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A Novel Method for One-pot Synthesis of Furo[3,2-*c*]coumarin Derivatives from 4-Hydroxycoumarin and Arylglyoxal under Microwave Irradiation

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A novel one-pot synthesis of furo[3,2-*c*]coumarins has been developed from readily available starting materials 4-hydroxycoumarin and arylglyoxal. This method is simple, rapid and good yielding.

Keywords furocoumarins, 4-hydroxycoumarin, arylglyoxal, microwave irradiation, one-pot synthesis

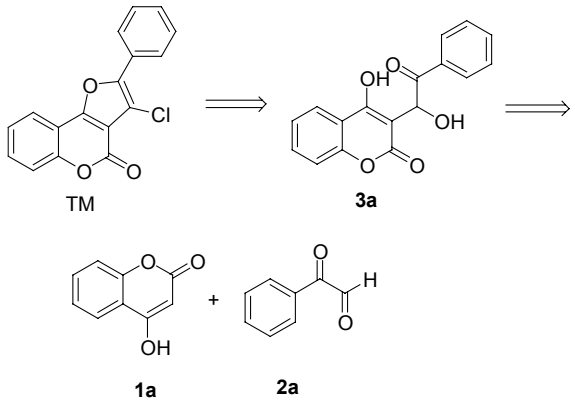
Introduction

Furocoumarins are widely present in numerous natural products, manifest a wide range of biological activities, such as antibacterial, anti-HIV, insecticides, antioxidants, antitumor and antiviral properties, and they are also widely applied in the pharmaceutical industry.[1] Synthesis and screening of furocoumarins compounds for drug discovery has been a vital subject of constant interest in organic and medicinal chemistry. To date, synthetic methodologies for the synthesis of furocoumarins have been studied for many years.[2]

Recently, Cheng[3] and coworkers have prepared 3-chloro-4*H*-furo[3.2-*c*]chromen derivatives from 3-alkynylchromone via one-pot reaction. Also, Xu[4] have prepared furo[3,2-*c*]chromen via coupling cyclization strategy with 3-bromo-4-acetoxycoumarins and 1-alkynes catalyzed by palladium/copper. These methods have their own merits in the preparation of the individual target compounds, however, these methods usually require rather specific substrates (*e.g.*, 3-alkynylchromone), most of which are commercially unavailable, long reaction time (20 h), heavy metal ($CuCl_2$, CuBr, CuCl, Pd) used. Therefore, there is an eager desire to explore a simple and very effective method for preparation of a wide variety of the furocoumarins.

As part of our continuing efforts on the development of new route for the synthesis of novel coumarin derivatives,[5] herein we report a novel and efficient route to one-pot syntheses of 3-chloro-4*H*-furo[3,2-*c*]chromen derivatives from readily available reagents. A retrosynthetic analysis suggested the formation of the furan ring via ring closure of **3a**, which results from the condensation reaction of 4-hydroxycoumarin **1a** and phenylglyoxal **2a** (Scheme 1).

Scheme 1



Results and Discussion

In the study of the condensation of 4-hydroxycoumarin with phenylglyoxal, it was found that generally two molecules of 4-hydroxycoumarin (**1a**) react with one of the phenylglyoxal (**2a**) to obtain the Michael adducts (**4a**) as the final product.[6] Herein, we hope to obtain the product **3a** from the reaction of 4-hydroxycoumarin **1a** with phenylglyoxal **2a**. As show in Table 1, no product **3a** was observed but **4a** was obtained in high yield when the reaction was kept in EtOH reflux for 2 h in the absence of catalyst. Disappointedly, the product **3a** was also not obtained when this reaction was heated at reflux in EtOH for 60 min in the presence of catalyst PTSA or DBU (Table 1, Entries 2—3). When 20 mol% DABCO, [dabco][HCOO]$_2$ and [dabco][CH_3COO]$_2$

