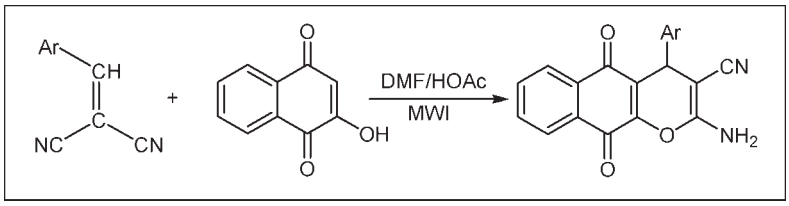
A Facile Route to the Synthesis of 1,4-Pyranonaphthoquinone Derivatives under Microwave Irradiation without Catalyst

Xing-Han Wang,[a] Xiao-Hong Zhang,[a] Shu-Jiang Tu,[a]* Feng Shi,[a] Xiang Zou,[b] Shu Yan,[a] Zheng-Guo Han,[a] Wen-Juan Hao,[a] Xu-Dong Cao,[a] and Shan-Shan Wu[a]

[a]School of Chemistry and Chemical Engineering, Xuzhou Normal University, Key Laboratory of Biotechnology for Medicinal Plant, Xuzhou, Jiangsu, 221116, People's Republic of China
[b]Department of Chemistry, Lianyungang Teachers College, Lianyungang, People's Republic of China
*E-mail: laotu2001@263.net

Received July 18, 2008
DOI 10.1002/jhet.153
Published online 25 August 2009 in Wiley InterScience (www.interscience.wiley.com).



A series of 1,4-pyranonaphthoquinone derivatives were synthesized *via* the reaction of arylidenemalononitrile and 2-hydroxynaphthalene-1,4-dione in the mixed solvent of N,N-dimethylformamide and glacial acetic acid (HOAc) under microwave irradiation without catalyst. This protocol has the notable advantages of short reaction time, high yield, and convenient operation.

J. Heterocyclic Chem., **46**, 832 (2009).

INTRODUCTION

Organic reactions under microwave irradiation (MWI) have attracted considerable attention in the past decade for the efficient and friendly synthesis of various organic compounds [1]. More attractively, many reactions that typically required hours or days with conventional heating could be realized in several minutes utilizing MWI [2]. The use of MWI for the formation of carbon-heteroatom and carbon-carbon bonds has been successfully demonstrated [3].

Pyran derivatives are important compounds, which exhibit antibacterial activity [4,5], antiproliferation [6] and antitumor activities [7], hypotensive effect [8], antiallergic effect [9,10], and biological activities of local anesthetic and antiarrhythmic [11]. Derivatives of 1,4-naphthoquinone possess potent and versatile biological activity, such as antiallergic and anticancer activities [12]. And they are also used as inhibitors of KB cells [13]. Derivatives of 1,4-pyranonaphthoquinone, possessing both pyran ring and 1,4-naphthoquinone motif were evaluated against human cancer cell lines, which are KB (human epidermoid carcinoma), HeLa (human cervical carcinoma) and $HepG_2$ (human hepatocellular carcinoma) cell lines employing the MTT colorimetric method [14].

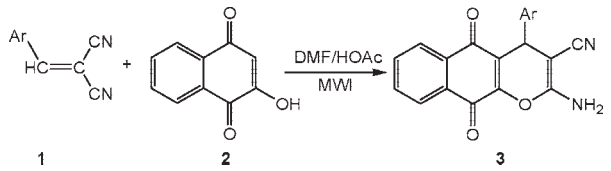
Due to their diverse biological activities, several groups [15] have been interested in the synthesis of derivatives of this structural type. For example, Abboub and coworkers [15a] have reported the reaction of 2-hydroxynaphthalene-1,4-dione and arylidenemalononitrile in methanol with Et_3N as catalyst under reflux condition. However, this protocol has drawbacks such as: (a) narrow application scope of substrates, (b) poor to moderate yields, (c) prolonged reaction time, (d) drastic reaction conditions and tedious work up. Therefore, the development of a relatively convenient method to prepare these compounds is still desirable.

