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An Efficient Synthesis of 4*H*-Benzo[*g*]chromene-5,10-dione Derivatives through Triethylbenzylammonium Chloride Catalyzed Multicomponent Reaction under Solvent-free Conditions

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A series of 4-aryl-5,10-dihydro-4*H*-benzo[*g*]chromene-5,10-dione derivatives were synthesized by a three-component reaction with aromatic aldehyde, 2-hydroxy-1,4-dihydronaphthalene-1,4-dione, and malononitrile catalyzed by triethylbenzylammonium chloride under solvent-free conditions. The novel efficient method has the advantages of environmental friendliness, high yield, simple work-up and ease of operation.

Keywords 4-aryl-4*H*-benzo[*g*]chromene-5,10-dione, solvent-free, three-component reaction, triethylbenzylammonium chloride

Introduction

In a multicomponent reaction (MCR), one can create highly complex molecules in a single reaction from readily available starting materials without the complicated purification operations; thus, MCR is a resource- and time-effective and therefore economically favorable process in diversity generation.[1] Recently, great efforts have been made to develop new MCR for the synthesis of compounds with potential bioactivity.[2]

Pyran derivatives have extensive bioactivities, such as antibacterial,[3] antiproliferation[4] and antitumor activities,[5] hypotensive effect,[6] antiallergic effect,[7] and biological activities of local anesthetization and antiarrhythmia.[8] Derivatives of 1,4-naphthoquinone also have antiallergic and anticancer activities,[9] and can be used as inhibitors of KB (human epidermoid carcinoma KB cells).[10] 1,4-Pyranonaphthoquinone derivatives possessing pyran and 1,4-naphthoquinone motifs exhibit much more anticancer activities against KB, HeLa (human cervical carcinoma) and $HepG_2$ (human hepatocellular carcinoma) cell lines.[11]

Due to their diverse biological activities, the synthesis of 1,4-pyranonaphthoquinone derivatives has attracted considerable attention. So far, several methods to these compounds have been reported.[12] However, most of them have many drawbacks, including high temperatures, long reaction time, drastic reaction conditions, tedious work-up, low yields and the use of organic solvents. Therefore, the development of simple, convenient and environmentally benign approaches for the synthesis of these potential bioactive compounds is still desirable. In past decades, solvent-free reaction has gained much application in organic synthesis. These processes are not only environmentally benign, but also economically beneficial because toxic wastes can be minimized or eliminated, so the costs of waste treatment are also reduced. An additional attractive feature is the operational simplicity.[13] To continue our work in the synthesis of heterocyclic compounds via MCR under solvent-free conditions,[14] here we shall report an efficient and green synthetic route to 4-aryl-5,10-dihydro-4*H*-benzo[*g*]chromene-5,10-dione derivatives **4** by a three-component reaction (which consists of condensation, Michael addition, and cyclization) with aromatic aldehyde 1,2-hydroxy-1,4-dihydronaphthalene-1,4-dione **2**, and malononitrile **3** catalyzed by TEBA (triethylbenzylammonium chloride) under solvent-free conditions (Scheme 1).

Results and discussion

The effect of solvent on the reaction was initially investigated by the reaction of 2-hydroxy-1,4-dihydronaphthalene-1,4-dione (1 mmol), malononitrile (1 mmol) and phenyl aldehyde (1 mmol) catalyzed by TEBA (0.1 mmol). As shown in Table 1, the synthesis in solvents gave the expected product, **4a**, in different yields (20%—88%). However, solvent-free reaction

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Scheme 1

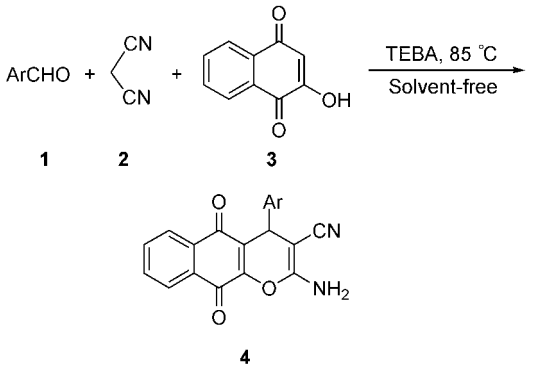


Table 1 Solvent effect on the synthesis of **4a**

Entry	Solvent	Temp./℃	Time/h	Isolated yield/%
1	CH_3CN	Reflux	5	20
2	$CHCl_3$	Reflux	6	26
3	EtOH	Reflux	4	88
4	HOAc	85	6	65
5	H_2O	85	8	82
6	Solvent-free	85	4	92

exhibited higher yield (92%) than their liquid-phase counterparts. So we synthesized the desired products via the solventless three-component reaction.