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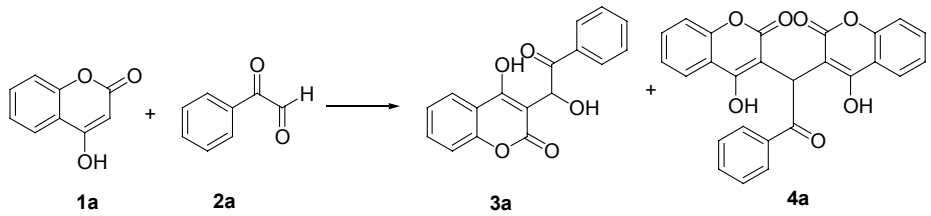
Table 1 Synthesis of product **3a** under different conditions[a]



Entry	Catalyst	Loading/mol%	Solvent	Temperature	Time/min	Yield[b]/%	
						3a	**4a**
1	none	—	EtOH	reflux	120	trace	52
2	PTSA	20	EtOH	reflux	60	trace	63
3	DBU	20	EtOH	reflux	60	trace	88
4	DABCO	20	EtOH	r.t.	28	21	63
5	[dabco][HCOO]$_2$	20	EtOH	r.t.	25	24	61
6	[dabco[CH_3COO]$_2$	20	EtOH	r.t.	26	27	57
7	[dabco[CH_3COO]$_2$	50	EtOH	r.t.	19	45	41
8	[dabco[CH_3COO]$_2$	100	EtOH	r.t.	25	76	9
9	[dabco[CH_3COO]$_2$	150	EtOH	r.t.	11	96	trace
10	DABCO	150	EtOH	r.t.	28	92	trace
11	[dabco][CH_3COO]$_2$	250	EtOH	r.t.	15	96	trace
12	[dabco][CH_3COO]$_2$	150	$ClCH_2CH_2Cl$	r.t.	16	95	trace
13	[dabco][CH_3COO]$_2$	150	CH_2Cl_2	r.t.	13	94	trace
14	[dabco][CH_3COO]$_2$	150	CH_3CN	r.t.	19	96	trace
15	[dabco][CH_3COO]$_2$	150	THF	r.t.	18	92	trace

[a] All reactions were run with the molar ratio of **1a** : **2a** = 1 : 1. [b] Isolated yield of **3a** based on **1a**.

were undertaken, it should be mentioned that besides **3a**, a noticeable amount of **4a** was also obtained (Table 1, Entries 4—6). To our surprise, when the loading amount of catalyst increased, the yield was improved (Table 1, Entries 7 — 11). It was found that 150 mol% [dabco][CH_3COO]$_2$ was enough to promote the reaction efficiently for preparing **3a** (Table 1, Entry 9). Next, different solvents were also tested in the presence of [dabco][CH_3COO]$_2$ as catalyst, for example, EtOH, THF, $ClCH_2CH_2Cl$, CH_2Cl_2 and CH_3CN, to our delight, they also resulted in high yields (Table 1, Entries 9, 12—15).

It is well-known that acids[7] (such as $HClO_4$, BF_3•Et_2O) and dehydrating agent[8] (such as $POCl_3$, P_2O_5) were employed for the Paal-Knorr furan synthesis. The close loop of the **3a** was chosen as a model reaction to optimize the reactions. It was found that when PTSA, $HClO_4$, Yb(OTf)$_3$, CF_3COOH, BF_3•Et_2O were used as catalysts, the expected product of 3-OH-4*H*-furo[3.2-*c*]chromen **6a** was not gotten, but much amount of by-product **4a** was obtained. A plausible mechanism for this reaction is proposed in Scheme 2. The product **3a** is not stable, first **3a** loses H_2O to afford II, next another molecule of 4-hydroxycoumarin is added to *α*,*β*-unsaturated carbonyl intermediate II to form III via 1,4-conjugate addition. Then, the subsequent keto-enol tautomerism affords the corresponding product **4a**.