Herein, we wish to report an efficient synthetic route to 1,4-Pyranonaphthoquinone derivatives by the reaction of arylidenemalononitrile and 2-hydroxynaphthalene-1,4-dione. The reaction was carried out in the mixed solvent of DMF and HOAc under MWI without catalyst (Scheme 1).

RESULTS AND DISCUSSION

Choosing an appropriate solvent is of crucial importance for successful MW promoted synthesis in view of a rapid rise of temperature in the reaction mixture. To search for the optimum solvent, different organic solvents such as ethanol, HOAc, DMF and mixed solvent of DMF, and HOAc were tested in the synthesis of **3c** at 100°C under MW irradiation (initial power 200 W and maximum power 250 W). As shown in Table 1, we could see the reaction in the mixed solvent of DMF and

Scheme 1



1 2 3

HOAc (the preferred volume ratio is 2:1) gave the best result (Table 1, Entry 5).

Moreover, to further optimize the reaction temperature, the synthesis of **3c** was performed in the mixed solvent of DMF and HOAc (2:1, V/V) at the temperatures ranging from 100 to 150°C in the increment of 10°C each time at 250 W. As illustrated in Table 2, when the temperature was increased from 100 to 130°C, the yield of **3c** obviously improved. However, no significant increase in the yield of **3c** was observed as the reaction temperature was raised from 130 to 150°C. Therefore, the temperature of 130°C was chosen for all further microwave-assisted reactions.

Under these optimized reaction conditions [mixed solvent (V_{DMF}/V_{HOAc}: 2:1, 1.5 mL), 130°C], a series of compounds **3** were synthesized with this simple procedure. The results were summarized in Table 3. As shown in Table 3, the applicability of this methodology is broad, not only to arylidenemalononitrile either with electron-donating groups or with electron-withdrawing groups, but also to heterocyclic arylidenemalononitrile (Table 3, entry 15). Therefore, we concluded that the electronic nature of the substituent has no significant effect on this reaction.

The proposed mechanism of this reaction may undergo a simple addition and cyclization progress (Scheme 2). The addition between arylidenemalononitrile **1** and 2-hydroxynaphthalene-1,4-dione **2** occurs to generate **4**, which subsequently undergoes intramolecular cyclization and isomerisation to afford final products **3**.

All the products were characterized by Mp, IR, ^{1}H NMR, and ^{13}C NMR spectral data, as well as by elemental analysis. The IR spectrum of compound **3b** showed strong absorptions at 3413 and 3329 cm^{-1} due to libration of NH_2 group, 2196 cm^{-1} due to CN group, 1662 and 1636 cm^{-1} due to C=O groups. The ^{1}H NMR spectrum of **3b** showed a singlet at δ 7.36 corresponding to proton from NH_2, and a singlet at δ 4.65 due to CH.

Table 1

Solvent optimization of synthesis **3c**.

Entry	Solvent	Time (min)	Yield (%)
1	Ethanol	10	72
2	HOAc	7	74
3	DMF	8	70
4	DMF/HOAc(1:1)	6	76
5	DMF/HOAc(2:1)	6	83
6	DMF/HOAc(3:1)	6	78

Table 2

Temperature optimization of synthesis **3c**.

Entry	Temp (°C)	Time (min)	Yield (%)
1	100	6	83
2	110	5	86
3	120	5	90
4	130	4	95
5	140	4	95
6	150	3	93

In summary, we have developed a rapid and facile method for the synthesis of highly functionalized 1,4-pyranonaphthoquinone derivatives of potential biological importance in excellent yields. Particularly, this protocol offers increased safety for small-scale high-speed synthesis, and the series of 1,4-pyranonaphthoquinone derivatives may provide expansive foreground for biomedical scopes.

