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Visible-light-promoted radical acylation/cyclization of alkynoates with aldehydes for the synthesis of 3-acylcoumarins†

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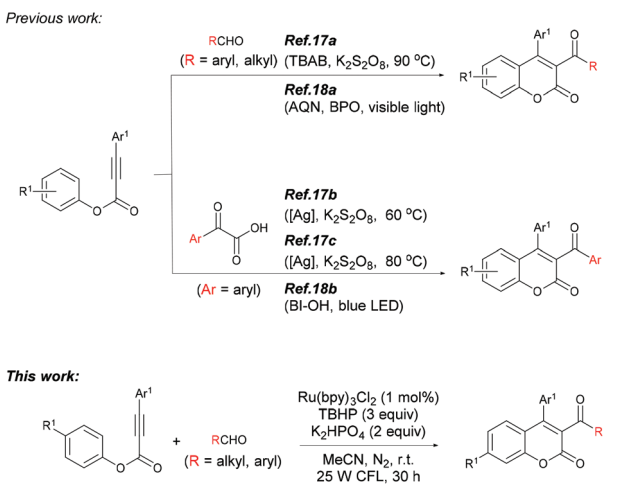
A new, efficient, and atom-economic visible-light-promoted radical acylation/cyclization of alkynoates with aldehydes was developed for the synthesis of 3-acylcoumarins. The reaction undergoes a domino radical addition/5-*exo* cyclization, and ester migration to afford the product in moderate to good yields with wide functional group tolerance. The significant feature of this new method is the excellent tolerance of aliphatic aldehydes, which leads to the efficient synthesis of aliphatic 3-acylcoumarins.

Introduction

Coumarin derivatives retain a high degree of importance in pharmaceuticals, agrochemical industries, food, and cosmetics because of their unique properties.[1] Among them, 3-acylcoumarins have received considerable attention owing to their important biological activities,[2] such as antioxidant,[2d] monoamine oxidase (MAO) inhibitor,[2a] anticancer,[2f] and anti-inflammatory activities,[2c,h] and their fluorescence properties.[3] These growing needs have stimulated interest in the design and efficient synthesis of highly functionalized coumarins. Initially, several named reactions, such as the Pechmann condensation,[4] the Perkin reaction,[5] the Claisen rearrangement,[6] the Knoevenagel reaction,[7] the Reformatsky reaction,[8] and the Wittig reaction,[9] were extended for the synthesis of coumarin derivatives. Then the transition metal catalyzed approaches to prepare coumarin derivatives became a powerful tool, since diverse processes were developed using transition-metal catalysts,[10] such as Pd,[11] Ru,[12] Rh,[13] Cu,[14] *etc*. However, the aforementioned methods suffered from some drawbacks, namely the necessity of the corresponding ligands.

As many efforts have been devoted to radical chemistry recently,[15] the generation of different radicals and subsequent radical cyclizations with alkynoates contribute significantly to the synthesis of coumarin derivatives.[16] In this regard, plenty of 3-substituted coumarins were successfully prepared[17,18] through a general sequence as follows: (1) generation of a functional radical from the radical donor, (2) selective radical addition to the C–C triple bond in alkynoates, (3) intramolecular radical cyclization and (4) rearomatization. Compared to the traditional thermal initiation of reactive radicals, visible-light promoted generation of radicals through single electron transfer (SET) with excited photoredox catalysts under remarkably mild reaction conditions has attracted more and more attention. For the synthesis of 3-acylcoumarins, aldehydes[17a,18a] and 2-keto acids[17b,c,18b] have been commonly employed as the acyl radical donors (Scheme 1). Selective radical addition to alkynoates gives vinyl radical intermediates, which could undergo 6-*exo* cyclization, or 5-*exo* cyclization and subsequent ester migration to deliver the desired products. Although a few processes have been developed to synthesize



Scheme 1 Synthesis of 3-acylcoumarins.

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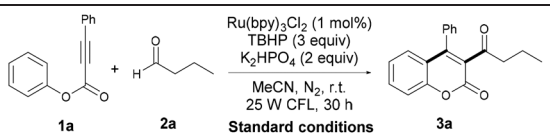
3-acylcoumarin derivatives under thermal or visible light initiation, most of them are limited to aromatic acyl radical donors (Scheme 1). Only a few examples involving aliphatic acyl radical donors were reported with low yields,[17a,c] which might come from the lower stability of aliphatic acyl radicals than aromatic ones.[18b] Herein, we describe a visible-light-promoted radical acylation/cyclization of alkynoates with aldehydes for the preparation of 3-acylcoumarins, which uses ruthenium as the photoredox catalyst and features the efficient synthesis of aliphatic 3-acylcoumarins.

