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Fluoride ion catalyzed multicomponent reactions for efficient synthesis of 4*H*-chromene and *N*-arylquinoline derivatives in aqueous media

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ABSTRACT

4*H*-Chromene and *N*-arylquinoline derivatives are obtained in good to excellent yields by proceeding through a simple, mild, and efficient procedure utilizing tetrabutylammonium fluoride (TBAF) as catalyst.

1. Introduction

The developments of multicomponent reactions (MCRs) have attracted much attention from the vantage point of combinatorial and medicinal chemistry.[1] Generally, the MCR strategy affords savings in synthetic time and effort, and has significant advantages over conventional two-component reactions in several aspects, such as variable and high bond forming efficiency. With a small set of start materials, very large libraries can be developed within a short time, which can apply to research on medicinal chemistry. The first MCR was described in 1850 by the Strecker's synthesis of α-amino acids.[2a] The other MCRs have been described successfully in Hantsch's synthesis of 1,4-dihydropyridines in 1882,[2b] Biginelli's synthesis of 3,4-dihydropyrimidin-2-ones in 1891,[2c] Mannich's synthesis of β-amino carbonyl compounds in 1912,[2d] Robinson's synthesis of alkaloid tropinone in 1917,[2e] Passerini synthesis of α-acyloxycarboxamide in 1921,[2f] Bucherer–Bergs's synthesis of hydantoins in 1934,[2g] Ugi's synthesis of bis-amide in 1959,[2h] and Pauson–Khand's synthesis of α,β-cyclopentenone in 1977.[2i]

Many important heterocycle syntheses are multicomponent reactions. Recently, the syntheses of 4*H*-chromene and quinoline derivatives have attracted great interest due to biological and pharmacological activities. The 4*H*-chromene derivatives show various pharmacological properties such as spasmolytic, diuretic, anticoagulant, anticancer, and antianaphylactic activities.[3] Quinoline derivatives are a class of important compounds, which are widely recognized to have antitumor, antibacterial, anticancer, and antimalarial activities.[4] The known procedure for the synthesis of 4*H*-chromene derivatives employ a three-component reaction of cyclic 1,3-diketones, aryl aldehydes, and malononitrile, and is performed under various reaction conditions. The conventional reported syntheses of 4*H*-chromene derivatives employ piperidine and triethylamine in organic solvents.[5] Other effective syntheses of 4*H*-chromene derivatives employ microwave[6] and electrogenerated base.[7] Recently, some two- and three-component reactions have been catalyzed by utilizing alkyl ammonium salts,[8] $Re(PFO)_3$,[9] KF–Al_2O_3,[10] (*S*)-proline,[11] and $(NH_4)_2HPO_4$.[12] The classical procedure for the synthesis of quinoline derivatives has been described in Skraup,[13] Doebner–Miller,[14] and Combes quinoline syntheses.[15] However, the synthesis of *N*-substituted quinoline derivative is few in the literature. The multicomponent reaction could be also successfully applied to various aryl aldehydes with cyclic 3-arylamino-2-enones and malononitrile to synthesize various *N*-arylquinoline derivative catalyzed by $[Bmim^+][BF_4^-]$[16] and TEBAC.[17]

Over the past years, tetrabutylammonium fluoride (TBAF) in organic synthesis has been widely used for most fluoride-assisted reactions,[18] deprotection of silyl groups,[19] desilyation,[20] and fluorination.[21] TBAF has been widely recognized as a convenient, organic-soluble source of naked fluoride ion. It has also been widely used for a variety of base-catalyzed reactions such as alkylation, elimination, Michael addition, and aldol condensation.[22] The potential ability of the fluoride ion to act as a base might be predicated on considering the strength of the H–F bond. Most ionic fluorides are easy to prepare and use and are stable over long periods of time. The fluoride ions are hygroscopic, but they do not react with water and may therefore be recovered from aqueous solution by conventional techniques. As part of our incessant research efforts with MCR chemistry,[23] we now report a simple and efficient catalyst, TBAF, for catalyzing the syntheses of 4*H*-chromene and *N*-arylquinoline derivatives via a one-pot three-component reaction in aqueous media (Scheme 1).

2. Results and discussion

Preliminary efforts were mainly focused on the evaluation of different additives, the yields of 4*H*-chromene derivatives obtained

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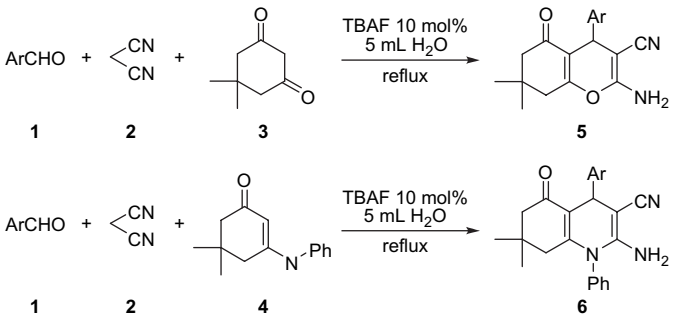
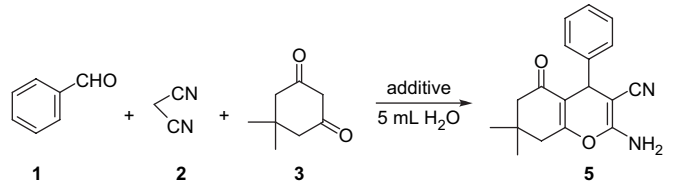


Scheme 1.

by reacting cyclic 1,3-diketones, aryl aldehydes, and malononitrile are shown in Table 1. First, it was clearly suggested that TBAF certainly catalyzed the multicomponent reactions (compare entries 1 and 2, Table 1). It is noteworthy to observe that corresponding product was obtained in excellent yield, no any benzylidenemalononitrile or 2,2-benzyliden-bis-(5,5-dimethyl-3-oxo-1-hydroxycyclohexene) was observed. The reactions carried out by using different ammonium halide such as chloride, bromide, and iodide showed that the fluoride ion was more active than other halides and the iodide anion did not avail against the reaction (entries 3–5, Table 1). The result accords with the literature and revealed that quaternary ammonium halides are known to give rise to an order of nucleophilicity for the halide ions, which parallels their electronegativities, i.e., fluoride>chloride>bromide>iodide. We tried to explore an effective system for multicomponent reactions by screening other fluoride sources under the same conditions, it was found that the fluoride ion of TBAF is the most reactive than other fluoride sources (entries 6–10, Table 1). The corresponding product was obtained in low yield in presence of H_2SiF_6 and HF–pyridine, because these prefer to afford acidic HF molecular, not basic F^- anion (entries 9–10, Table 1). Besides the basic F^- anion, the

