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Paper

Synthesis of 3-(4-oxo-4*H*-chromen-3-yl)acrylates through the tandem reaction of 3-(2-buta-2,3-dienoylphenoxy)acrylates

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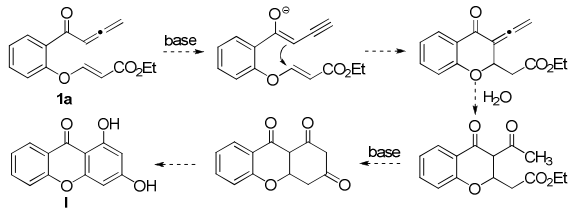
In this paper, we report a novel synthesis of 2-substituted 3-(4-oxo-4*H*-chromen-3-yl)acrylates through base-catalyzed tandem reaction of the readily available 3-(2-buta-2,3-dienoylphenoxy)acrylates. This new synthetic strategy features with extremely mild conditions and good to excellent yields.

Introduction

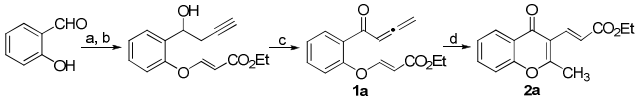
Allene units connected with a carbonyl group are electrophilic and the protons attached to them are thus acidic enough to be abstracted by bases to form alkynylenolate intermediates. Recently, these intermediates have been used as efficient nucleophiles by Hammond et al in the synthesis of carbinol allenate[1] and α,α-disubstituted alkynyl ester.[2] Using similar strategy, we have developed a synthesis of tricarbonyl compounds through reaction of 1,2-allenic ketones with α-halocarbonyl compounds under the promotion of TBAF in water.[3] Inspired by those results, we envisioned a synthetic approach toward the biologically interesting xanthone derivative (**I**) *via* a cascade reaction of ethyl 3-(2-buta-2,3-dienoylphenoxy)acrylate (**1a**) initiated by an intramolecular Michael type reaction of the *in situ* formed alkynylenolate onto the acrylate moiety (Scheme 1).



Scheme 1. Proposed synthetic pathway toward xanthone (**I**).

Results and discussion

To check the feasibility of our proposal, **1a** was prepared *via* a three-step procedure with a total yield of 71% (Scheme 2). Then, it was treated with TBAF in water at 80 °C for 1 h. From this reaction, to our surprise, ethyl 3-(2-methyl-4-oxo-4*H*-chromen-3-yl)acrylate (**2a**), instead of the expected xanthone, was obtained in a yield of 50% (Scheme 2).



Scheme 2. Reaction conditions: (a) 3-bromoprop-1-yne, zinc powder, THF/DMF, r.t.; (b) ethyl propiolate, DABCO, CH_2Cl_2, 0 ºC; (c) Jones reagent, acetone, 0 ºC; (d) TBAF, H_2O, 80 ºC, 1 h.

Although the envisioned xanthone (**I**) was not obtained, we realized that the unexpected formation of **2a** might be equally rewarding. It is well known that chromone ring system is not only a common framework found in numerous natural products (Figure 1),[4] but also considered as a privileged structure[5] in the search for new lead compounds in pharmaceutical chemistry.[6,7] In addition, among various chromone derivatives, those bearing an electron-withdrawing vinyl moiety on the C-3 position are found in many pharmaceutically important compounds with anti-tumor, anti-microbial, anti-inflammatory, and anti-allergic activities.[8] The C-3 functionalized chromones are also versatile synthetic building blocks for the construction of more advanced structures.[9] Due to their importance, several strategies to introduce an electron-withdrawing vinyl moiety, including an acrylate unit, onto the C-3 position of chromone scaffold, such as Heck coupling reaction between 3-halochromones and alkene coupling parters,[9d,10] Pd(II)-catalyzed direct intermolecular alkenylation of chromones,[11] condensation of 3-formyl chromone with phenylacetic acid[12] or malonic acid in the presence of pyridine under reflux condition,[8b] have been developed. In addition, preparation of 3-(4-oxo-4*H*-chromen-3-yl)acrylate through the classical Wittig reaction or Horner-Wadsworth-Emmons (HWE) reaction has also been reported.[9f] While the above mentioned literature synthetic methods are generally reliable and efficient, they usually started from precursors already having a chromone scaffold. Moreover, some of the syntheses were realized with the aid of transition metal catalyst or under harsh reaction conditions. Under this circumstance, the reaction of **1a** deserves thorough exploration with the aim to develop it into a practical approach toward chromon-3-acrylates without using costly catalyst and realized under mild conditions.