To address the aforementioned challenge, butyraldehyde **2a** was employed as the initial model reagent to optimize the reaction conditions. Indeed, the desired acylation/cyclization product **3a** was obtained in up to 80% yield with $Ru(bpy)_3Cl_2$/TBHP (*tert*-butyl hydroperoxide) as the photoredox catalyst/oxidant combination, K_2HPO_4 as the base, and MeCN as the solvent (Table 1, entry 1). Further control experiments indicated that the photoredox catalyst, TBHP, base, and light source were all essential for this transformation (entries 2–5). When $Ru(bpy)_3Cl_2$ was replaced by other photoredox catalysts including eosin-Y (organic dye photoredox catalyst) and *fac*-Ir(ppy)$_3$ (metal photoredox catalyst), no improved outcomes were observed (entries 6 and 7). Among all the bases tested, the performance of K_2HPO_4 was superior to that of the others, while a weaker base such as $NaHCO_3$ led to a lower yield (entry 8) and a stronger base such as Cs_2CO_3 completely restrained the reaction (entry 9). Most of the solvents tested prohibited the product formation except toluene (entry 10). In addition, changing the concentration of the reactants from 0.10 M to 0.05 M dramatically decreased the yield (entry 11). The attempt to improve the yield by changing the light source was unsuccessful (entry 12).

Table 1 Optimization of conditions[a]

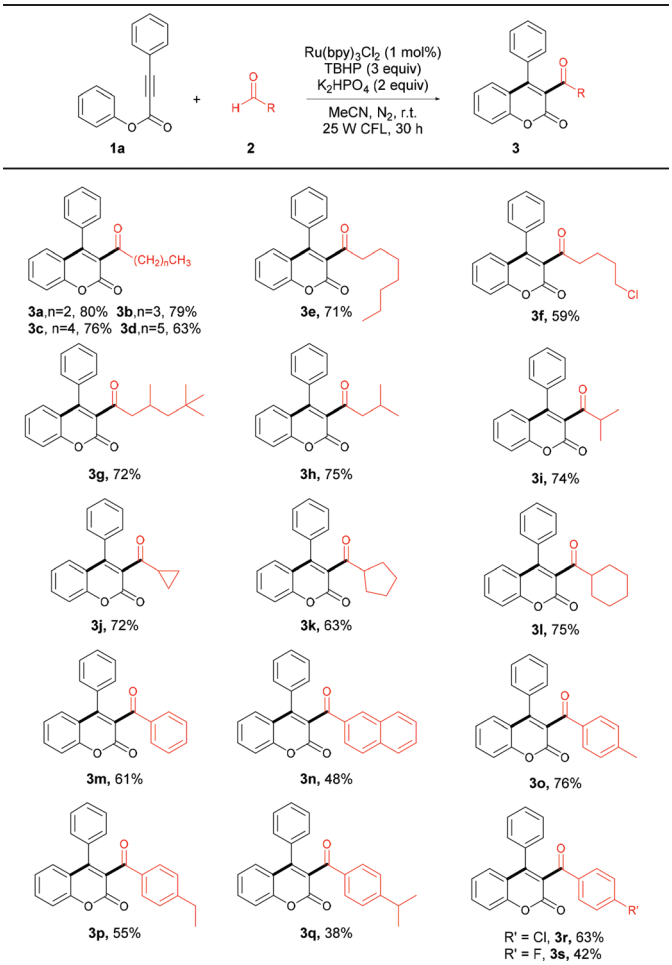


Entry	Change from standard conditions	Yield[b] (%)
1	None	80
2	No $Ru(bpy)_3Cl_2$	0
3	No TBHP	0
4	No base	0
5	No light	0
6	Eosin-Y instead of $Ru(bpy)_3Cl_2$	0
7	*fac*-Ir(ppy)$_3$ instead of $Ru(bpy)_3Cl_2$	47
8	$NaHCO_3$ instead of K_2HPO_4	52
9	Cs_2CO_3 instead of K_2HPO_4	0
10	Toluene instead of MeCN	35
11	0.05 mmol mL^{-1} instead of 0.1 mmol mL^{-1}	57
12	36 W blue LED instead of 25 W CFL	38

[a] Reaction conditions: Phenyl 3-phenylpropiolate (**1a**, 0.10 mmol), butyraldehyde (**2a**, 0.30 mmol), photoredox catalyst (1.0 mol%), TBHP (3.0 equiv.), base (2.0 equiv.), solvent (1.0 mL) at room temperature under light irradiation in N_2 for 30 h. [b] Isolated yields.

