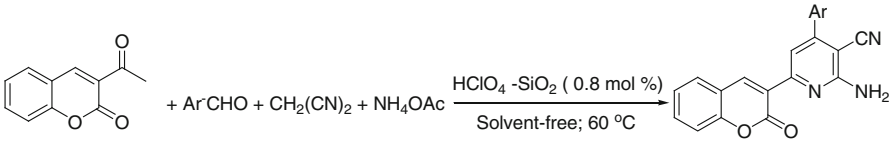
Results and discussion

3-Acetylcoumarin was synthesized by the reaction of salicylaldehyde with ethyl acetoacetate in the presence of a catalytic amount of piperidine [21] (Scheme 2) to undergo a condensation reaction with substituted benzaldehdyes, malononitrile, and ammonium acetate to afford 2-amino-6-(2-oxo-2*H*-chromen-3-yl)-4-phenylnicotinonitrile derivatives.

To find out the suitable conditions for the reaction, a series of experiments were performed with the standard reaction of 3-acetylcoumarin, benzaldehyde, malononitrile, and ammonium acetate as a model reaction.

Effect of catalyst

Initially, a systematic study was carried out for catalytic evaluation of $HClO_4$–SiO_2 for the preparation of 2-amino-6-(2-oxo-2*H*-chromen-3-yl)-4-phenylpyridine-3-carbonitrile at a temperature of 60 °C (Table 1). Our studies showed that when



4a - 4l

Scheme 1 Synthesis of various 2-amino-6-(2-oxo-2*H*-chromen-3-yl)-4-arylnicotinonitrile derivatives

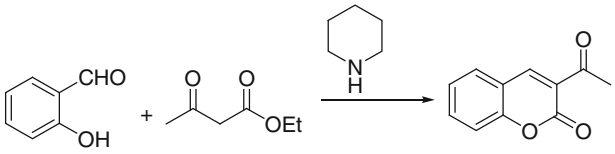
less than 0.8 mol% of $HClO_4$–SiO_2 was applied, lower yields of the corresponding product (Table 1, Entries 2–4) resulted, whereas use of 0.8 mol% $HClO_4$–SiO_2 gives excellent results in terms of yield and time required for completion of the reaction (Table 1, Entry 5). However, use of more than 0.8 mol% of catalyst did not improve the yield (Table 1, Entry 6). In the absence of a catalyst, the product was synthesized in low yield (Table 1, Entry 1).

Effect of temperature

In addition, the effect of temperature on rate of reaction was studied at different temperatures for the preparation of 2-amino-6-(2-oxo-2*H*-chromen-3-yl)-4-phenyl-nicotinonitrile (**4a**) (Table 2). It was observed that the reaction is very slow at room temperature. At 40 °C, the reaction proceeded smoothly and almost complete conversion of product was observed. Further increases in temperature to 50, 60, 70, and 80 °C increased the rate of reaction. However, at 70 and 80 °C, the reaction time reduced and the yield of the product was also reduced. Therefore, we kept the reaction temperature at 60 °C. At this temperature, the reaction is completed within 1.5 h with 92 % yield.

Finally, the optimum conditions selected were: 3-acetylcoumarin (1 mmol), aldehyde (1 mmol), malononitrile (1 mmol), ammonium acetate (1 mmol), $HClO_4$–SiO_2 (0.8 mol%), solvent-free condition and 60 °C as the reaction temperature.

To demonstrate the versatility of the developed protocol, several types of aromatic aldehydes substituted with different groups possessing both electron-



Scheme 2 Preparation of 3-Acetylcoumarin

Table 1 The reaction of 3-acetylcoumarin, benzaldehyde, malononitrile and ammonium acetate: Effect of catalysis

Entry	Catalyst	Amount of catalyst (mol%)	Time (h)	Yield (%)[a]
1	$HClO_4$–SiO_2	0.0	3.0	28
2	$HClO_4$–SiO_2	0.2	3.0	55
3	$HClO_4$–SiO_2	0.4	3.0	69
4	$HClO_4$–SiO_2	0.6	2.0	81
5	$HClO_4$–SiO_2	0.8	1.5	92
6	$HClO_4$–SiO_2	1.0	1.2	84

