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Microwave-promoted Synthesis of Novel Fused Osthole Analogues

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Osthole is a natural coumarin derivative and has a broad scope of biological activities. Two series of novel fused osthole analogues were designed, and synthesized through a highly efficient microwave-promoted synthetic protocol via the reaction of 4-hydroxycoumarins and *β*-ketoesters. The reaction conditions including solvent, catalyst, microwave power and irradiation time were also optimized. The pyrano[3,2-*c*]chromene-2,5-diones and furo[3,2-*c*]-coumarins were obtained through two distinct intramolecular cyclization processes, and the proposed mechanism was also discussed.

Keywords osthole, microwave-promoted synthesis, pyrano[3,2-*c*]chromene-2,5-diones, furo[3,4-*c*]coumarins, mechanism

Introduction

Osthole, a natural occurring coumarin derivative (Figure 1), is reported as the active ingredient of *Cnidium Monnieri*, a traditional Chinese herbal medicine. Osthole chemically known as an *O*-methylated coumarin was also found in many plants and possesses a broad scope of pharmacological and biochemical activities,[1-4] including antiarrhythmia, antidiabetic, anticancer, anti-osteoporosis, antiinflammatory, hepatoprotection and neuroprotection. It has been widely used as a fungicide in China for a long history,[5] displaying a range of antifungal activities against *Rhizoctonia solani* and other phytopathogenic fungi.[6]

As the structural core, coumarin is used regularly as a scaffold in medicinal and agricultural chemistry.[7-9] As shown in Figure 1, warfarin, phenprocoumon and acenocoumarol are coumarin anticoagulant agents, function as vitamin K antagonists that inhibit coagulation by blocking synthesis of coagulation factors.[10,11] Methoxsalen is a natural coumarin drug used to treat psoriasis, eczema and some cutaneous lymphomas in conjunction with exposing the skin to UVA light from lamps or sunlight.[12] Dicoumarol is a naturally coumarin occurring anticoagulant that functions as a functional

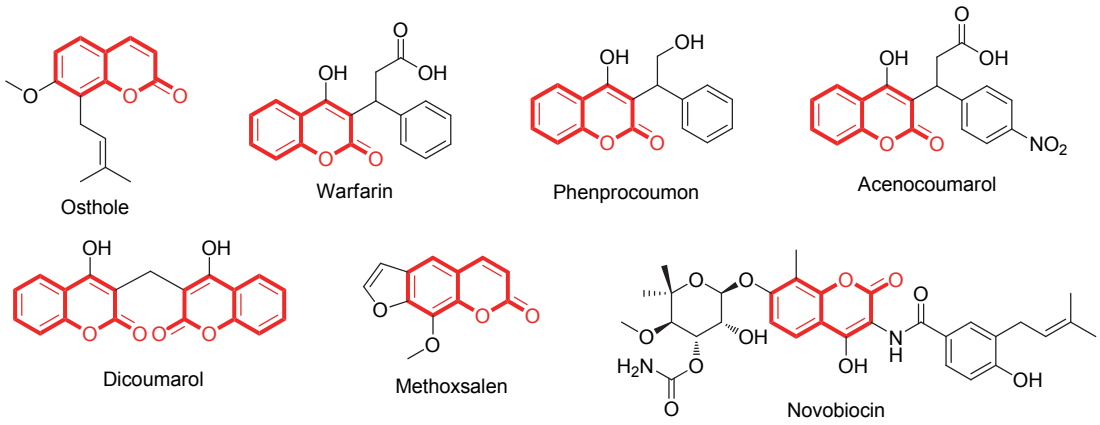

Figure 1 Structures of osthole and coumarin-containing drugs.

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vitamin K depleter (similar to warfarin).[13] Novobiocin is an aminocoumarin antibiotic obtained from an actinomycete and used to treat infections by Gram-positive bacteria.[14]

The prominence of coumarins in natural products and biologically active molecules has promoted considerable efforts toward their synthesis,[15,16] while, based on the chemical structures characteristics of these approved drugs, and the results of substructure search in DrugBank database (http://www.drugbank.ca/), we can notice that the fused coumarin derivatives on C-3 and C-4 were rarely reported in the research of medicinal and agricultural chemistry, some related publications mainly focus on the synthetic approaches to furo[3,2-*c*]-coumarin and Furtinone A derivatives.[17-19] Though Gupta and coworkers[20] have previously described the synthesis and antifungal activity of some fused coumarin compounds, some of which possessed effective control with EC_{50} values ranging from 0.2 to 2.5 μg/mL against five tested phytopathogenic fungi in culture, other than this, few literatures reported the further structural modification and antifungal activity of fused coumarin analogues.

Osthole was treated as the lead compound to carry out structural optimization in our previous work,[21-23] as the 2*H*-pyran-2-one substructure in osthole can be considered as configuration ring-closed analogue of (*E*)-methyl 3-methoxy-2-phenylacrylate (Figure 2), which is the pharmacophore of the strobilurin fungicides. Our published data showed that the designed compounds with coumarin as the scaffold are very potent against the phytopathogenic fungi on which they were tested.[7,24] As continuation of our studies on natural product based pesticide discovery, we report our research focused on microwave-promoted synthesis of novel fused oxygen-bearing osthole analogues.

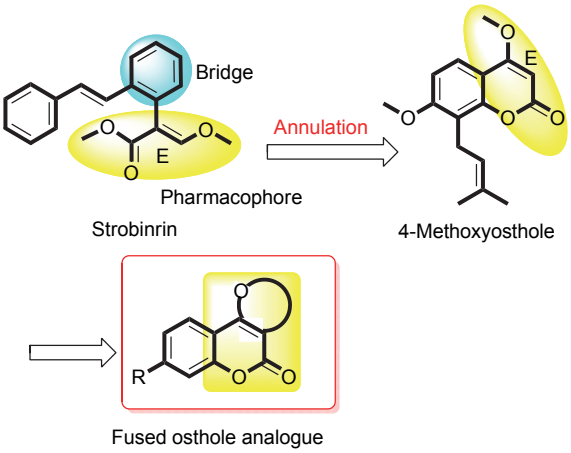


Figure 2 Design strategies of target molecules.

Results and Discussion

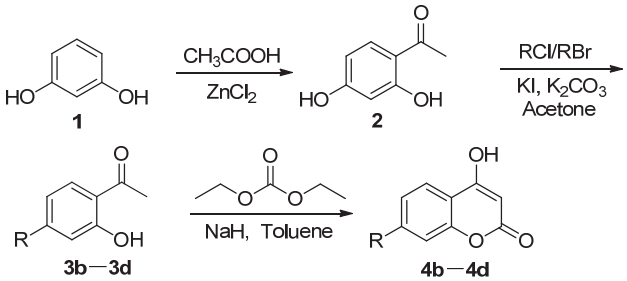
Synthetic chemistry

Aiming to discover synthetic analogues with simpler chemical structures, our research in this study is to use the natural product osthole as a lead to carry out the structural modification, to improve the bioactivity by exploring the chemistry, thus, a highly efficient reaction protocol *e.g.* microwave-promoted synthesis is preferred for building up the compounds library.