EXPERIMENTAL

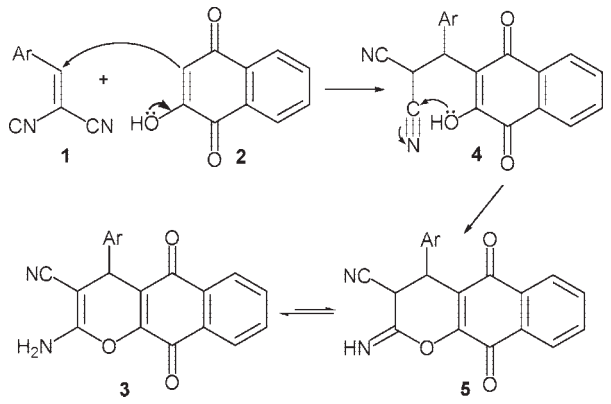
MWI was carried out with an Emrys™ Creator microwave oven from Personal Chemistry, Uppsala, Sweden. Melting points were determined in open capillaries and were uncorrected. IR spectra were recorded on a FTIR-Tensor 27 spectrometer in KBr. ^{1}H NMR spectra were measured on a DPX 400 MHz spectrometer using TMS as an internal standard and DMSO-d_6 as solvent. ^{13}C NMR spectra were measured on a DPX 100 MHz spectrometer using TMS as an internal standard and DMSO-d_6 as solvent. Elemental analysis was

Table 3

Physical data of products **3**.

Entry	Product	Ar	Time (min)	Yield (%)	Mp (°C)
1	**3a**	4-FC_6H_4	5	92	286–288
2	**3b**	4-ClC_6H_4	5	93	278–280
3	**3c**	4-BrC_6H_4	4	95	291–294
4	**3d**	4-$CH_3OC_6H_4$	6	81	257–259
5	**3e**	4-$CH_3C_6H_4$	6	83	254–257
6	**3f**	4-$NO_2C_6H_4$	4	94	247–248
7	**3g**	2-ClC_6H_4	5	90	>300
8	**3h**	3-$NO_2C_6H_4$	5	84	295–297
9	**3i**	3,4-$OCH_2OC_6H_3$	5	87	281–283
10	**3j**	2,4-$Cl_2C_6H_3$	4	86	293–295
11	**3k**	3,4-$(CH_3O)_2C_6H_3$	6	81	270–272
12	**3l**	4-OH-3-$NO_2C_6H_3$	4	80	237–239
13	**3m**	C_6H_5	5	88	>300
14	**3n**	3,4,5-$(CH_3O)_3C_6H_2$	6	85	290–293
15	**3o**	Thien-2-yl	6	82	274–276

Scheme 2



determined with a Perkin-Elmer 240c elemental analysis instrument.

General procedure for 2-arylidenemalononitrile (1). A mixture of aromatic aldehyde (5 mmol), malononitrile (5 mmol), and ethanol (2 mL) was added to a 10 mL reaction vessel of the monomodal Emrys™ Creator microwave synthesizer and allowed to react under MWI at 150 W power and 100°C for 2–3 min. The reaction mixture was cooled to room temperature, then filtered to give the crude product, which was further purified by recrystallization from EtOH (95%).

General procedure for 2-Amino-5,10-dihydro-5,10-dioxo-4-aryl-4*H*-benzo-[*g*]chromene-3-carbonitrile derivatives (3). The reactions were performed in a 10 mL Emrys™ reaction vial, arylidenemalononitrile **1** (1 mmol), 2-hydroxynaphthalene-1,4-dione **2** (1 mmol), and DMF/HOAc (1.5 mL) (2:1, V/V) were mixed and then capped. The mixture was irradiated for a given time at 130°C under MWI (initial power 200 W and maximum power 250 W). Upon completion, monitored by TLC, the reaction mixture was cooled to room temperature, then filtered to give the crude product, which was further purified by recrystallization from EtOH (95%) to give pure 2-amino-5,10-dihydro-5,10-dioxo-4-aryl-4*H*-benzo[*g*]chromene-3-carbonitrile derivatives **3**.

2-Amino-4-(4-fluorophenyl)-5,10-dihydro-5,10-dioxo-4*H*-benzo [*g*]chromene-3-carbonitrile (3a). This compound was obtained according to above general procedure; ir (potassium bromide): 3407, 3324, 2210, 1667, 1635 cm^{-1}; ^1H nmr (DMSO-d_6): δ 8.06–8.04 (m, 1H, ArH), 7.88–7.83 (m, 3H, ArH), 7.38 (t, 2H, J = 5.6 Hz, ArH), 7.35 (s, 2H, NH_2), 7.13 (t, 2H, J = 8.8 Hz, ArH), 4.65 (s, 1H, CH); ^{13}C NMR (100 MHz) (δ, ppm): 182.55, 176.81, 162.37, 159.96, 158.28, 148.92, 139.82, 134.49, 134.12, 130.99, 130.64, 129.73, 129.65, 121.62, 119.24, 115.35, 57.33, 35.79. Anal. Calcd. for $C_{20}H_{11}FN_2O_3$: C, 69.36; H, 3.20; N, 8.09. Found: C, 69.54; H, 3.19; N, 8.11.