With the aim to obtain the product **5a**, $POCl_3$ was used, the results were summarized in Table 2. It was found that **3a** was treated with 2.0 equiv. of $POCl_3$ in CH_2ClCH_2Cl at room temperature for 8 h, the desired product **5a** was obtained in 35% (Table 2, Entry 2). Increasing the reaction temperature, the yield was improved obviously. When the reaction of **3a** with 2.0 equiv. of $POCl_3$ was performed in reflux condition for 2 h, the yield of **5a** reached to 65% (Table 2, Entry 4).

Organic reactions accelerated by microwave irradiation has attracted considerable attention over the past number of years for the efficient synthesis of a variety of organic compounds.[9] Microwave-assisted reactions are particularly effective when small polar molecules are part of the reaction transformation.[10-12] With the aim to reduce reaction time and improve the yield, microwave heating was employed. After optimization of the reaction conditions, the reaction was generally completed in the presence of $POCl_3$ at 130 ℃ in CH_2ClCH_2Cl for 15 min under microwave irradiation of **3a**. Finally, the two-step sequence can be carried out in a one-pot manner without the isolation of the product **3a**, the reaction would be greatly improved and the yield was increased from 65% to 81%.

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Scheme 2

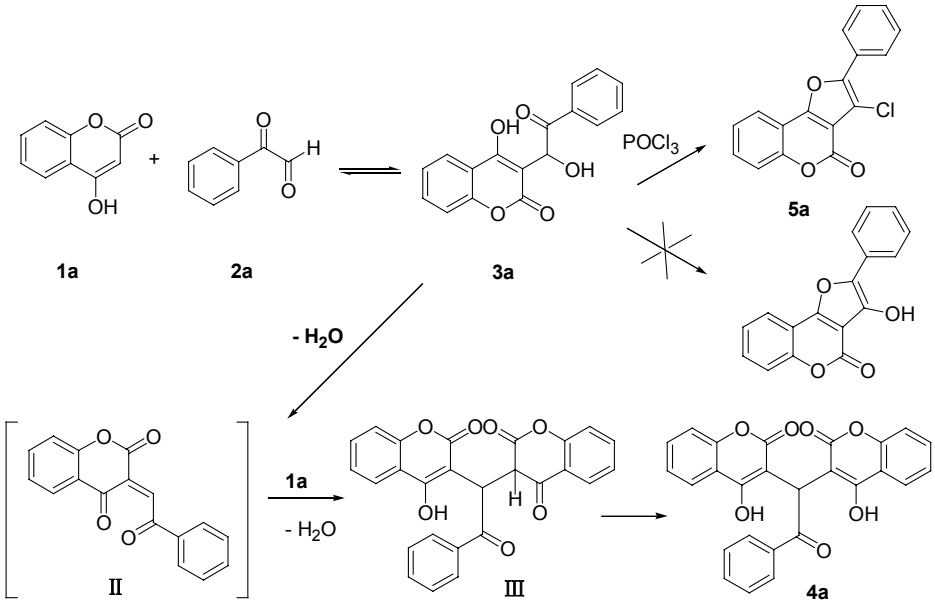


Table 2 Synthesis of **5a** under different conditions

Entry	Reagent	Loading/ mol%	Condition	Yield[a]/%	
				5a	**4a**
1	$POCl_3$	100	$ClCH_2CH_2Cl$, r.t., 8 h	trace	13
2	$POCl_3$	200	$ClCH_2CH_2Cl$, r.t., 8 h	35	9
3	$POCl_3$	200	r.t., 8 h	37	7
4	$POCl_3$	200	$ClCH_2CH_2Cl$, reflux, 2 h	65	4
5[b]	$POCl_3$	200	$ClCH_2CH_2Cl$, 110 ℃, 20 min	72	trace
6[b]	$POCl_3$	200	$ClCH_2CH_2Cl$, 120 ℃, 18 min	74	trace
7[b]	$POCl_3$	200	$ClCH_2CH_2Cl$, 130 ℃, 15 min	79	trace
8[b]	$POCl_3$	300	$ClCH_2CH_2Cl$, 130 ℃, 15 min	78	trace

[a] Isolated yields based on **3a**. [b] Under microwave heating.