With the optimum reaction conditions in hand, various aldehydes **2** were first investigated with phenyl 3-phenylpropiolate **1a**. As illustrated in Table 2, a number of linear alkyl aldehydes, such as *n*-valeraldehyde, *n*-hexanaldehyde and *n*-octanaldehyde, reacted smoothly with **1a**, giving the corresponding 3-acylcoumarins in good yields (**3a–3e**, 63%–80% yields). Alkyl aldehydes bearing a chlorine atom, which could easily transform into other functional groups,[19] were also explored, providing **3f** in 59% yield. Higher yields were observed with branched alkyl aldehydes (**3g–3i**, 72%–75% yields) and cyclic aldehydes (**3j–3l**, 63%–75% yields) as the radical donors, compared to a previous report.[17a] Moreover, this newly developed catalytic protocol was not only applicable to alkyl aldehydes, but also applicable to aromatic aldehydes. Benzaldehyde and 2-naphthalene aldehyde delivered the products in moderate yields (**3m** and **3n**, 61% and 48% yields). It seems that the size of the alkyl group of substituted benzaldehydes has an effect on this protocol. Benzaldehydes bearing a methyl group gave

Table 2 Scope of the aldehydes[a,b]

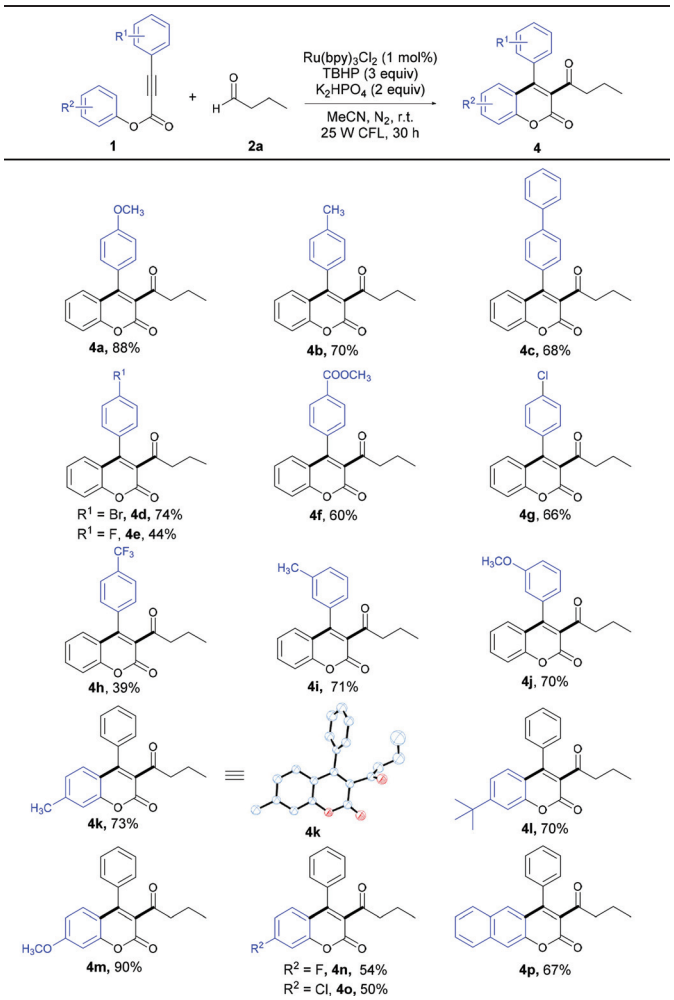


[a] Reaction conditions: Phenyl 3-phenylpropiolate (**1a**, 0.10 mmol), aldehydes (**2**, 0.30 mmol), $Ru(bpy)_3Cl_2$ (1.0 mol%), TBHP (3.0 equiv.), K_2HPO_4 (2.0 equiv.), MeCN (1.0 mL) at room temperature under light irradiation in N_2 for 30 h. [b] Isolated yields.

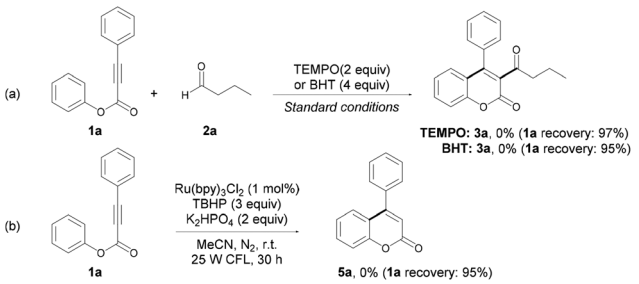
76% yield (**3o**), while benzaldehydes with ethyl or isopropyl led to poor yields (**3p** and **3q**, 55% and 38% yields). Benzaldehydes bearing halogen atoms (chlorine, fluorine) at the *para*-position were also compatible (**3r** and **3s**, 63% and 42% yields).

