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Multicomponent reaction for the synthesis of novel fluorinated 2-amino-4*H*-benzo[*g*]chromene-5,10-dione-3-carbonitriles

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Abstract. Chromene is a significant class of heterocyclic compounds prossessing a simple structure as well as important biological activities. Many studies have been done to find new approaches for the preparation of chromene derivatives. Notably, the introduction of fluorine into heterocyclic molecules resulted in a significant improvement of their biological activities. In this study, a simple, straightforward, and highly efficient microwave-assisted three-component synthesis of novel 2-amino-4*H*-benzo[*g*]chromene-5,10-dione-3-carbonitrile derivatives bearing fluorine atoms has been developed using 1,4-diazabicyclo[2.2.2]octane (DABCO) as an eco-friendly catalyst, and acetonitrile as a solvent. Starting from 2-hydroxy-1,4-dihydronaphthalene-1,4-dione, malononitrile, and fluorinated aromatic aldehyde, 2-amino-4*H*-benzo[*g*]chromene-5,10-dione-3-carbonitrile derivatives have been afforded in good yields (71 - 76 %). The plausible reaction mechanism was described. Products were synthesized through a sequential Knoevenagel condensation, Michael addition, intramolecular cyclization, and [1,3]-hydrogen shift step. The structure of products was completely elucidated by ^{1}H NMR, ^{13}C NMR, and mass spectra. The particularly valuable feature of this process is mild reaction conditions, short reaction times, and good yields.

Keywords: 2-Amino-3-cyano-chromene, fluorine heterocyclic molecule, 1,4-diazabicyclo[2.2.2]octane, multicomponent domino reaction, 2-hydroxy-1,4-naphthoquinone.

Classification numbers: 2.10.2, 2.10.3.

1. INTRODUCTION

Chromenes have been known as a common structural feature in numerous natural compounds such as calanolides [1, 2], and calophyllolides [3]. They have exhibited a broad

range of significant biological activities including anticancer [4, 5], anti-HIV [6, 7], antitumor [8], anti-proliferation [9], antibacterial [10], antimalarial [11,12], and many more. Noticeably, 2-amino-4*H*-chromene-3-carbonitriles have played an important role in drug discovery. For example, crolibulin (**1**) has been used in phase I/II clinical trials for the treatment of advanced solid tumors [13], 2-amino-4-(3-nitrophenyl)-4*H*-benzo[*h*]chromene-3-carbonitrile (**2**) has been known as a potent anti-proliferative agent as well as a mitotic inhibitor [14, 15], and 2-amino-5-oxo-4-phenyl-4,5-dihydropyrano[3,2-*c*]chromene-3-carbonitrile (**3**) as a blood anticoagulant analog of warfarin (Figure 1) [16]. For this reason, many efforts were made to synthesize this structure type, especially, 2-amino-4*H*-benzo[*g*]chromene-5,10-dione-3-carbonitrile derivatives [17 - 25]. Moreover, scientific studies have indicated that the introduction of fluorine into heterocyclic molecules resulted in a significant improvement of their biological activities [26-28]. Recently, fluorinated compounds have exhibited a wide range of biological and pharmaceutical activities [29 - 32]. Therefore, in continuing our interest on developing new potent bioactive heterocyclic molecules [33 - 41], herein, we reported the synthesis of 2-amino-4*H*-benzo[*g*]chromene-5,10-dione-3-carbonitrile derivatives bearing fluorines.

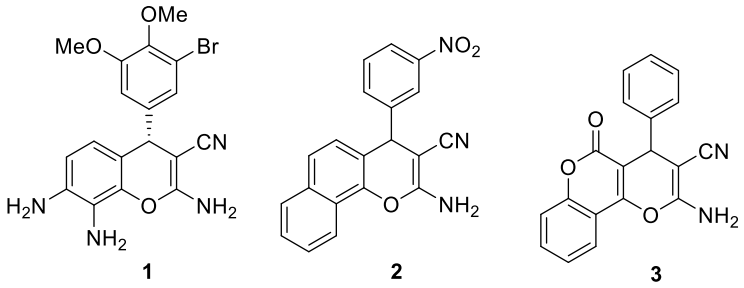


Figure 1. Some bioactive 2-amino-4*H*-chromene-3-carbonitriles.