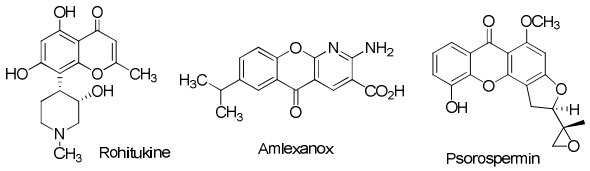
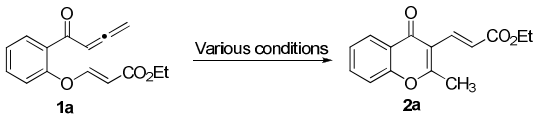


Figure 1. Some naturally occurring products with a chromone unit.

For this purpose, the reaction of **1a** was run again under various conditions. To our delight, when the reaction medium was changed from water to THF, the reaction could proceed smoothly at room temperature and the yield of **2a** increased to 68% over 20 min (Table 1, entry 2). With THF as the solvent, different bases were then tried (entries 2-9). Among them, Cs_2CO_3 gave much higher yield than TBAF, TEA, *t*-BuOK, DBU, DABCO, pyridine, or K_2CO_3. As for the amount of base, we were pleased to find that 0.1 equiv of Cs_2CO_3 could give **2a** in a similar yield as that of 1 equiv of Cs_2CO_3 (entries, 7, 10-11). With 0.1 equiv of Cs_2CO_3 as the base, other solvents were also tried (entries 12-16). It was demonstrated that while CH_3CN, CH_3OH, C_2H_5OH, and DMF were less effective in mediating this reaction, a mixed solvent of THF/H_2O (10:1) could afford **2a** in a yield of 82% albeit the reaction period was longer (entry 12). In summary of the optimization study, treatment of **1a** with 0.1 equiv of Cs_2CO_3 in THF at room temperature for 10 min gave **2a** in an optimum yield of 86% (entry 11).

Table 1 Optimization studies for the preparation of **2a**[a]



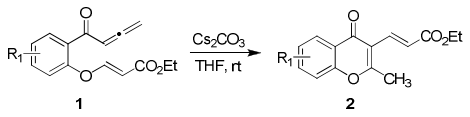
1a **2a**

Entry	Solvent	Base (equiv)	t (min)	T (ºC)	Yield (%)[b]
1	H_2O	TBAF (1)	60	80	50
2	THF	TBAF (1)	20	rt	68
3	THF	TEA (1)	20	rt	42
4	THF	*t*-BuOK (1)	20	rt	62
5	THF	DBU (1)	30	rt	31
6	THF	DABCO (1)	30	rt	47
7	THF	Cs_2CO_3 (1)	10	rt	87
8	THF	pyridine (1)	60	rt	trace
9	THF	K_2CO_3 (1)	10	rt	72
10	THF	Cs_2CO_3 (0.5)	10	rt	86
11	**THF**	**Cs_2CO_3 (0.1)**	**10**	**rt**	**86**
12	THF/H_2O (10/1)	Cs_2CO_3 (0.1)	60	rt	82
13	CH_3CN	Cs_2CO_3 (0.1)	10	rt	78
14	CH_3OH	Cs_2CO_3 (0.1)	10	rt	trace
15	C_2H_5OH	Cs_2CO_3 (0.1)	10	rt	trace
16	DMF	Cs_2CO_3 (0.1)	10	rt	63

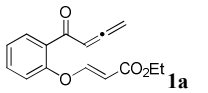
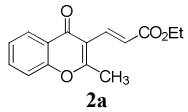
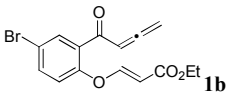
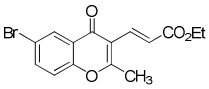
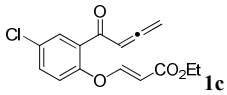
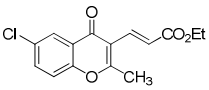
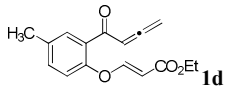
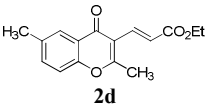
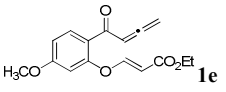
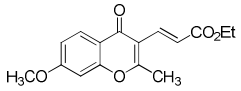
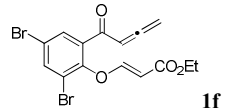
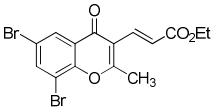
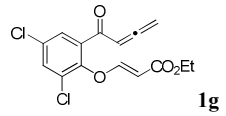
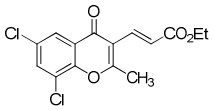
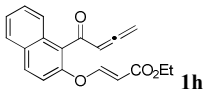
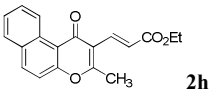
[a] Reaction conditions: 0.5 mmol of **1a**, 3 mL of solvent; [b] Isolated yield.