Subsequently, various alkynoate derivatives were explored with butyraldehyde **2a** in this acylation/cyclization procedure, and the representative results are summarized in Table 3. Generally, different functional groups at the benzene rings of the 3-phenylpropiolic acids (as R1) and the phenols (as R2) showed a concerted effect regarding their electronic properties. The substrates bearing electron-donating groups, such as methoxyl, methyl or *tert*-butyl, gave higher yields (for *para*-position: **4a**, **4b** and **4k–4m**, for *meta*-position: **4i–4j**, 70%–90% yields) than alkynoates with the electron-withdrawing substituents (**4d–4g** and **4n–4o**, 44%–74% yields). The crystal structure of **4k** is shown in the table to confirm its structure.[20] An

Table 3 Scope of alkynoates with aldehyde **2a**[a,b]



[a] Reaction conditions: Phenyl 3-phenylpropiolate (**1a**, 0.10 mmol), aldehydes (**2**, 0.30 mmol), $Ru(bpy)_3Cl_2$ (1.0 mol%), TBHP (3.0 equiv.), K_2HPO_4 (2.0 equiv.), MeCN (1.0 mL) at room temperature under light irradiation in N_2 for 30 h. [b] Isolated yields.

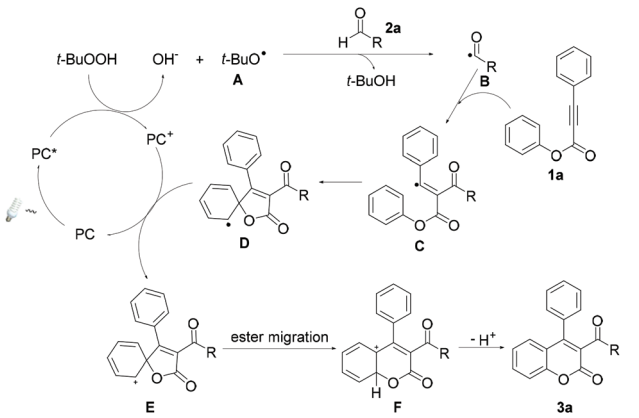


Scheme 2 Control experiments.

alkynoate with a strong electron-withdrawing trifluoromethyl group on the benzene ring was also tested for this transformation, however a much lower yield was observed (**4h**, 39% yield). In addition, substrates bearing weak electron-donating groups, a phenyl group and a benzo ring provided **4c** and **4p** in 68% and 67% yields, respectively.

In order to explore the reaction mechanism, control experiments were carried out (Scheme 2). When TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy) (2.0 equiv.) or BHT (2,6-di-*tert*-butyl-4-methyl-phenol) (4.0 equiv.) was added under the standard conditions, the formation of **3a** was completely inhibited (Scheme 2a). Meanwhile, the cyclization product **5a** was not observed when the reaction was conducted without aldehyde **2a** under the standard conditions (Scheme 2b). Furthermore, it was found that the transformation is substantially dependent upon photoirradiation. The reaction stopped in the dark and could be switched on by turning on the light (see Fig. S1†). These results indicated that a radical intermediate was involved in this transformation and the process is not a chain reaction pathway.

On the basis of the above results, the previous investigations and the crystal structure of **4k**, a possible mechanism for the photoreaction of **1a** and **2a** is proposed, as shown in Scheme 3. Initially, a *tert*-butoxy radical **A** is produced by a SET process from the reaction of the excited state of $[Ru(bpy)_3Cl_2]^*$ with TBHP. Then, the abstraction of a hydrogen radical from aldehydes gives the corresponding acyl radical **B** and *tert*-



Scheme 3 Speculative reaction mechanism.

butanol. The addition of **B** to **1a** delivers the radical intermediate **C**, which tends to undergo an intramolecular 5-*exo* cyclization to give radical intermediate **D**. The intermediate **D** is then oxidized by $[Ru(bpy)_3Cl_2]^+$ to give the cation **E**, followed by the 1,2-ester migration process to furnish cation **F**. Finally, **F** is deprotonated in the presence of bases, regenerating the aromatic system and affording the desired 3-acylcoumarin product **3a**.

Conclusions

In conclusion, we have developed a new, efficient and atom-economic method for the synthesis of 3-acylcoumarins starting with readily prepared alkynoates and the commercially available aldehydes under visible light irradiation. A series of coumarin derivatives could be conveniently and efficiently obtained in moderate to good yields with excellent functional group tolerance and good compatibility for aliphatic aldehydes. We anticipate further development of the presented method and its application toward the synthesis of bioactive compounds.