As most synthetic procedures are costly, time consuming and not environmentally friendly, usually giving relatively poor yields, the application of microwave irradiation has rapidly gained acceptance as a valuable tool in modern combinatorial and medicinal chemistry. Compared with traditional heating for organic reactions, the main benefits of microwave-promoted organic synthesis are significant enhancements in rate and higher product yields, representing a very efficient and green synthetic approach.[25]

4-Hydroxycoumarins **4b** — **4d** were synthesized through the reported synthetic route (Scheme 1),[7] yields for **4b**, **4c**, and **4d** are 85%, 86%, and 82%, respectively. 4-Hydroxycoumarins (**4a**) was purchased from a commercial source.

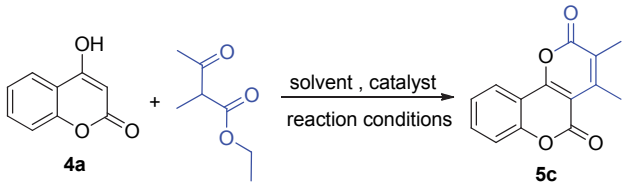
Scheme 1 Synthetic route for 4-hydroxycoumarins **4b**—**4d**



b: R = Methoxyl; **c**: R = Allyloxy; **d**: R = *n*-Butoxy.

In our initial study, the reaction of 4-hydroxycoumarin (**4a**) with ethyl 2-methylacetoacetate in the presence of toluene was chosen as a model to optimize the reaction conditions (Table 1). As shown in Table 1, compound **5c** could be prepared in a moderate yield with toluene as the best solvent (Table 1, Entries 3, 5, 6), using 640 W microwave irradiation (Table 1, Entries 6, 7, 8), and 4-dimethylaminopyridine (DMAP) as the catalyst (Table 1, Entries 4, 6). The yields increased consistently with time, from 34% (10 min) to a maximum of 69% (15 min) under these conditions, however, when extending the reaction time longer than 20 min, the yield did not increase significantly (shown in Table 1, Entries 5, 6 and 9). Therefore, we can conclude that the optimal conditions include using toluene as the solvent in the presence of DMAP under microwave irradia tion (640 W) for 15 min. This optimized method was used to synthesize the designed coumarin derivatives. Furthermore, compared with conventional heating (Table 1, Entries 13, 14), the reaction times for the target compounds can be reduced from about 6 h to 15 min at minimum (Table 1, Entry 6). We also explored the green conditions (Table 1, Entries 15, 16), unfortunately, the reaction was not suitable to conduct under water or solvent-free conditions, duct under water or solvent-free

Table 1 Reaction condition optimization for compound **5c**



Entry	Solvent	Catalyst	MW/W	Temperature	Time/min	Yield[a]/%
1	DMF	NH_4OAc	640	r.t.	15	45
2	DMF	NH_4OAc	640	r.t	20	40
3	DMF	DMAP	640	r.t.	15	35
4	Toluene	NH_4OAc	640	r.t	15	45
5	Toluene	DMAP	640	r.t.	10	34
6	**Toluene**	**DMAP**	**640**	**r.t.**	**15**	**69**
7	Toluene	DMAP	560	r.t.	15	55
8	Toluene	DMAP	720	r.t.	15	20
9	Toluene	DMAP	640	r.t.	20	65
10	Ethanol	NH_4OAc	640	r.t.	20	48
11	Ethanol	DMAP	640	r.t.	20	54
12	DMF	NH_4OAc	—[b]	Reflux	360	30
13	DMF	DMAP	—[b]	Reflux	360	40
14	Toluene	DMAP	—[b]	Reflux	360	45
15	H_2O	DMAP	640	r.t.	15	—[c]
16	—[d]	DMAP	640	r.t.	15	—[c]

[a] Yields after recrystallization from ethanol. [b] Conventional heating, no microwave irradiation. [c] Reaction failed. [d] Solvent free.

conditions, as the starting materials are insoluble in water or conglomerate together under solvent-free condition.

With this efficient method, a focused compounds library of pyrano[3,2-*c*]chromene-2,5-diones (**5a**—**9d**) and furo[3,2-*c*]coumarins (**10a** — **13d**), including 3-(trifluoro)methyl (**5a**—**5e**), 8-alkoxy (**6a**—**6d**, **8a**—**8c**) and 8-allyloxy (**7a** — **7c**) pyrano[3,2-*c*]chromene-2,5-diones have been designed and synthesized (Schemes 2 and 3). All of the target compounds were characterized by ^{1}H NMR, ^{13}C NMR, IR and HRMS, and the structures of **5b**, **6b**, **10b** and **12a** were further confirmed by X-ray diffraction crystallography (Figure 3).

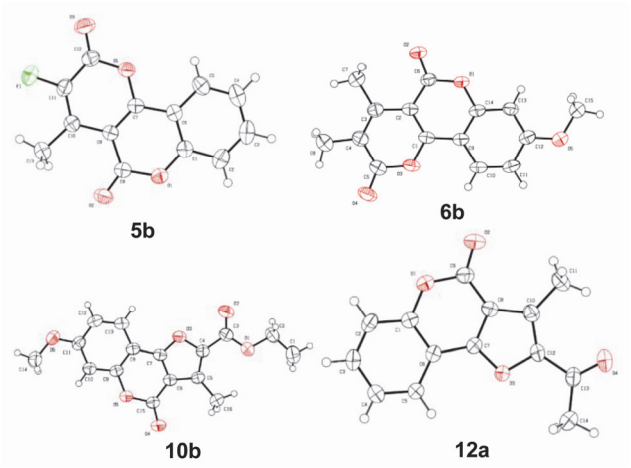
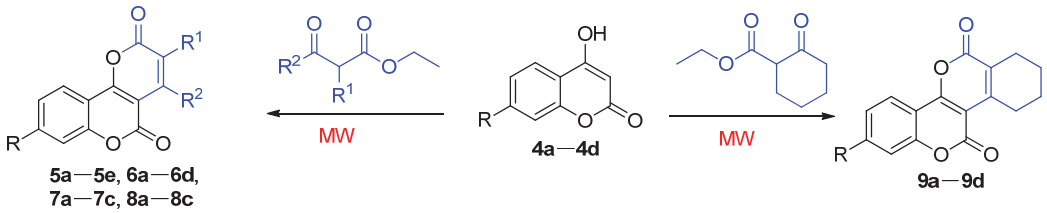


Figure 3 X-ray structures of compounds **5b**, **6b**, **10b** and **12a**.

Proposed reaction mechanisms

A plausible reaction pathway is proposed in Scheme 4. Nucleophilic attack of compound **4** on the ketone carbonyl of *β*-ketoesters followed by protonation gives intermediate **E**, which could undergo two distinct intramolecular cyclization processes (Routes 1 and 2) depending on the R^1 substituent. When R^1 is H, Me, Et or F, intermediate **E** proceeds via dehydration of **F** and subsequent intramolecular cyclization of **G** to afford six-membered-ring product **A** (Route 1). Due to their good leaving ability, Cl or Br-substituted **E** would undergo an alternative cyclization, in which the intramolecular nucleophilic substitution occurs on the *α*-site of the ester, process shown in **H**, then is the subsequent dehydration of intermediate **I** to generate five-membered ring **B** (Route 2).