Diazabicyclo[2.2.2]octane (DABCO) has been extensively used as an inexpensive, eco-friendly, highly reactive, and non-toxic base catalyst for the synthesis of various organic products [42 - 44]. Especially, DABCO has catalyzed efficiently multicomponent reactions for the synthesis of benzochromene derivatives [43, 44]. However, there is not any research on using DABCO as a catalyst in the synthesis of 2-amino-4*H*-benzo[*g*]chromene-5,10-dione-3-carbonitrile derivatives bearing fluorines. Therefore, this study investigated the synthesis of 2-amino-4*H*-benzo[*g*]chromene-5,10-dione-3-carbonitrile derivatives bearing fluorines *via* the microwave-assisted three-component reaction of 2-hydroxy-1,4-naphthoquinone, malononitrile, and several fluorinated aromatic aldehydes using DABCO catalyst.

2. MATERIALS AND METHODS

2.1. Materials

All reagents and solvents were purchased from Aldrich or Merck unless noted otherwise. TLC was performed using Merck silica gel 60 F_{254} plates and visualized under UV light at 254 nm. Purification of compounds was carried out using silica gel column chromatography (CC).

2.2. Methods

Reactions were performed in an Anton Paar Microwave Synthetic Reactor Monowave 400. IR spectra were recorded on a PerkinElmer Spectrum Two spectrometer in KBr pellets. ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance III spectrometers 600 MHz and 500 MHz.

HR-ESI-MS were recorded on a SCIEX X500 QTOF mass spectrometer. Melting points were determined using the Buchi B-545 melting point apparatus and are uncorrected.

2.3. Synthesis procedure of compounds 7a-j

A mixture of 2-hydroxy-1,4-naphthoquinone (**4**) (174 mg, 1.0 mmol), aromatic aldehydes **5a–j** (1.0 mmol), malononitrile (**6**) (66 mg, 1.0 mmol), and DABCO (22.5 mg, 0.2 mmol) in acetonitrile (10 ml) was subjected to microwave irradiation at 82 °C. After 20 - 25 min, the reaction was cooled to room temperature, added water, extracted with dichloromethane, washed with brine, and dried over Na_2SO_4. Evaporation of the solvent gave crude products **7a-j**, purified by CC using CH_2Cl_2–EtOAc, 20:1, v/v, as eluent.

2-Amino-4-(2-fluoro-4-methoxyphenyl)-5,10-dihydro-4*H*-benzo[*g*]chromene-5,10-dione-3-carbonitrile (7a). Reaction time: 20 min. Yield 271 mg (72 %), orange solid, mp. 240 ºC. IR (KBr) ν_{max} (cm^{-1}): 3407, 3325, 3216, 3191, 2200, 1664, 1633, 1603, 1504, 1438, 1406, 1363, 1333, 1299, 1240, 1197, 1093, 1025, 951, 830, and 718. ^{1}H NMR (DMSO-d_6, 600 MHz): δ 8.05 (1H, dd, J = 2.4, 7.8 Hz), 7.89-7.86 (1H, m), 7.86 - 7.82 (2H, m), 7.29 (2H, s, N$\underline{H}_2$), 7.26 (1H, t, J = 8.4 Hz), 6.78 (1H, dd, J = 2.4, 12.6 Hz), 6.69 (1H, dd, J = 2.4, 9.0 Hz), 4.83 (1H, s), and 3.74 (3H, s). ^{13}C NMR (DMSO-d_6, 150 MHz) δ 182.4, 176.8, 160.2 (1C, d, J = 244.5 Hz), 159.7 (1C, d, J = 12.0 Hz), 158.5, 149.1, 134.6, 134.1, 130.9, 130.6 (1C, d, J = 6.0 Hz), 130.5, 126.1, 125.8, 122.2 (1C, d, J = 13.5 Hz), 121.0 119.1, 110.7, 101.3 (1C, d, J = 25.5 Hz), 56.3, 55.5, and 29.9. HR-ESI-MS *m/z* 377.0929 $[M+H]^+$ (calcd. for $C_{21}H_{14}FN_2O_4^+$: 377.0933).