Experimental section

General methods

Unless otherwise stated, all reactions were performed under a N_2 atmosphere. Reactions were monitored with analytical thin-layer chromatography (TLC) on a silica gel GF 254 plate. Purification of the reaction products was carried out by column chromatography using silica gel. Silica gel 60H (200–300 mesh) manufactured by Qingdao Haiyang Chemical Group Co. (China) was used for general chromatography. ^1H and ^{13}C NMR spectra were recorded with Bruker AV-300 and AV-500 spectrometers operating at 300 MHz/500 MHz and 75 MHz/126 MHz using $CDCl_3$ as the solution, respectively. Chemical shifts δ are reported in ppm relative to Me_4Si (δ = 0.00 ppm) or residual $CHCl_3$ (δ = 7.26 ppm). The multiplicity of signals is designated by the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). High-resolution mass spectra (HRMS) were obtained on an Agilent mass spectrometer using ESI-TOF (electrospray ionization-time of flight). Commercial reagents were purchased from J&K, Energy, Bide, Alfa Aesar, Acros Organics, Strem Chemicals, and TCI, and if not mentioned otherwise all chemicals were used as received.

Preparation of substrates

The alkynoate substrates were prepared following the procedure in previous reports.[17a,b]

General procedure for the synthesis of 3-acylcoumarins

A mixture of **1** (0.1 mmol), **2** (0.3 mmol), $Ru(bpy)_3Cl_2$ (1 mol%), TBHP (0.3 mmol), and K_2HPO_4 (0.2 mmol) in MeCN (1 mL) was stirred under 25 W CFL (CFL = compact fluorescent light) under an atmosphere of N_2 in a sealed tube at room temperature for 30 h. After completion of the reaction, the reaction mixture was purified by flash chromatography on silica gel with a mixture of petroleum ether and ethyl acetate (30 : 1–10 : 1) as the eluent to give the desired product **3** or **4**.

3-Butyryl-4-phenyl-2*H*-chromen-2-one (3a).[17a] White solid (23.3 mg, 80%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.51–7.47 (m, 3H), 7.40 (d, J = 8.5 Hz, 1H), 7.34–7.29 (m, 2H), 7.22 (s, 2H), 2.44 (t, J = 7.1 Hz, 2H), 1.46 (dd, J = 14.6, 7.3 Hz, 2H), 0.70 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.74, 158.56, 153.34, 151.33, 132.55, 132.40, 129.62, 128.72, 127.95, 124.56, 119.38, 117.00, 45.46, 16.46, 13.30. HRMS (ESI-TOF) m/z calcd for $C_{19}H_{17}O_3$ $[M + H]^+$ 293.1172, found 293.1175.

3-Pentanoyl-4-phenyl-2*H*-chromen-2-one (3b). White solid (24.1 mg, 79%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.60–7.54 (m, 1H), 7.53–7.46 (m, 3H), 7.40 (d, J = 8.2 Hz, 1H), 7.34–7.28 (m, 2H), 7.25–7.16 (m, 2H), 2.45 (t, J = 7.3 Hz, 2H), 1.47–1.34 (m, 2H), 1.16–1.04 (m, 2H), 0.75 (t, J = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.99, 158.65, 153.44, 151.37, 132.64, 132.53, 129.73, 128.81, 128.05, 124.66, 119.47, 117.10, 43.37, 25.14, 21.92, 13.76. HRMS (ESI-TOF) m/z calcd for $C_{20}H_{19}O_3$ $[M + H]^+$ 307.1329, found 307.1331.

3-Hexanoyl-4-phenyl-2*H*-chromen-2-one (3c). White solid (24.3 mg, 76%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.57 (ddd, J = 8.6, 6.0, 2.8 Hz, 1H), 7.53–7.46 (m, 3H), 7.41 (d, J = 8.2 Hz, 1H), 7.32 (dd, J = 6.5, 2.9 Hz, 2H), 7.25–7.17 (m, 2H), 2.45 (t, J = 7.3 Hz, 2H), 1.48–1.39 (m, 2H), 1.20–1.11 (m, 2H), 1.08–0.99 (m, 2H), 0.79 (t, J = 7.3 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.96, 158.63, 153.44, 151.34, 132.62, 132.53, 129.71, 128.83, 128.80, 128.10, 128.04, 124.64, 119.48, 117.09, 43.62, 30.95, 22.74, 22.32, 13.89. HRMS (ESI-TOF) m/z calcd for $C_{21}H_{21}O_3$ $[M + H]^+$ 321.1485, found 321.1489.

3-Heptanoyl-4-phenyl-2*H*-chromen-2-one (3d). White solid (21.1 mg, 63%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.56 (t, J = 7.2 Hz, 1H), 7.52–7.46 (m, 3H), 7.39 (d, J = 8.3 Hz, 1H), 7.33–7.28 (m, 2H), 7.24–7.18 (m, 2H), 2.45 (t, J = 7.3 Hz, 2H), 1.47–1.37 (m, 2H), 1.22–1.14 (m, 2H), 1.07 (ddd, J = 23.8, 14.7, 7.4 Hz, 4H), 0.81 (t, J = 7.2 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.97, 158.64, 153.43, 151.34, 132.62, 132.52, 129.72, 128.83, 128.80, 128.09, 128.03, 124.65, 119.47, 117.09, 43.66, 31.47, 28.46, 23.00, 22.45, 14.04. HRMS (ESI-TOF) m/z calcd for $C_{22}H_{23}O_3$ $[M + H]^+$ 335.1642, found 335.1644.