After optimizing the reaction conditions, the scope of this method was evaluated using coumarins **1a**—**1c**, and phenylglyoxals **2a** — **2h**, and the corresponding 3-chloro-4*H*-furo[3.2-*c*]chromen compounds **5a** — **5k** were obtained in moderate to excellent yields, as summarized in Table 3. The nature of R^1 group on the 4-hydroxycoumarin **1a** showed no significant effect on the yield, electron-withdrawing group substituted compounds showed slightly higher yields than electron-donating group on arylglyoxals. But, this reaction was carried out with glyoxals such as 2-furanylglyoxal and ethylglyoxal, the TLC and ^{1}H-NMR spectra of the crude reaction mixture showed the presence of a combination of starting materials and numerous by-products, and the yield of the expected product was very poor.

Experimental

All microwave irradiation experiments were carried out in a Discover-CEM monomode microwave apparatus. Melting points were determined on a Büchi B-540 capillary melting point apparatus and uncorrected. IR spectra was recorded on an AVATAR-370, samples were prepared as KBr plates. ^{1}H NMR and ^{13}C NMR spectra were recorded at VARAIN-400 using DMSO or $CDCl_3$ as the solvent with tetramethylsilane (TMS) as an internal standard. Chemical shifts (δ) are given relative to TMS, the coupling constants J are given in Hz. Mass spectra were measured with Thermo Finnigan LCQ-Advantage. High resolution mass spectral (HRMS) analyses were measured on an Agilent 6210 TOF LC/MS using ESI or EI (electrospray ionization) techniques.

General procedure for the preparation of [dabco]-[CH_3COO]$_2$

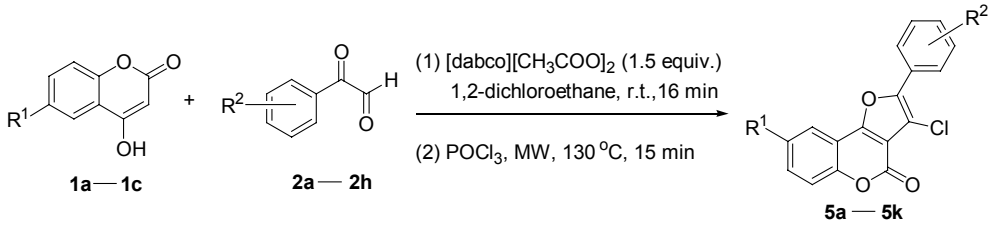
To a solution of dabco (10 mmol) in EtOH (3 mL) was added CH_3COOH (20.2 mmol) in portion within 30 min, and then the mixture was stirred at room for 1 h and evaporated under reduced pressure to give [dabco]-[CH_3COO]$_2$ as a white solid; m.p. 69.5—73.2 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.90 (s, 12H), 1.94 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 175.6, 45.2, 22.3. MS (ESI) m/z: 113 [M−(CH_3COOH)$_2$]$^+$.

General procedure for the synthesis of 3a

To a mixture of 4-hydroxycoumarin **1a** (1 mmol), phenylglyoxal **2a** (1 mmol) was added [dabco]-[CH_3COO]$_2$ (1.5 mmol) in EtOH (2 mL), and the reaction mixture was stirred at room temperature and monitored by TLC [V(CH_2Cl)∶V(CH_3OH)=10∶1). After completion of the reaction, compounds were purified by column chromatography on silica to give the corresponding compound **3a**.

4-Hydroxy-3-(1-hydroxy-2-oxo-2-phenylethyl)-2*H*-chromen-2-one (3a) White solid; m.p. ＞300 ℃; ^{1}H NMR (400 MHz, DMSO) δ: 7.98—7.96 (m, 2H), 7.77

Table 3 One-pot, two-step synthesis of 3-chloro-4*H*-furo[3.2-*c*]chromen derivatives



1a—1c 2a—2h 5a—5k

Entry	R^1	R^2	Product	Yield[a]/%
1	H (**1a**)	H (**2a**)	**5a**	81
2	H	4-F (**2b**)	**5b**	84
3	H	4-Cl (**2c**)	**5c**	83
4	H	4-Br (**2d**)	**5d**	82
5	H	4-Me (**2e**)	**5e**	79
6	H	4-MeO (**2f**)	**5f**	78
7	H	3-Cl (**2g**)	**5g**	82
8	H	3-MeO (**2h**)	**5h**	74
9	Me (**1b**)	H	**5i**	80
10	Me	3-Cl	**5j**	83
11	*t*-Bu (**1c**)	H	**5k**	82

[a] Isolated yields based on **1a**—**1c**.