Scheme 2 Microwave-promoted synthetic route for compounds **5a**—**9d**



Compd.	R	R^1	R^2	Yield/%	Compd.	R	R^1	R^2	Yield/%
5a	H	H	CH_3	72	**7b**	Allyloxy	CH_3	CH_3	66
5b	H	F	CH_3	13	**7c**	Allyloxy	Et	CH_3	69
5c	H	CH_3	CH_3	68	**8a**	*n*-Butoxy	H	CH_3	70
5d	H	Et	CH_3	64	**8b**	*n*-Butoxy	CH_3	CH_3	62
5e	H	H	CF_3	20	**8c**	*n*-Butoxy	Et	CH_3	64
6a	Methoxy	H	CH_3	75	**9a**	H	$(CH_2)_4$		74
6b	Methoxy	CH_3	CH_3	71	**9b**	Methoxy	$(CH_2)_4$		65
6c	Methoxy	Et	CH_3	69	**9c**	Allyloxy	$(CH_2)_4$		67
6d	Methoxy	H	CF_3	31	**9d**	*n*-Butoxy	$(CH_2)_4$		75
7a	Allyloxy	H	CH_3	76	**9a**	H			74

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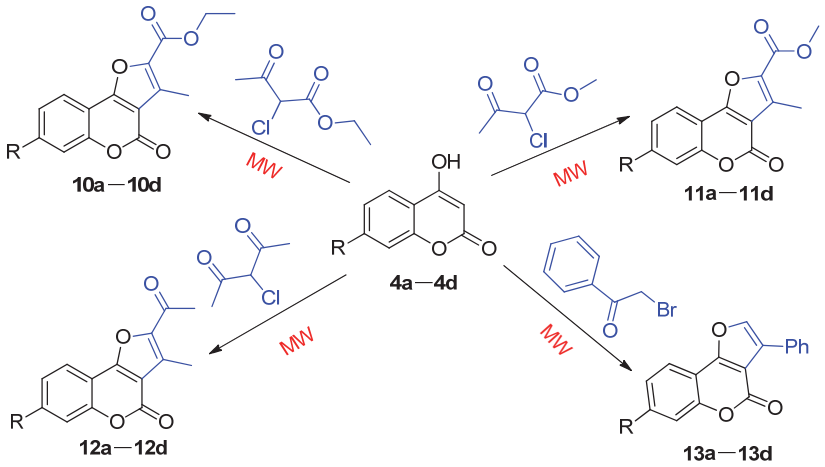
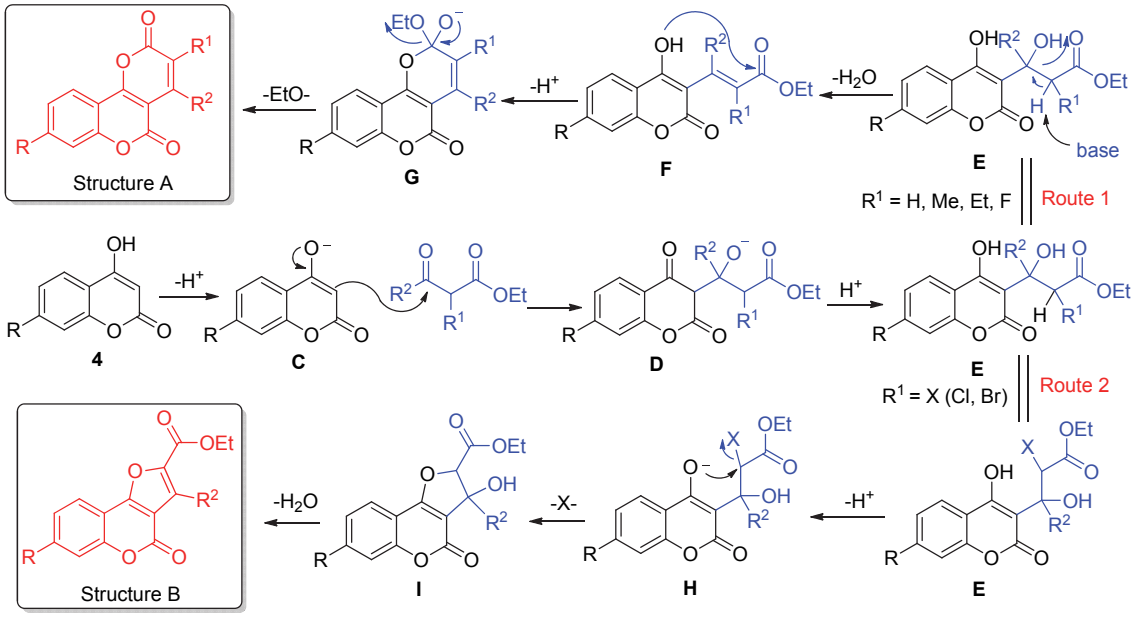
Scheme 3 Microwave-promoted synthetic routes for compounds **10a**—**13d**



Compd.	Time/min	R	Yield/%	Compd.	Time/min	R	Yield/%
10a	10	H	65	**12a**	10	H	69
10b	15	Methoxy	77	**12b**	15	Methoxy	73
10c	10	Allyloxy	67	**12c**	15	Allyloxy	65
10d	10	*n*-Butoxy	63	**12d**	15	*n*-Butoxy	62
11a	10	H	67	**13a**	15	H	67
11b	15	Methoxy	73	**13b**	15	Methoxy	73
11c	15	Allyloxy	65	**13c**	15	Allyloxy	65
11d	15	*n*-Butoxy	61	**13d**	15	*n*-Butoxy	61

Scheme 4 Proposed mechanism for the formation of structures **A** and **B**



Experimental

Chemicals and instruments

All chemicals were purchased from commercial sources (*e.g.*, Adamas, Crystal Chemicals) and used without further purification unless otherwise stated. The microwave treatment was carried out in a microwave oven (WBFY-201, Gongyi Yuhua Instrument Co., Ltd.) with an emission frequency of 2450 MHz and a maximum output power of 800 W. The melting points of the ester derivatives of coumarin derivatives were determined on an X-4 apparatus (uncorrected), which was purchased from Shanghai Tech. Infrared (IR) spectra were recorded on a Bruker Tensor 27 spectrometer, and samples were prepared as KBr plates. ^{1}H NMR and ^{13}C NMR spectra were obtained by using a Bruker Avance 400 MHz spectrometer in $CDCl_3$ solution with TMS as an internal standard. HR-MS (ESI) spectra were carried out with a Thermo Exactive spectrometer, and X-rays were measured at 296 K on a Bruker SMART APEX2

CCD area detector diffractometer. Most reaction yields were not optimized.

