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Note

Efficient synthesis of 3-(4-methyl-3-phenyl-furo [3,2-*c*] quinoline-2-carbonyl)- chromen-2-ones under microwave irradiation

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A rapid and efficient method for the preparation of 3-(4-methyl-3-phenyl-furo[3,2-*c*]quinoline-2-carbonyl)-chromen-2-ones by the reaction between 3-(2-bromo-acetyl)-chromen-2-ones and (4-hydroxy-2-methyl-quinolin-3-yl)-phenyl-methanones using dimethyl formamide and anhydrous potassium carbonate under microwave irradiation is reported. Microwave assisted reactions have resulted in better yields of the desired products than prepared under conventional conditions. The structures of the compounds are supported by spectral and analytical data.

Keywords: Quinolines, chromene-2-ones, potassium carbonate, microwave irradiation

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Quinolines[1] and coumarins constitute an important class of heterocyclic molecules. Various substituted quinolines are reported to possess a wide range of biological activities including antimicrobial[2], antitumor[3], anticonvulsant[4], antidepressant[5], antimalarial[6], antihistamine[7] etc.

The application of microwave (MW) irradiation in organic synthesis has been the focus of considerable attention in recent years and is becoming an increasingly popular technology[8-10] the salient features of the microwave approach are the rapid reaction rates, cleaner reaction conditions and the operational simplicity. In view of this and in continuation of our interest on conventional[11] and microwave[12] assisted organic transformations on quinoline derivatives we wish to report here in a rapid convenient and efficient microwave assisted synthesis of 3-(4-methyl-3-phenyl-furo [3,2-*c*] quinolin-2-carbonyl)-chromen-2-ones using dimethyl formamide and anhydrous potassium carbonate.

Results and Discussion

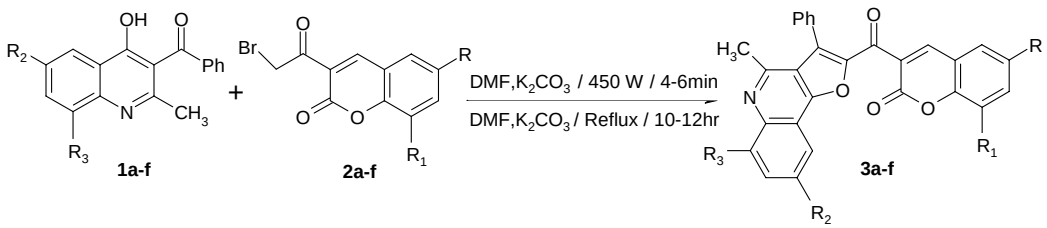
Condensation of 3-(2-bromo-acetyl)-chromen-2-ones[13] **2a-f** with (4-hydroxy-2-methyl-quinolin-3-yl)-phenyl-methanones in the presence of DMF and K_2CO_3. The mixture was refluxed for about 10-12 hr furnished **3a-f**, alternatively when **2a-f** with **1a-f** taken in a domestic MW oven at 450W level is irradiated in an open vessel for 4-6 min in DMF and K_2CO_3, furnished **3a-f** in good yields (**Scheme I**). The results are summarized in **Table I**. A comparison between the two methods shows that in the microwave technique the reaction time is drastically reduced, and the yields are comparable. The compounds **3a-f** were characterized by IR, ^{1}H NMR and mass spectral data.

The IR spectra of the products **3a-f** show absorption range at 1700-1740, 1675-1695, 1610-1675, 1570-1580 cm^{-1} which are characteristic of C=O (lactone), C=O, C=N, and C=C stretching, respectively.

The ^{1}H NMR spectra of **3a** shows a multiplet at δ 7.3-7.6 for the 5′, 6′, 7′ and 8′ of aromatic region of the coumarin protons. Another multiplet is obtained at δ 7.7-8 due to 4 protons of C-5, C-6, C-7 and C-8 of quinoline. One more multiplet is obtained at δ 7-7.2 due to 5 protons of the phenyl group. One sharp singlet is obtained at δ 2.3 due to three protons of quinoline methyl group. One more singlet at δ 8.9 integrating for one proton is assigned to C-4′H. The mass spectrum of **3a** shows molecular ion peak at m/z 431 (60%), which is consistent with its molecular formula $C_{28}H_{17}NO_4$.