(dd, J=1.6, 8.0 Hz, 1H), 7.48—7.44 (m, 1H), 7.37—7.31 (m, 3H), 7.08—7.00 (m, 2H), 6.08 (s, 1H); ^{13}C NMR (100 MHz, DMSO) δ: 197.7, 172.8, 163.3, 153.5, 135.5, 132.2, 130.2, 127.8, 127.29, 124.6, 122.4, 121.7, 115.5, 93.4, 78.2; IR (KBr) v: 1671, 1638, 1600, 1522, 1449, 1419, 1353, 1061 cm^{-1}; MS (ESI) m/z: 295 (M−H)$^-$. HRMS calcd for $C_{17}H_{13}O_5$ 297.0763, found 297.0763.

Typical procedure for the one-pot synthesis of 5a

In a 10 mL pressurized vial "snap-on" cap, a mixture of 4-hydroxycoumarin **1a** (1 mmol), and phenylglyoxal **2a** (1 mmol) was added [dabco][CH_3COO]$_2$ (1.5 mmol) in $ClCH_2CH_2Cl$ (4 mL). The reaction mixture was stirred at room temperature and monitored by TLC. After completion of the first reaction, 0.3 g $POCl_3$ (2.0 mmol) was added and the reaction mixture was irradiated for 15 min at 130 ℃, the reaction mixture was then allowed to cool to room temperature and poured into crushed ice (10 mL), the aqueous phase was extracted with CH_2Cl_2 (10 mL×3), the combined organic extracts were washed with brine (10 mL) and then dried over Na_2SO_4, filtered, compounds were then purified by column chromatography on silica to give the corresponding compound. Other products (**5b**—**5k**) were prepared according to the same method of **5a**.

3-Chloro-2-phenyl-4*H*-furo[3,2-*c*]chromen-4-one (5a) White solid, m.p. 163—165 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.04 (d, J=7.6 Hz, 1H), 7.92 (d, J=8.0 Hz, 1H), 7.56—7.35 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 156.2, 155.4, 152.5, 149.8, 131.3, 129.4, 128.8, 127.7, 125.7, 124.7, 120.8, 117.4, 112.1, 110.2, 110.2; IR (KBr) v: 1757, 1633,1489, 1446, 1419, 1095, 1029 cm^{-1}; MS (EI) m/z: 296 (M$^+$, 100). HRMS calcd for $C_{17}H_9ClO_3$ 296.0240, found 296.0245.

3-Chloro-2-(4-fluorophenyl)-4*H*-furo[3,2-*c*]-chromen-4-one (5b) White solid, m.p. 171—173 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.03 (dd, J=5.6, 8.0 Hz, 2H), 7.90 (d, J=8.0 Hz, 1H), 7.57—7.53 (m, 1H), 7.44—7.36 (m, 2H), 7.22—7.17 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.5, 162.0, 155.8, 155.6, 152.9, 149.4, 131.4, 128.1, 128.0, 124.7, 124.4, 120.8, 117.5, 116.3, 116.0, 112.4, 110.4, 110.3; IR (KBr) v: 2925, 1754, 1632, 1496, 1408, 1167, 1095 cm^{-1}; MS (EI) m/z: 314 (M$^+$, 100). HRMS calcd for $C_{17}H_8ClFO_3$ 314.0146, found 314.0131.