Reaction conditions: 3-acetylcoumarin (1 mmol), benzaldehyde (1 mmol), malononitrile (1 mmol), and ammonium acetate (2 mmol) under solvent-free condition at 60 °C

[a] Isolated yields

Table 2 Effect of temperature using $HClO_4$–SiO_2 (0.8 mol%)

Entry	Temperature (°C)	Time (h)	Yield (%)[a]
1	RT	4.0	39
2	40	4.0	72
3	50	3.5	82
4	60	1.5	92
5	70	1.2	85
6	80	1.2	80

Reaction conditions: 3-acetylcoumarin (1 mmol), benzaldehyde (1 mmol), malononitrile (1 mmol), and ammonium acetate (2 mmol) in the presence of $HClO_4$–SiO_2 (0.8 mol %) under solvent-free condition

[a] Isolated yields

withdrawing and electron-releasing groups were chosen and results are summarized in Table 3. In all cases, aromatic aldehydes with substituents carrying either electron-donating or electron-withdrawing groups reacted successfully and gave the products in high yields. It was shown that the aromatic aldehydes with electron-withdrawing groups reacted faster than the aromatic aldehydes with electron-releasing groups as would be expected. The structures of isolated products **4a–4l** were deducted by physical and spectroscopic data such as: IR, ^{1}H NMR and ^{13}C NMR spectroscopy, and elemental analysis.

Mechanism

On the basis of all our experimental results, together with a literature report [22], a mechanistic rationale portraying the probable sequence of events is given in Scheme 3. The reaction is believed to proceed through the formation of an enamine. It is suggested that the 3-acetylcoumarin (ketone) is first reacted with ammonium acetate to form enamine (**a**). In a second step, aromatic aldehyde undergoes condensation with malononitrile to form arylidenemalononitrile (**b**). The enamine (**a**) reacts with (**b**) to give intermediate (**c**). The intermediate (**c**) undergoes cyclo-addition, isomerization, and aromatization to afford the final product.

Reusability of the catalyst

The reusability of the catalyst is one of the most important benefits and makes it useful for commercial applications. Thus, the reusability of the catalyst was tested in the synthesis of 2-amino-6-(2-oxo-2*H*-chromen3-yl)-4-phenylnicotinonitrile (**4a**), as shown in Fig. 1 and Table 4. Interestingly, the heterogeneity of $HClO_4$–SiO_2 facilitates efficient recovery from the reaction mixture during the work-up procedure by simple filtration and by washing the catalyst two times with an aliquot of fresh CH_2Cl_2 (2 × 10 mL), then drying to make ready for a later run. The catalyst was tested for four runs. It was seen that the recovered catalyst was

Table 3 Synthesis of various 2-amino-6-(2-oxo-2*H*-chromen-3-yl)-4-phenylnicotinonitrile derivatives in the presence of $HClO_4$–SiO_2

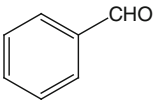
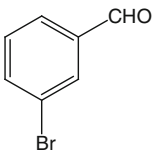
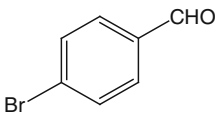
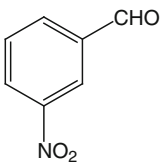
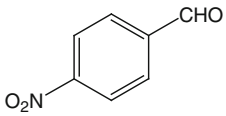
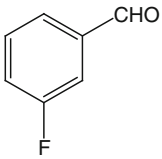
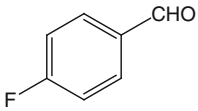
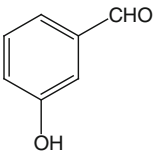
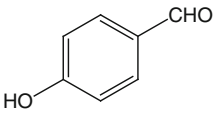
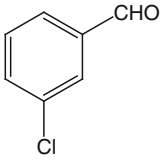
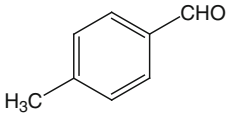
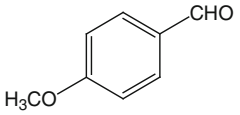
Entry	Aldehyde	Product	Time (h)	Yield (%)[a]	Mp (°C)	
					Found	Reported
1		**4a**	1.5	92	232–234	234–236 [13]
2		**4b**	1.2	95	242–244	–
3		**4c**	1.2	96	224–226	–
4		**4d**	1.5	90	287–289	286–288 [13]
5		**4e**	1.5	93	250–252	252–254 [13]
6		**4f**	1.2	94	248–250	–
7		**4g**	1.2	92	232–234	–
8		**4h**	1.5	90	238–240	–