Table 1
One-pot synthesis of 4*H*-chromene derivatives in presence of various additives[a]



Entry	Additive (equiv)	Time (min)	Temp (°C)	**5** Yield[b] (%)
1	—	30	Reflux	57[c]
2	TBAF (0.1)	30	Reflux	>99
3	TBACl (0.1)	30	Reflux	80
4	TBABr (0.1)	30	Reflux	73
5	TBAI (0.1)	30	Reflux	56[d]
6	KF (0.1)	30	Reflux	88
7	CsF (0.1)	30	Reflux	85
8	NH_4F (0.1)	30	Reflux	73
9	H_2SiF_6 (0.1)	30	Reflux	28[e]
10	HF–pyridine (0.1)	30	Reflux	20[f]
11	NaOH (0.1)	30	Reflux	72
12	$NaHCO_3$ (0.1)	30	Reflux	84
13	Na_2CO_3 (0.1)	30	Reflux	82
14	K_2CO_3 (0.1)	30	Reflux	85

[a] Condition: the reaction was performed by using 2 mmol of **1**, 2 mmol of **2**, and 2 mmol of **3** in the presence of 10 mol% of additive in 5 mL H_2O under reflux condition.
[b] NMR yield.
[c] 18% Benzylidenemalononitrile was observed.
[d] 7% Benzylidenemalononitrile was observed.
[e] 32% Benzylidenemalononitrile was observed.
[f] 25% Benzylidenemalononitrile was observed.

corresponding product was obtained in 72–85% yield in presence of NaOH, $NaHCO_3$, Na_2CO_3, and K_2CO_3 (entries 11–14, Table 1). On the basis of the optimization of the reaction conditions, the scope of these fluoride anion catalyzed multicomponent reactions was explored. Not only electron-rich aryl aldehyde, but also electron-deficient aryl aldehyde in the reactions afforded 4*H*-chromene derivatives in 73–98% yields and *N*-arylquinoline derivatives in 88–96% yields (Table 2). The 4*H*-chromene and *N*-arylquinoline derivatives thus formed can be obtained in pure form by recrystallizing or passing the crude through a short plug of silica. As shown in Table 2, the periods of reaction time of cyclic 1,3-diketones with aryl aldehyde containing either electron-withdrawing

Table 2
Fluoride ion catalyzed one-pot synthesis of 4*H*-chromene and *N*-arylquinoline derivatives[a]

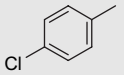
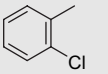
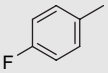
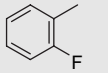
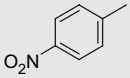
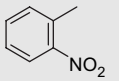
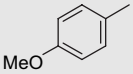
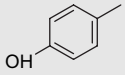
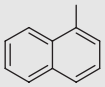
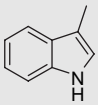
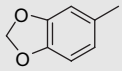
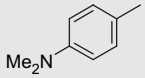
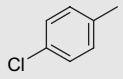
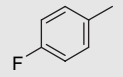
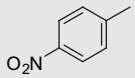
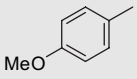
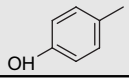
Entry	Ar		Time (min)	Yield[b] (%)
1		**5a**	30	97
2		**5b**	30	94
3		**5c**	30	84
4		**5d**	30	98
5		**5e**	30	87
6		**5f**	30	75
7		**5g**	30	73
8		**5h**	30	96
9		**5i**	30	97
10		**5j**	100	98
11		**5k**	150	76
12		**5l**	30	98
13		**5m**	10	97
14		**5n**	300	96
15		**6a**	30	96

Table 2 (*continued*)

Entry	Ar		Time (min)	Yield[b] (%)
16		**6b**	120	98
17		**6c**	30	97
18		**6d**	60	90
19		**6e**	240	88
20		**6f**	300	98

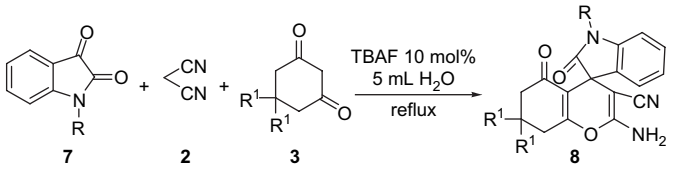
[a] Condition: the reaction was performed by using 2 mmol of **1**, 2 mmol **2**, and 2 mmol of **3** or **4** in the presence of 10 mol % of TABF in 5 mL H_2O under reflux condition.
[b] Isolated yield.

group or electron-donating group are similar (entries 1–14, Table 2). Comparatively, the rate of the reaction of cyclic 3-arylamino-2-enones with electron-deficient aryl aldehyde is faster than with electron-rich aryl aldehyde (entries 15–20, Table 2). In order to extend the scope of fluoride ion catalyzed multicomponent reaction could been also successfully applied to various isatin derivatives with cyclic 1,3-diketones and malononitrile to synthesize various spirooxindoles derivatives (Table 3). For isatin derivatives, both isatin and *N*-substituted isatins could undergo multicomponent reactions to give the spirochromene in 87–98% isolated yields. The fused chromene system is the core structure of many pharmacological and biological activities.[24] The scope of fluoride ion catalyzed-multicomponent reactions has been demonstrated by using a wide range of aryl aldehyde as well as isatin with different groups or substituents.

3. Conclusion

In conclusion, we have developed an efficient procedure for the synthesis of 4*H*-chromene and *N*-arylquinoline derivatives, which are often encountered in molecules of biologically active compounds. The procedures described here are simple, mild, and efficient. The use of TBAF as a base has the advantages of being economically viable and more efficient for multicomponent reactions in aqueous media. The reaction system can be successfully applied to a variety of aryl aldehyde as well as isatin to synthesize a wide variety of heterocycles in good to excellent yields.