With the optimized reaction conditions in hand, we then studied the scope and generality of the above reaction leading to 3-(4-oxo-4*H*-chromen-3-yl)acrylates (**2**). Firstly, the effect of different substituents attached on the phenyl ring was studied (Table 2). To our delight, substrates bearing methyl, methoxy, chloro, bromo, dichloro or dibromo substituted phenyl or naphthyl scaffold underwent the reactions smoothly to give the corresponding products in good yields (Table 2, entries 1-8). It is also noted that the structure of (*E*)-ethyl 3-(2,6-dimethyl-4-oxo-4*H*-chromen-3-yl)acrylate (**2d**) was confirmed by X-ray diffraction analysis.[13]

Table 2 Scope of the reaction leading to **2** (I)[a]



1 **2**

Entry	Substrate (**1**)	Product (**2**)	Yield (%)[b]
1	 **1a**	 **2a**	86
2	 **1b**	 **2b**	84
3	 **1c**	 **2c**	83
4	 **1d**	 **2d**	85
5	 **1e**	 **2e**	86
6	 **1f**	 **2f**	86
7	 **1g**	 **2g**	88
8	 **1h**	 **2h**	87

[a] Reaction conditions: 0.5 mmol of **1**, 0.05 mmol (10 mol %) of Cs_2CO_3, 3 mL of THF, rt, 10 min; [b] Isolated yield.

Secondly, reactions of substrates with a substituent on the terminal position of the allenic moiety were also studied (Table 3). It was found that with phenyl, 2-cyanophenyl, 3,5-dimethoxyl phenyl, 4-methylphenyl, or 2-methyl-5-chlorophenyl substituted allene derivatives, the tandem reaction proceeded with an efficient manner (entries 1-9). Moreover, the reaction was also compatible with a terminal methyl group (Table 3, entry 10), thus resulting chromones with diverse substitution patterns.

Based on the above observations and previous reports,[14] the formation of **2a** can be explained on the basis of the process as outlined in Scheme 3. It is postulated that an alkynylenolate intermediate **A** is firstly formed *via* Cs_2CO_3 promoted deprotonation of **1a**.[1,2] **A** then undergoes an intramolecular Michael type reaction to give intermediate **B**. Subsequent elimination reaction of **B** results in the formation of intermediate **C**. C-C single bond rotation followed by propargyl-allenyl isomerization of **C** gives **D**, which then undergoes another intramolecular conjugate addition to give intermediate **E**.

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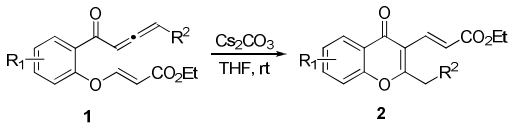
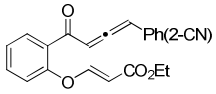
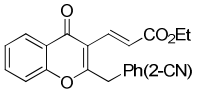
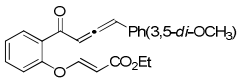
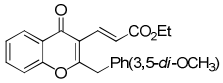
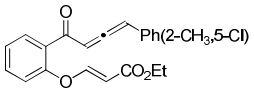
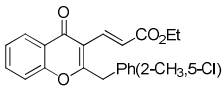
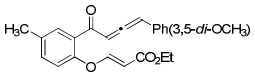
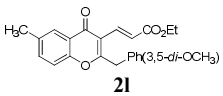
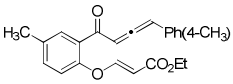
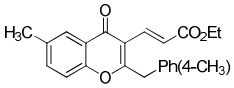
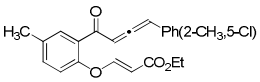
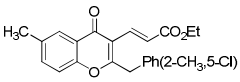
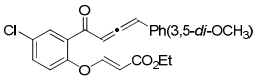
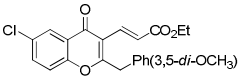
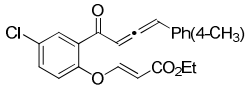
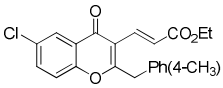
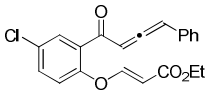
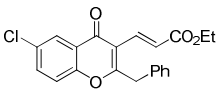
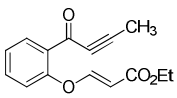
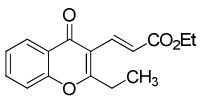
Table 3 Scope of the reaction leading to **2** (II)[a]