2-Amino-4-(3-fluoro-4-methoxyphenyl)-5,10-dihydro-4*H*-benzo[*g*]chromene-5,10-dione-3-carbonitrile (7b). Reaction time: 20 min. Yield 274 mg (73 %), orange solid, mp. 258 ºC. IR (KBr) ν_{max} (cm^{-1}) 3397, 3329, 3254, 3216, 3068, 2962, 2840, 2193, 1729, 1663, 1603, 1519, 1414, 1368, 1334, 1243, 1204, 1124, 1095, 1074, 1026, 953, 776, 719, 621, and 524. ^{1}H NMR (DMSO-d_6, 600 MHz): δ 8.05 (1H, dd, J = 1.8, 7.2 Hz), 7.90 - 7.88 (1H, m), 7.87 - 7.82 (2H, m), 7.30 (2H, s, N$\underline{H}_2$), 7.17 (1H, dd, J = 1.8, 11.4 Hz), 7.10 - 7.08 (2H, m), 4.60 (1H, s), and 3.80 (3H, s). ^{13}C NMR (DMSO-d_6, 150 MHz) δ 182.6, 176.9, 158.2, 151.4 (1C, d, J = 241.5 Hz), 148.9, 146.2 (1C, d, J = 10.5 Hz), 136.6 (1C, d, J = 4.5 Hz), 134.5, 134.1, 131.0, 130.7, 126.0, 125.8, 123.9, 121.4, 119.2, 115.2 (1C, d, J = 18 Hz), 113.8, 57.3, 56.0, and 35.6.

2-Amino-4-(2-fluoro-4-hydroxyphenyl)-5,10-dihydro-4*H*-benzo[*g*]chromene-5,10-dione-3-carbonitrile (7c). Reaction time: 20 min. Yield 257 mg (71 %), orange solid, mp. 270 ºC. IR (KBr) ν_{max} (cm^{-1}) 3436, 3391, 3293, 3177, 2959, 2925, 2855, 2198, 1730, 1664, 1624, 1595, 1510, 1460, 1369, 1292, 1259, 1206, 1095, 1070, 1021, 968, 953, 841, 802, 713, and 549. ^{1}H NMR (DMSO-d_6, 600 MHz): δ 9.83 (1H, s, O$\underline{H}$), 8.05 (1H, dd, J = 1.8, 7.2 Hz), 7.90 - 7.87 (1H, m), 7.87-7.83 (2H, m), 7.26 (2H, s, N$\underline{H}_2$), 7.12 (1H, t, J = 8.4 Hz), 6.54-6.49 (2H, m), and 4.77 (1H, s). ^{13}C NMR (DMSO-d_6, 125 MHz) δ 182.4, 176.9, 160.2 (1C, d, J = 243.75 Hz), 158.5, 158.0 (1C, d, J = 11.25 Hz), 149.1, 134.6, 134.1, 131.096, 130.5 (1C, d, J = 8.75 Hz), 130.5, 126.1, 125.8, 121.3, 120.5 (1C, d, J = 13.75 Hz), 119.2, 111.8, 102.4 (1C, d, J = 23.75 Hz), 56.6, and 29.8.