2-Amino-4-(4-chlorophenyl)-5,10-dihydro-5,10-dioxo-4*H*-benzo [*g*]chromene-3-carbonitrile (3b). This compound was obtained according to above general procedure; ir (potassium bromide): 3413, 3329, 2196, 1662, 1636 cm^{-1}; ^1H nmr (DMSO-d_6): δ 8.06–8.05 (m, 1H, ArH), 7.88–7.84 (m, 3H, ArH), 7.38 (s, 4H, ArH), 7.36 (s, 2H, NH_2), 4.65 (s, 1H, CH); ^{13}C NMR (100 MHz) (δ, ppm): 182.53, 176.78, 158.31, 149.03, 142.59, 134.51, 134.14, 131.67, 130.98, 130.63, 129.65, 128.47, 126.03, 125.78, 121.37, 119.16, 57.07, 36.98. Anal. Calcd. for $C_{20}H_{11}ClN_2O_3$: C, 66.22; H, 3.06; N, 7.72. Found: C, 66.43; H, 3.05; N, 7.74.

2-Amino-4-(4-bromophenyl)-5,10-dihydro-5,10-dioxo-4*H*-benzo [*g*]chromene-3-carbonitrile (3c). This compound was obtained according to above general procedure; ir (potassium bromide): 3406, 3326, 2194, 1665, 1603 cm^{-1}; ^1H nmr (DMSO-d_6): δ 8.07–8.04 (m, 1H, ArH), 7.89–7.83 (m, 3H, ArH), 7.50 (d, 2H, J = 8.4 Hz, ArH), 7.39 (s, 2H, NH_2), 7.31 (d, 2H, J = 8.4 Hz, ArH), 4.63 (s, 1H, CH); ^{13}C NMR (100 MHz) (δ, ppm): 182.52, 176.78, 158.30, 149.04, 143.01, 134.51, 134.14, 131.40, 130.97, 130.63, 130.02, 126.04, 125.78, 121.31, 120.20, 119.15, 57.00, 36.06. Anal. Calcd. for $C_{20}H_{11}BrN_2O_3$: C, 58.99; H, 2.72; N, 6.88. Found: C, 59.16; H, 2.73; N, 6.86.

2-Amino-5,10-dihydro-4-(4-methoxyphenyl)-5,10-dioxo-4*H*-benzo[*g*]chromene-3-carbonitrile (3d). This compound was obtained according to above general procedure; ir (potassium bromide): 3396, 3329, 2204, 1672, 1635 cm^{-1}; ^1H nmr (DMSO-d_6): δ 8.06–8.04 (m, 1H, ArH), 7.87–7.83 (m, 3H, ArH), 7.30 (s, 2H, NH_2), 7.22 (d, 2H, J = 8.4 Hz, ArH), 6.86 (d, 2H, J = 8.8 Hz, ArH), 4.56 (s, 1H, CH), 3.71 (s, 3H, OCH_3); ^{13}C NMR (100 MHz) (δ, ppm): 182.58, 176.88, 158.29, 148.55, 135.64, 134.49, 134.09, 131.02, 130.56, 128.82, 128.29, 126.02, 125.76, 122.25, 119.37, 113.93, 57.70, 55.04, 35.67. Anal. Calcd. for $C_{21}H_{14}N_2O_4$: C, 70.39; H, 3.94; N, 7.82. Found: C, 70.62; H, 3.95; N, 7.87.