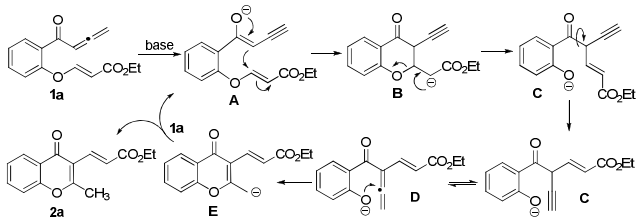


1 **2**

Entry	Substrate (**1**)	Product (**2**)	Yield (%)[b]
1	 **1i**	 **2i**	73
2	 **1j**	 **2j**	70
3	 **1k**	 **2k**	78
4	 **1l**	 **2l**	80
5	 **1m**	 **2m**	72
6	 **1n**	 **2n**	74
7	 **1o**	 **2o**	79
8	 **1p**	 **2p**	71
9	 **1q**	 **2q**	74
10	 **1r**	 **2r**	65

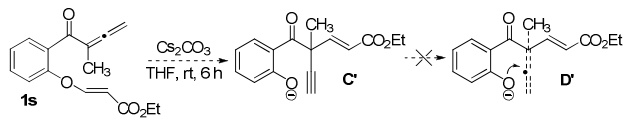
[a] Reaction conditions: 0.5 mmol of **1**, 0.05 mmol (10 mol %) of Cs_2CO_3, 3 mL of THF, rt, 10 min; [b] Isolated yield.

Subsequently, **E** abstracts a proton from **1a** to give the final chromone product **2a** as well as anion **A** for the next round of the reaction.



Scheme 3. Plausible pathway for the formation of **2a** from **1a**.

Based on the proposed mechanism as shown in Scheme 3, substrate with a substituent attached on the internal position of the allene moiety, such as (*E*)-ethyl 3-(2-(2-methylbuta-2,3-dienoyl)phenoxy)acrylate (**1s**, Scheme 4), should not take part in this tandem reaction since with such a substrate the proposed allenic ketone intermediate (**D'**) could not be formed. In consistent with this deduction, no reaction was observed when **1s** was treated with Cs_2CO_3 in THF for as long as 6 h.



Scheme 4. Experiment of substrate with an α methyl group.

Conclusions

In this paper, we have developed a straightforward preparation of 3-(4-oxo-4*H*-chromen-3-yl)acrylate derivatives *via* Cs_2CO_3 catalyzed tandem reaction of the readily obtainable 3-(2-buta-2,3-dienoylphenoxy)acrylates. Notably, the synthesis did not involve a chromone precursor and was realized in the presence of catalytic amount of base without using any expensive transition metal catalyst. Compared with literature procedures toward C-3 functionalized chromones, the strategy developed in this paper showed remarkable advantages such as readily available starting materials, simple procedure, high efficiency, and extremely mild reaction conditions. We expect this protocol to be valuable in expanding the scaffold space of chromone derivatives as valuable candidates in pharmaceutical industry and versatile intermediates in synthetic chemistry.

Experimental

The ^1H, ^{13}C NMR spectra were recorded at 400 MHz or 100 MHz, respectively. Chemical shifts were reported in ppm from tetramethylsilane (TMS) as internal standard in $CDCl_3$ solutions. Multiplicity was indicated as follows: s (singlet); d (doublet); t (triplet); m (multiplet); dd (doublet of doublets), etc., and coupling constants were given in Hz. High resolution mass

spectra (HRMS) were performed on a time-of-flight (microTOF) mass spectrometer. The conversion of starting materials were monitored by thin layer chromatography (TLC) using silica gel plates (silica gel 60 F254 0.25 mm) and components were visualized by observation under UV light (254 and 365 nm).

Synthetic procedures for **1a** and **1j**, copies of ^{1}H and ^{13}C NMR spectra for **1a**-**1h**, **1j** and **2a**-**2r**, X-ray crystal structure of **2d** are available as electronic supporting information.

A typical procedure for the synthesis of (*E*)-ethyl 3-(2-methyl-4-oxo-4*H*-chromen-3-yl)acrylate (2a)

To a flask containing (*E*)-ethyl 3-(2-buta-2,3-dienoylphenoxy) acrylate (**1a**, 0.5 mmol) in THF (3 mL) was added Cs_2CO_3 (0.05 mmol). The mixture was stirred at room temperature for 10 min. Then, the reaction was quenched by addition of aqueous NH_4Cl solution and extracted with ethyl acetate (3×10 mL). The combined organic layer was washed with brine, and then dried over anhydrous Na_2SO_4. The solvent was evaporated under vacuum and the crude product was purified by column chromatography on silica gel using petroleum ether-ethyl acetate (10:1) as the eluent to give (*E*)-ethyl 3-(2-methyl-4-oxo-4*H*-chromen-3-yl)acrylate (**2a**, 86%). **2b-2r** were obtained in a similar manner.