The catalytic efficiency of $KHSO_4$, DMAP (4-dimethylaminopyridine), HTMAB (hexadecyltrimethylaminium bromide) and K_2CO_3 in the reaction was also studied. In all cases 10 mol% of the catalyst was used and the reaction was carried out under solvent-free conditions. As shown in Table 2, the catalytic effects of DMAP, HTMAB, and K_2CO_3 were similar. $KHSO_4$ gave the lowest yield, while TEBA gave the highest yield. Therefore, TEBA is the best among the five catalysts in this study.

Table 2 Catalyst optimization for the synthesis of **4a**[a]

Entry	Catalyst	Time/h	Isolated yield/%
1	None	8	Trace
2	$KHSO_4$	6	Trace
3	DMAP	3	80
4	HTMAB	4	83
5	K_2CO_3	4	85
6	TEBA	4	92

[a] Reaction conditions: 2-hydroxy-1,4-dihydronaphthalene-1,4-dione (1 mmol), malononitrile (1 mmol) and phenyl aldehyde (1 mmol), solvent-free, 85 ℃.

To find the optimal reaction temperature, the synthesis of **4a** was studied in the presence of 10 mol% TEBA at different temperatures. The results in Table 3 show that the reaction at 85 ℃ proceeded in the highest yield among the seven tested temperatures. So 85 ℃ was chosen for the reaction.

Table 3 Temperature optimization for synthesis of **4a**

Entry	Temp./℃	Time/h	Isolated yield/%
1	r.t.	8	trace
2	45	6	20
3	65	6	71
4	75	5	85
5	85	4	92
6	95	4	91
7	105	4	88

To optimize the catalyst loading, 5 mol%, 10 mol%, 15 mol%, and 20 mol% of TEBA were tested respectively. The results are listed in Table 4. A 10 mol% loading of TEBA was sufficient to push the reaction forward.

Table 4 Effect of amount of catalyst on reaction

Entry	Catalyst/mol%	Time/h	Isolated yield/%
1	0	8	Trace
2	5	4	64
3	10	4	92
4	15	4	91
5	20	4	92

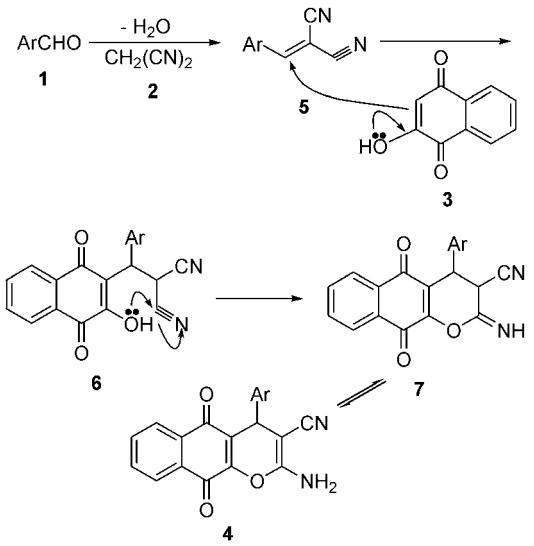
Under these optimized reaction conditions (solvent-free, 85 ℃, 10 mol% TEBA), a series of 4-aryl-5,10-dihydro-4*H*-benzo[*g*]chromene-5,10-dione derivatives (**4**) were synthesized with high yields. The results are summarized in Table 5. The methodology can be applied to aromatic aldehydes either with electron-withdrawing groups (such as nitro group, halogen) or electron-donating groups (such as methoxy group) with moderate to excellent yields under the same conditions. Therefore we conclude that the electronic nature of substituents of the aromatic aldehyde has no significant effect on the reaction. However, when the aliphatic aldehyde was applied to this reaction, no expected product was obtained.