Microwave-promoted synthetic procedure for the preparation of compounds 5a—9d

Take the synthesis of compoubd **5c** as an example. To a stirred solution of 4-hydroxycoumarin (**4**, 1.62g, 10.0 mmol) and *β*-ketoester (ethyl 2-methyl-3-oxobutanoate, 1.73 g, 12.0 mmol) in toluene (30 mL) was added DMAP (1.46 g, 12.0 mmol), and the reaction mixture was irradiated in a microwave apparatus (640 W) under room temperature for 15 min. After the reaction mixture was cooled down to ambient temperature, the mixture was concentrated, and the crude product was purified by column chromatography using petroleum ether/acetone (*V*∶*V*, 20∶1 to 10∶1) as eluent to give the title compound **5c** (1.67 g) as a white solid, yield 69%.

Traditional synthetic procedure for the preparation of compound 5c

4-Hydroxycoumarin **4** (1.62 g, 10.0 mmol), ethyl 2-methyl-3-oxobutanoate (1.73 g, 12.0 mmol) and DMAP (1.46 g, 12.0 mmol) were dissolved in toluene (30 mL). The mixture was stirred under conventional heating reflux for about 6 h till full conversion of the substrates was indicated by TLC analysis, then cooled to ambient temperature and concentrated at reduced pressure. The crude product was purified by column chromatography to give the title compound **5c** (1.09 g) as a white solid, yield 45%.

4-Methyl-pyrano[3,2-*c*]chromene-2,5-dione (**5a**): white solid; m.p. 257.6—262.5 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.16 (s, 1H), 7.71 (s, 1H), 7.44 (s, 2H), 6.27 (s, 1H), 2.69 (s, 3H); ^{13}C NMR (101 MHz, DMSO) *δ*: 135.09, 125.63, 123.99, 117.14, 114.29, 40.51, 40.40, 40.19, 39.91, 39.78, 39.59, 39.46, 22.31; IR (KBr) *ν*: 1711, 1623, 1446, 1272 cm^{-1}; HR-MS (ESI) calcd for $C_{13}H_9O_4$ $[M+H]^+$ 229.05009, found 229.04944.

3-Fluoro-4-methyl-pyrano[3,2-*c*]chromene-2,5-dione (**5b**): white solid; m.p. 247.3—247.5 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.05 (s, 1H), 7.69 (s, 1H), 7.41 (s, 2H), 2.64 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 158.03, 157.69, 152.61, 145.45, 142.95, 134.91, 134.34, 125.30, 123.69, 116.96, 112.73, 103.25, 12.84; IR (KBr) *ν*: 1695, 1616, 1446, 1268 cm^{-1}; HR-MS (ESI) calcd for $C_{13}H_9FO_4$ $[M+H]^+$ 247.04066, found 247.03992.

3,4-Dimethyl-pyrano[3,2-*c*]chromene-2,5-dione (**5c**): white solid; m.p. 223.5—223.5 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.15 (s, 1H), 7.69 (s, 1H), 7.41 (s, 2H), 2.69 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 159.52, 159.36, 158.65, 152.73, 149.46, 133.86, 124.90, 123.64, 122.41, 116.67, 113.20, 104.18, 18.18, 13.23; IR (KBr) *ν*: 1727, 1660, 1446, 1191 cm^{-1}; HR-MS (ESI) calcd for $C_{14}H_{10}O_4$ $[M+H]^+$ 243.06573, found 243.06502.

3-Ethyl-4-methyl-pyrano[3,2-*c*]chromene-2,5-dione (**5d**): white solid; m.p. 143.4—144.3 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.14 (d, *J*=7.9 Hz, 1H), 7.69 (t, *J*=7.8 Hz, 1H), 7.42 (dd, *J*=13.8, 8.0 Hz, 2H), 2.73 (dd, *J*=15.2, 7.7 Hz, 2H), 2.70 (s, 3H), 1.21 (q, *J*=7.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 159.54, 159.13, 158.71, 152.75, 149.08, 133.86, 128.15, 124.88, 123.67, 116.66 , 113.24, 104.31, 20.76, 17.67, 12.52; IR (KBr) *ν*: 1715, 1620, 1537, 1449 cm^{-1}; HR-MS (ESI) calcd for $C_{15}H_{12}O_4$ $[M+H]^+$ 257.08139, found 257.08069.

4-Trifluoromethyl-pyrano[3,2-*c*]chromene-2,5-dione (**5e**): white solid; m.p. 200.5—203.0 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.13 (dd, *J*=8.0, 1.4 Hz, 1H), 7.80—7.72 (m, 1H), 7.49—7.41 (m, 2H), 6.88 (d, *J*=0.7 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 163.80, 156.30, 154.66, 153.70, 142.35, 141.93, 135.75, 125.38, 124.15, 117.16, 115.97 (q, *J*=7.3 Hz, 1C), 112.37, 99.63; IR (KBr) *ν*: 1724, 1607, 1530, 1458, 1389, 1099, 833 cm^{-1}; HR-MS (ESI) calcd for $C_{13}H_5F_3O_4$ $[M+H]^+$ 283.02182, found 283.02127.

8-Methoxy-4-methyl-pyrano[3,2-*c*]chromene-2,5-dione (**6a**): white solid; m.p. 242.0—242.1 ℃; ^{1}H NMR (400 MHz,$CDCl_3$) *δ*: 8.02 (s, 1H), 6.99 (s, 1H), 6.87 (s, 1H), 6.17 (s, 1H), 3.97 (s, 3H), 2.66 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 165.13, 162.71, 158.69, 158.18, 156.45, 155.36, 125.40, 113.70, 112.72, 106.30, 101.51, 100.55, 56.04, 22.67; IR (KBr) *ν*: 1709, 1611, 1541, 1281 cm^{-1}; HR-MS (ESI) calcd for $C_{14}H_{10}O_5$ $[M+H]^+$ 259.06065, found 259.05988.

8-Methoxy-3,4-dimethyl-pyrano[3,2-*c*]chromene-2,5-dione (**6b**): white solid; m.p. 212.3—212.9 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.01 (s, 1H), 6.97 (s, 1H), 6.85 (s, 1H), 3.95 (s, 3H), 2.67 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 164.54, 159.80, 159.70, 159.01, 154.74, 149.83, 124.85, 120.69, 113.44, 106.33, 101.83, 100.34, 55.98, 18.14, 13.06; IR (KBr) *ν*: 1702, 1609, 1550, 1275 cm^{-1}; HR-MS (ESI) calcd for $C_{15}H_{12}O_5$ $[M+H]^+$ 273.07630, found 273.07553.

3-Ethyl-8-methoxy-4-methyl-pyrano[3,2-*c*]chromene-2,5-dione (**6c**): white solid; m.p. 143.1—143.3 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.01 (dd, *J*=18.7, 8.9 Hz, 1H), 7.00—6.94 (m,1H), 6.84 (dd, *J*=12.5, 2.2 Hz, 1H), 3.95 (s, 3H), 2.71 (dd, *J*=14.6, 7.1 Hz, 2H), 2.68 (s, 3H), 1.18 (t, *J*=7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 164.56, 160.10, 159.36, 159.12, 154.80, 149.47, 126.48, 124.92, 113.40, 106.41, 101.97, 100.35, 55.97, 20.63, 17.64, 12.60; IR (KBr) *ν*: 1715, 1607, 1397, 1275, 1022 cm^{-1}; HR-MS (ESI) calcd for $C_{16}H_{13}O_5$ $[M+H]^+$ 287.09195, found 287.09115.