3a: 3-(4-Methyl-3-phenyl-furo[3,2-*c*]quinoline-2-carbonyl)-chromen-2-one. ^{1}H NMR (DMSO-d_6): δ 7.3-7.6 (m, 4H, C-5′, C-6′, C-7′ and C-8′H), 7.7-8 (m, 4H, C-5, C-6, C-7 and C-8), 2.3 (S, 3H, CH_3), 7-7.2 (m, 5H, Ar-H), 8.9 (S, 1H C-4′H,); ^{13}C NMR (75 MHz, DMSO-d_6): δ 175.0, 172.9,162.0, 159.3, 152.6, 150.8, 146.8,148.0, 141.0, 136.5, 134.9, 130.5, 129.3, 129.0, 128.9, 128.5, 127.5, 127.1, 126.6, 126.0, 125.8, 125.2, 125.0, 124.0, 122.8, 121.3, 19.8; MS: = 431 (M^+ 60%), 355 (12), 185 (25), 174 (40), 154(30), 146(100).

3b: 6-Bromo-3-(4,8-dimethyl-3-phenyl-furo[3,2-*c*]quinoline-2-carbonyl)-chromen-2-one. ^{1}H NMR (DMSO-d_6): δ 7.3-7.5 (m, 3H, C-5′, C-7′ and C-8′), 7.8-8 (m, 3H, C-5, C-7 and C-8), 2.3 (S, 3H, CH_3), 2.5 (S,3H C- 6), 7-7.2 (m, 5H, Ar-H), 8.9 (S, IH, C-



Scheme I

Compd	R	R_1	R_2	R_3
3a	H	H	H	H
3b	Br	H	CH_3	H
3c	Br	Br	CH_3	H
3d	NO_2	H	CH_3	H
3e	NO_2	H	H	CH_3
3f	Cl	H	CH_3	H

Table I—Analytical data of title compounds **3a-f**

Compd	Mol.formula (Mol. Wt)	M^+	m.p (ºC)	Method A		Method B		Calcd (Found)%		
				Yield (%)	Time (min)	Yield (%)	Time (hr)	C	H	N
3a	$C_{28}H_{17}NO_4$ (431)	431	240	85	4.15	82	10.30	77.95 (77.94)	3.97 (3.95)	3.25 (3.26)
3b	$C_{29}H_{18}BrNO_4$ (524)	524	185	80	4.00	79	10.00	66.43 (66.40)	3.46 (3.45)	2.67 (2.69)
3c	$C_{29}H_{17}Br_2NO_4$ (603)	603	250	72	4.30	66	10.30	66.17 (66.19)	3.32 (3.33)	2.73 (2.70)
3d	$C_{29}H_{18}N_2O_6$ (490)	490	245	75	5.30	70	11.00	71.02 (71.00)	3.70 (3.71)	5.71 (5.72)
3e	$C_{29}H_{18}N_2O_6$ (490)	490	250	77	5.00	75	11.40	71.02 (71.05)	3.70 (3.72)	5.71 (5.71)
3f	$C_{29}H_{18}ClNO_4$ (479)	479	260	74	6.00	69	12.00	72.58 (72.56)	3.78 (3.76)	2.92 (2.90)

4′H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 178.2, 172.5, 162.5, 159.0, 152.0, 149.8, 146.0, 144.8,141.5, 134.6, 131.0, 130, 129.9, 128.9, 128.2, 127.8, 127.2, 126.0, 125.9, 125.2, 124.5, 123.9, 119.8, 117.9, 111.9, 20.6, 20.0; MS: = 524 (M^+, 10%), 448 (45), 252 (50), 197 (30), 146 (100).

3c: 6,8-Dibromo-3-(4,8-dimethyl-3-phenyl-furo-[3,2-*c*]quinoline-2-carbonyl)-chromen-2-one. ^{1}H NMR (DMSO-d_6): δ 7-7.2 (m, 2H, C-5′, C-7′), 7.7-8 (m,3H, C-5, C-7 and C-8), 2.3 (S, 3H, CH_3), 2.5 (S, 3H C-6), 7-7.2 (m, 5H, Ar-H), 8.9 (S, IH, C-4′H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 176.0, 172.5, 162.0, 159.6, 153.1, 152.6, 148.5, 144.5, 134.7, 133.9, 133.0, 132.9, 131.9, 130.6, 128.9, 127.9, 126.9, 126.0, 125.9, 124.8, 124.0, 123.9, 122.0, 118.1, 111.5, 20.5, 18.0; MS: = 603 (M^+, 20%), 527 (50), 330 (9), 197 (30), 146 (100);

3d: 6-Nitro-3-(4,8-dimethyl-3-phenyl-furo [3,2-*c*]quinoline-2-carbonyl)-chromen-2-one. ^{1}H NMR (DMSO-d_6): δ 7.5-7.7 (m, 3H, C-5′, C-7′ and C-8′), 7.8-8.1(m, 3H, C-5, C-7 and C-8), 2.3 (S, 3H, CH_3), 2.6 (S, 3H, C- 6), 7-7.2 (m, 5H, Ar-H), 9.2 (S, IH, C-4′H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 179.0, 174.0, 165.0, 159.3, 152.6, 149.0, 146.2, 145.1, 133.5, 133.0, 132.8, 131.5, 130.5, 129.0, 128.7, 127.9, 126.9, 126.0, 125.7, 124.9, 124.0, 123.2, 122.8, 121.7, 117.8, 111.5, 22.5, 18.5; MS: = 490 (M^+, 30%), 414 (60), 219 (50), 197 (40), 146(100).