3-Chloro-2-(4-chlorophenyl)-4*H*-furo[3,2-*c*]-chromen-4-one (5c) White solid, m.p. 169—170 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.99 (d, J=8.0 Hz, 2H), 7.92 (d, J=8.0 Hz, 1H), 7.59—7.37 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 155.9, 155.5, 152.5, 148.7, 135.2, 131.4, 129.0, 126.8, 125.1, 124.7, 120.7, 117.4, 111.9, 110.7, 100.1; IR (KBr) v: 2923, 1746, 1629, 1486, 1402, 1098, 1033 cm^{-1}; MS (EI) m/z: 330 (M$^+$, 100). HRMS calcd for $C_{17}H_8Cl_2O_3$ 329.9850, found 329.9846.

2-(4-Bromophenyl)-3-chloro-4*H*-furo[3,2-*c*]-chromen-4-one (5d) White solid, m.p. 239—241 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.93 (d, J=8.4 Hz, 3H), 7.63 (d, J=8.8 Hz, 2H), 7.59—7.55 (m, 1H), 7.46—7.37 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 155.7, 152.8, 149.0, 132.1, 131.5, 127.2, 126.8, 124.8, 123.7, 120.9, 117.5, 112.2, 111.1, 110.4; IR (KBr) v: 2924, 1747, 1616, 1483, 1412, 1091, 1082 cm^{-1}; MS (EI) m/z: 376 (M$^+$, 100).

3-Chloro-2-*p*-tolyl-4*H*-furo[3,2-*c*]chromen-4-one (5e) White solid, m.p. 169—170 ℃; ^{1}H NMR (400

MHz, $CDCl_3$) δ: 7.96—7.92 (m, 3H), 7.55 (t, J=8.0 Hz, 1H), 7.45 (d, J=8.0 Hz, 1H), 7.38 (t, J=8.0 Hz, 1H), 7.31 (t, J=8.4 Hz, 2H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 156.2, 155.0, 152.4, 149.9, 139.6, 131.1, 129.4, 125.4, 124.8, 124.6, 120.6, 117.2, 112.0, 110.0, 109.3, 21.4; IR (KBr) v: 2920, 1747, 1631, 1495, 1454, 1360, 1095, 1028 cm^{-1}; MS (EI) m/z: 310 (M^+, 100).

3-Chloro-2-(4-methoxyphenyl)-4*H*-furo[3,2-*c*]-chromen-4-one (5f) White solid, m.p. 182—184 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.00 (d, J=8.0 Hz, 2H), 7.92 (d, J=8.0 Hz, 1H), 7.54 (t, J=4.0 Hz, 1H), 7.56—7.36 (m, 2H), 7.03 (d, J=8.0 Hz, 2H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 160.4, 156.3, 155.0, 152.6, 150.2, 131.1, 130.8, 127.5, 124.7, 120.7, 120.6, 117.4, 114.4, 112.4, 110.3, 55.6; IR (KBr) v: 2923, 1750, 1607, 1498, 1305, 1259, 1189 cm^{-1}; MS (EI) m/z: 326 (M^+, 100).

3-Chloro-2-(3-chlorophenyl)-4*H*-furo[3,2-*c*]-chromen-4-one (5g) White solid, m.p. 198—200 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.00 (s, 1H), 7.95 (t, J=8.0 Hz, 2H), 7.57 (t, J=8.0 Hz, 1H), 7.45—7.38 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 155.7, 155.60, 152.5, 148.0, 134.7, 131.5, 130.0, 129.1, 125.2, 124.7, 123.4, 120.7, 117.3, 111.7, 111.3, 110.0; IR (KBr) v: 2924, 1755, 1632, 1570, 1476, 1400, 1278, 1003 cm^{-1}; MS (EI) m/z: 330 (M^+, 100), HRMS calcd for $C_{17}H_8Cl_2O_3$: 329.9850, found 329.9850.