Table 3 continued

Entry	Aldehyde	Product	Time (h)	Yield (%)[a]	Mp (°C)	
					Found	Reported
9		**4i**	1.5	91	262–264	268–264 [13]
10		**4j**	1.2	96	254–256	–
11		**4k**	2.0	86	270–272	271–273 [13]
12		**4l**	2.0	88	266–268	268–270 [13]

Reaction conditions: 3-Acetylcoumarin (1 mmol), benzaldehyde (1 mmol), malononitrile (1 mmol), and ammonium acetate (2 mmol) in the presence of $HClO_4$–SiO_2 (0.8 mol%) under solvent-free condition

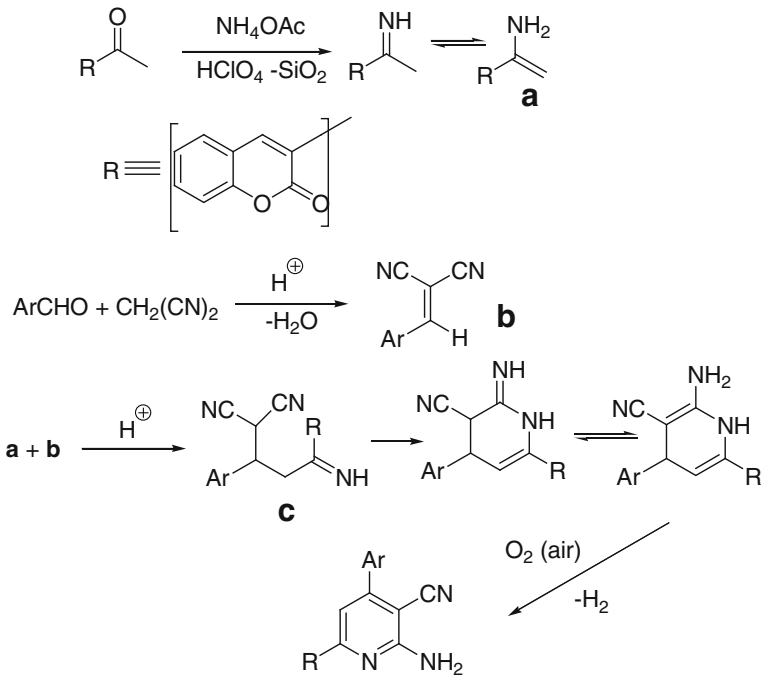
All reactions were carried out at 60 °C

[a] Isolated yields

recycling in subsequent runs without observing significant decreases in activity even after four runs.

Experimental

The general procedure for the synthesis of 2-amino-6-(2-oxo-2*H*-chromen-3-yl)-4-phenylnicotinonitrile derivatives was as follows. In a general experimental procedure, a mixture of the 3-acetylcoumarin (1 mmol), aromatic aldehyde (1 mmol), malononitrile (1 mmol), and ammonium acetate (1 mmol) in the presence of $HClO_4$–SiO_2 (0.8 mol%) were taken into a 50-ml flask equipped with a reflux condenser and heated at 60 °C for the appropriate time (Table 3). After completion of the reaction (TLC monitoring), the reaction mixture was cooled to ambient temperature, CH_2Cl_2 was added, and the $HClO_4$–SiO_2 was filtered off. The filtrate was concentrated to dryness, and the crude solid product was crystallized from EtOH to afford the pure 2-amino-6-(2-oxo-2*H*-chromen-3-yl)-4-phenylnicotinonitrile.