(*E*)-Ethyl 3-(2-methyl-4-oxo-4*H*-chromen-3-yl)acrylate (2a)

Eluent: petroleum ether-ethyl acetate (10:1); white solid (111 mg, 86%), mp 80-82 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.30 (t, J = 6.8 Hz, 3H), 2.59 (s, 3H), 4.22 (q, J = 6.8 Hz, 2H), 7.32-7.38 (m, 3H), 7.53 (d, J = 16.0 Hz, 1H), 7.59-7.64 (m, 1H), 8.16-8.18 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 19.2, 60.4, 116.1, 117.6, 123.0, 123.4, 125.4, 126.2, 133.6, 134.9, 155.0, 167.8, 167.9, 176.2. HRMS (ESI) calcd for $C_{15}H_{15}O_4$: 259.0970 [M+H], found: 259.0977.

(*E*)-Ethyl 3-(6-bromo-2-methyl-4-oxo-4*H*-chromen-3-yl) acrylate (2b)

Eluent: petroleum ether-ethyl acetate (10:1); white solid (141 mg, 84%), mp 161-163 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.32 (t, J = 7.2 Hz, 3H), 2.61 (s, 1H), 4.24 (q, J = 7.2 Hz, 2H), 7.29-7.34 (m, 2H), 7.52 (d, J = 15.2 Hz, 1H), 7.71 (dd, J_1 = 8.8 Hz, J_2 = 2.4 Hz 1H), 8.30 (d, J = 2.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 19.2, 60.5, 116.3, 118.0, 119.6, 123.6, 124.7, 128.8, 134.4, 136.6, 153.8, 167.8, 167.9, 174.9. HRMS (ESI) calcd for $C_{15}H_{14}BrO_4$: 337.0075 [M+H], found: 337.0081.

(*E*)-Ethyl 3-(6-chloro-2-methyl-4-oxo-4*H*-chromen-3-yl) acrylate (2c)

Eluent: petroleum ether-ethyl acetate (10:1); white solid (121 mg, 83%), mp 153-155 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.30 (t, J = 7.2 Hz, 3H), 2.42 (s, 3H), 4.22 (q, J = 6.8 Hz, 2H), 7.27 (d, J = 8.0 Hz, 1H), 7.34 (d, J = 15.2 Hz, 1H), 7.41 (d, J = 8.4 Hz, 1H), 7.53 (d, J = 15.6 Hz, 1H), 7.94 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 21.0, 60.4, 115.8, 117.4, 122.7, 123.0, 125.4, 134.8, 135.1, 135.4, 153.3, 167.7, 168.0, 176.3. HRMS (ESI) calcd for $C_{15}H_{14}ClO_4$: 293.0580 [M+H], found: 293.0582.

(*E*)-Ethyl 3-(2,6-dimethyl-4-oxo-4*H*-chromen-3-yl)acrylate (2d)

Eluent: petroleum ether-ethyl acetate (10:1); white solid (116 mg, 85%), mp 113-115 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.31 (t, J = 6.8 Hz, 3H), 2.42 (s, 3H), 2.58 (s, 3H), 4.23 (q, J = 7.2 Hz, 2H), 7.27 (d, J = 8.8 Hz, 1H), 7.34 (d, J = 15.6 Hz, 1H), 7.42 (dd, J_1 = 8.0 Hz, J_2 = 2.0 Hz, 1H), 7.54 (d, J = 16.0 Hz, 1H), 7.95 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 19.2, 21.0, 60.4, 115.9, 117.4, 122.8, 123.1, 125.5, 134.8, 135.1, 135.4, 153.3, 167.7, 168.0, 176.3. HRMS (ESI) calcd for $C_{16}H_{17}O_4$: 273.1127 [M+H], found: 273.1120.

(*E*)-Ethyl 3-(7-methoxy-2-methyl-4-oxo-4*H*-chromen-3-yl) acrylate (2e)

Eluent: petroleum ether-ethyl acetate (10:1); white solid (124 mg, 86%), mp 118-120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.27 (t, J = 7.2 Hz, 3H), 2.50 (s, 1H), 3.83 (s, 3H), 4.20 (q, J = 6.8 Hz, 2H), 6.70 (s, 1H), 6.87 (d, J = 8.0 Hz, 1H), 7.28 (d, J = 16.0 Hz, 1H), 7.46 (d, J = 16.0 Hz, 1H), 8.01 (d, J = 8.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 19.0, 55.8, 60.4, 99.8, 114.6, 115.7, 117.1, 122.7, 127.4, 135.0, 156.6, 164.0, 167.3, 167.9, 175.6. HRMS (ESI) calcd for $C_{16}H_{17}O_5$: 289.1076 [M+H], found: 289.1092.