Table 5 TEBA catalyzed synthesis of **4**

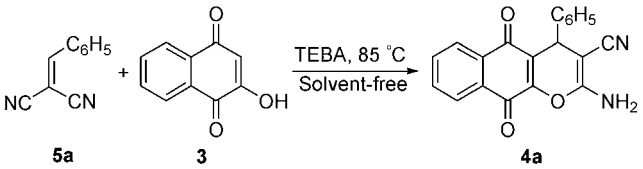
Entry	Product	Ar	Reaction time/h	Isolated yield/%
1	**4a**	C_6H_5	4.0	92
2	**4b**	4-ClC_6H_4	3.5	93
3	**4c**	4-BrC_6H_4	4.0	95
4	**4d**	4-$NO_2C_6H_4$	3.0	94
5	**4e**	2-ClC_6H_4	3.5	90
6	**4f**	3-$NO_2C_6H_4$	3.0	84
7	**4g**	2,4-$Cl_2C_6H_3$	3.5	86
8	**4h**	4-FC_6H_4	3.5	92
9	**4i**	3,4,5-$(CH_3O)_3C_6H_2$	6.0	85

A plausible mechanism of the reaction was presented in Scheme 2. Product **4** may be synthesized via sequential Knoevenagel condensation, Michael addition, cyclization and isomerization. First, Knoevenagel condensation between aryl aldehyde and malononitrile gave an intermediate **5**, 2-arylmethylidenemalononitrile. Michael addition between **5** and **3** furnished **6**, which upon intramolecular cyclization and isomerization gave rise to product **4**. To test the proposed reaction pathway, a solvent-free reaction of **5a** and **3** catalyzed by TEBA was carried out at 85 ℃. To our delight, it proceeded smoothly and gave product **4a** with a similar yield to the three-component reaction (Scheme 3). The fact supported the supposed reaction mechanism. However, the reactivity of aliphatic aldehyde is much lower than that of their aromatic counterparts. The intermediate **5** could not be formed via condensation under solvent-free conditions, so no expected products were obtained.

Scheme 2



Scheme 3



Encouraged by these results, the three-component reaction was carried out using ethyl 2-cyanoacetate as the substituent of malononitrile. However, no desired product was obtained. This should be attributed to the low reactivity of ethyl 2-cyanoacetate, for ethyl 2-cyano-3-arylacrylates **8** reacted with **3** smoothly and gave the desired products **9** successfully (Table 6, Scheme 4).

All of the products were characterized by IR, ^{1}H NMR, ^{13}C NMR and HRMS. To further confirm the structure of product, a single crystal of **9e** was prepared and determined by X-ray diffraction (Figure 1).

Scheme 4

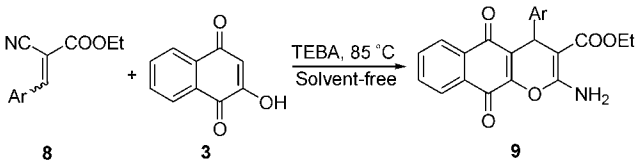


Table 6 TEBA catalyzed synthesis of **9**

Entry	Product	Ar	Reaction time/h	Isolated yield/%
1	**9a**	4-BrC_6H_4	4.0	92
2	**9b**	3-$NO_2C_6H_4$	3.5	93
3	**9c**	4-$NO_2C_6H_4$	4.0	95
4	**9d**	3-BrC_6H_4	4.5	83
5	**9e**	4-FC_6H_4	3.0	88

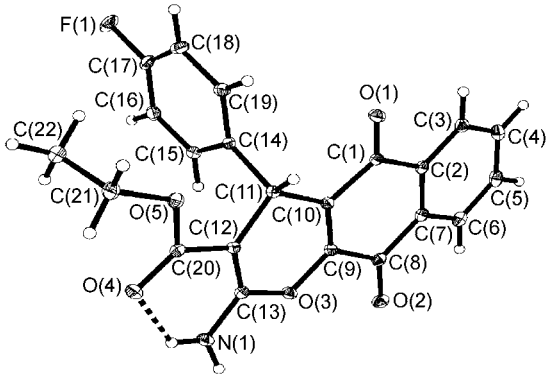


Figure 1 Crystal structure of **9e**.

Conclusion

In summary, an efficient and simple method for the synthesis of 5,10-dihydro-4*H*-benzo[*g*]chromene-5,10-dione derivatives by three-component reaction of aldehyde, 2-hydroxy-1,4-dihydronaphthalene-1,4-dione, and malononitrile was successfully established under solvent-free conditions catalyzed by TEBA. Particularly valuable features of this protocol include high yields, mild reaction conditions, easy work-up, short reaction time and environmentally friendly procedure.