Table 3
Fluoride ion catalyzed one-post synthesis spirochromene derivatives[a]



7 2 3 8

Entry	R	R^1		Time (min)	Yield[b] (%)
1	H	Me	**8a**	30	97
2	Me	Me	**8b**	20	98
3	Boc	Me	**8c**	10	91
4	Benzyl	Me	**8d**	15	96
5	Acetyl	Me	**8e**	60	90
6	H	H	**8f**	20	96
7	Me	H	**8g**	20	97
8	Boc	H	**8h**	15	94
9	Benzyl	H	**8i**	20	96
10	Acetyl	H	**8j**	60	87

[a] Condition: the reaction was performed using 2 mmol of **7**, 2 mmol of **2**, and 2 mmol of **3** in the presence of 10 mol % of TBAF in 5 mL H_2O under reflux condition.
[b] Isolated yield.

4. Experimental

4.1. General

All Analytical thin layer chromatography was performed with E. Merck silica gel $60F_{254}$ aluminum sheets and was visualized with UV light. Flash column chromatography, following the method of still, was carried out with E. Merck silica gel 60 (Kieselgel 60, 230–400 mesh) using the indicated eluents. ^{1}H nuclear magnetic resonance (NMR) spectra were recorded routinely with a Bruker Avance 400 (400 MHz) spectrometer. The ^{1}H NMR data are described as following: chemical shifts (δ, given in ppm with DMSO-d_6 (2.50 ppm) as internal reference), multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, br=broad, m=multiplet), coupling constants (J, given in Hz), with integration. ^{13}C NMR spectra were obtained with a Bruker Avance 400 (100 MHz) spectrometer using DMSO-d_6 (39.51 ppm) as internal reference. Mass spectra were given on a JOEL SX-102A spectrometer at an ionization potential of 70 eV and reported as mass/charge (m/z) with percent relative abundance. High-resolution mass spectra (HRMS) were acquired with a FINNIGAN MAT-95XL spectrometer. Solvent for extraction and chromatography were reagent grade.

4.2. Procedures and analytical data

To a mixture of benzaldehyde (213 mg, 2 mmol), malononitrile (133 mg, 2 mmol), 5,5-dimethyl-1,3-cyclohexanedione (295 mg, 2 mmol), and water (5 mL), TBAF·$3H_2O$ (64 mg, 0.2 mmol) was added and the mixture was stirred under reflux condition for 30 min. After completion of reaction (monitored by NMR), the generated solid was filtered off and recrystallized from ethyl acetate to obtain **5a** (499 mg, 97% isolated yield).

*4.2.1. 2-Amino-7,7-dimethyl-5-oxo-4-phenyl-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (**5a**)*

White solid with the melting point of 234–235 °C; IR (KBr, neat) ν_{max} 3397, 3325, 3214, 2961, 2200, 1681, 1661, 1605, 1371, 1249, 1214, 1160, 1139, 1036, 696; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.28 (t, J=7.3 Hz, 2H), 7.21–7.12 (m, 3H), 6.98 (s, 2H), 4.17 (s, 1H), 2.51 (s, 2H), 2.25 (d, J=16.1 Hz, 1H), 2.10 (d, J=16.1 Hz, 1H), 1.04 (s, 3H), 0.96 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.59, 162.45, 158.47, 144.71, 128.29, 127.11, 126.53, 119.67, 112.73, 58.23, 49.96, 38.67, 35.56, 31.77, 28.36, 26.78; HRMS (EI) m/z calcd for $C_{18}H_{18}N_2O_2$ (M^+): 294.1368, found: 294.1361.

*4.2.2. 2-Amino-4-(4-chlorophenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (**5b**)*

White solid with the melting point of 215–216 °C; IR (KBr, neat) ν_{max} 3395, 3322, 3257, 3214, 2964, 2193, 1741, 1684, 1655, 1605, 1368, 1214, 1041; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.34 (d, J=8.4 Hz, 2H), 7.17 (d, J=8.4 Hz, 2H), 7.04 (s, 2H), 4.19 (s, 1H), 2.50 (s, 2H), 2.24 (d, J=16.1 Hz, 1H), 2.10 (d, J=16.1 Hz, 1H), 1.03 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.71, 162.65, 158.52, 143.74, 131.14, 129.12, 128.30, 119.55, 112.36, 57.85, 49.97, 40.14, 35.13, 31.80, 28.32, 26.88; HRMS (EI) m/z calcd for $C_{18}H_{17}ClN_2O_2$ (M^+): 328.0979, found: 328.0965.

*4.2.3. 2-Amino-4-(2-chlorophenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (**5c**)*

White solid with the melting point of 191–192 °C; IR (KBr, neat) ν_{max} 3363, 3185, 2963, 2190, 1738, 1683, 1651, 1604, 1506, 1371, 1216, 1142, 1038, 850; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.22–7.14 (m, 2H), 7.10 (t, J=8.8 Hz, 2H), 7.02 (s, 1H), 4.21 (s, 1H), 2.50 (s, 2H), 2.24 (d, J=16.1 Hz, 1H), 2.10 (d, J=16.1 Hz, 1H), 1.02 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 196.14, 162.95, 162.59, 160.19, 158.98, 141.43, 141.40, 129.57, 129.49, 120.11, 115.60, 115.39, 113.11, 58.62, 50.46, 35.41, 32.27, 28.81, 27.33; HRMS (EI) m/z calcd for $C_{18}H_{17}ClN_2O_2$ (M^+): 328.0979, found: 328.0977.

*4.2.4. 2-Amino-4-(4-fluorophenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (**5d**)*

White solid with the melting point of 210–211 °C; IR (KBr, neat) ν_{max} 3479, 3335, 3181, 2954, 2202, 2186, 1688, 1668, 1598, 1366, 1252, 1210, 1140, 1036, 749; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.21–7.15 (m, 2H), 7.10 (t, J=8.6 Hz, 2H), 7.02 (s, 2H), 4.20 (s, 1H), 3.35 (s, 2H), 2.50 (s, 2H), 2.24 (d, J=16.1 Hz, 1H), 2.10 (d, J=16.1 Hz, 1H), 1.02 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 196.15, 162.96, 162.59, 160.19, 158.98, 141.43, 141.40, 129.57, 129.49, 120.11, 115.60, 115.39, 113.11, 58.62, 50.46, 35.41, 32.27, 28.81, 27.33.