2-Amino-4-(3-fluoro-4-hydroxyphenyl)-5,10-dihydro-4*H*-benzo[*g*]chromene-5,10-dione-3-carbonitrile (7d). Reaction time: 20 min. Yield 257 mg (71 %), orange solid, mp. 285 ºC. IR (KBr) ν_{max} (cm^{-1}) 3400, 3309, 3193, 2205, 1672, 1644, 1609, 1592, 1522, 1446, 1403, 1365, 1299, 1243, 1207, 1112, 1074, 1028, 955, 827, 770, 715, and 491. ^{1}H NMR (DMSO-d_6, 600 MHz): δ 9.78 (1H, s, O$\underline{H}$), 8.05 (1H, dd, J = 1.8, 7.2 Hz), 7.91 - 7.88 (1H, m), 7.87 - 7.83 (2H, m), 7.27 (2H, s), 7.08 (1H, dd, J = 2.4, 12.0 Hz), 6.94 (1H, dd, J = 2.4, 7.8 Hz), 6.87 (1H, t, J = 9.0 Hz), and 4.54 (1H, s). ^{13}C NMR (DMSO-d_6, 150 MHz) δ 182.6, 176.9, 158.3, 150.8 (1C, d, J

= 240 Hz), 148.8, 143.9 (1C, d, *J* = 16.5 Hz), 135.1 (1C, d, *J* = 4.5 Hz), 134.5, 134.1, 131.0, 130.7, 126.0, 125.8, 123.8, 121.7, 119.3, 117.7, 115.4 (1C, d, *J* = 18 Hz), 57.5, 35.5. HR-ESI-MS *m/z* 363.0753 $[M+H]^+$ (calcd. for $C_{20}H_{12}FN_2O_4^+$: 363.0776).

2-Amino-4-(4-methoxy-2-(trifluoromethyl)phenyl)-5,10-dihydro-4*H*-benzo[*g*]chromene-5,10-dione-3-carbonitrile (7e). Reaction time: 20 min. Yield 320 mg (75 %), orange solid, mp. 273 ºC. IR (KBr) ν_{max} (cm^{-1}) 3489, 3358, 2201, 1659, 1629, 1587, 1502, 1431, 1407, 1362, 1314, 1244, 1197, 1166, 1108, 1032, 942, 907, 781, and 716. ^{1}H NMR (DMSO-d_6, 600MHz): δ 8.06 (1H, dd, *J* = 1.8, 7.2 Hz), 7.87-7.80 (3H, m), 7.44 (1H, d, *J* = 9.0 Hz), 7.27 (2H, s, N$\underline{H}_2$), 7.16 (1H, d, *J* = 2.4 Hz), 7.11 (1H, dd, *J* = 2.4, 8.4 Hz), 4.91 (1H, s), and 3.80 (3H, s). ^{13}C NMR (DMSO-d_6, 125MHz) δ 182.3, 176.9, 158.3, 157.9, 149.3, 134.7, 134.6, 134.1, 132.3, 131.0, 130.5, 127.3 (1C, d, *J* = 30 Hz), 126.0, 125.8, 124.0 (1C, d, *J* = 272.5 Hz, CF_3), 121.6, 118.6, 118.6, 110.9 (1C, d, *J* = 6.25 Hz), 57.7, 55.5, and 31.8.

2-Amino-4-(4-(4-fluorophenoxy)phenyl)-5,10-dihydro-4*H*-benzo[*g*]chromene-5,10-dione-3-carbonitrile (7f). Reaction time: 25 min. Yield 311 mg (71 %), orange solid, mp. 260 ºC. IR (KBr) ν_{max} (cm^{-1}) 3418, 3191, 2207, 1672, 1637, 1605, 1501, 1410, 1365, 1330, 1301, 1247, 1208, 1195, 1076, 1017, 951, 847, 831, 716, 528, and 495. ^{1}H NMR (DMSO-d_6, 600MHz): δ 8.05 (1H, dd, *J* = 2.4, 7.2 Hz), 7.91-7.89 (1H, m), 7.86-7.83 (2H, m), 7.32 (2H, d, *J* = 9.0 Hz), 7.31 (2H, s, N$\underline{H}_2$), 7.20 (2H, t, *J* = 9.0 Hz), 7.06-7.03 (2H, m), 6.91 (2H, t, *J* = 9.0 Hz), and 4.62 (1H, s). ^{13}C NMR (DMSO-d_6, 125 MHz) δ 182.6, 176.9, 158.4, 158.3 (1C, d, *J* = 238.75 Hz), 156.2, 152.3 (1C, d, *J* = 1.25 Hz), 148.8, 138.4, 134.5, 134.2, 131.0, 130.6, 129.3 (2C), 126.1, 125.8, 122.0, 120.9 (2C, d, *J* = 8.75 Hz), 119.3, 117.9 (2C), 116.6 (2C, d, *J* = 23.75 Hz), 57.5, and 35.8.