Experimental

Reaction progress was monitored with analytical TLC on 0.25 mm silica gel precoated glass plates with a fluorescent indicator UV254. Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a TENSOR 27 spectrometer in KBr. ^{1}H NMR spectra were measured on a DPX 400 spectrometer operating at 400 MHz, using DMSO-d_6 as solvent and TMS as an internal standard. HRMS data were obtained on a Varian IonSpec QFT-MS spectrometer with the technique of electrospray ionization. Solvents and commercial reagents of analytical reagent grade were purchased and used without any further purification.

General procedure for the synthesis of 5,10-dihydro-4*H*-benzo[*g*]chromene-5,10-dione derivatives (4a—4n)

The mixture of aldehyde **1** (1 mmol), TEBA (0.1 mmol) and malononitrile (**2**) (1 mmol) was triturated together in an agate mortar for 5 min. After the mixture was kept at 85 ℃ for 0.5 h, 2-hydroxy-1,4-dihydronaphthalene-1,4-dione (**3**) (1 mmol) was added and triturated. The reaction mixture was heated at 85 ℃ for a certain time (monitored by TLC). After completion of the reaction, the reaction mixture was allowed to cool to room temperature, washed with water and recrystallized from 95% ethanol to give products **4** with high purities.

2-Amino-4-phenyl-5,10-dihydro-5,10-dioxo-4*H*-benzo[*g*]chromene-3-carbonitrile (4a) Red powder, m.p. 260—262 ℃ (Lit.[12h] 256 ℃); ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 4.61 (s, 1H, CH), 7.22—7.23 (m, 1H, ArH), 7.31 (d, J=4.4 Hz, 4H, ArH), 7.34 (s, 2H, NH_2), 7.83—7.90 (m, 3H, ArH), 8.05—8.07 (m, 1H, ArH); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 182.5, 176.8, 158.4, 148.9, 143.5, 134.5, 134.1, 131.0, 130.6, 128.6, 127.6, 127.0, 126.0, 125.8, 122.0, 119.3, 57.5, 36.5; IR (KBr) v: 3401, 3325, 3215, 3194, 2200, 1671, 1636, 1602, 1580, 1523, 1406, 1366, 1331, 1302, 1245, 1206, 1179, 1071, 1056, 949, 884, 720, 622 cm^{-1}; HRMS calcd for $C_{20}H_{12}N_2O_3Na$ (M^++Na) 351.0746, found 351.0761.

2-Amino-4-(4-chlorophenyl)-5,10-dihydro-5,10-dioxo-4*H*-benzo[*g*]chromene-3-carbonitrile (4b) Red powder, m.p. 278—280 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 4.65 (s, 1H, CH), 7.13 (t, J=8.8 Hz, 2H, ArH), 7.35 (s, 2H, NH_2), 7.38 (t, J=5.6 Hz, 2H, ArH), 7.83—7.88 (m, 3H, ArH), 8.04—8.06 (m, 1H, ArH); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 182.5, 176.8, 158.3, 149.0, 142.6, 134.5, 134.1, 131.7, 131.0, 130.6, 129.6, 128.5, 126.0, 125.8, 121.4, 119.2, 57.1, 36.0; IR (KBr) v: 3407, 3324, 3208, 3194, 2210, 1667, 1635, 1594, 1507, 1408, 1364, 1240, 1200, 1158, 1072, 1015, 939, 835, 742, 718, 628 cm^{-1}; HRMS calcd for $C_{20}H_{11}ClN_2O_3Na$ (M^++Na) 385.0356, found 385.0368.

2-Amino-4-(4-bromophenyl)-5,10-dihydro-5,10-dioxo-4*H*-benzo[*g*]chromene-3-carbonitrile (4c) Red powder, m.p. 291—293 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 4.63 (s, 1H, CH), 7.31 (d, J=8.4 Hz, 2H, ArH), 7.39 (s, 2H, NH_2), 7.50 (d, J=8.4 Hz, 2H, ArH), 7.83—7.89 (m, 3H, ArH), 8.04—8.07 (m, 1H, ArH); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 182.5, 176.8, 158.3, 149.0, 143.0, 134.5, 134.1, 131.4, 131.0, 130.6, 130.0, 126.0, 125.8, 121.3, 120.2, 119.2, 57.0, 36.1; IR (KBr) v: 3406, 3326, 3214, 3192, 2194, 1665, 1603, 1593, 1487, 1411, 1365, 1302, 1243, 1207, 1180, 1073, 1010, 942, 841, 734, 719, 628 cm^{-1}; HRMS calcd for $C_{20}H_{11}BrN_2O_3Na$ (M^++Na) 428.9851, found 428.9837.