*4.2.5. 2-Amino-4-(2-fluorophenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (**5e**)*

Yellow solid with the melting point of 232–233 °C; IR (KBr, neat) ν_{max} 3397, 3328, 3214, 2966, 2879, 2198, 1683, 1661, 1605, 1487, 1372, 1215, 1140, 1037, 753; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.28–7.09 (m, 4H), 7.04 (s, 2H), 4.47 (s, 1H), 3.35 (s, 2H), 2.52 (q, J=16.8 Hz, 2H), 2.28 (d, J=16.1 Hz, 1H), 2.10 (d, J=16.1 Hz, 1H), 1.06 (s, 3H), 0.97 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.56, 163.09, 161.16, 157.75, 131.24, 131.11, 129.68, 129.65, 128.60, 128.52, 124.39, 119.48, 115.50, 115.29, 111.38, 56.75, 49.89, 31.77, 29.83, 28.47; HRMS (EI) m/z calcd for $C_{18}H_{17}FN_2O_2$ (M^+): 312.1274, found: 312.1269.

*4.2.6. 2-Amino-7,7-dimethyl-4-(4-nitrophenyl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (**5f**)*

Yellow solid with the melting point of 151–152 °C; IR (KBr, neat) ν_{max} 3392, 3322, 3256, 3213, 2960, 2193, 1736, 1684, 1651, 1605, 1525, 1367, 1347, 1253, 1215, 1042, 867, 827; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.17 (d, J=8.1 Hz, 2H), 7.44 (d, J=8.1 Hz, 2H), 7.17 (s, 2H), 4.36 (s, 1H), 2.50 (s, 2H), 2.26 (d, J=15.7 Hz, 1H), 2.11 (d, J=15.7 Hz, 1H), 1.04 (s, 3H), 0.96 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.75, 163.14, 158.61, 152.29, 146.29, 128.63, 123.68, 119.32, 111.75, 57.04, 49.88, 35.68, 34.84, 28.26, 26.96; HRMS (EI) m/z calcd for $C_{18}H_{17}N_3O_4$ (M^+): 339.1219, found: 339.1214.

*4.2.7. 2-Amino-7,7-dimethyl-4-(2-nitrophenyl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (**5g**)*

Yellow solid with the melting point of 233–234 °C; IR (KBr, neat) ν_{max} 3473, 3333, 3257, 3213, 3188, 2959, 2870, 2194, 1689, 1667, 1597, 1525, 1365, 1254, 1214, 1143, 1041, 756, 736; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.81 (d, J=8.1 Hz, 1H), 7.66 (t, J=7.3 Hz, 1H), 7.42 (t, J=7.7 Hz, 1H), 7.35 (d, J=8.1 Hz, 1H), 7.17 (s, 2H), 4.93 (s, 1H), 2.50 (s, 2H), 2.20 (d, J=16.1 Hz, 1H), 2.01 (d, J=16.1 Hz, 1H), 1.01 (s, 3H), 0.88 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.79, 162.72, 159.17, 148.95, 138.93, 133.34, 130.26, 127.85, 123.71, 119.03, 112.30, 56.37, 49.56, 31.83, 29.94, 28.27, 26.70.

*4.2.8. 2-Amino-4-(4-methoxyphenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (**5h**)*

Yellow solid with the melting point of 201–202 °C; IR (KBr, neat) ν_{max} 3352, 3188, 2967, 2194, 1684, 1655, 1606, 1509, 1371, 1256, 1214, 1033, 844; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.05 (d, J=8.1 Hz, 2H), 6.94 (s, 2H), 6.84 (d, J=8.1 Hz, 2H), 4.12 (s, 1H), 3.71 (s, 1H), 2.50 (s, 2H), 2.24 (d, J=16.1 Hz, 1H), 2.09 (d, J=16.1 Hz, 1H), 1.03 (s, 3H), 0.94 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.65, 162.12, 158.51, 157.92, 136.84, 128.20, 119.78, 113.67, 112.99, 58.57, 54.99, 50.01, 34.75, 31.77, 28.40, 26.77; HRMS (EI) m/z calcd for $C_{19}H_{20}N_2O_3$ (M^+): 324.1474, found: 324.1478.

*4.2.9. 2-Amino-4-(4-hydroxyphenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (**5i**)*

Yellow solid with the melting point of 224–226 °C; IR (KBr, neat) ν_{max} 3478, 3315, 3160, 2962, 2202, 1683, 1661, 1615, 1592, 1515, 1451, 1367, 1214, 1041, 849; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.30 (s, 1H), 6.96–6.89 (m, 4H), 6.67 (d, J=8.4 Hz, 2H), 4.07 (s, 1H), 2.55–2.43 (m, 2H), 2.24 (d, J=16.1 Hz, 1H), 2.09 (d, J=16.1 Hz, 1H), 1.03 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 196.23, 162.53, 158.89, 156.44, 135.67, 128.63, 120.36, 115.50, 113.67, 59.34, 50.53, 40.18, 35.18, 32.25, 28.90, 27.23; HRMS (EI) m/z calcd for $C_{18}H_{18}N_2O_3$ (M^+): 310.1317, found: 310.1327.

*4.2.10. 2-Amino-7,7-dimethyl-4-(naphthalen-1-yl)-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (**5j**)*

White solid with the melting point of 214–215 °C; IR (KBr, neat) ν_{max} 3420, 3319, 3254, 3208, 3062, 2959, 2185, 1679, 1659, 1596, 1377, 1351, 1248, 1205, 1158, 1141, 1033, 789; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.38 (d, J=7.7 Hz, 1H), 7.92 (d, J=7.7 Hz, 1H), 7.78 (d, J=8.4 Hz, 1H), 7.59–7.49 (m, 2H), 7.45 (t, J=7.5 Hz, 1H), 7.25 (d, J=7.3 Hz, 1H), 6.96 (s, 2H), 2.59 (s, 2H), 2.24 (d, J=16.1 Hz, 1H), 2.07 (d, J=16.1 Hz, 1H), 1.06 (s, 3H), 1.00 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 196.22, 163.26, 158.94, 133.83, 131.25, 128.87, 127.46, 126.31, 126.15, 126.07, 125.70, 124.10, 12.011, 113.94, 59.43, 50.51, 40.22, 32.32, 28.87, 27.48; HRMS (EI) m/z calcd for $C_{22}H_{20}N_2O_2$ (M^+): 344.1525, found: 344.1526.