3-Chloro-2-(3-methoxyphenyl)-4*H*-furo[3,2-*c*]-chromen-4-one (5h) White solid, m.p. 137—140 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.96 (d, J=8.0 Hz, 1H), 7.53—7.33 (m, 5H), 7.18 (s, 1H), 6.94 (s, 1H), 3.91 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 159.9, 158.1, 156.7, 156.3, 152.5, 130.6, 130.1, 128.8, 124.5, 120.8, 117.4, 117.1, 114.6, 112.7, 112.4, 110.1, 103.0, 55.5; IR (KBr) v: 2927, 1747, 1634, 1579, 1461, 1280, 1274, 1237 cm^{-1}; MS (EI) m/z: 327 (M^+, 94).

3-Chloro-9-methyl-2-phenyl-4*H*-furo[3,2-*c*]-chromen-4-one (5i) White solid, m.p. 181—183 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.06 (dd, J=1.2, 8.4 Hz, 1H), 7.70 (s, 1H), 7.53—7.49 (m, 2H), 7.45—7.41 (m, 2H), 7.36—7.30 (m, 2H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 156.1, 155.2, 150.7, 149.5, 134.7, 132.3, 129.3, 128.8, 127.8, 125.5, 120.3, 117.0, 111.7, 110.3, 110.0, 21.2; IR (KBr) v: 2921, 1739, 1634, 1572, 1487, 1419, 1264, 1090 cm^{-1}; MS (EI) m/z: 310 (M^+, 100). HRMS calcd for $C_{18}H_{11}ClO_3$ 310.0397, found 310.0389.

3-Chloro-2-(3-chlorophenyl)-9-methyl-4*H*-furo[3,2-*c*]chromen-4-one (5j) White solid, m.p. 196—198 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.02 (s, 1H), 7.98 (d, J=8.0 Hz, 1H), 7,72 (s, 1H), 7.46—7.32 (m, 4H), 2.50 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 155.9, 155.5, 150.6, 147.7, 134.7, 134.7, 132.5, 129.9, 129.1, 129.0, 125.1, 123.3, 120.3, 116.9, 111.3, 109.8, 21.0; IR (KBr) v: 2922, 1764, 1638, 1573, 1474, 1401, 1086, 1002 cm^{-1}; MS (EI) m/z: 344 (M^+, 100). HRMS calcd for $C_{18}H_{10}Cl_2O_3$ 344.0007, found 343.9997.

9-*tert*-Butyl-3-chloro-2-(3-chlorophenyl)-4*H*-furo-[3,2-*c*]chromen-4-one (5k) White solid, m.p. 218—220 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 (d, J=8.0 Hz, 2H), 7.89 (d, J=4.0 Hz, 1H), 7.61 (dd, J=4.0, 8.0 Hz, 1H), 7.53 (t, J=8.0 Hz, 2H), 7.42 (dd, J=8.0, 24.0 Hz, 2H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 156.4, 155.9, 150.7, 149.6, 148.0, 129.3, 129.0, 128.7, 127.9, 125.8, 117.0, 111.6, 110.3, 110.0, 77.4, 77.1, 76.8, 35.0, 31.6; IR (KBr) v: 2962, 1749, 1635, 1568, 1487, 1258, 1123, 1003 cm^{-1}; MS (EI) m/z: 352 (M^+, 65). HRMS calcd for $C_{21}H_{17}ClO_3$ 352.0866, found 352.0858.

3,3'-(2-Oxo-2-phenylethane-1,1-diyl)bis(4-hydroxy-2*H*-chromen-2-one) (4a) White solid, m.p. 200—203 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 11.23 (s, 2H, OH), 8.06 (dd, J=1.6, 8 Hz, 2H), 7.83—7.81 (m, 2H), 7.62—7.58 (m, 2H), 7.49—7.45 (m, 1H), 7.40—7.32 (m, 6H), 6.09 (s, 1H); MS (ESI) m/z: 439($M-H)^-$.

Conclusions

In conclusion, an extremely efficient method has been developed for the one-pot synthesis of 3-chloro-4*H*-furo[3.2-*c*]chromen derivatives form 4-hydroxy-coumarin derivatives and arylglyoxals. The methodology is efficient, simple work-up, heavy metal catalyst-free and using commercially available reagents. This class of compounds may be used to construct some bioactive compounds.