2-Amino-4-(4-nitrophenyl)-5,10-dihydro-5,10-dioxo-4*H*-benzo[*g*]chromene-3-carbonitrile (4d) Red powder, m.p. 247—248 ℃; ^{1}H NMR (DMSO-d_6) δ: 4.88 (s, 1H, CH), 7.49 (s, 2H, NH_2), 7.63 (t, J=8.0 Hz, 1H, ArH), 7.84—7.88 (m, 4H, ArH), 8.06 (d, J=7.6 Hz, 1H, ArH), 8.11 (d, J=8.4 Hz, 1H, ArH), 8.21 (s, 1H, ArH); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 182.6, 176.8, 158.5, 149.4, 147.9, 145.8, 134.8, 134.5, 134.1, 131.0, 130.7, 130.0, 126.0, 125.8, 122.5, 122.2, 120.6, 119.0, 56.6, 36.3; IR (KBr) v: 3421, 3328, 3221, 3196, 2201, 1673, 1604, 1591, 1530, 1410, 1358, 1300, 1244, 1199, 1099, 1038, 1022, 956, 859, 721, 616 cm^{-1}; HRMS calcd for $C_{20}H_{12}N_3O_5$ (M^+ + H) 374.0777, found 374.0766.

2-Amino-4-(2-chlorophenyl)-5,10-dihydro-5,10-dioxo-4*H*-benzo[*g*]chromene-3-carbonitrile (4e) Red powder, m.p.＞300 ℃; ^{1}H NMR (DMSO-d_6) δ: 5.15 (s, 1H, CH), 7.24—7.26 (m, 2H, ArH), 7.37 (s, 2H, NH_2), 7.40—7.45 (m, 2H, ArH), 7.84—7.87 (m, 3H, ArH), 8.06—8.08 (m, 1H, ArH); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 182.4, 176.8, 158.4, 149.5, 140.9, 134.6, 134.2, 132.0, 130.9, 130.6, 130.5, 129.4, 128.7, 127.8, 126.1, 125.8, 121.3, 118.8, 56.3, 33.5; IR (KBr) v: 3434, 3327, 3213, 3184, 2192, 1663, 1635, 1595, 1473, 1414, 1366, 1301, 1246, 1202, 1077, 1040, 1016, 956, 860, 723, 623 cm^{-1}; HRMS calcd for $C_{20}H_{11}ClN_2O_3Na$ (M^++Na) 385.0356, found 385.0343.

2-Amino-4-(3-nitrophenyl)-5,10-dihydro-5,10-dioxo-*H*-benzo[*g*]chromene-3-carbonitrile (4f) Red powder, m.p. 295—297 ℃; ^{1}H NMR (DMSO-d_6) δ: 4.88 (s, 1H, CH), 7.49 (s, 2H, NH_2), 7.63 (t, J=8.0 Hz, 1H, ArH), 7.84—7.87 (m, 4H, ArH), 8.07 (d, J=7.6 Hz, 1H, ArH), 8.11 (d, J=9.6 Hz, 1H, ArH), 8.21 (s, 1H, ArH); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 182.6, 176.8, 158.4, 149.4, 147.9, 145.8, 134.8, 134.5, 134.1, 131.0, 130.7, 130.0, 126.0, 125.8, 122.5, 122.2, 120.5, 119.0, 56.6, 36.3; IR (KBr) v: 3421, 3328, 3222, 3196, 2202, 1671, 1639, 1605, 1591, 1531, 1411, 1359, 1300, 1243, 1199, 1064, 1038, 1021, 962, 859, 715, 613 cm^{-1}; HRMS calcd for $C_{20}H_{11}N_3O_5Na$ (M^++Na) 396.0596, found 396.0577.