3e: 6,8-Dinitro-3-(4,8-dimethyl-3-phenyl-furo-[3,2-*c*]quinoline-2-carbonyl)-chromen-2-one. ^{1}H NMR (DMSO-d_6): δ 7.5-7.7 (m, 3H, C-5′, C-7′ and C-8′), 7.8-8.1 (m, 3H, C-5, C-7 and C-8), 2.3 (S, 3H, CH_3), 2.8 (S, 3H C- 6), 7-7.2 (m, 5H, Ar-H), 9.2 (S, IH, C-4′H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 177.0, 172.3, 163.0, 155.0, 146.9, 135.2, 134.6, 133.9, 133.4, 132.9, 132.5, 131.9, 131.4, 130.5, 129.5, 127.9, 127.0, 126.5, 125.8, 125.3, 123.2, 122.5, 121.9, 120.5 117.9, 111.9, 20.8, 15.8; MS: = 490 (M^+, 12%), 414 (60), 219 (50), 197 (45), 146 (100).

3f: 6-Chloro-3-(4,8-dimethyl-3-phenyl-furo[3,2-*c*]quinoline-2-carbonyl)-chromen-2-one. ^{1}H NMR (DMSO-d_6): δ 7.4 -7.6 (m, 3H, C-5′, C-7′ and C-8′),

7.8-8 (m, 3H, C-5, C-7 and C-8), 2.3 (S, 3H, CH_3), 2.5 (S, 3H C- 6), 7-7.2 (m, 5H, Ar-H), 8.6 (S, IH, C-4′H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 178.0, 172.5, 165.0, 162.0, 159.0, 146.0, 142.6, 136.0, 135.2, 134.0, 133.2, 132.5, 131.0, 130.5, 129.2, 128.5, 128.2, 127.9, 127.0, 125.8, 123.9, 123.0, 122.7, 117.5, 110.5, 22.0, 18.5; MS: = 479 (M^+, 15%), 403 (60), 208 (50), 197 (30), 146 (100), 129 (9).

Experimental Section

All the melting points were determined in open capillary in liquid paraffin bath and are uncorrected. The purity of the compounds was checked by TLC. IR spectra (KBr) were recorded on a Shimadzu FTIR model 8010 spectrometer and the ^{1}H NMR spectra on a Varian Gemini 200 MHz spectrometer using TMS as an internal standard. The C, H, and N analysis of the compounds was done on a Carlo Erba model EA1108. Mass spectra on a Jeol JMS D-300 spectrometer. For the microwave irradiation experiments (BPL 800T) was used.

Synthesis of 3-(4-methyl-3-phenyl-furo [3,2-*c*] quinoline-2-carbonyl)-chromen-2-one 3a

Method A (Microwave irradiation method): A mixture of (4-hydroxy-2-methyl-quinoline-3-yl)-phenyl-methanone **1a** (0.001 mole), 3-(2-bromo-acetyl)- chromene-2-one **2a** (0.001 mole), anhydrous K_2CO_3 (0.001 mole), and DMF (2 mL), was subjected to microwave irradiation at 450W level for 4.15 min. The reaction was monitored over TLC. After completion of the reaction, the reaction mixture was filtered to remove the potassium salt and the filtrate was poured over crushed ice and the resulting solid was crystallized from ethanol as shining needles.

Compounds **3b-f** were prepared similarly.

Method B (Conventional method): (4-Hydroxy-2-methyl-quinoline-3-yl)-phenyl-methanone **1a** (0.001 mole) is treated with 3-(2-bromo-acetyl)-chromene-2-one **2a** (0.001 mole), anhydrous K_2CO_3 (0.001 mole), and DMF (5 mL) was added and the reaction mixture was refluxed for 10.30 hr. The reaction mixture was monitored over TLC. After completion of the reaction, the reaction mixture was filtered and the filtrate was poured over crushed ice, and the resulting solid was crystallized from ethanol as shinning needles.

Compounds **3b-f** were prepared similarly.

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