2-Amino-4-(2,6-difluoro-4-methoxyphenyl)-5,10-dihydro-4*H*-benzo[*g*]chromene-5,10-dione-3-carbonitrile (7g). Reaction time: 20 min. Yield 284 mg (72 %), orange solid, mp. 223 ºC. IR (KBr) ν_{max} (cm^{-1}) 3441, 3340, 3183, 2923, 2848, 2195, 1667, 1634, 1593, 1498, 1441, 1407, 1365, 1302, 1246, 1203, 1142, 1075, 1039, 1021, 948, 797, 720, 550, and 525. ^{1}H NMR (DMSO-d_6, 600MHz): δ 8.11-8.09 (1H, m), 7.97-7.95 (1H, m), 7.93-7.90 (2H, m), 7.44 (2H, s, N$\underline{H}_2$), 6.75 (2H, d, *J* = 10.2 Hz), 5.02 (1H, s), and 3.80 (3H, s). ^{13}C NMR (DMSO-d_6, 125MHz) δ 182.4, 176.8, 161.2 (1C, d, *J* = 243.75 Hz), 161.1 (1C, d, *J* = 243.75 Hz), 160.0 (1C, d, *J* = 15.0 Hz), 159.1, 149.1, 134.8, 134.3, 130.8, 130.2, 126.2, 125.9, 120.4, 119.1, 110.2 (1C, t, *J* = 17.5 Hz), 98.5 (2C, d, *J* = 28.75 Hz), 56.0, 54.2, and 25.8.

2-Amino-4-(4-(difluoromethoxy)-3-hydroxyphenyl)-5,10-dihydro-4*H*-benzo[*g*]chromene-5,10-dione-3-carbonitrile (7h). Reaction time: 25 min. Yield 299 mg (73 %), orange solid, mp. 234 ºC. IR (KBr) ν_{max} (cm^{-1}) 3402, 3322, 3195, 2202, 1670, 1603, 1508, 1439, 1406, 1365, 1245, 1208, 1139, 1041, 950, 761, and 715. ^{1}H NMR (DMSO-d_6, 600MHz): δ 9.91 (1H, s, O$\underline{H}$), 8.07-8.04 (1H, m), 7.92-7.90 (1H, m), 7.87 - 7.84 (2H, m), 7.33 (2H, s, N$\underline{H}_2$), 7.02 (1H, d, *J* = 8.4 Hz), 6.97 (1H, t, *J* = 75 Hz, C$\underline{H}F_2$), 6.90 (1H, d, *J* = 1.8 Hz), 6.76 (1H, dd, *J* = 1.8, 8.4 Hz), and 4.54 (1H, s). ^{13}C NMR (DMSO-d_6, 125MHz) δ 182.6, 176.9, 158.5, 148.8, 141.9, 137.6, 134.7, 134.3, 131.0, 130.6, 126.2, 125.9, 122.1, 121.8, 119.4, 118.7, 118.6, 116.7 (1C, t, *J* = 256.25 Hz), 116.4, 57.3, and 36.0. HR-ESI-MS *m/z* 411.0784 $[M+H]^+$ calcd. for $C_{21}H_{13}F_2N_2O_5^+$: 411.0787.