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References

[1] (a) Santana, L.; Uriarte, E.; Roleira, F.; Milhazes, N.; Borges, F. *Curr. Med. Chem*. **2004**, *11*, 3239; (b) Wang, X. H.; Bastow, K. F.; Sun, C. M.; Lin, Y. L.; Yu, H. J. *J. Med. Chem.* **2004**, *47*, 5816; (c) Dong, Y. H.; Shi, Q.; Pai, H. C.; Peng, C. Y.; Pan, S. H.; Teng, C. M. *J. Med. Chem*. **2010**, *53*, 2299.

[2] (a) Guillaume, R.; Marion, R.; Geneviève, B.; Nuno, M. *Org. Lett.* **2009**, *22*, 5254; (b) Elisa, A.; Massimiliano, C.; Giovanni, G.; Francesco, R.; Angela, S. *Tetrahedron* **2010**, *66*, 9493; (c) Abdullah, G. A.; Sameh, R. E. *Chin. J. Chem.* **2012**, *30*, 316.

[3] (a) Cheng, G.; Hu, Y. H. *Chem. Commun.* **2007**, 3285; (b) Cheng, G.; Hu, Y. H. *J. Org. Chem.* **2008**, *73*, 4732.

[4] Chen, L.; Li, Y.; Xu, M. H. *Org. Biomol. Chem.* **2010**, *8*, 3073.

[5] Chen, Z. W.; Zhu, Q.; Su, W. K. *Tetrahedron Lett*. **2011**, *52*, 2601.

[6] (a) Kolos, N. N.; Gozalishvili, L. L.; Sivokon, E. N.; Knyazeva, I. V. *Russ. J. Org. Chem.* **2009**, *45*, 119; (b) Kolos, N. N.; Gozalishvili, L. L.; Yaremenko, F. G.; Shishkin, O. V.; Shishkina, S. V.; Konovalovac, I. S. *Russ. Chem. Bull.* **2007**, *56*, 2277.

[7] (a) Fajarií, L.; Brillas, E.; Alemán, C.; Juliá, L. *J. Org. Chem.* **1998**, *63*, 5324; (b) Wu, A. X.; Wang, M. Y.; Gan, Y. H.; Pan, X. F. *J. Chem. Res.* **1998**, *30*, 136; (c) Jones, R. A.; Civcir, P. U. *Tetrahedron* **1997**, *53*, 11529; (d) Stauffer, F.; Neier, R. *Org. Lett.* **2000**, *2*, 3535; (e) Yin, G. D.; Wang, Z. H.; Chen, A. H.; Gao, M.; Wu, A. X.; Pan, Y. J. *J. Org. Chem.* **2008**, *73*, 3377.

[8] (a) Venugopal, M.; Balasundaram, B.; Perumal, P. T. *Synth.*

Commun. **1993**, *23*, 2593; (b) Nicolaou, K. C.; Hao, J. L.; Reddy, M. V. *J. Am. Chem. Soc.* **2004**, *126*, 12897.

[9] (a) Kappe, C. O. *Angew. Chem., Int. Ed. Engl.* **2004**, *43*, 6250; (b) Lidström, 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; (d) Yang, X. H.; Zhang, P. H.; Zhou, Y. H.; Wang, J. S.; Liu, H. J. *Chin. J. Chem.* **2012**, *30*, 670; (e) Maher, A. E.; Ahmed, Y. E.; Mamdouh, A. T.; Ibrahim, E. E. *Chin. J. Chem*. **2012**, *30*, 616.

[10] Nagariya, A. K.; Meena, A. K.; Yadav, A. K.; Niranjan, U. S.; Pathak, A. K.; Singh, B.; Rao, M. M. *J. Pharm. Res.* **2010**, *3*, 575.

[11] Kappe, C. O.; Dallinger, D.; Murphree, S. S. *Practical Microwave Synthesis for Organic Chemists*, Wiley-VCH, Weinheim, **2009**.

[12] Kappe, C. O. *Chem. Sov. Rev.* **2008**, *37*, 1127.

(Cheng, F.)