2-Amino-4-(2,4-dichlorophenyl)-5,10-dihydro-5,10-dioxo-4*H*-benzo[*g*]chromene-3-carbonitrile (4g) Red powder, m.p. 293—295 ℃; ^{1}H NMR (DMSO-d_6) δ: 5.14 (s, 1H, CH), 7.33 (d, J=8.4 Hz, 1H, ArH), 7.42 (s, 2H, NH_2), 7.49 (d, J=8.4 Hz, 1H, ArH), 7.60 (s, 1H, ArH), 7.85—7.88 (m, 3H, ArH), 8.06—8.08 (m, 1H, ArH); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 182.4, 176.7, 158.4, 149.6, 140.2, 134.6, 134.2, 132.9, 132.3, 131.9, 130.9, 130.6, 128.7, 128.0, 126.1, 125.8, 120.7, 118.7, 55.8, 33.2; IR (KBr) v: 3467, 3341, 3166, 3073, 2202, 1671, 1632, 1592, 1469, 1400, 1386, 1365, 1302, 1248, 1199, 1070, 1048, 946, 847, 718, 615 cm^{-1}; HRMS calcd for $C_{20}H_{10}Cl_2N_2O_3Na$ (M^++Na) 418.9966, found 418.9974.

2-Amino-4-(4-fluorophenyl)-5,10-dihydro-5,10-dioxo-4*H*-benzo[*g*]chromene-3-carbonitrile (4h) Red powder, m.p. 286—288 ℃; ^{1}H NMR (DMSO-d_6) δ: 4.65 (s, 1H, CH), 7.13 (t, J=8.8 Hz, 2H, ArH), 7.35 (s, 2H, NH_2), 7.38 (t, J=5.6 Hz, 2H, ArH), 7.83—7.88 (m, 3H, ArH), 8.04—8.06 (m, 1H, ArH); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 182.5, 176.8, 161.2 (^{C-F}J=

243.2 Hz), 158.3, 148.9, 139.8 (^{C-F}J=2.9 Hz), 134.5, 134.1, 131.0, 130.6, 129.7 (^{C-F}J=8.1 Hz), 126.0, 125.8, 121.6, 119.2, 115.23 (^{C-F}J=21.4 Hz), 57.3, 35.8; IR (KBr) *v*: 3407, 3324, 3208, 3194, 2210, 1667, 1635, 1594, 1507, 1408, 1364, 1240, 1200, 1158, 1072, 1015, 939, 835, 742, 718, 628 cm^{-1}; HRMS calcd for $C_{20}H_{11}FN_2O_3Na$ (M^++Na) 369.0651, found 369.0649.

2-Amino-4-(3,4,5-trimethoxyphenyl)-5,10-dihydro-5,10-dioxo-4*H*-benzo[*g*]chromene-3-carbonitrile (4i) Red powder, m.p. 286—288 ℃; ^{1}H NMR (DMSO-d_6) δ: 3.62 (s, 3H, OCH_3) , 3.74 (s, 6H, 2×OCH_3), 4.57 (s, 1H, CH), 6.57 (s, 2H, ArH), 7.30 (s, 2H, NH_2), 7.84—7.92 (m, 3H, ArH), 8.05—8.07 (m, 1H, ArH); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 182.6, 176.9, 158.3, 152.9, 149.0, 139.3, 136.6, 134.4, 134.0, 131.1, 130.7, 126.0, 125.8, 121.5, 119.4, 105.1, 59.9, 57.5, 56.0, 36.8; IR (KBr) *v*: 3418, 3327, 3223, 3190, 2196, 1662, 1634, 1594, 1505, 1461, 1411, 1365, 1326, 1302, 1246, 1204, 1182, 1129, 1083, 1007, 947, 886, 723, 612 cm^{-1}; HRMS calcd for $C_{23}H_{18}N_2O_6Na$ (M^++Na) 441.1063, found 441.1062.

General procedure for the synthesis of 5,10-dihydro-4*H*-benzo[*g*]chromene-5,10-dione derivatives (9a—9e)

The mixture of ethyl 2-cyano-3-arylacrylates **8** (1 mmol), TEBA (0.1 mmol) and 2-hydroxy-1,4-dihydronaphthalene-1,4-dione (**3**) (1 mmol) was triturated together in an agate mortar for 5 min. Then the mixture was kept at 85 ℃ for a certain time (monitored by TLC). After completion of the reaction, the reaction mixture was allowed to cool to room temperature, washed with water and recrystallized from 95% ethanol to give products **9** with high purities.