2-Amino-4-(4-(trifluoromethoxy)phenyl)-5,10-dihydro-4*H*-benzo[*g*]chromene-5,10-dione-3-carbonitrile (7i). Reaction time: 20 min. Yield 317 mg (77 %), orange solid, mp. 276 ºC. IR (KBr) ν_{max} (cm^{-1}) 3402, 3331, 3196, 2203, 1670, 1639, 1604, 1508, 1410, 1366, 1333, 1282, 1246, 1207, 1157, 1077, 1018, 953, 842, 776, 717, and 530. ^{1}H NMR (DMSO-d_6, 600MHz): δ 7.99 (1H, dd, *J* = 1.8, 7.2 Hz), 7.82 (1H, dd, *J* = 1.8, 7.2 Hz), 7.78 (1H, td, *J* = 1.8, 7.2 Hz), 7.76 (1H, td, *J* = 1.8, 7.2 Hz), 7.40 (2H, dt, *J* = 2.4, 9.0 Hz), 7.29 (2H, s, N$\underline{H}_2$), 7.23 (2H, d, *J* = 7.8

Hz), and 4.62 (1H, s). ^{13}C NMR (DMSO-d_6, 125MHz) δ 182.7, 176.9, 158.5, 149.2, 147.4, 143.0, 134.6, 134.3, 131.0, 130.7, 129.7 (2C), 126.1, 125.9, 121.5, 121.2 (2C), 120.1 (1C, d, J = 256.25 Hz), 119.3, 57.2, and 36.0.

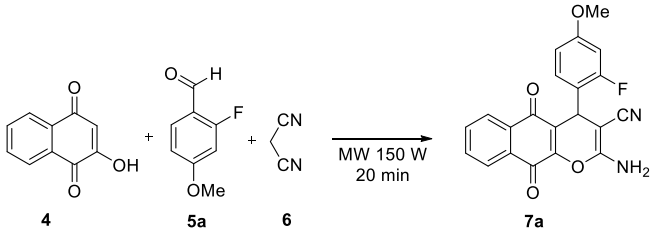
2-Amino-4-(2,5-difluoro-4-methoxyphenyl)-5,10-dihydro-4*H*-benzo[*g*]chromene-5,10-dione-3-carbonitrile (7j). Reaction time: 20 min. Yield 299 mg (76 %), orange solid, mp. 256 ºC. IR (KBr) ν_{max} (cm^{-1}) 3418, 3090, 2254, 2201, 2127, 1674, 1603, 1516, 1416, 1362, 1323, 1298, 1246, 1198, 1094, 1025, 1005, 871, 825, 761, and 622. ^{1}H NMR (DMSO-d_6, 600MHz): δ 8.06 (1H, dd, J = 1.8, 7.2 Hz), 7.90-7.87 (1H, m), 7.87-7.82 (2H, m), 7.33 (2H, s, N$\underline{H}_2$), 7.31 (1H, dd, J = 7.2, 12.0 Hz), 7.09 (1H, dd, J = 7.2, 12.0 Hz), 4.85 (1H, s), and 3.83 (3H, s). ^{13}C NMR (DMSO-d_6, 125MHz) δ 182.5, 176.8, 158.5, 155.5 (1C, d, J = 240 Hz), 149.5, 147.9 (1C, d, J = 238.75 Hz), 147.1 (1C, d, J = 11.25 Hz), 134.5, 134.2, 131.0, 130.7, 126.1, 125.8, 121.9 (1C, d, J = 16.25 Hz), 120.2, 119.0, 116.2 (1C, dd, J = 5.0, 21.25 Hz), 102.0 (1C, d, J = 28.75 Hz), 56.5, 56.0, and 29.7.

3. RESULTS AND DISCUSSION

Initially, investigation on the synthesis of 2-amino-4-(2-fluoro-4-methoxyphenyl)-5,10-dihydro-4*H*-benzo[*g*]chromene-5,10-dione-3-carbonitrile (**7a**) by using the microwave-assisted three-component reaction of 2-hydroxy-1,4-naphthoquinone (**4**), 2-fluoro-4-methoxybenzaldehyde (**5a**), and malononitrile (**6**) was performed in acetonitrile (CH_3CN), at 80 ºC, for 20 min, and with the presence of several different catalysts (20 mol %) including DABCO, ammonium acetate (NH_4OAc), 4-dimethylaminopyridine (DMAP), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), triethylamine (Et_3N). As shown in Table 1. Optimization of catalysts and reaction solvents for the synthesis of compound **7a***.