8-Methoxy-4-trifluoromethyl-pyrano[3,2-*c*]chromene-2,5-dione (**6d**): white solid; m.p. 225.6—225.8 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.01 (dd, *J*=21.3, 8.4 Hz, 1H), 7.09—6.94 (m, 1H), 6.94—6.74 (m, 2H), 3.98 (d, *J*=8.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 166.08, 164.17, 156.66, 156.05, 155.09,143.37, 142.29, 125.49, 115.09, 114.38—113.99 (m, 1C), 105.54, 100.57, 97.02, 56.21; IR (KBr) *ν*: 1765, 1731, 1609, 1376, 1150 cm^{-1}; HR-MS (ESI) calcd for $C_{14}H_7F_3O_5$ $[M+H]^+$ 313.03238, found 313.03183.

8-Allyloxy-4-methyl-pyrano[3,2-*c*]chromene-2,5-dione (**7a**): white solid; m.p. 178.1—178.3 ℃; ^{1}H

NMR (400 MHz, $CDCl_3$) δ: 8.03 (s, 1H), 7.01 (s, 1H), 6.88 (s, 1H), 6.17 (s, 1H), 6.09 (s, 1H), 5.46 (s, 2H), 4.70 (s, 2H), 2.66 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 164.02, 162.62, 158.63, 158.12, 156.41, 155.21, 131.70, 125.36, 118.89, 114.14, 112.72, 106.34, 101.51, 101.35, 69.53, 22.65; IR (KBr) ν: 1711, 1609, 1544, 1489, 1279, 1089 cm^{-1}; HR-MS (ESI) calcd for $C_{16}H_{11}O_5$ $[M+H]^+$ 285.07630, found 285.07554.

8-Allyloxy-3,4-dimethyl-pyrano[3,2-*c*]chromene-2,5-dione (**7b**): white solid; m.p. 192.7－193.3 ℃; ^{1}H NMR (400 MHz, DMSO) δ: 7.79 (s, 1H), 7.15 (s, 1H), 6.32 (s, 1H), 6.10 (s, 1H), 5.39 (d, J=40.7 Hz, 2H), 4.78 (s, 2H), 3.33 (s, 3H), 2.21 (s, 3H); ^{13}C NMR (101 MHz, CDCl3) δ: 163.44, 159.77, 159.02, 154.63, 149.81, 131.80, 124.86, 120.72, 118.80, 113.92, 106.41, 101.86, 101.17, 69.45, 18.15, 13.07; IR (KBr) ν: 1718, 1605, 1541, 1489, 1291, 1105 cm^{-1}; HR-MS (ESI) calcd for $C_{17}H_{14}O_5$ $[M+H]^+$ 299.09195, found 299.09109.

8-Allyloxy-3-ethyl-4-methyl-pyrano[3,2-*c*]chromene-2,5-dione (**7c**): white solid; m.p. 143.1－143.3 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.98 (d, J=8.9 Hz, 1H), 7.00－6.88 (m, 1H), 6.82 (d, J=2.3 Hz, 1H), 6.05 (ddd, J=22.5, 10.6, 5.3 Hz, 1H), 5.41 (ddd, J=13.9, 11.6, 1.1 Hz, 2H), 4.63 (d, J=5.3 Hz, 2H), 2.67 (dd, J=14.9, 7.4 Hz, 2H), 2.63 (s, 3H), 1.14 (t, J=7.5 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 163.46, 160.04, 159.31, 159.09, 154.67, 149.43, 131.81, 126.52, 124.90, 118.79, 113.92, 106.47, 101.98, 101.17, 69.46, 20.63, 17.63, 12.59; IR (KBr) ν: 1704, 1616, 1544, 1503, 1277, 1205 cm^{-1}; HR-MS (ESI) calcd for $C_{18}H_{16}O_5$ $[M+H]^+$ 313.10760, found 313.10669.

8-Butoxy-4-methyl-pyrano[3,2-*c*]chromene-2,5-dione (**8a**): white solid; m.p. 183.0－183.9 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.03 (d, J=8.9 Hz, 1H), 6.99 (dd, J=8.9, 2.2 Hz, 1H), 6.85 (d, J=2.2 Hz, 1H), 6.17 (d, J=1.0 Hz, 1H), 4.11 (t, J=6.5 Hz, 2H), 2.66 (d, J=0.9 Hz, 3H), 1.91－1.79 (m, 2H), 1.55 (dt, J=14.7, 7.4 Hz, 2H), 1.04 (t, J=7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 164.74, 162.73, 158.73, 158.21, 156.48, 155.35, 125.30, 114.07, 112.59, 106.02, 101.36, 100.93, 68.73, 30.90, 22.67, 19.14, 13.77; IR (KBr) ν: 1744, 1627, 1546, 1438, 1276, 1087 cm^{-1}; HR-MS (ESI) calcd for $C_{17}H_{16}O_5$ $[M+H]^+$ 301.10760, found 301.10675.

8-Butoxy-3,4-dimethyl-pyrano[3,2-*c*]chromene-2,5-dione (**8b**): white solid; m.p. 172.5－172.7 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.97 (d, J=8.9 Hz, 1H), 6.93 (dd, J=8.9, 2.3 Hz, 1H), 6.79 (d, J=2.2 Hz, 1H), 4.05 (t, J=6.5 Hz, 2H), 2.63 (s, 3H), 2.19 (s, 3H), 1.88－1.73 (m, 2H), 1.52 (dq, J=14.7, 7.4 Hz, 2H), 1.00 (t, J=7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 164.17, 159.98, 159.77, 159.13, 154.78, 149.89, 124.80, 120.56, 113.84, 106.11, 101.73, 100.76, 68.62, 30.92, 19.15, 18.15, 13.77, 13.05; HR-MS (ESI) calcd for $C_{18}H_{18}O_5$ $[M+H]^+$ 315.12325, found 315.12239.

8-Butoxy-3-ethyl-4-methyl-pyrano[3,2-*c*]chromene-2,5-dione (**8c**): white solid; m.p. 144.3－144.7 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.97 (dd, J=8.9, 1.3 Hz, 1H), 6.92 (dd, J=8.9, 2.1 Hz, 1H), 6.79 (s, 1H), 4.05 (t, J=6.4 Hz, 2H), 2.67 (dd, J=13.2, 5.7 Hz, 2H), 2.63 (s, 3H), 1.88－1.76 (m, 2H), 1.51 (dt, J=14.9, 7.4 Hz, 2H), 1.26 (s, 1H), 1.14 (t, J=7.5 Hz, 3H), 1.00 (t, J=7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 164.17, 160.15, 159.38, 159.18, 154.80, 149.51, 126.35, 124.83, 113.83, 106.15, 101.83, 100.74, 68.61, 30.93, 20.61, 19.15, 17.64, 13.77, 12.60; HR-MS (ESI) calcd for $C_{19}H_{20}O_5$ $[M+H]^+$ 329.13890, found 329.13809.