(*E*)-Ethyl 3-(6,8-dibromo-2-methyl-4-oxo-4*H*-chromen-3-yl) acrylate (2f)

Eluent: petroleum ether-ethyl acetate (10:1); white solid (178 mg, 86%), mp 182-184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.33 (t, J = 7.2 Hz, 3H), 2.68 (s, 3H), 4.26 (q, J = 7.2 Hz, 2H), 7.32 (d, J = 16.0 Hz, 1H), 7.51 (d, J = 16.0 Hz, 1H), 7.98 (d, J = 2.4 Hz, 1H), 8.27 (d, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 19.2, 60.6, 112.4, 116.4, 118.7, 124.3, 125.4, 128.3, 133.8, 139.2, 150.8, 167.5, 167.9, 174.2. HRMS (ESI) calcd for $C_{15}H_{13}Br_2O_4$: 414.9180 [M+H], found: 414.9196.

(*E*)-Ethyl 3-(6,8-dichloro-2-methyl-4-oxo-4*H*-chromen-3-yl) acrylate (2g)

Eluent: petroleum ether-ethyl acetate (10:1); white solid (143 mg, 88%), mp 190-191 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.33 (t, J = 7.2 Hz, 3H), 2.68 (s, 3H), 4.25 (q, J = 7.2 Hz, 2H), 7.32 (d, J = 15.6 Hz, 1H), 7.52 (d, J = 16.0 Hz, 1H), 7.68 (d, J = 2.4 Hz, 1H), 8.07 (d, J = 2.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 19.1, 60.6, 116.4, 123.9, 124.3, 124.4, 125.2, 131.1, 133.7, 133.8, 149.5, 167.5, 167.8, 174.4. HRMS (ESI) calcd for $C_{15}H_{13}Cl_2O_4$: 327.0191 [M+H], found: 327.0196.

(*E*)-Ethyl 3-(3-methyl-1-oxo-1*H*-benzo[*f*]chromen-2-yl) acrylate (2h)

Eluent: petroleum ether-ethyl acetate (10:1); white solid (134 mg, 87%), mp 186-188 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.34 (t, J = 7.2 Hz, 1H), 2.58 (s, 3H), 4.27 (q, J = 7.2 Hz, 2H), 7.32-7.39 (m, 2H), 7.57-7.61 (m, 2H), 7.72 (t, J = 8.0 Hz, 1H), 7.84 (d, J = 8.0 Hz, 1H), 7.99 (d, J = 8.8 Hz, 1H), 9.98 (d, J = 9.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.4, 18.8, 60.5, 116.4, 117.2, 118.3, 123.2, 126.6, 127.0, 128.3, 129.3, 130.4, 130.7, 135.2, 135.5, 156.1, 165.0, 167.9, 178.0. HRMS (ESI) calcd for $C_{19}H_{17}O_4$: 309.1127 [M+H], found: 309.1122.

(*E*)-Ethyl 3-(2-(2-cyanobenzyl)-4-oxo-4*H*-chromen-3-yl) acrylate (2i)

Eluent: petroleum ether-ethyl acetate (20:1); pale yellow solid (131 mg, 73%), mp 141-143 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.32 (t, J = 7.2 Hz, 1H), 4.25 (q, J = 7.2 Hz, 2H), 4.49 (s, 2H), 7.34 (d, J = 8.0 Hz, 1H), 7.38-7.42 (m, 4H), 7.53-7.57 (m, 1H), 7.62-7.69 (m, 2H), 7.73 (dd, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 1H), 8.21 (dd, J_1 = 8.4 Hz, J_2 = 1.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 36.4, 60.6, 113.4, 116.9, 117.6, 117.9, 123.3, 124.8, 125.8, 126.3, 128.2, 129.5, 133.39, 133.41, 133.7, 134.0, 138.8, 155.1, 165.7, 167.5, 176.4. HRMS (ESI) calcd for $C_{22}H_{18}NO_4$: 360.1236 [M+H], found: 360.1249.

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(*E*)-Ethyl 3-(2-(3,5-dimethoxybenzyl)-4-oxo-4*H*-chromen-3-yl) acrylate (2j)

Eluent: petroleum ether-ethyl acetate (20:1); white solid (138 mg, 70%), mp 149-151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.32 (t, J = 7.2 Hz, 3H), 3.76 (s, 6H), 4.16 (s, 2H), 4.24 (q, J = 6.8 Hz, 2H), 6.36 (t, J = 2.4 Hz, 1H), 6.45 (d, J = 1.2 Hz, 2H), 7.40 (d, J = 7.6 Hz, 3H), 7.62-7.66 (m, 1H), 7.72 (d, J = 15.2 Hz, 1H), 8.21-8.23 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 38.4, 55.3, 60.4, 99.1, 106.8, 116.4, 117.8, 123.4, 123.9, 125.5, 126.3, 133.8, 134.5, 137.3, 155.1, 161.2, 167.8, 168.1, 176.6. HRMS (ESI) calcd for $C_{23}H_{23}O_6$: 395.1494 [M+H], found: 395.1498.