, Entries 1-5, the synthesis in different catalysts gave the expected product **7a**, in different yields (31 % - 72 %).

Table 1. Optimization of catalysts and reaction solvents for the synthesis of compound **7a***.



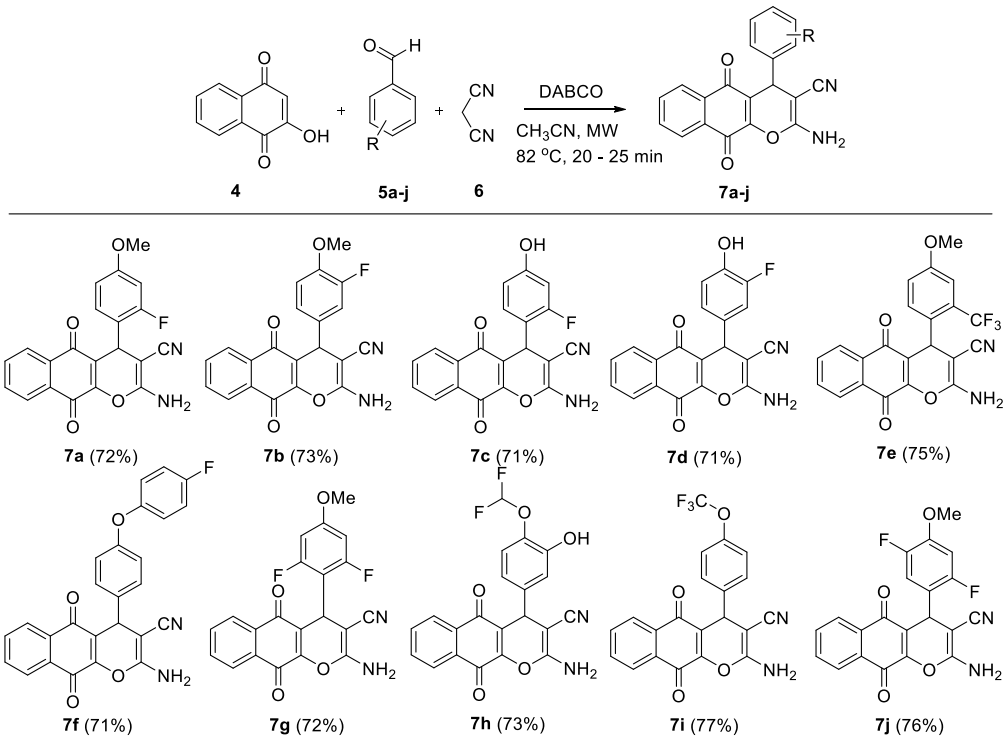
Entry	Catalyst	Solvent	Temperature, ºC	Yield, %
1	NH_4OAc	CH_3CN	82	44
2	DMAP	CH_3CN	82	56
3	DBU	CH_3CN	82	33
4	Et_3N	CH_3CN	82	31
5	**DABCO**	**CH_3CN**	**82**	**72**
6	DABCO	EtOH	78	60
7	DABCO	MeOH	65	55
8	DABCO	H_2O	100	36
9	DABCO	EtOH/H_2O (1:1)	reflux	63

All the reactions were carried out in 1 mmol scale in 10 ml solvent for 20 min in 20 mol% of the catalyst under MW at 150 W at the equimolar ratio of reactants **4, **5a**, and **6**.*

Among the catalysts, DABCO gave the highest yield of product **7a** (Table 1. Optimization of catalysts and reaction solvents for the synthesis of compound **7a***.