Scheme 3 Proposed mechanism for the synthesis of 2-amino-6-(2-oxo-2*H*-chromen-3-yl)-4-arylnicotinonitrile derivatives

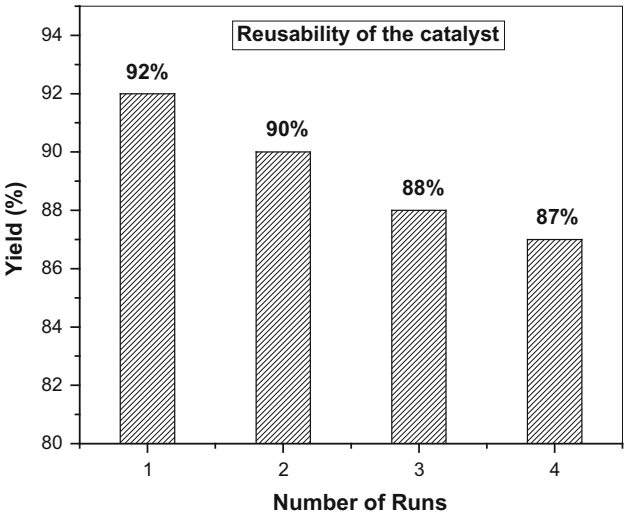


Fig. 1 Reusability of the catalyst $HClO_4$–SiO_2 for the synthesis of 2-amino-6-(2-oxo-2*H*-chromen-3-yl)-4-phenylnicotinonitrile

Table 4 The effect of recyclability of $HClO_4$–SiO_2 (0.8 mol%) catalyst on the product **4a** yield

Entry	Cycle	Time (h)	Yield (%)[a]
1	0	1.5	92
2	1	1.5	90
3	2	1.5	88
4	3	1.5	87

Reaction conditions: 3-acetylcoumarin (1 mmol), benzaldehyde (1 mmol), malononitrile (1 mmol), and ammonium acetate (2 mmol) in the presence of $HClO_4$–SiO_2 (0.8 mol%) under solvent-free condition at 60 °C

[a] Isolated yields

Spectral data for the synthesized compounds

*2-Amino-6-(2-oxo-2H-chromen-3-yl)-4-phenylnicotinonitrile (**4a**)* IR (KBr, cm^{-1}): 3,450 and 3,359 (NH_2), 3,132 (ArH), 2,215 (CN), 1,725 (C=O), 1,612 (C–O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 8.82 (s, 1H, coumarin 4-H), 7.77 (s, 1H, PyrH), 7.88–7.54 (m, 9H, ArH), 7.02 (s, 2H, NH_2);; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 86.4, 114.2, 117.8, 125.1, 125.6, 127.2, 127.6, 128.3, 129.4, 129.9, 130.3, 134.5, 136.1, 142.3, 147.2, 153.0, 158.9, 184.8 ppm; MS(ESI): *m/z* 340 $(M + H)^+$; Anal. Calcd. for $C_{21}H_{13}N_3O_2$: C, 74.34; H, 3.83; N, 12.39 %. Found: C, 74.30; H, 3.80; N, 12.34 %.

*2-Amino-6-(2-oxo-2H-chromen-3-yl)-4-(3-bromophenyl)nicotinonitrile (**4b**)* IR (KBr, cm^{-1}): 3,453 and 3,344 (NH_2), 3,120 (ArH), 2,218 (CN), 1,721 (C=O), 1,622 (C–O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 8.77 (s, 1H, coumarin 4-H), 7.85 (s, 1H, PyrH), 7.77–7.51 (m, 8H, ArH), 7.07 (s, 2H, NH_2) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 85.8, 114.0, 117.4, 125.3, 125.8, 127.4, 127.8, 128.5, 129.5, 129.9, 130.5, 134.3, 136.3, 142.1, 147.5, 152.8, 158.7, 184.5 ppm; MS(ESI): *m/z* 418.9 $(M + H)^+$; Anal. Calcd. for $C_{21}H_{12}BrN_3O_2$: C, 60.30; H, 2.87; N, 10.05 %. Found: C, 60.22; H, 2.85; N, 10.03 %.