(*E*)-Ethyl 3-(2-(5-chloro-2-methylbenzyl)-4-oxo-4*H*-chromen-3-yl)acrylate (2k)

Eluent: petroleum ether-ethyl acetate (20:1); white solid (149 mg, 78%), mp 126-128 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.32 (t, J = 7.2 Hz, 3H), 2.36 (s, 3H), 4.19 (s, 2H), 4.24 (q, J = 7.2 Hz, 2H), 7.08 (d, J = 2.0 Hz, 1H), 7.13-7.18 (m, 2H), 7.33-7.44 (m, 3H), 7.60-7.66 (m, 2H), 8.24 (dd, J_1 = 8.4 Hz, J_2 = 1.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 19.4, 35.5, 60.5, 116.8, 117.8, 123.4, 124.3, 125.7, 126.3, 127.6, 128.7, 131.9, 132.0, 133.9, 134.0, 134.9, 135.4, 155.1, 167.2, 167.6, 176.4, 177.2. HRMS (ESI) calcd for $C_{22}H_{20}ClO_4$: 383.1050 [M+H], found: 383.1056.

(*E*)-Ethyl 3-(2-(3,5-dimethoxybenzyl)-6-methyl-4-oxo-4*H*-chromen-3-yl)acrylate (2l)

Eluent: petroleum ether-ethyl acetate (20:1); white solid (163 mg, 80%), mp 119-120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.26 (t, J = 7.2 Hz, 1H), 2.35 (s, 3H), 3.76 (s, 6H), 4.14 (s, 2H), 4.24 (q, J = 7.2 Hz, 2H), 6.35 (t, J = 2.0 Hz, 1H), 6.44 (d, J = 2.0 Hz, 1H), 7.30 (d, J = 9.2 Hz, 1H), 7.39 (d, J = 15.6 Hz, 1H), 7.44 (dd, J_1 = 8.4 Hz, J_2 = 2.0 Hz, 1H), 7.72 (d, J = 15.6 Hz, 1H), 7.99 (d, J = 1.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 21.0, 38.4, 55.3, 60.4, 99.0, 106.8, 109.4, 116.2, 117.5, 123.6, 125.5, 134.7, 135.0, 137.4, 153.4, 160.4, 161.1, 167.8, 168.0, 176.6. HRMS (ESI) calcd for $C_{24}H_{25}O_6$: 409.1651 [M+H], found: 409.1642.

(*E*)-Ethyl 3-(6-methyl-2-(4-methylbenzyl)-4-oxo-4*H*-chromen-3-yl)acrylate (2m)

Eluent: petroleum ether-ethyl acetate (20:1); pale yellow solid (130 mg, 72%), mp 145-147 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.33 (t, J = 7.2 Hz, 3H), 2.31 (s, 3H), 2.44 (s, 3H), 4.17 (s, 2H), 4.25 (q, J = 7.2 Hz, 2H), 7.12 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 8.4 Hz, 2H), 7.29 (d, J = 8.8 Hz, 1H), 7.39-7.45 (m, 2H), 7.74 (d, J = 15.6 Hz, 1H), 7.98 (d, J = 1.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 20.98, 21.04, 37.9, 60.4, 115.9, 117.5, 123.1, 123.6, 125.5, 128.5, 129.7, 132.2, 134.8, 134.9, 135.5, 137.1, 153.4, 167.9, 168.6, 176.7. HRMS (ESI) calcd for $C_{23}H_{23}O_4$: 363.1596 [M+H], found: 363.1599.

(*E*)-Ethyl 3-(2-(5-chloro-2-methylbenzyl)-6-methyl-4-oxo-4*H*-chromen-3-yl)acrylate (2n)

Eluent: petroleum ether-ethyl acetate (20:1); pale yellow solid (146 mg, 74%), mp 145-148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.32 (t, J = 7.2 Hz, 3H), 2.35 (s, 3H), 2.45 (s, 3H), 4.17 (s, 2H), 4.24 (q, J = 7.2 Hz, 2H), 7.07 (s, 1H), 7.13-7.17 (m, 2H), 7.23 (d, J = 8.8 Hz, 1H), 7.36 (d, J = 15.6 Hz, 1H), 7.44 (d, J = 8.8 Hz, 1H), 7.62 (d, J = 15.6 Hz, 1H), 8.01 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 19.4, 21.0, 35.5, 60.5, 116.7, 117.5, 123.0, 124.1, 125.6, 127.5, 128.7, 131.8, 132.0, 134.2, 134.9, 135.1, 135.4, 135.7, 153.4, 167.0, 167.7, 176.5. HRMS (ESI) calcd for $C_{23}H_{22}ClO_4$: 397.1206 [M+H], found: 397.1193.