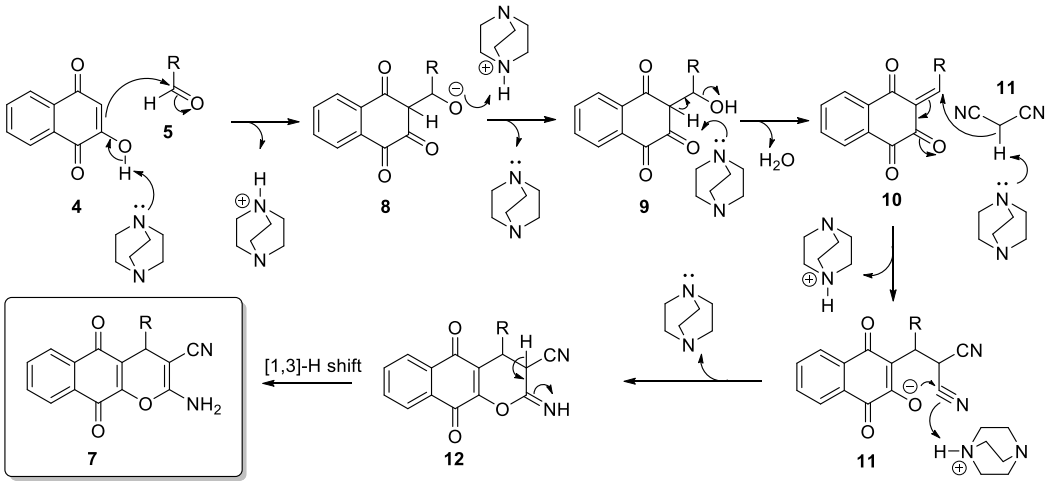
Entry 5). To optimize the more suitable reaction solvent, the microwave-assisted three-component reaction was carried out in the presence of DABCO 20 mol% in 20 min in different solvents including CH_3CN, ethanol (EtOH), methanol (MeOH), H_2O, and EtOH/H_2O (1:1) at reflux (Table 1, Entries 5-9). The results indicated that among five reaction solvent systems tested, the reaction in CH_3CN proceeded the highest yield (Table 1, Entry 5). Therefore, DABCO 20 mol% and CH_3CN were chosen as the optimized catalyst and solvent for the synthesis of product **7a**.

With the optimized conditions, various fluorinated aromatic aldehydes (**5a-j**) were subjected to the microwave-assisted reaction of 2-hydroxy-1,4-naphthoquinone (**4**), malononitrile (**6**), using DABCO 20 mol% in CH_3CN in 20 - 25 min to furnish products **7a-j** (Scheme 1). Compounds **7a-j** were obtained in good yields (71 – 76 %) and completely characterized by IR, ^1H, ^{13}C NMR, and mass spectra.



Scheme 1. Synthesis of compounds **7a–j** under microwave irradiation.

DABCO as a catalyst has played a key role in the formation of 2-amino-4*H*-benzo[*g*]chromene-5,10-dione-3-carbonitrile derivatives bearing fluorine atoms. As described in the Scheme 2, the formation of products **7a-j** underwent a sequential Knoevenagel condensation, Michael addition, intramolecular cyclization, and [1,3]-hydrogen shift reactions. Based on this plausible mechanism, DABCO effectively catalyzed the Knoevenagel condensation between aromatic aldehydes and naphthoquinone to form (*E*)-3-arylidenenaphthalene-1,2,4(3*H*)-triones **10**. DABCO was also employed to generate dicyanomethanide ion from malononitrile, a Michael donor. Then, dicyanomethanide ion could react with Michael acceptors **10** to form intermediates **11.**



Scheme 2. Reaction mechanism for the synthesis of 2-amino-4*H*-benzo[*g*]chromene-5,10-dione-3-carbonitrile derivatives **7a-j**.

4. CONCLUSIONS

In summary, an efficient and simple approach for the synthesis of novel 2-amino-4*H*-benzo[*g*]chromene-5,10-dione-3-carbonitrile derivatives bearing fluorine atoms *via* three-component reaction of 2-hydroxy-1,4-dihydronaphthalene-1,4-dione, malononitrile, and fluorinated aromatic aldehyde was successfully established under the presence of DABCO as a base catalyst in acetonitrile. Products were successfully synthesized with good yields and confirmed by ^{1}H NMR, ^{13}C NMR, and mass spectra. This method has the advantages of high yields, mild reaction conditions, easy work-up, short reaction time, and the use of an eco-friendly catalyst.

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Declaration of competing interest. The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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