2-Amino-5,10-dihydro-5,10-dioxo-4-*p*-tolyl-4*H*-benzo[*g*]-chromene-3-carbonitrile (3e). This compound was obtained according to above general procedure; ir (potassium bromide): 3404, 3327, 2197, 1662, 1603 cm^{-1}; ^1H nmr (DMSO-d_6): δ 8.06–8.04 (m, 1H, ArH), 7.87–7.83 (m, 3H, ArH), 7.32 (s, 2H, NH_2), 7.19 (d, 2H, J = 8.0 Hz, ArH), 7.11 (d, 2H, J = 7.6 Hz, ArH), 4.57 (s, 1H, CH), 2.25 (s, 3H, CH_3); ^{13}C NMR (100 MHz) (δ, ppm): 182.53, 176.86, 158.29, 148.73, 140.63, 136.25, 134.51, 134.10, 131.01, 130.58, 129.12, 127.56, 126.03, 125.77, 122.16, 119.33, 57.59, 36.09, 20.59. Anal. Calcd. for $C_{21}H_{14}N_2O_3$: C, 73.68; H, 4.12; N, 8.18. Found: C, 73.88; H, 4.11; N, 8.20.

2-Amino-5,10-dihydro-4-(4-nitrophenyl)-5,10-dioxo-4*H*-benzo [*g*]chromene-3-carbonitrile (3f). This compound was obtained according to above general procedure; ir (potassium bromide): 3421, 3328, 2201, 1673, 1604 cm^{-1}; ^1H nmr (DMSO-d_6): δ 8.21–8.19 (m, 1H, ArH), 8.11 (d, 1H, J = 8.4 Hz, ArH), 8.06 (d, 1H, J = 7.6 Hz, ArH), 7.88–7.84 (m, 4H, ArH), 7.63 (t, 1H, J = 8.0 Hz, ArH), 7.49 (s, 2H, NH_2), 4.88 (s, 1H, CH); ^{13}C NMR (100 MHz) (δ, ppm): 182.56, 176.75, 158.46, 149.37, 147.94, 145.81, 134.77, 134.47, 134.14, 130.97, 130.05, 126.02, 125.79, 122.49, 120.58, 119.01, 56.63, 36.33. Anal. Calcd. for $C_{20}H_{11}N_3O_5$: C, 64.35; H, 2.97; N, 11.26. Found: C, 64.51; H, 2.96; N, 11.29.

2-Amino-4-(2-chlorophenyl)-5,10-dihydro-5,10-dioxo-4*H*-benzo[*g*]chromene-3-carbonitrile (3g). This compound was obtained according to above general procedure; ir (potassium bromide): 3434, 3327, 2192, 1663, 1635 cm^{-1}; ^1H nmr (DMSO-d_6): δ 8.08–8.06 (m, 1H, ArH), 7.87–7.84 (m, 3H, ArH), 7.45–7.40 (m, 2H, ArH), 7.37 (s, 2H, NH_2), 7.26–7.24 (m, 2H, ArH), 5.15 (s, 1H, CH); ^{13}C NMR (100 MHz) (δ, ppm): 182.39, 176.78, 158.40, 149.52, 140.92, 134.57, 134.15, 132.01, 130.93, 130.57, 130.50, 129.38, 128.67, 127.79, 126.06, 125.80, 121.29, 118.77, 56.33, 33.55. Anal. Calcd. for $C_{20}H_{11}ClN_2O_3$: C, 66.22; H, 3.06; N, 7.72. Found: C, 66.41; H, 3.07; N, 7.70.

2-Amino-5,10-dihydro-4-(3-nitrophenyl)-5,10-dioxo-4*H*-benzo[*g*] chromene-3-carbonitrile (3h). This compound was obtained according to above general procedure; ir (potassium bromide): 3421, 3328, 2202, 1671, 1639 cm^{-1}; ^1H nmr (DMSO-d_6): δ 8.21–8.18 (m, 1H, ArH), 8.11 (d, 1H, J = 7.6 Hz, ArH), 8.07 (d, 1H, J = 7.6 Hz, ArH), 7.87–7.84 (m, 4H, ArH), 7.63 (t, 1H, J = 8.0 Hz, ArH), 7.49 (s, 2H, NH_2), 4.88 (s, 1H, CH); ^{13}C NMR (100 MHz) (δ, ppm): 182.57, 176.76, 158.44, 149.37, 147.93, 145.82, 134.79, 134.47, 134.14, 130.96, 130.73, 130.05, 126.02, 125.79, 122.49, 122.16, 120.54, 119.03, 56.59, 36.32. Anal. Calcd. for $C_{20}H_{11}N_3O_5$: C, 64.35; H, 2.97; N, 11.26. Found: C, 64.51; H, 2.98; N, 11.23.