*4.2.11. 2-Amino-4-(1H-indol-3-yl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (**5k**)*

Yellow solid with the melting point of 185–186 °C; IR (KBr, neat) ν_{max} 3521, 3405, 3303, 3124, 2959, 2187, 1683, 1661, 1608, 1368, 1248, 1213, 1143, 1030, 742; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.85 (s, 1H), 7.39–7.31 (m, 2H), 7.14–7.12 (m, 1H), 7.05 (t, J=7.1 Hz, 1H), 6.99–6.92 (m, 1H), 6.85 (s, 2H), 4.51 (d, J=6.2 Hz, 1H), 2.51 (q, J=17.6 Hz, 2H), 2.23 (d, J=16.1 Hz, 1H), 2.06 (d, J=16.1 Hz, 1H), 1.02 (s, 3H), 0.87 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.75, 161.67, 158.63, 136.59, 125.34, 120.76, 120.18, 118.39, 118.35, 117.58, 112.79, 111.67, 58.64, 50.15, 39.72, 31.66, 28.50, 27.26, 26.76; HRMS (EI) m/z calcd for $C_{20}H_{18}N_3O_2$ (M^+): 332.1399, found: 332.1395.

*4.2.12. 2-Amino-4-(benzo[d][1,3]dioxol-5-yl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (**5l**)*

White solid with the melting point of 224–225 °C; IR (KBr, neat) ν_{max} 3358, 3261, 3192, 2965, 2899, 2197, 1683, 1651, 1607, 1490, 1375, 1359, 1250, 1215, 1038, 561; ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.96 (s, 2H), 6.81 (d, J=7.7 Hz, 1H), 6.65 (s, 1H), 6.61 (d, J=7.7 Hz, 1H), 4.11 (s, 1H), 2.50 (s, 2H), 2.24 (d, J=15.7 Hz, 1H), 2.12 (d, J=15.7 Hz, 1H), 1.03 (s, 3H), 0.96 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.63, 162.28, 158.39, 147.15, 145.81, 138.82, 120.25, 119.63, 112.73, 107.96, 107.49, 110.83, 58.45, 50.00, 35.18, 31.75, 28.24, 26.91; HRMS (EI) m/z calcd for $C_{19}H_{18}N_2O_4$ (M^+): 338.1267, found: 338.1260.

*4.2.13. 2-Amino-4-(furan-2-yl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (**5m**)*

White solid with the melting point of 226–228 °C; IR (KBr, neat) ν_{max} 3398, 3329, 3255, 3216, 2966, 2932, 2875, 2197, 1681, 1661, 1604, 1364, 1218, 1038, 1013, 736; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.47 (s, 1H), 7.06 (s, 2H), 6.32 (s, 1H), 6.05 (d, J=2.2 Hz, 1H), 4.32 (s, 1H), 2.48 (q, J=17.9 Hz, 2H), 2.28 (d, J=16.1 Hz, 1H), 2.16 (d, J=16.1 Hz, 1H), 1.04 (s, 3H), 0.98 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.40, 163.25, 159.30, 155.72, 141.72, 119.52, 110.43, 110.37,

105.04, 55.44, 59.90, 39.72, 31.79, 28.99, 28.41, 26.55; HRMS (EI) m/z calcd for $C_{16}H_{16}N_2O_3$ (M^+): 284.1161, found: 284.1167.

*4.2.14. 2-Amino-4-(4-(dimethylamino)phenyl)-7,7-dimethyl-5-oxo-5,6,7,8-tetrahydro-4H-chromene-3-carbonitrile (**5n**)*

Yellow solid with the melting point of 217–218 °C; IR (KBr, neat) ν_{max} 3195, 2959, 2922, 2804, 2361, 2339, 2192, 1681, 1658, 1607, 1520, 1368, 1247, 1213, 1159, 1141, 1034, 826; ^{1}H NMR (400 MHz, DMSO-d_6) δ 6.94 (d, J=8.4 Hz, 2H), 6.87 (s, 2H), 6.63 (d, J=8.4 Hz, 2H), 4.05 (s, 1H), 2.84 (s, 6H), 2.48 (q, J=17.2 Hz, 2H), 2.24 (d, J=16.1 Hz, 1H), 2.08 (d, J=16.1 Hz, 1H), 1.03 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.67, 161.85, 158.35, 149.23, 132.52, 127.72, 119.94, 113.29, 112.33, 58.98, 50.07, 40.22, 39.72, 34.57, 31.77, 28.48, 26.75; HRMS (EI) m/z calcd for $C_{20}H_{23}N_3O_2$ (M^+): 337.1790, found: 337.1798.

*4.2.15. 2-Amino-7,7-dimethyl-5-oxo-1,4-diphenyl-1,4,5,6,7,8-hexahydroquinoline-3-carbonitrile (**6a**)*

White solid with the melting point of 246–247 °C; IR (KBr, neat) ν_{max} 3462, 3335, 3221, 3056, 3021, 2958, 2179, 1660, 1620, 1572, 1490, 1415, 1374, 1259, 1145, 1041, 738, 697, 575; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.66–7.51 (m, 3H), 7.46–7.25 (m, 6H), 7.19 (t, J=6.8 Hz, 1H), 5.34 (s, 2H), 4.46 (s, 1H), 2.20 (dd, J=16.5, 5.5 Hz, 2H), 2.00 (d, J=16.1 Hz, 1H), 1.71 (d, J=17.6 Hz, 1H), 0.88 (s, 3H), 0.73 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.88, 51.16, 150.25, 146.52, 136.27, 130.24, 129.97, 129.77, 128.43, 126.81, 126.32, 121.55, 111.73, 60.43, 49.32, 40.99, 36.39, 31.90, 29.10, 26.30; HRMS (EI) m/z calcd for $C_{24}H_{23}N_3O$ (M^+): 369.1841, found: 369.1845.