Ethyl 2-amino-4-(4-bromophenyl)-5,10-dihydro-5,10-dioxo-4*H*-benzo[*g*]chromene-3-carboxylate (9a) Red powder, m.p. 183—185 ℃; ^{1}H NMR (DMSO-d_6) δ: 1.15 (t, *J*=7.2 Hz, 3H, $OCH_2C\mathbf{H}_3$), 4.02 (q, *J*=7.2 Hz, 2H, $OC\mathbf{H}_2CH_3$), 4.88 (s, 1H, ArH), 7.26 (d, *J*=8.0 Hz, 2H, ArH), 7.44 (d, *J*=8.0 Hz, 2H, ArH), 7.85—7.88 (m, 5H, NH_2+ArH), 8.05—8.07 (m, 1H, ArH); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 182.9, 177.6, 168.4, 158.4, 148.2, 143.4, 134.5, 133.8, 131.6, 131.3, 130.5, 130.4, 126.6, 126.5, 126.0, 120.8, 78.6, 60.0, 34.7, 14.2; IR (KBr) *v*: 3426, 3299, 2987, 1681, 1613, 1594, 1509, 1483, 1403, 1359, 1330, 1303, 1274, 1248, 1194, 1097, 1065, 1012, 947, 932, 846, 823, 805, 791, 732, 715, 656, 608 cm^{-1}; HRMS calcd for $C_{22}H_{16}BrNO_5Na$ (M^++Na) 476.0110, found 476.0067.

Ethyl 2-amino-4-(3-nitrophenyl)-5,10-dihydro-5,10-dioxo-4*H*-benzo[*g*]chromene-3-carboxylate (9b) Red powder, m.p. 223—224 ℃; ^{1}H NMR (DMSO-d_6) δ: 1.13 (t, *J*=7.2 Hz, 3H, $OCH_2C\mathbf{H}_3$), 4.01 (q, *J*=7.2 Hz, 2H, $OC\mathbf{H}_2CH_3$), 5.01 (s, 1H, CH), 7.57 (t, *J*=8.0 Hz, 2H, ArH), 7.77—8.07 (m, 7H, NH_2+ArH), 8.12 (s, 1H, ArH); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 182.8, 177.4, 168.1, 158.4, 148.5, 148.3, 146.6, 134.8, 134.7, 134.0, 131.5, 130.5, 129.0, 126.7, 126.7, 125.2, 123.7, 122.0, 78.1, 60.2, 35.3, 14.2; IR (KBr) *v*: 3434, 3313, 3100, 2981, 2931, 1684, 1623, 1537, 1477, 1455, 1405, 1386, 1345, 1241, 1101, 1071, 1012, 954, 940, 905, 820, 806, 789, 745, 728, 717, 705, 677, 600 cm^{-1}; HRMS calcd for $C_{22}H_{16}N_2O_7Na$ (M^++Na) 443.0855, found 443.0849.

Ethyl 2-amino-4-(4-nitrophenyl)-5,10-dihydro-5,10-dioxo-4*H*-benzo[*g*]chromene-3-carboxylate (9c) Red powder, m.p. 192—193 ℃; ^{1}H NMR (DMSO-d_6) δ: 1.14 (t, *J*=7.2 Hz, 3H, $OCH_2C\mathbf{H}_3$), 4.03 (q, *J*=7.2 Hz, 2H, $OC\mathbf{H}_2CH_3$), 5.01 (s, 1H, CH), 7.60 (d, *J*=8.0 Hz, 2H, ArH), 7.82—7.91 (m, 3H, ArH), 7.98 (s, 2H, NH_2), 8.05—8.07 (m, 1H, ArH), 8.13 (d, *J*=8.0 Hz, 2H, ArH); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 182.8, 177.4, 168.1, 158.5, 151.6, 149.9, 148.5, 146.8, 134.7, 134.0, 131.4, 130.5, 129.6, 126.7, 125.2, 123.5, 77.9, 60.2, 35.4, 14.3; IR (KBr) *v*: 3415, 3299, 2985, 1693, 1625, 1592, 1524, 1460, 1404, 1349, 1299, 1248, 1244, 1195, 1166, 1108, 1061, 1018, 946, 857, 834, 792, 722, 706, 610 cm^{-1}; HRMS calcd for $C_{22}H_{16}N_2O_7Na$ (M^++Na) 443.0855, found 443.0860.