2-Amino-4-(benzo[*d*][1,3]dioxol-5-yl)-5,10-dihydro-5,10-dioxo-4*H*-benzo[*g*]chromene-3-carbonitrile (3i). This compound was obtained according to above general procedure; ir (potassium bromide): 3427, 3396, 2207, 1673, 1637 cm^{-1}; ^1H nmr (DMSO-d_6): δ 8.06–8.04 (m, 1H, ArH), 7.89–7.83 (m, 3H, ArH), 7.29 (s, 2H, NH_2), 6.89–6.86 (m, 1H, ArH), 6.83 (d, 1H, J = 8.0 Hz, ArH), 6.78 (d, 1H, J = 7.6 Hz, ArH), 5.97 (s, 2H, CH_2), 4.55 (s, 1H, CH); ^{13}C NMR (100 MHz) (δ, ppm): 182.59, 176.84, 158.21, 148.82, 147.39, 146.23, 137.66, 134.45, 134.07, 131.04, 130.67, 126.00, 125.77, 121.75, 120.98, 119.29, 112.71, 108.13, 100.97, 57.70, 36.12. Anal. Calcd. for $C_{21}H_{12}N_2O_5$: C, 67.74; H, 3.25; N, 7.52. Found: C, 67.94; H, 3.26; N, 7.50.

2-Amino-4-(2,4-dichlorophenyl)-5,10-dihydro-5,10-dioxo-4*H*-benzo[*g*]chromene-3-carbonitrile (3j). This compound was obtained according to above general procedure; ir (potassium bromide): 3467, 3341, 2202, 1671, 1632 cm^{-1}; ^1H nmr (DMSO-d_6): δ 8.08–8.06 (m, 1H, ArH), 7.88–7.85 (m, 3H, ArH), 7.60–7.58 (m, 1H, ArH), 7.49 (d, 1H, J = 8.4 Hz, ArH), 7.42 (s, 2H, NH_2), 7.33 (d, 1H, J = 8.4 Hz, ArH), 5.14 (s, 1H, CH); ^{13}C NMR (100 MHz) (δ, ppm): 182.43, 176.73, 158.37, 149.63, 140.21, 134.57, 134.20, 132.92, 132.26, 131.94, 130.89, 130.59, 128.66, 127.97, 126.07, 125.80, 120.70, 118.69, 55.77, 33.15. Anal. Calcd. for $C_{20}H_{10}Cl_2N_2O_3$: C, 60.48; H, 2.54; N, 7.05. Found: C, 60.67; H, 2.55; N, 7.02.

2-Amino-5,10-dihydro-4-(3,4-dimethoxyphenyl)-5,10-dioxo-4*H*-benzo[*g*]chromene-3-carbonitrile (3k). This compound was obtained according to above general procedure; ir (potassium bromide): 3418, 3324, 2195, 1688, 1632 cm^{-1}; ^1H nmr (DMSO-d_6): δ 8.06–8.04 (m, 1H, ArH), 7.90–7.83 (m, 3H, ArH), 7.28 (s, 2H, NH_2), 6.88–6.86 (m, 2H, ArH), 6.80 (d, 1H, J = 8.4 Hz, ArH), 4.56 (s, 1H, CH), 3.72 (s, 3H, OCH_3), 3.70 (s, 3H, OCH_3); ^{13}C NMR (100 MHz) (δ, ppm): 182.62, 176.91, 158.27, 148.66, 148.63, 147.96, 136.22, 134.47, 134.06, 131.07, 130.62, 126.01, 125.78, 122.04, 119.89, 119.38, 111.95, 111.68, 57.70, 55.62, 55.52, 36.05. Anal. Calcd. for $C_{22}H_{16}N_2O_5$: C, 68.04; H, 4.15; N, 7.21. Found: C, 68.26; H, 4.16; N, 7.23.