*4.2.16. 2-Amino-4-(4-chlorophenyl)-7,7-dimethyl-5-oxo-1-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carbonitrile (**6b**)*

White solid with the melting point of 268–269 °C; IR (KBr, neat) ν_{max} 3467, 3331, 3218, 2952, 2179, 1652, 1618, 1593, 1568, 1486, 1415, 1372, 1258, 1144, 1011, 841, 696; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.64–7.51 (m, 3H), 7.45–7.33 (m, 4H), 7.30 (d, J=8.4 Hz, 2H), 5.37 (s, 2H), 4.48 (s, 1H), 2.19 (d, J=16.5 Hz, 2H), 2.00 (d, J=15.7 Hz, 1H), 1.70 (d, J=17.2 Hz, 1H), 0.87 (s, 3H), 0.72 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.79, 151.23, 150.34, 145.42, 136.09, 130.78, 130.18, 129.95, 129.78, 128.70, 128.32, 121.28, 111.35, 59.85, 49.24, 40.95, 35.98, 31.85, 28.98, 26.28; HRMS (EI) m/z calcd for $C_{24}H_{22}ClN_3O$ (M^+): 403.1451, found: 403.1455.

*4.2.17. 2-Amino-4-(4-fluorophenyl)-7,7-dimethyl-5-oxo-1-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carbonitrile (**6c**)*

Yellow solid with the melting point of 260–261 °C; IR (KBr, neat) ν_{max} 3455, 3339, 3210, 2959, 2361, 2339, 2177, 1640, 1592, 1557, 1505, 1417, 1371, 1257, 1216, 1153, 1045, 849, 702; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.64–7.51 (m, 3H), 7.40 (d, J=7.0 Hz, 2H), 7.30 (dd, J=8.4, 5.9 Hz, 2H), 7.14 (t, J=8.8 Hz, 2H), 5.34 (s, 2H), 4.48 (s, 1H), 2.19 (d, J=16.8 Hz, 2H), 2.00 (d, J=16.1 Hz, 1H), 1.70 (d, J=17.2 Hz, 1H), 0.87 (s, 3H), 0.72 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.81, 161.98, 159.57, 151.15, 150.16, 142.66, 136.14, 130.17, 129.92, 129.76, 128.63, 128.55, 121.34, 115.11, 114.90, 111.66, 60.24, 49.27, 40.95, 35.74, 31.84, 28.98, 26.26; HRMS (EI) m/z calcd for $C_{24}H_{22}FN_3O$ (M^+): 387.1747, found: 387.1741.

*4.2.18. 2-Amino-7,7-dimethyl-4-(4-nitrophenyl)-5-oxo-1-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carbonitrile (**6d**)*

Yellow solid with the melting point of 275–276 °C; IR (KBr, neat) ν_{max} 3460, 3321, 3218, 3070, 2959, 2180, 1651, 1620, 1592, 1565, 1519, 1374, 1346, 1258, 1146, 1042, 872, 697; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.22 (d, J=8.8 Hz, 2H), 7.65–7.52 (m, 5H), 7.46 (d, J=7.0 Hz, 2H), 5.47 (s, 2H), 4.62 (s, 1H), 2.20 (d, J=16.5 Hz, 2H), 2.01 (d, J=16.8 Hz, 1H), 1.73 (d, J=17.6 Hz, 1H), 0.88 (s, 3H), 0.73 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.79, 153.88, 151.45, 150.97, 146.08, 135.92, 130.21, 130.01, 129.88, 128.14, 123.81, 121.05, 110.68, 59.07, 49.15, 41.00, 31.89, 30.65, 28.90, 26.39; HRMS (EI) m/z calcd for $C_{24}H_{22}N_4O_3$ (M^+): 414.1692, found: 414.1685.

*4.2.19. 2-Amino-4-(4-methoxyphenyl)-7,7-dimethyl-5-oxo-1-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carbonitrile (**6e**)*

White solid with the melting point of 244–245 °C; IR (KBr, neat) ν_{max} 3459, 3332, 3219, 2991, 2956, 2836, 2177, 1464, 1645, 1590, 1564, 1508, 1412, 1374, 1256, 1239, 1177, 1143, 1030, 852, 705; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.63–7.51 (m, 3H), 7.39 (d, J=7.0 Hz, 2H), 7.20 (d, J=8.4 Hz, 2H), 6.89 (d, J=8.4 Hz, 2H), 5.26 (s, 2H), 4.42 (s, H), 3.73 (s, 3H), 2.21 (d, J=4.4 Hz, 1H), 2.17 (d, J=2.2 Hz, 1H), 2.00 (d, J=16.1 Hz, 1H), 1.69 (d, J=17.2 Hz, 1H), 0.87 (s, 3H), 0.73 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.79, 157.74, 150.98, 149.78, 138.70, 136.30, 130.16, 12.90, 129.68, 127.78, 121.51, 113.71, 112.06, 60.80, 54.95, 49.33, 10.93, 35.45, 31.82, 29.06, 26.25; HRMS (EI) m/z calcd for $C_{25}H_{25}N_3O_2$ (M^+): 399.1947, found: 399.1943.

*4.2.20. 2-Amino-4-(4-hydroxyphenyl)-7,7-dimethyl-5-oxo-1-phenyl-1,4,5,6,7,8-hexahydroquinoline-3-carbonitrile (**6f**)*

Yellow solid with the melting point of 267–268 °C; IR (KBr, neat) ν_{max} 3472, 3333, 3276, 3217, 2962, 2360, 2339, 2179, 1652, 1634, 1614, 1591, 1566, 1510, 1415, 1377, 1259, 1168, 1041, 852, 703, 577; ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.22 (s, 1H), 7.64–7.49 (m, 3H), 7.37 (d, J=6.6 Hz, 2H), 7.07 (d, J=8.1 Hz, 2H), 6.70 (d, J=8.4 Hz, 2H), 5.23 (s, 2H), 4.37 (s, 1H), 2.18 (d, J=17.2 Hz, 2H), 1.99 (d, J=16.1 Hz, 1H), 1.68 (d, J=17.2 Hz, 1H), 0.87 (s, 3H), 0.73 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.85, 155.77, 150.94, 149.64, 137.06, 136.36, 130.17, 129.92, 129.68, 127.75, 121.61, 115.04, 112.29, 61.02, 49.39, 40.94, 35.36, 31.84, 29.08, 26.24; HRMS (EI) m/z calcd for $C_{24}H_{23}N_3O_2$ (M^+): 385.1790, found: 385.1793.