7,8,9,10-Tetrahydro-5,12-dioxa-chrysene-6,11-dione (**9a**): white solid; m.p. 211.2－212.3 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 (s, 1H), 7.65 (s, 1H), 7.37 (s, 2H), 3.14 (s, 2H), 2.59 (s, 2H), 1.80 (s, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 159.29, 159.17, 158.40, 152.73, 150.76, 133.77, 124.87, 123.79, 123.56, 116.67, 113.27, 103.83, 28.55, 24.50, 21.53, 20.84; IR (KBr) ν: 1720, 1620, 1605, 1541, 1189 cm^{-1}; HR-MS (ESI) calcd for $C_{16}H_{12}O_4$ $[M+H]^+$ 269.08139, found 269.08072.

2-Methoxy-7,8,9,10-tetrahydro-5,12-dioxa-chrysene-6,11-dione (**9b**): white solid, m.p. 238.2－240.8 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.98 (s, 1H), 6.95 (s, 1H), 6.82 (s, 1H), 3.91 (s, 3H), 3.12 (s, 2H), 2.56 (s, 2H), 1.78 (s, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 164.48, 159.88, 159.42, 158.81, 154.77, 151.13, 124.81, 122.11, 113.41, 106.44, 101.49, 100.39, 55.96, 28.55, 24.37, 21.57, 20.93; IR (KBr) ν: 1702, 1605, 1528, 1275 cm^{-1}; HR-MS (ESI) calcd for $C_{17}H_{14}O_5$ ($[M+H]^+$) 299.09195, found 299.09109.

2-Allyloxy-7,8,9,10-tetrahydro-5,12-dioxa-chrysene-6,11-dione (**9c**): a white solid, m.p. 206.9－207.3 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.02 (d, J=8.9 Hz, 1H), 7.07－6.93 (m, 1H), 6.86 (d, J=2.2 Hz, 1H), 6.09 (ddd, J=22.4, 10.6, 5.3 Hz, 1H), 5.45 (dd, J=36.7, 13.9 Hz, 2H), 4.68 (d, J=5.3 Hz, 2H), 3.16 (s, 2H), 2.60 (s, 2H), 1.87－1.71 (m, 4H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 163.40, 159.85, 159.40, 158.81, 154.67, 151.11, 131.83, 124.82, 122.15, 118.78, 113.89, 106.53, 101.53, 101.23, 69.45, 28.54, 24.37, 21.57, 20.92; IR (KBr) ν: 1702, 1611, 1550, 1277, 1110 cm^{-1}; HR-MS (ESI) calcd for $C_{19}H_{16}O_5$ ($[M+H]^+$) 325.10760, found 325.10675.

2-Butoxy-7,8,9,10-tetrahydro-5,12-dioxa-chrysene-6,11-dione (**9d**): white solid; m.p. 146.7－147.1 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.97 (d, J=8.9 Hz, 1H), 6.92 (dd, J=8.9, 2.3 Hz, 1H), 6.79 (d, J=2.2 Hz, 1H), 4.05 (t, J=6.5 Hz, 2H), 3.11 (s, 2H), 2.56 (s, 2H), 1.89－1.69 (m, 6H), 1.60－1.42 (m, 2H), 1.00 (t, J=7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 162.71, 159.17, 158.84, 158.19, 155.43, 141.00, 130.49, 122.90, 113.44, 109.11, 105.24, 101.85, 68.45, 61.27, 30.98, 29.70, 19.17, 14.24, 13.78, 10.17; HR-MS (ESI) calcd for $C_{20}H_{20}O_5$ ($[M+H]^+$) 341.13890, found 341.13835.

Microwave-promoted synthesis for compounds 10a－13d

Based on the above microwave-promoted method, α-halo-β-ketoesters *e.g.* ethyl 2-chloro-3-oxobutanoate were employed as the starting materials, while, the obtained products were furo[3,2-*c*]coumarins rather than pyrano[3,2-*c*]chromene-2,5-diones, and furo[3,2-*c*]-

coumarins **10a**－**13d** could be prepared in moderate yields with toluene as the solvent, using 640 W microwave irradiation, and DMAP as the catalyst. The yields vary from 61% to 77% considerably depending upon the irradiative time.

3-Methyl-4-oxo-4*H*-furo[3,2-*c*]chromene-2-carboxylic acid ethyl ester (**10a**): white solid; m.p. 140.2－140.6 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.07 (dd, J=7.9, 1.4 Hz, 1H), 7.69－7.58 (m, 1H), 7.56－7.37 (m, 2H), 4.50 (q, J=7.1 Hz, 2H), 2.75 (s, 3H), 1.50 (t, J=7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 159.01, 158.07, 157.79, 153.50, 141.85, 132.09, 130.31, 124.74, 121.90, 117.40, 112.18, 111.52, 61.45, 14.36, 10.15; IR (KBr) v: 1708, 1631, 1446, 1321, 1139, 1087 cm^{-1}; HR-MS (ESI) calcd for $C_{15}H_{12}O_5$ $[M+H]^+$ 273.07630, found 273.07575.

7-Methoxy-3-methyl-4-oxo-4*H*-furo[3,2-*c*]chromene-2-carboxylic acid ethyl ester (**10b**): white solid; m.p. 186.4－187.1 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.07 (dd, J=7.9, 1.4 Hz, 1H), 7.69－7.58 (m, 1H), 7.56－7.37 (m, 2H), 4.50 (q, J=7.1 Hz, 2H), 2.75 (s, 3H), 1.50 (t, J=7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 163.07, 159.14, 158.71, 158.10, 155.37, 141.03, 130.45, 122.95, 113.03, 109.18, 105.41, 101.37, 61.32, 55.85, 14.37, 10.17; IR (KBr) v: 1739, 1627, 1442, 1323, 1241, 963 cm^{-1}; HR-MS (ESI) calcd for $C_{16}H_{14}O_6$ $[M+H]^+$ 303.08686, found 303.08631.

7-Allyloxy-3-methyl-4-oxo-4*H*-furo[3,2-*c*]chromene-2-carboxylic acid ethyl ester (**10c**): white solid; m.p. 155.5－156.2 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.95 (d, J=8.7 Hz, 1H), 7.00 (dd, J=12.6, 3.8 Hz, 2H), 6.10 (ddd, J=16.6, 10.4, 5.2 Hz, 1H), 5.45 (dd, J=39.7, 13.9 Hz, 2H), 4.67 (d, J=5.2 Hz, 2H), 4.49 (q, J=7.1 Hz, 2H), 2.73 (s, 3H), 1.49 (t, J=7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 162.01, 159.14, 158.70, 158.11, 155.30, 141.08, 132.02, 130.45, 122.97, 118.66, 113.57, 109.25, 105.55, 102.25, 69.35, 61.31, 14.37, 10.17; IR (KBr) v: 1720, 1607, 1450, 1317, 1244, 1083, 994 cm^{-1}; HR-MS (ESI) calcd for $C_{18}H_{16}O_6$ $[M+H]^+$ 329.10252, found 329.10196.