*2-Amino-6-(2-oxo-2H-chromen-3-yl)-4-(4-bromophenyl)nicotinonitrile (**4c**)* IR (KBr, cm^{-1}): 3,54 and 3,342 (NH_2), 3,128 (ArH), 2,216 (CN), 1,722 (C=O), 1,615 (C–O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 8.81 (s, 1H, coumarin 4-H), 7.73 (s, 1H, PyrH), 7.78–7.52 (m, 8H, ArH), 7.06 (s, 2H, NH_2) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 86.2, 114.4, 117.5, 125.0, 125.4, 127.4, 127.7, 128.5, 129.6, 129.9, 130.3, 134.7, 136.0, 143.0, 147.4, 153.2, 158.8, 184.5 ppm; MS(ESI): *m/z* 418.90 $(M + H)^+$; Anal. Calcd. for $C_{21}H_{12}BrN_3O_2$: C, 60.30; H, 2.87; N, 10.05 %. Found: C, 60.25; H, 2.80; N, 10.02 %.

*2-Amino-6-(2-oxo-2H-chromen-3-yl)-4-(3-nitrophenyl)nicotinonitrile (**4d**)* IR (KBr, cm^{-1}): 3,453 and 3,388 (NH_2), 3,130 (ArH), 2,208 (CN), 1,718 (C=O), 1,609 (C–O); 3,452, 3,395, 3,130, 2,203, 1,723, 1,606; ^{1}H NMR (500 MHz, DMSO-d_6) δ: 8.80 (s, 1H, coumarin 4-H), 7.88 (s, 1H, PyrH), 7.82–7.40 (m, 8H, ArH), 7.12 (s, 2H, NH_2) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 87.0, 114.0, 117.5, 125.0,

125.5, 127.0, 127.4, 128.0, 129.6, 129.9, 130.1, 134.3, 136.1, 142.0, 147.2, 153.5, 159.4, 186.2 ppm; MS(ESI): *m/z* 385 $(M + H)^+$; Anal. Calcd. for $C_{21}H_{12}N_4O_4$: C, 65.62; H, 3.12; N, 14.58 %. Found: C, 65.52; H, 3.11; N, 14.54 %.

2-Amino-6-(2-oxo-2H-chromen-3-yl)-4-(4-nitrophenyl)nicotinonitrile ***(4e)*** IR (KBr, cm^{-1}): 3,455 and 3,365 (NH_2), 3,127 (ArH), 2,11 (CN), 1,724 (C=O), 1,628 (C–O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 8.78 (s, 1H, coumarin 4-H), 7.75 (s, 1H, PyrH), 7.96–7.58 (m, 8H, ArH), 7.18 (s, 2H, NH_2) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 86.0, 114.0, 117.5, 125.0, 125.5, 127.1, 127.6, 128.3, 129.3, 129.8, 130.1, 134.5, 136.3, 142.1, 146.9, 152.5, 157.9, 186.0 ppm; MS(ESI): *m/z* 385 $(M + H)^+$; Anal. Calcd. for $C_{21}H_{12}N_4O_4$: C, 65.62; H, 3.12; N, 14.58 %. Found: C, 65.55; H, 3.09; N, 14.56 %.