3-Octanoyl-4-phenyl-2*H*-chromen-2-one (3e). White solid (23.0 mg, 71%). ^1H NMR (500 MHz, $CDCl_3$) δ 7.57 (ddd, J = 8.6, 6.0, 2.8 Hz, 1H), 7.53–7.48 (m, 3H), 7.41 (d, J = 8.3 Hz, 1H), 7.32 (dd, J = 6.4, 2.9 Hz, 2H), 7.25–7.18 (m, 2H), 2.46 (t, J = 7.3 Hz, 2H), 1.50–1.34 (m, 2H), 1.22 (dt, J = 14.1, 7.2 Hz, 2H), 1.19–1.09 (m, 4H), 1.05 (dd, J = 14.2, 6.6 Hz, 2H), 0.89–0.79 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.96, 158.64, 153.45, 151.33, 132.61, 132.54, 129.70, 128.83, 128.80, 128.11, 128.03, 124.64, 119.49, 117.09, 43.67, 31.62, 28.94, 28.75, 23.05, 22.59, 14.10. HRMS (ESI-TOF) m/z calcd for $C_{23}H_{25}O_3$ $[M + H]^+$ 349.1798, found 349.1801.

3-(5-Chloropentanoyl)-4-phenyl-2*H*-chromen-2-one (3f). White solid (20.0 mg, 59%). ^1H NMR (300 MHz, $CDCl_3$) δ 7.62–7.52 (m, 1H), 7.51–7.44 (m, 3H), 7.38 (d, J = 8.2 Hz, 1H),

7.30 (dd, J = 6.3, 2.4 Hz, 2H), 7.23–7.17 (m, 2H), 3.35 (t, J = 6.1 Hz, 2H), 2.49 (t, J = 6.4 Hz, 2H), 1.56 (dt, J = 8.3, 5.2 Hz, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.20, 158.61, 153.43, 151.64, 132.79, 132.41, 129.86, 128.89, 128.77, 128.08, 127.78, 124.75, 119.38, 117.09, 44.54, 42.50, 31.38, 20.34. HRMS (ESI-TOF) m/z calcd for $C_{20}H_{18}ClO_3$ $[M + H]^+$ 341.0939, found 341.0945.

4-Phenyl-3-(3,5,5-trimethylhexanoyl)-2*H*-chromen-2-one (3g). White solid (26.1 mg, 72%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (dt, J = 8.6, 4.4 Hz, 1H), 7.50–7.43 (m, 3H), 7.38 (d, J = 8.3 Hz, 1H), 7.31 (dt, J = 7.0, 3.4 Hz, 2H), 7.20 (d, J = 4.2 Hz, 2H), 2.48 (dd, J = 18.3, 4.7 Hz, 1H), 2.32 (dd, J = 18.3, 8.2 Hz, 1H), 2.05–1.94 (m, 1H), 0.92–0.89 (m, 2H), 0.77 (s, 9H), 0.69 (d, J = 6.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.11, 158.59, 153.43, 151.10, 132.54, 132.38, 129.68, 129.02, 128.93, 128.79, 128.27, 127.97, 124.60, 119.55, 117.08, 53.31, 50.59, 31.06, 29.95, 24.60, 22.33. HRMS (ESI-TOF) m/z calcd for $C_{24}H_{27}O_3$ $[M + H]^+$ 363.1955, found 363.1957.

3-(3-Methylbutanoyl)-4-phenyl-2*H*-chromen-2-one (3h).[17a] White solid (22.9 mg, 75%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59–7.54 (m, 1H), 7.51–7.46 (m, 3H), 7.39 (d, J = 8.3 Hz, 1H), 7.31 (dt, J = 7.4, 3.3 Hz, 2H), 7.23–7.18 (m, 2H), 2.34 (d, J = 6.7 Hz, 2H), 2.09–1.98 (m, 1H), 0.68 (d, J = 6.7 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.24, 158.62, 153.42, 151.32, 132.62, 132.40, 129.70, 128.94, 128.79, 128.11, 128.02, 124.64, 119.52, 117.07, 52.56, 23.53, 22.27. HRMS (ESI-TOF) m/z calcd for $C_{20}H_{19}O_3$ $[M + H]^+$ 307.1329, found 307.1333.