7-Butoxy-3-methyl-4-oxo-4*H*-furo[3,2-*c*]chromene-2-carboxylic acid ethyl ester (**10d**): white solid; m.p. 189.3－192.3 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.07 (dd, J=7.9, 1.4 Hz, 1H), 7.69－7.58 (m, 1H), 7.56－7.37 (m, 2H), 4.50 (q, J=7.1 Hz, 2H), 2.75 (s, 3H), 1.50 (t, J=7.1 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 173.09, 165.25, 162.73, 155.77, 155.45, 126.39, 122.94, 113.73, 113.48, 108.54, 101.87, 100.77, 68.54, 61.30, 30.95, 19.16, 14.38, 13.78, 10.20; IR (KBr) v: 1732, 1696, 1623, 1442, 1309, 1135, 962 cm^{-1}; HR-MS (ESI) calcd for $C_{19}H_{20}O_6$ $[M+H]^+$ 345.13382, found 345.13331.

3-Methyl-4-oxo-4*H*-furo[3,2-*c*]chromene-2-carboxylic acid methyl ester (**11a**): white solid; m.p. 152.2－152.4 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.05 (d, J=7.8 Hz, 1H), 7.59 (t, J=26.3 Hz, 1H), 7.43 (dt, J=34.3, 17.6 Hz, 2H), 4.04 (t, J=16.4 Hz, 3H), 2.76 (t, J=16.6 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 159.34, 158.12, 157.72, 153.50, 141.59, 132.16, 130.64, 124.78, 121.85, 117.41, 112.11, 111.49, 52.21, 10.12; IR (KBr) v: 1700, 1623, 1446, 1325, 1232, 1131, 1083 cm^{-1}; HR-MS (ESI) calcd for $C_{14}H_{10}O_5$ $[M+H]^+$ 259.06065, found 259.06010.

7-Methoxy-3-methyl-4-oxo-4*H*-furo[3,2-*c*]chromene-2-carboxylic acid methyl ester (**11b**): white solid; m.p. 216.0 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.91 (d, J=8.6 Hz, 1H), 7.31 (t, J=14.7 Hz, 1H), 6.96 (d, J=11.6 Hz, 1H), 4.01 (dd, J=17.9, 11.4 Hz, 3H), 3.95－3.88 (m, 3H), 2.72 (dd, J=17.9, 11.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 163.15, 159.51, 158.83, 158.09, 155.45, 140.83, 130.83, 122.95, 113.10, 109.21, 105.41, 101.43, 55.87, 52.12, 10.16; IR (KBr) v: 1736, 1699, 1617, 1445, 1325, 1235, 1082, 960 cm^{-1}; HR-MS (ESI) calcd for $C_{15}H_{10}O_5$ $[M+H]^+$ 289.07122, found 289.07066.

7-Allyloxy-3-methyl-4-oxo-4*H*-furo[3,2-*c*]chromene-2-carboxylic acid methyl ester (**11c**): white solid; m.p. 151.0－154.9 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.98－7.85 (m, 1H), 7.04－6.89 (m, 2H), 6.12－5.99 (m, 1H), 5.43 (dd, J=49.7, 13.8 Hz, 2H), 4.65 (s, 2H), 4.07－3.94 (m, 3H), 2.77－2.65 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 162.05, 159.46, 158.73, 158.02, 155.31, 140.82, 132.00, 130.79, 122.91, 118.74, 113.55, 109.22, 105.47, 102.25, 69.46, 52.09, 10.13; IR (KBr) v: 1732, 1623, 1446, 1333, 1260, 1091, 994 cm^{-1}; HR-MS (ESI) calcd for $C_{17}H_{14}O_6$ $[M+H]^+$ 315.08686, found 315.08631.

7-Butoxy-3-methyl-4-oxo-4*H*-furo[3,2-*c*]chromene-2-carboxylic acid methyl ester (**11d**): white solid; m.p. 145.9－146.8 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.90 (dd, J=8.6, 3.5 Hz, 1H), 6.94 (dd, J=11.6, 5.9 Hz, 2H), 4.10－4.03 (m, 2H), 4.00 (d, J=3.5 Hz, 3H), 2.70 (t, J=9.4 Hz, 3H), 1.84 (s, 2H), 1.56 (dd, J=16.8, 5.8 Hz, 3H), 1.10－0.96 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 159.34, 158.12, 157.72, 153.50, 141.59, 132.16, 130.64, 124.78, 121.85, 117.41, 112.11, 111.49, 68.46, 52.21, 30.98, 19.18, 13.80, 10.12; IR (KBr) v: 1758, 1711, 1614, 1453, 1329, 1132, 999 cm^{-1}; HR-MS (ESI) calcd for $C_{18}H_{18}O_6$ $[M+H]^+$ 331.11816, found 331.11761.

2-Acetyl-furo[3,2-*c*]chromen-4-one (**12a**): white solid; m.p. 178.7－179.5 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.98 (dd, J=7.8, 1.2 Hz, 1H), 7.66－7.56 (m, 1H), 7.52－7.35 (m, 2H), 2.75 (s, 3H), 2.65 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 188.73, 157.79, 157.33, 153.66, 149.14, 132.28, 129.54, 124.84, 121.57, 117.54, 112.12, 112.04, 27.66, 10.24; IR (KBr) v: 1739, 1683, 1623, 1548, 1442, 1360, 1229, 1185, 994 cm^{-1}; HR-MS (ESI) calcd for $C_{14}H_{10}O_4$ $[M+H]^+$ 243.06573, found 243.06519.

2-Acetyl-7-methoxy-furo[3,2-*c*]chromen-4-one (**12b**): white solid; m.p. 200.9－203.2 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.87 (d, J=8.6 Hz, 1H), 7.03－6.90 (m, 2H), 3.96－3.87 (m, 3H), 2.74 (s, 3H), 2.62 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ: 188.56, 163.23, 158.06, 158.03, 155.61, 148.61, 129.77, 122.62, 113.22, 109.69,

105.35, 101.46, 55.95, 27.60, 10.28; IR (KBr) *v*: 1744, 1627, 1546, 1438, 1276, 1087 cm^{-1}; HR-MS (ESI) calcd for $C_{15}H_{12}O_5$ $[M+H]^+$ 273.07630, found 273.007575.