2-Amino-6-(2-oxo-2H-chromen-3-yl)-4-(3-fluorophenyl)nicotinonitrile ***(4f)*** IR (KBr, cm^{-1}): 3,450 and 3,353 (NH_2), 3,133 (ArH), 2,218 (CN), 1,722 (C=O), 1,616 (C–O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 8.78 (s, 1H, coumarin 4-H), 7.71 (s, 1H, PyrH), 7.83–7.54 (m, 8H, ArH), 7.03 (s, 2H, NH_2) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 85.9, 113.9, 118.0, 124.9, 125.6, 127.2, 127.7, 128.6, 129.6, 129.9, 130.6, 134.6, 135.9, 142.4, 147.6, 152.9, 158.7, 185.1 ppm; MS(ESI): *m/z* 358 $(M + H)^+$; Anal. Calcd. for $C_{21}H_{12}FN_3O_2$: C, 70.59; H, 3.36; N, 11.76 %. Found: C, 70.55; H, 3.32; N, 11.72 %.

2-Amino-6-(2-oxo-2H-chromen-3-yl)-4-(4-fluorophenyl)nicotinonitrile ***(4g)*** IR (KBr, cm^{-1}): 3,452 and 3,355 (NH_2), 3,128 (ArH), 2,220 (CN), 1,718 (C=O), 1,622 (C–O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 8.80 (s, 1H, coumarin 4-H), 7.86 (s, 1H, PyrH), 7.75–7.48 (m, 8H, ArH), 7.00 (s, 2H, NH_2) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 86.6, 114.7, 117.7, 125.0, 125.7, 127.4, 127.8, 128.1, 129.3, 129.9, 130.3, 134.2, 136.2, 141.9, 147.0, 152.7, 158.7, 184.5 ppm; MS(ESI): *m/z* 358 $(M + H)^+$;Anal. Calcd. for $C_{21}H_{12}FN_3O_2$: C, 70.59; H, 3.36; N, 11.76 %. Found: C, 70.57; H, 3.29; N, 11.69 %.

2-Amino-6-(2-oxo-2H-chromen-3-yl)-4-(3-hydroxylphenyl)nicotinonitrile ***(4h)*** IR (KBr, cm^{-1}): 3,444 and 3,377 (NH_2), 3,342 (OH), 3,133 (ArH), 2,211 (CN), 1,722 (C=O), 1,611 (C–O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 8.64 (s, 1H, coumarin 4-H), 7.82 (s, 1H, PyrH), 7.89–7.65 (m, 8H, ArH), 7.15 (s, 2H, NH_2), 9.89 (s, 1 H, OH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 85.3, 113.3, 118.2, 125.0, 125.4, 127.1, 127.6, 128.1, 129.4, 130.0, 130.5, 134.5, 136.1, 142.5, 147.0, 153.6, 159.7, 185.8 ppm; MS(ESI): *m/z* 408 $(M + H)^+$; Anal. Calcd. for $C_{21}H_{13}N_3O_3$: C, 70.98; H, 3.66; N, 11.83 %. Found: C, 70.94; H, 3.64; N, 11.80 %.

2-Amino-6-(2-oxo-2H-chromen-3-yl)-4-(4-hydroxyphenyl)nicotinonitrile ***(4i)*** IR (KBr, cm^{-1}): 3,438 and 3,375 (NH_2), 3,348 (OH), 3,128 (ArH), 2,216 (CN), 1,716 (C=O), 1,617 (C–O); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 8.58 (s, 1H, coumarin 4-H), 7.78 (s, 1H, PyrH), 7.94–7.68 (m, 8H, ArH), 7.14 (s, 2H, NH_2), 9.94 (s, 1 H, OH) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ 85.9, 113.9, 117.9, 125.2, 125.7, 127.4, 127.7,

128.1, 129.4, 130.2, 130.6, 134.7, 136.3, 142.2, 147.4, 153.5, 159.7, 186.2 ppm; MS(ESI): *m/z* 408 $(M + H)^+$; Anal. Calcd. for $C_{21}H_{13}N_3O_3$: C, 70.98; H, 3.66; N, 11.83 %. Found: C, 70.90; H, 3.65; N, 11.84 %.