*4.2.21. 2-Amino-7,7-dimethyl-2′,5-dioxo-5,6,7,8-tetrahydrospiro-[chromene-4,3′-indoline]-3-carbonitrile (**8a**)*

White solid with the melting point of >300 °C; IR (KBr, neat) ν_{max} 3380, 3316, 3141, 2960, 2929, 2885, 2193, 1723, 1683, 1658, 1605, 1471, 1349, 1327, 1223, 1166, 1055, 902, 745, 615; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.38 (s, 1H), 7.21 (s, 2H), 7.14 (t, J=7.3 Hz, 1H), 6.97 (d, J=7.3 Hz, 1H), 6.89 (t, J=7.5 Hz, 1H), 6.78 (d, J=7.7 Hz, 1H), 2.56 (q, J=17.9 Hz, 2H), 2.13 (q, J=16.1 Hz, 2H), 1.03 (s, 3H), 1.00 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.80, 177.96, 164.08, 158.73, 142.03, 134.37, 128.11, 122.96, 121.62, 117.26, 110.77, 109.19, 57.53, 49.98, 46.79, 39.93, 31.85, 27.55, 27.00.

*4.2.22. 2-Amino-1′,7,7-trimethyl-2′,5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3′-indoline]-3-carbonitrile (**8b**)*

White solid with the melting point of 265–266 °C; IR (KBr, neat) ν_{max} 3461, 3371, 3298, 3247, 3167, 2959, 2892, 2870, 2195, 1712, 1669, 1609, 1493, 1471, 1353, 1323, 1222, 1052, 904, 744, 562, 542; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.29–7.22 (m, 3H), 7.20 (d, J=7.0 Hz, 1H), 7.01–6.95 (m, 2H), 3.13 (s, 3H), 2.57 (s, 2H), 2.15 (d, J=15.7 Hz, 1H), 2.08 (d, J=15.7 Hz, 1H), 1.03 (s, 3H), 0.99 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.88, 176.54, 164.25, 158.88, 143.57, 133.54, 128.40, 122.76, 122.43, 117.19, 110.74, 108.17, 57.07, 49.96, 46.47, 31.96, 27.53, 27.07, 26.36; HRMS (EI) m/z calcd for $C_{20}H_{19}N_3O_3$ (M^+): 349.1426, found: 349.1422.

*4.2.23. tert-Butyl 2-amino-3-cyano-7,7-dimethyl-2′,5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3′-indoline]-1′-carboxylate (**8c**)*

White solid with the melting point of >300 °C; IR (KBr, neat) ν_{max} 3379, 3328, 3247, 3205, 2961, 2937, 2870, 2196, 1791, 1673, 1601, 1479, 1466, 1352, 1311, 1248, 1149, 1053, 857, 841, 750, 560; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.74 (d, J=8.4 Hz, 1H), 7.44 (s, 2H), 7.35–7.28 (m, 1H), 7.14 (d, J=3.7 Hz, 2H), 2.60 (s, 2H), 2.16 (q, J=16.1 Hz, 2H), 1.58 (s, 9H), 1.04 (s, 3H), 1.01 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.64, 175.49, 165.15, 159.15, 149.14, 139.43,

132.86, 129.09, 125.26, 123.84, 117.50, 114.78, 111.36, 84.22, 57.77, 50.10, 47.72, 40.28, 32.55, 28.17, 28.01, 27.61; HRMS (EI) *m*/*z* calcd for $C_{24}H_{25}N_3O_5$ (M^+): 435.1794, found: 435.1818.

*4.2.24. 2-Amino-1′-benzyl-7,7-dimethyl-2′,5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3′-indoline]-3-carbonitrile (**8d**)*

Yellow solid with the melting point of 285–286 °C; IR (KBr, neat) ν_{max} 3387, 3322, 3248, 3207, 2964, 2922, 2878, 2197, 1715, 1681, 1661, 1600, 1487, 1467, 1352, 1220, 1167, 1051, 749; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.49 (d, J=7.3 Hz, 2H), 7.33–7.23 (m, 5H), 7.13 (t, J=7.7 Hz, 1H), 7.08 (d, J=7.3 Hz, 1H), 6.96 (t, J=7.3 Hz, 1H), 6.68 (d, J=7.7 Hz, 1H), 4.90 (q, J=16.1 Hz, 2H), 2.60 (q, J=17.9 Hz, 2H), 2.17 (q, J=16.1 Hz, 2H), 1.05 (s, 3H), 1.02 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.01, 176.70, 164.48, 158.94, 142.61, 136.12, 133.58, 128.34, 128.24, 127.13, 127.08, 122.92, 122.54, 117.36, 110.67, 108.87, 57.28, 49.93, 46.60, 43.34, 39.98, 31.94, 27.60, 27.03; HRMS (EI) *m*/*z* calcd for $C_{26}H_{23}N_3O_3$ (M^+): 425.1739, found: 425.1736.

*4.2.25. 1′-Acetyl-2-amino-7,7-dimethyl-2′,5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3′-indoline]-3-carbonitrile (**8e**)*

Yellow solid with the melting point of 249–250 °C; IR (KBr, neat) ν_{max} 3409, 3327, 3247, 3199, 2967, 2900, 2190, 1715, 1683, 1661, 1593, 1464, 1352, 1266, 1167, 1046, 969, 907, 796, 763, 597, 560, 512; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.07 (d, J=8.4 Hz, 1H), 7.52 (s, 2H), 7.35–7.30 (m, 1H), 7.20 (d, J=3.7 Hz, 2H), 2.62 (d, J=1.5 Hz, 2H), 2.57 (s, 3H), 2.17 (q, J=16.3 Hz, 2H), 1.04 (s, 3H), 1.01 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.34, 177.86, 170.26, 164.85, 158.66, 139.20, 132.69, 128.64, 125.52, 123.33, 116.92, 115.33, 110.84, 57.03, 49.48, 47.44, 39.72, 32.07, 27.50, 27.03, 25.89; HRMS (EI) *m*/*z* calcd for $C_{21}H_{19}N_3O_4$ (M^+): 377.1376, found: 377.1372.