3-Isobutyryl-4-phenyl-2*H*-chromen-2-one (3i).[21] White solid (21.6 mg, 74%). ^{1}H NMR (500 MHz, CDCl3) δ 7.57 (ddd, J = 8.7, 6.6, 2.2 Hz, 1H), 7.51–7.46 (m, 3H), 7.41 (d, J = 8.2 Hz, 1H), 7.33 (dt, J = 7.5, 3.2 Hz, 2H), 7.25–7.19 (m, 2H), 2.66–2.52 (m, 1H), 0.92 (d, J = 7.0 Hz, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.66, 158.78, 153.49, 151.49, 132.65, 132.61, 129.72, 129.05, 128.73, 128.04, 127.69, 124.63, 119.45, 117.11, 41.25, 17.62. HRMS (ESI-TOF) m/z calcd for $C_{19}H_{17}O_3$ $[M + H]^+$ 293.1172, found 293.1175.

3-(Cyclopropanecarbonyl)-4-phenyl-2*H*-chromen-2-one (3j).[17a] White solid (20.9 mg, 72%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (t, J = 7.6 Hz, 1H), 7.49 (s, 3H), 7.41 (d, J = 8.3 Hz, 1H), 7.37–7.30 (m, 2H), 7.25 (dd, J = 22.9, 7.8 Hz, 2H), 2.04 (s, 1H), 0.97 (s, 2H), 0.81 (d, J = 4.1 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.68, 158.56, 153.58, 152.08, 132.99, 132.71, 129.65, 128.86, 128.70, 128.18, 124.63, 119.49, 117.12, 23.25, 12.85. HRMS (ESI-TOF) m/z calcd for $C_{19}H_{15}O_3$ $[M + H]^+$ 291.1016, found 291.1019.

3-(Cyclopentanecarbonyl)-4-phenyl-2*H*-chromen-2-one (3k). White solid (20.1 mg, 63%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59–7.54 (m, 1H), 7.51–7.46 (m, 3H), 7.41 (d, J = 8.2 Hz, 1H), 7.33 (dd, J = 6.6, 2.9 Hz, 2H), 7.25–7.18 (m, 2H), 2.92–2.84 (m, 1H), 1.63 (d, J = 7.3 Hz, 2H), 1.58–1.39 (m, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 204.91, 158.76, 153.49, 151.22, 132.68, 132.53, 129.66, 129.10, 128.69, 128.36, 128.04, 124.58, 119.53, 117.09, 52.02, 28.94, 25.82. HRMS (ESI-TOF) m/z calcd for $C_{21}H_{19}O_3$ $[M + H]^+$ 319.1329, found 319.1332.

3-(Cyclohexanecarbonyl)-4-phenyl-2*H*-chromen-2-one (3l). White solid (24.9 mg, 75%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (ddd, J = 8.7, 6.4, 2.4 Hz, 1H), 7.51–7.46 (m, 3H), 7.40 (d, J = 8.2 Hz, 1H), 7.32 (dd, J = 6.5, 2.9 Hz, 2H), 7.24–7.18 (m, 2H), 2.38–2.29 (m, 1H), 1.65 (d, J = 8.4 Hz, 5H), 1.10 (dd, J = 29.0, 17.2 Hz, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 204.85, 158.82, 153.48, 151.51, 132.67, 132.55, 129.65, 129.13, 128.64, 128.03, 127.70, 124.59, 119.52, 117.07, 50.82, 27.90, 25.70, 25.59. HRMS (ESI-TOF) m/z calcd for $C_{22}H_{21}O_3$ $[M + H]^+$ 333.1485, found 332.1489.

3-Benzoyl-4-phenyl-2*H*-chromen-2-one (3m).[17a] White solid (19.9 mg, 61%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, J = 7.6 Hz, 2H), 7.61 (dd, J = 11.3, 4.1 Hz, 1H), 7.47 (dt, J = 12.2, 7.6 Hz, 2H), 7.37–7.30 (m, 5H), 7.27 (ddd, J = 12.8, 9.4, 4.3 Hz, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.21, 158.87, 153.78, 153.04, 136.25, 133.91, 132.80, 132.35, 129.57, 129.31, 128.76, 128.66, 128.64, 128.04, 126.02, 124.76, 119.48, 117.23. HRMS (ESI-TOF) m/z calcd for $C_{22}H_{15}O_3$ $[M + H]^+$ 327.1016, found 327.1021.

3-(2-Naphthoyl)-4-phenyl-2*H*-chromen-2-one (3n). White solid (18.0 mg, 48%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (s, 1H), 7.88 (dd, J = 12.4, 4.8 Hz, 2H), 7.81 (t, J = 9.2 Hz, 2H), 7.67–7.61 (m, 1H), 7.58 (t, J = 7.5 Hz, 1H), 7.51 (dd, J = 7.9, 4.7 Hz, 2H), 7.33–7.27 (m, 7H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 192.12, 158.99, 153.87, 153.16, 136.03, 133.74, 132.81, 132.44, 132.00, 129.76, 129.57, 128.96, 128.70, 128.66, 128.10, 127.87, 126.86, 126.19, 124.77, 124.12, 119.57, 117.30. HRMS (ESI-TOF) m/z calcd for $C_{26}H_{17}O_3$ $[M + H]^+$ 377.1172, found 377.1175.