2-Amino-5,10-dihydro-4-(4-hydroxy-3-nitrophenyl)-5,10-dioxo-4*H*-benzo[*g*]chromene-3-carbonitrile (3l). This compound was obtained according to above general procedure; ir (potassium bromide): 3446, 3350, 2197, 1667, 1642 cm^{-1}; ^1H nmr (DMSO-d_6): δ 10.95 (s, 1H, OH), 8.06–8.04 (m, 1H, ArH), 7.90–7.83 (m, 4H, ArH), 7.53 (d, 1H, J = 8.4 Hz, ArH), 7.41 (s, 2H, NH_2), 7.07(d, 1H, J = 8.8 Hz, ArH), 4.68 (s, 1H, CH); ^{13}C NMR (100 MHz) (δ, ppm): 182.60, 176.82, 158.37, 150.96, 149.01, 136.73, 134.87, 134.59, 134.47, 134.11, 131.02, 130.68, 125.99, 125.79, 124.03, 120.98, 119.15, 119.10, 56.89, 35.46. Anal. Calcd. for $C_{20}H_{11}N_3O_6$: C, 61.70; H, 2.85; N, 10.79. Found: C, 61.90; H, 2.84; N, 10.82.

2-Amino-5,10-dihydro-5,10-dioxo-4-phenyl-4*H*-benzo[*g*]-chromene-3-carbonitrile (3m). This compound was obtained according to above general procedure; ir (potassium bromide): 3401, 3325, 2200, 1671, 1636 cm^{-1}; ^1H nmr (DMSO-d_6): δ 8.07–8.05 (m, 1H, ArH), 7.90–7.83 (m, 3H, ArH), 7.34 (s, 2H, NH_2), 7.31 (d, 4H, J = 4.4 Hz, ArH), 7.23–7.22 (m, 1H, ArH), 4.61 (s, 1H, CH); ^{13}C NMR (100 MHz) (δ, ppm): 182.53, 176.84, 158.37, 148.91, 143.55, 134.51, 134.12, 131.03, 130.63, 128.56, 127.65, 127.05, 126.05, 125.79, 122.04, 119.27, 57.54, 36.50. Anal. Calcd. for $C_{20}H_{12}N_2O_3$: C, 73.16; H, 3.68; N, 8.53. Found: C, 73.38; H, 3.69; N, 8.51.

2-Amino-5,10-dihydro-4-(3,4,5-trimethoxyphenyl)-5,10-dioxo-4*H*-benzo[*g*]chromene-3-carbonitrile (3n). This compound was obtained according to above general procedure; ir (potassium bromide): 3418, 3327, 2196, 1662, 1634 cm^{-1}; ^1H nmr (DMSO-d_6): δ 8.07–8.05 (m, 1H, ArH), 7.92–7.84 (m, 3H, ArH), 7.30 (s, 2H, NH_2), 6.57–6.55 (m, 2H, ArH), 4.57 (s, 1H, CH), 3.74 (s, 6H, $2OCH_3$), 3.62 (s, 3H, OCH_3); ^{13}C NMR (100 MHz) (δ, ppm): 182.64, 176.88, 158.29, 152.87, 149.00, 139.28, 136.59, 134.43, 134.04, 131.08, 130.72, 125.99, 125.82, 121.48, 119.35, 105.13, 59.89, 57.54, 55.99, 36.76. Anal. Calcd. for $C_{23}H_{18}N_2O_6$: C, 66.02; H, 4.34; N, 6.70. Found: C, 66.24; H, 4.35; N, 6.72.

2-Amino-5,10-dihydro-5,10-dioxo-4-(thiophen-2-yl)-4*H*-benzo[*g*]chromene-3-carbonitrile (3o). This compound was obtained according to above general procedure; ir (potassium bromide): 3409, 3328, 2196, 1665, 1638 cm^{-1}; ^1H nmr (DMSO-d_6): δ 8.05–8.04 (m, 1H, ArH), 7.98–7.96 (m, 1H, ArH), 7.88–7.86 (m, 2H, ArH), 7.49 (s, 2H, NH_2), 7.40 (d, 1H, J = 4.0 Hz, ArH), 7.01 (d, 1H, J = 3.2 Hz, ArH), 6.95 (t, 1H, J = 2.8 Hz, ArH), 4.97 (s, 1H, CH); ^{13}C NMR (100 MHz) (δ, ppm): 182.38, 176.81, 158.93, 148.18, 147.10, 134.69, 134.29, 130.91, 130.48, 127.18, 126.16, 125.92, 125.41, 125.35, 121.87, 119.19, 57.10, 31.17. Anal. Calcd. for $C_{18}H_{10}N_2O_3S$: C, 64.66; H, 3.01; N, 8.38; S, 9.59. Found: C, 64.83; H, 3.00; N, 8.35; S, 9.61.