*4.2.26. 2-Amino-2′,5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3′-indoline]-3-carbonitrile (**8f**)*

White solid with the melting point of 276–277 °C; IR (KBr, neat) ν_{max} 3370, 3298, 3131, 2191, 1705, 1683, 1652, 1606, 1466, 1353, 1334, 1316, 1210, 1194, 1076, 1011, 763, 680; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.38 (s, 1H), 7.20 (s, 2H), 7.13 (t, J=7.5 Hz, 1H), 7.00 (d, J=7.0 Hz, 1H), 6.88 (t, J=7.3 Hz, 1H), 2.68–2.62 (m, 2H), 2.30–2.15 (m, 2H), 1.96–1.87 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.94, 178.08, 165.98, 158.60, 141.98, 134.51, 128.09, 123.15, 121.59, 117.30, 111.87, 109.10, 57.58, 46.87, 36.35, 26.71, 19.76; HRMS (EI) *m*/*z* calcd for $C_{17}H_{13}N_3O_3$ (M^+): 307.0957, found: 307.0964.

*4.2.27. 2-Amino-1′-methyl-2′,5-dioxo-5,6,7,8-tetrahydrospiro-[chromene-4,3′-indoline]-3-carbonitrile (**8g**)*

White solid with the melting point of 277–278 °C; IR (KBr, neat) ν_{max} 3566, 3468, 3357, 3302, 3151, 2962, 2195, 1705, 1675, 1645, 1602, 1492, 1470, 1424, 1350, 1309, 1215, 1075, 1012, 758, 686, 540; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.27–7.22 (m, 3H), 7.07 (d, J=7.3 Hz, 1H), 7.00–6.94 (m, 2H), 3.13 (s, 3H), 2.69–2.64 (m, 2H), 2.28–2.13 (m, 2H), 1.92 (quint, J=6.2 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 194.96, 176.60, 166.12, 158.72, 143.49, 133.66, 128.33, 122.91, 122.35, 117.18, 111.81, 108.05, 46.52, 36.30, 26.71, 26.32, 19.73; HRMS (EI) *m*/*z* calcd for $C_{18}H_{15}N_3O_3$ (M^+): 321.1113, found: 321.1106.

*4.2.28. tert-Butyl 2-amino-3-cyano-2′,5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3′-indoline]-1′-carboxylate (**8h**)*

White solid with the melting point of 296–297 °C; IR (KBr, neat) ν_{max} 3323, 3188, 2981, 2197, 1791, 1730, 1683, 1602, 1479, 1351, 1310, 1250, 1148, 1073, 1009, 839, 757, 538; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.72 (d, J=8.1 Hz, 1H), 7.43 (s, 2H), 7.31 (td, J=7.5, 1.5 Hz, 1H), 7.19–7.11 (m, 2H), 2.69 (t, J=5.9 Hz, 2H), 2.32–2.16 (m, 2H), 1.94 (quint, J=5.9 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.28, 175.03, 166.54, 158.48, 148.68, 138.89, 132.48, 128.52, 124.69, 123.52, 117.03, 114.15, 111.93, 83.66, 57.28, 47.27, 35.97, 27.65, 26.60, 19.67; HRMS (EI) *m*/*z* calcd for $C_{22}H_{21}N_3O_5$ (M^+): 407.1481, found: 407.1484.

*4.2.29. 2-Amino-1′-benzyl-2′,5-dioxo-5,6,7,8-tetrahydrospiro-[chromene-4,3′-indoline]-3-carbonitrile (**8i**)*

White solid with the melting point of 284–285 °C; IR (KBr, neat) ν_{max} 3375, 3291, 3176, 2195, 1694, 1683, 1667, 1605, 1488, 1466, 1348, 1313, 1213, 1173, 1075, 1012, 942, 881, 867, 748, 707, 689, 615, 538; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.49 (d, J=7.3 Hz, 2H), 7.34–7.22 (m, 5H), 7.16–7.08 (m, 2H), 6.95 (t, J=7.3 Hz, 1H), 6.68 (d, J=7.7 Hz, 1H), 4.90 (q, J=16.5 Hz, 2H), 2.77–2.63 (m, 2H), 2.34–2.18 (m, 2H), 1.95 (quint, J=6.2 Hz, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.11, 176.77, 166.36, 158.77, 142.56, 136.16, 133.70, 128.31, 128.18, 127.09, 123.08, 122.46, 117.36, 111.71, 108.74, 57.27, 46.63, 43.31, 36.29, 26.77, 19.74; HRMS (EI) *m*/*z* calcd for $C_{24}H_{19}N_3O_3$ (M^+): 397.1426, found: 397.1422.

*4.2.30. 1′-Acetyl-2-amino-2′,5-dioxo-5,6,7,8-tetrahydrospiro-[chromene-4,3′-indoline]-3-carbonitrile (**8j**)*

White solid with the melting point of 272–273 °C; IR (KBr, neat) ν_{max} 3594, 3533, 3318, 3183, 2204, 1755, 1722, 1678, 1658, 1603, 1465, 1423, 1372, 1350, 1334, 1305, 1211, 1172, 1073, 1014, 759, 599; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.07 (d, J=8.1 Hz, 1H), 7.50 (s, 2H), 7.32 (t, J=7.3 Hz, 1H), 7.24–7.17 (m, 2H), 2.78–2.64 (m, 2H), 2.57 (s, 3H), 2.34–2.18 (m, 2H), 1.99–1.90 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 195.52, 177.95, 170.31, 166.80, 158.53, 139.16, 132.86, 128.61, 125.50, 123.55, 116.98, 115.24, 111.95, 57.10, 47.51, 35.88, 26.60, 25.93, 19.67.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2008.06.061.

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