2-Amino-6-(2-oxo-2H-chromen-3-yl)-4-(3-chlorophenyl)nicotinonitrile ***(4j)*** IR (KBr, cm^{-1}): 3,458 and 3,347 (NH_2), 3,126 (ArH), 2,212 (CN), 1,718 (C=O), 1,625 (C–O); ^1H NMR (500 MHz, DMSO-d_6) δ: 8.79 (s, 1H, coumarin 4-H), 7.80 (s, 1H, PyrH), 7.80–7.56 (m, 8H, ArH), 7.07 (s, 2H, NH_2) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 86.3, 114.1, 117.7, 125.1, 125.6, 127.0, 127.5, 128.2, 129.5, 129.8, 130.6, 134.6, 136.2, 142.5, 147.5, 153.4, 159.2, 185.3 ppm; MS(ESI): *m/z* 374.45 $(M + H)^+$; Anal. Calcd. for $C_{21}H_{12}ClN_3O_2$: C, 67.48; H, 3.21; N, 11.25 %. Found: C, 67.44; H, 3.20; N, 11.22 %.

2-Amino-6-(2-oxo-2H-chromen-3-yl)-4-(4-methylphenyl)nicotinonitrile ***(4k)*** IR (KBr, cm^{-1}): 3,440 and 3,376 (NH_2), 3,130 (ArH), 2,210 (CN), 1,723 (C=O), 1,612 (C–O); ^1H NMR (500 MHz, DMSO-d_6) δ: 8.61 (s, 1H, coumarin 4-H), 7.85 (s, 1H, PyrH), 7.84–7.60 (m, 8H, ArH), 7.11 (s, 2H, NH_2), 2.42 (s, 3H, CH_3) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 31.2, 85.5, 113.8, 118.1, 125.1, 125.5, 127.1, 127.5, 128.1, 129.2, 130.0, 130.3, 134.7, 136.1, 142.2, 146.9, 153.4, 159.4, 186.0 ppm; MS(ESI): *m/z* 354 $(M + H)^+$; Anal. Calcd. for $C_{22}H_{15}N_3O_2$: C, 74.79; H, 4.25; N, 11.90 %. Found: C, 74.72; H, 4.26; N, 11.86 %.

2-Amino-6-(2-oxo-2H-chromen-3-yl)-4-(4-methoxyphenyl)nicotinonitrile ***(4l)*** IR (KBr, cm^{-1}): 3,416 and 3,352 (NH_2), 3,118 (ArH), 2,216 (CN), 1,717 (C=O), 1,608 (C–O); ^1H NMR (500 MHz, DMSO-d_6) δ: 8.74 (s, 1H, coumarin 4-H), 7.87 (s, 1H, PyrH), 7.87–7.66 (m, 8H, ArH), 7.13 (s, 2H, NH_2), 3.84 (s, 3H, OCH_3) ppm; ^{13}C NMR (125 MHz, DMSO-d_6) δ: 86.1, 114.1, 117.4, 125.0, 125.4, 127.0, 127.7, 128.0, 129.7, 129.9, 130.1, 134.3, 136.3, 142.5, 147.6, 153.2, 158.5, 161.4, 184.7 ppm; MS(ESI): *m/z* 370 $(M + H)^+$; Anal. Calcd. for $C_{22}H_{15}N_3O_3$: C, 71.54; H, 4.06; N, 11.38 %. Found: C, 71.44; H, 4.04; N, 11.33 %.

Conclusions

In summary, we have developed a simple and new procedure for the synthesis of 2-amino-6-(2-oxo-2*H*-chromen-3-yl)-4-arylnicotinonitrile by a four-component condensation of 3-acetylcoumarin, benzaldehyde, malononitrile, and ammonium acetate in one-pot using $HClO_4$–SiO_2 as catalyst at 60 °C under solvent-free condition. This method offers several advantages such as catalyst recyclability, inexpensive catalyst, environmental friendly procedure, short reaction time, high yields, simple work-up procedure, and easy isolation. We expect this method will find extensive applications in the field of combinatorial chemistry, diversity-oriented synthesis, and drug discovery.

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