2-Acetyl-7-allyloxy-furo[3,2-*c*]chromen-4-one (**12c**): white solid; m.p. 146.2－146.3 ℃; ^1H NMR (500 MHz, $CDCl_3$) *δ*: 7.83 (d, *J*=8.7 Hz, 1H), 6.99－6.87 (m, 2H), 4.05 (t, *J*=6.5 Hz, 2H), 2.77－2.66 (m, 3H), 2.58 (d, *J*=17.9 Hz, 3H), 1.87－1.76 (m, 2H), 1.52 (dt, *J*=14.8, 7.5 Hz, 2H), 1.00 (t, *J*=7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 188.58, 162.14, 158.10, 158.04, 155.50, 148.61, 131.95, 129.76, 122.63, 118.76, 113.73, 109.72, 105.44, 102.30, 69.39, 27.62, 10.29; IR (KBr) *v*: 1736, 1607, 1438, 1333, 1252, 1099, 998 cm^{-1}; HR-MS (ESI) calcd for $C_{17}H_{14}O_5$ $[M+H]^+$ 289.09195, found 289.09140.

2-Acetyl-7-butoxy-furo[3,2-*c*]chromen-4-one (**12d**): a white solid; m.p. 149.7 ℃; ^1H NMR (500 MHz, $CDCl_3$) *δ*: 7.83 (d, *J*=8.7 Hz, 1H), 6.99－6.87 (m, 2H), 4.05 (t, *J*=6.5 Hz, 2H), 2.77－2.66 (m, 3H), 2.58 (d, *J*=17.9 Hz, 3H), 1.87－1.76 (m, 2H), 1.52 (dt, *J*=14.8, 7.5 Hz, 2H), 1.00 (t, *J*=7.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 188.52, 162.84, 158.12, 158.09, 155.62, 148.56, 129.78, 122.54, 113.59, 109.58, 105.11, 101.89, 68.50, 30.98, 27.58, 19.18, 13.80, 10.28; IR (KBr) *v*: 1744, 1667, 1627, 1595, 1458, 1256, 1011 cm^{-1}; HR-MS (ESI) calcd for $C_{18}H_{18}O_5$ $[M+H]^+$ 315.12325, found 315.12270.

3-Phenyl-furo[3,2-*c*]chromen-4-one (**13a**): white solid; m.p. 209.1－210.2 ℃; ^1H NMR (500 MHz, $CDCl_3$) *δ*: 7.95 (dd, *J*=7.8, 1.2 Hz, 1H), 7.80 (dd, *J*=6.3, 2.0 Hz, 2H), 7.57 (ddd, *J*=8.8, 7.3, 1.5 Hz, 1H), 7.51－7.47 (m, 3H), 7.44－7.38 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 158.80, 157.86, 152.61, 141.28, 130.97, 129.09, 128.68, 128.59, 128.39, 126.74, 124.51, 120.99, 117.13, 112.77, 108.48; IR (KBr) *v*: 1732, 1627, 1490, 1438, 1317, 1079, 962 cm^{-1}; HR-MS (ESI) calcd for $C_{17}H_{10}O_3$ $[M+H]^+$ 263.07082, found 263.07027.

7-Methoxy-3-phenyl-furo[3,2-*c*]chromen-4-one (**13b**): white solid; m.p. 162.1－162.4 ℃; ^1H NMR (500 MHz, $CDCl_3$) *δ*: 7.95 (dd, *J*=7.8, 1.2 Hz, 1H), 7.80 (dd, *J*=6.3, 2.0 Hz, 2H), 7.57 (ddd, *J*=8.8, 7.3, 1.5 Hz, 1H), 7.51－7.47 (m, 3H), 7.44－7.38 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 162.18, 159.46, 158.17, 154.39, 140.38, 129.29, 128.62, 128.54, 128.27, 126.47, 121.95, 112.88, 106.14, 106.05, 101.04, 55.78; IR (KBr) *v*: 1732, 1627, 1454, 1337, 1236, 1131 cm^{-1}; HR-MS (ESI) calcd for $C_{18}H_{12}O_4$ $[M+H]^+$ 293.08139, found 293.08084.

7-Allyloxy-3-phenyl-furo[3,2-*c*]chromen-4-one (**13c**): white solid; m.p. 167.4－168.5 ℃; ^1H NMR (500 MHz, $CDCl_3$) *δ*: 7.80 (ddd, *J*=14.9, 11.1, 6.3 Hz, 3H), 7.72 (d, *J*=1.7 Hz, 1H), 7.53－7.38 (m, 3H), 6.99 (td, *J*=4.6, 2.3 Hz, 2H), 6.09 (ddt, *J*=17.3, 10.6, 5.3 Hz, 1H), 5.55－5.34 (m, 2H), 4.69－4.62 (m, 2H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 161.11, 159.44, 158.14, 154.31, 140.40, 132.22, 129.29, 128.62, 128.54, 128.27, 126.49, 121.95, 118.55, 113.41, 106.29, 106.13, 101.96, 69.29; IR (KBr) *v*: 1739, 1611, 1451, 1232, 1138, 1068, 941 cm^{-1}; HR-MS (ESI) calcd for $C_{20}H_{14}O_4$ $[M+H]^+$ 319.09704, found 319.09649.

7-Butoxy-3-phenyl-furo[3,2-*c*]chromen-4-one (**13d**): white solid; m.p. 182.0－182.1 ℃; ^1H NMR (500 MHz, $CDCl_3$) *δ*: 7.84－7.77 (m, 3H), 7.71 (d, *J*=1.6 Hz, 1H), 7.51－7.44 (m, 2H), 7.44－7.38 (m, 1H), 6.98－6.94 (m, 2H), 4.06 (t, *J*=6.5 Hz, 2H), 1.91－1.79 (m, 2H), 1.55 (td, *J*=14.8, 7.3 Hz, 3H), 1.06－0.97 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 161.80, 159.56, 158.20, 154.44, 140.30, 132.17, 129.35, 128.62, 128.52, 128.24, 126.49, 121.87, 113.29, 105.97, 101.54, 68.36, 31.04, 19.21, 13.83; IR (KBr) *v*: 1728, 1623, 1510, 1446, 1272, 1244 cm^{-1}; HR-MS (ESI) calcd for $C_{21}H_{18}O_4$ $[M+H]^+$ 335.12834, found 335.12779.

X-ray diffraction analysis

The crystallographic data have been deposited with the Cambridge Crystallographic Data Centre (CCDC) as supplementary publication number: 1047356 (**5b**), 1419461 (**6b**), 1055787 (**10b**), 1417754 (**12a**). Copies of the data can be obtained free of charge via http://www.ccdc.cam.ac.uk/, or on application to CCDC, 12 Union Road, Cambridge CB12 1EZ, UK (Fax＋44 1223 336033 or E-mail: deposit@ccdc.cam.ac.uk).

Conclusions

In summary, a highly efficient microwave-promoted protocol was developed for the synthesis of two series of fused osthole analogues, and the optimal reaction conditions include using toluene as the solvent in the presence of DMAP under microwave irradiation (640 W). Compared with conventional heating, the isolated yields of microwave-promoted method can be improved from 30% to 76% at maximum, and the reaction times for the target compounds can be even reduced from about 6 h to 15 min at minimum. The proposed mechanism of the formation of two fused osthole derivatives: pyrano[3,2-*c*]chromene-2,5-diones and furo[3,2-*c*]-coumarins was also discussed in this study.

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