Acknowledgment. We thank the National Natural Science Foundation of China (No. 20672090), the Natural Science Foundation of the Jiangsu Province (No. BK2006033) for financial support, Six Kinds of Professional Elite Foundation of the Jiangsu Province (No. 06-A-039), the Qing Lan Project (No. 08QLT001), and the Open Foundation of Jiangsu Key Laboratory for Chemistry of Low-Dimensional Materials (No. JSKC07035).

REFERENCES AND NOTES

[1] (a) Kappe, C. O. Angew Chem Int Engl 2004, 43, 6250; (b) Lidstrom, P.; Tierney, J.; Wathey, B.; Westman, J. Tetrahedron 2001, 57, 9225; (c) Gabriel, C.; Gabriel, S.; Grant, E. H.; Halstead, B. S. J.; Mingos, D. M. P. Chem Soc Rev 1998, 27, 213.

[2] Shi, L.; Wang, M.; Fan, C. A.; Zhang, F. M.; Tu, Y. Q. Org Lett 2003, 5, 3515.

[3] (a) Loupy, A. Microwave in Organic Synthesis; Wiley-VCH: Weiheim, 2002; (b) Larhed, M.; Moberg, C.; Hallberg, A. Acc Chem Res 2002, 35, 717; (c) Varma, R. S. J Heterocycl Chem 1999, 36, 1565; (d) Dallinger, D.; Kappe, C. O. Chem Rev 2007, 107, 2563.

[4] El-Agrody, A. M.; El-Hakim, M. H.; Abd El-Latif, M. S. A.; Fakery, A. H.; El-Sayed, M.; El-Ghareab, K. A. Acta Pharm 2000, 50, 111.

[5] Zamocka, J.; Misikova, E.; Durinda, J. Cesk Farm 1992, 41, 170.

[6] Brunavs, M.; Dell, C. P.; Owton, W. M. J Fluor Chem 1994, 68, 201.

[7] Mohr, S. J.; Chirigos, M. A.; Fuhrman, F. S.; Pryor, J. W. Cancer Res 1975, 35, 3750.

[8] Tandon, V. K.; Vaish, M.; Jain, S.; Bhakuni, D. S.; Srimal, R. C. Indian J Pharm Sci 1991, 53, 22.

[9] Banzatti, C.; Branzoli, U.; Lovisolo, P. P.; Melloni, P.; Orsini, G. Salvadori, P. Arzneimittel Forschung 1984, 34, 864.

[10] (a) Hatakeyama, S.; Ochi, N.; Numata, H.; Takano, S. J Chem Soc Chem Commun 1988, 1202; (b) O'Callaghan, C. N.; McMurry, T. B. H. J Chem Res Synop 1995, 214.

[11] Coudert, P.; Coyquelet, J. M.; Bastide, J.; Marion, Y.; Fialip, J. Ann Pharm Fr 1988, 46, 91.

[12] Kongkathip, N.; Kongkathip, B.; Siripong, P.; Sangma, C.; Luangkamin, S.; Niyomdecha, M.; Pattanapa, S.; Piyaviriyagul, S.; Kongsaeree, P. Bioorg Med Chem 2003, 11, 3179.

[13] Hayashi, T.; Smith, F. T.; Lee, K. H. J Med Chem 1987, 30, 2005.

[14] Skehan, P.; Storeng, R.; Scudiero, D.; Monks, A.; McMahon, J.; Vistica, D.; Warren, J. T.; Bokesch, H.; Kenney, S.; Boyd, M. R. J Natl Cancer Inst 1990, 82, 1107.

[15] (a) Abboub, F.; Amari, M.; Kolli, B. J Soc Alger Chim 2001, 11, 223; (b) Khodeir, M.; El-Taweel, F.; Elagamey, A. Pharmazie, 1992, 47, 486.