(*E*)-Ethyl 3-(6-chloro-2-(3,5-dimethoxybenzyl)-4-oxo-4*H*-chromen-3-yl)acrylate (2o)

Eluent: petroleum ether-ethyl acetate (20:1); white solid (169 mg, 79%), mp 144-146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.32 (t, J = 7.2 Hz, 3H), 3.76 (s, 6H), 4.14 (s, 2H), 4.25 (q, J = 7.2 Hz, 2H), 6.43 (d, J = 2.0 Hz, 2H), 6.49 (d, J = 2.0 Hz, 1H), 7.35-7.39 (m, 2H), 7.53-7.59 (m, 1H), 7.69 (d, J = 16.4 Hz, 1H), 8.17 (d, J = 2.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.1, 38.0, 55.4, 60.6, 99.2, 106.8, 109.3, 116.5, 119.4, 124.4, 125.5, 131.7, 134.1, 136.9, 153.8, 160.6, 161.2, 167.6, 168.5, 175.5. HRMS (ESI) calcd for $C_{23}H_{22}ClO_6$: 429.1105 [M+H], found: 429.1118.

(*E*)-Ethyl 3-(6-chloro-2-(4-methylbenzyl)-4-oxo-4*H*-chromen-3-yl)acrylate (2p)

Eluent: petroleum ether-ethyl acetate (20:1); white solid (136 mg, 71%), mp 150-152 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.33 (t, J = 7.2 Hz, 3H), 2.32 (s, 3H), 4.18 (s, 2H), 4.26 (q, J = 7.2 Hz, 2H), 7.12-7.20 (m, 4H), 7.35-7.41 (m, 2H), 7.57 (dd, J_1 = 8.4 Hz, J_2 = 2.8 Hz, 1H), 7.71 (d, J = 16.0 Hz, 1H), 8.17 (d, J = 2.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 21.1, 37.8, 60.5, 116.2, 119.5, 124.3, 125.7, 128.5, 129.1, 129.6, 129.8, 131.9, 133.9, 134.1, 137.3, 153.3, 167.7, 168.9, 175.3. HRMS (ESI) calcd for $C_{22}H_{20}ClO_4$: 383.1050 [M+H], found: 383.1052.

(*E*)-Ethyl 3-(2-benzyl-6-chloro-4-oxo-4*H*-chromen-3-yl) acrylate (2q)

Eluent: petroleum ether-ethyl acetate (20:1); white solid (136 mg, 74%), mp 148-150 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.33 (t, J = 7.2 Hz, 3H), 4.23-4.28 (m, 4H), 7.28-7.41 (m, 7H), 7.58 (dd, J_1 = 9.2 Hz, J_2 = 1.6 Hz, 1H), 7.71 (d, J = 15.6 Hz, 1H), 8.18 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 14.3, 38.2, 60.5, 116.3, 119.5, 124.4, 125.7, 127.6, 128.6, 129.1, 131.5, 134.0, 135.0, 153.5, 167.6, 168.5, 175.4. HRMS (ESI) calcd for $C_{21}H_{18}ClO_4$: 369.0893 [M+H], found: 369.0896.

(*E*)-Ethyl 3-(2-ethyl-4-oxo-4H-chromen-3-yl)acrylate (2r)

Eluent: petroleum ether-ethyl acetate (20:1); white solid (88 mg, 65%), mp 80-82 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.32 (t, J = 7.2 Hz, 3H), 1.38 (t, J = 7.6 Hz, 3H), 2.95 (q, J = 7.2 Hz, 2H), 4.25 (q, J = 7.2 Hz, 2H), 7.39-7.44 (m, 1H), 7.59 (d, J = 15.2 Hz, 1H), 7.63-7.68 (m, 1H), 8.22 (dd, J_1 = 8.0 Hz, J_2 = 0.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 12.0, 14.2, 25.8, 60.4, 115.2, 117.6, 123.3, 123.4, 125.4, 126.3, 133.6, 134.4, 155.2, 168.0, 172.0, 176.5. HRMS (ESI) calcd for $C_{16}H_{17}O_4$: 273.1127 [M+H], found: 273.1133.

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Notes and references

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13 The molecular structure of (*E*)-ethyl 3-(2,6-dimethyl-4-oxo-4*H*-chromen-3-yl)acrylate (**2d**) was determined by X-ray crystallographic analysis. CCDC-979580 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
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A graphical contents entry

Synthesis of 3-(4-oxo-4*H*-chromen-3-yl)acrylates through the tandem reaction of 3-(2-buta-2,3-dienoylphenoxy)acrylates

Xuesen Fan,* Nana Shen, Bin Li, Shenghai Guo, and Xinying Zhang*

A straightforward and efficient synthesis of 2-substituted 3-(4-oxo-4*H*-chromen-3-yl)acrylates through base-catalyzed tandem reaction of the readily available 3-(2-buta-2,3-dienoylphenoxy) acrylates under extremely mild conditions has been developed.