Ethyl 2-amino-4-(3-bromophenyl)-5,10-dihydro-5,10-dioxo-4*H*-benzo[*g*]chromene-3-carboxylate (9d) Red powder, m.p. 194—196 ℃; ^{1}H NMR (DMSO-d_6) δ: 1.16 (t, *J*=7.2 Hz, 3H, $OCH_2C\mathbf{H}_3$), 4.04 (q, *J*=7.2 Hz, 2H, $OC\mathbf{H}_2CH_3$), 4.86 (s, 1H, CH), 7.23 (t, *J*=8.0 Hz, 2H, ArH), 7.30 (d, *J* = 8.0 Hz, 2H, ArH), 7.83—7.87 (m, 2H, ArH), 7.91 (s, 3H, NH_2+ArH), 8.04—8.06 (m, 1H, ArH); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 182.8, 177.6, 168.3, 158.4, 148.3, 146.5, 134.5, 133.8, 131.7, 131.6, 130.6, 130.0, 129.7, 127.4, 126.6, 126.6, 125.9, 122.3, 78.6, 60.1, 35.0, 14.2; IR (KBr) *v*: 3469, 3312, 3064, 2995, 2980, 2933, 2908, 2873, 1867, 1681, 1609, 1594, 1572, 1504, 1472, 1405, 1385, 1358, 1329, 1287, 1276, 1249, 1194, 1158, 1116, 1097, 1060, 1005, 970, 939, 903, 885, 820, 795, 784, 728, 716, 688, 664, 640, 601 cm^{-1}; HRMS calcd for $C_{22}H_{16}BrNO_5Na$ (M^++Na) 476.0110, found 476.0091.

Ethyl 2-amino-4-(4-fluorophenyl)-5,10-dihydro-5,10-dioxo-4*H*-benzo[*g*]chromene-3-carboxylate (9e) Red powder, m.p. 203—205 ℃; ^{1}H NMR (DMSO-d_6) δ: 1.11 (t, *J*=7.2 Hz, 3H, $OCH_2C\mathbf{H}_3$), 3.98 (q, *J*=7.2 Hz, 2H, $OC\mathbf{H}_2CH_3$), 4.90 (s, 1H, ArH), 7.03 (t, *J*=8.4 Hz, 2H, ArH), 7.29 (dd, *J*=8.4, 5.6 Hz, 2H, ArH), 7.83—7.92 (m, 5H, ArH+NH_2), 8.03—8.06 (m, 1H, ArH); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 183.0, 177.6, 168.4, 161.7 (^{C-F}J=245.3 Hz), 158.4, 148.1, 140.1 (^{C-F}J=3.3 Hz), 134.5, 133.8, 131.6, 130.5, 130.1 (^{C-F}J=8.1 Hz), 126.6, 126.5, 126.4, 115.0 (^{C-F}J=21.4 Hz), 79.0, 60.0, 34.4, 14.2; IR (KBr) *v*: 3465, 3410, 3292, 1679, 1657, 1615, 1595, 1508, 1443, 1405, 1360, 1332, 1290, 1276, 1242, 1195, 1159, 1098, 1065, 1016, 951, 932, 841, 793, 716, 615 cm^{-1}; HRMS calcd for $C_{22}H_{16}FNO_5Na$ (M^++Na) 416.0910, found 416.0920.

Crystallographic data

The single-crystal growth was carried out in ethanol at room temperature. X-ray crystallographic analysis was performed with a Rigaku Saturn diffractometer. Crystal data for **9e**: $C_{22}H_{16}FNO_5$, crystal dimension 0.20 mm×0.18 mm×0.14 mm, monoclinic, space group $P121/c1$, $a = 0.8575(3)$ nm, $b = 9590(3)$ nm, $c = 2.1431(6)$ nm, $\beta = 91.172(3)°$, $V = 1.7621(9)$ nm^3, $M_r = 393.36$, $Z = 4$, $D_c = 1.483$ g/cm^3, $\lambda = 0.71070$ Å, μ(Mo Kα) = 0.113 mm^{-1}, $F(000) = 816$, $S = 1.005$, $R_1 = 0.0366$, and $wR_2 = 0.0941$.

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