3-(4-Methylbenzoyl)-4-phenyl-2*H*-chromen-2-one (3o).[17a] White solid (25.8 mg, 76%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, J = 8.1 Hz, 2H), 7.64–7.58 (m, 1H), 7.46 (d, J = 8.3 Hz, 1H), 7.33 (dd, J = 6.3, 3.0 Hz, 3H), 7.31–7.22 (m, 4H), 7.16 (d, J = 8.1 Hz, 2H), 2.35 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.08, 158.28, 153.13, 152.11, 144.35, 133.20, 132.02, 131.81, 128.86, 128.77, 128.12, 127.97, 127.37, 125.61, 124.04, 118.92, 116.59, 21.20. HRMS (ESI-TOF) m/z calcd for $C_{23}H_{17}O_3$ $[M + H]^+$ 341.1172, found 341.1174.

3-(4-Ethylbenzoyl)-4-phenyl-2*H*-chromen-2-one (3p).[18b] White solid (19.5 mg, 55%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, J = 8.2 Hz, 2H), 7.60 (t, J = 7.7 Hz, 1H), 7.46 (d, J = 8.2 Hz, 1H), 7.36–7.30 (m, 3H), 7.30–7.22 (m, 4H), 7.18 (d, J = 8.1 Hz, 2H), 2.65 (q, J = 7.6 Hz, 2H), 1.21 (t, J = 7.6 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 191.73, 158.92, 153.77, 152.78, 151.03, 134.06, 132.64, 132.46, 129.59, 129.49, 128.76, 128.60, 128.22, 128.01, 126.30, 124.67, 119.58, 117.21, 29.07, 15.01. HRMS (ESI-TOF) m/z calcd for $C_{24}H_{19}O_3$ $[M + H]^+$ 355.1329, found 355.1334.

3-(4-Isopropylbenzoyl)-4-phenyl-2*H*-chromen-2-one (3q). White solid (14.0 mg, 38%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, J = 8.3 Hz, 2H), 7.64–7.58 (m, 1H), 7.46 (d, J = 8.2 Hz, 1H), 7.37–7.32 (m, 3H), 7.27 (dd, J = 12.8, 11.0 Hz, 4H), 7.21 (d, J = 8.3 Hz, 2H), 3.02–2.81 (m, 1H), 1.22 (d, J = 6.9 Hz, 6H). ^{13}C NMR (126 MHz, CDCl3) δ 191.72, 158.94, 155.52, 153.76, 152.83, 134.20, 132.64, 132.46, 129.61, 129.47, 128.78, 128.59, 128.03, 126.82, 126.33, 124.67, 119.60, 117.22, 34.36, 23.58. HRMS (ESI-TOF) m/z calcd for $C_{25}H_{21}O_3$ $[M + H]^+$ 369.1485, found 369.1489.

3-(4-Chlorobenzoyl)-4-phenyl-2*H*-chromen-2-one (3r).[17a] White solid (22.7 mg, 63%). ^{1}H NMR (300 MHz, CDCl3) δ 7.74

(d, J = 6.7 Hz, 2H), 7.68–7.59 (m, 1H), 7.47 (d, J = 8.1 Hz, 1H), 7.35 (dd, J = 7.4, 4.6 Hz, 5H), 7.31–7.23 (m, 4H). ^{13}C NMR (126 MHz, CDCl3) δ 190.96, 158.74, 153.82, 153.38, 140.40, 134.66, 132.95, 132.23, 130.62, 129.72, 129.05, 128.72, 128.70, 128.08, 125.54, 124.81, 119.38, 117.30. HRMS (ESI-TOF) m/z calcd for $C_{22}H_{14}ClO_3$ $[M + H]^+$ 361.0626, found 361.0629.

3-(4-Fluorobenzoyl)-4-phenyl-2*H*-chromen-2-one (3s).[17a] White solid (14.5 mg, 42%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (dd, J = 8.6, 5.4 Hz, 2H), 7.62 (t, J = 7.0 Hz, 1H), 7.46 (d, J = 8.3 Hz, 1H), 7.34 (d, J = 3.4 Hz, 3H), 7.28 (dd, J = 18.6, 5.2 Hz, 4H), 7.02 (t, J = 8.5 Hz, 2H). HRMS (ESI-TOF) m/z calcd for $C_{22}H_{14}FO_3$ $[M + H]^+$ 345.0921, found 345.0925.

3-Butyryl-4-(4-methoxyphenyl)-2*H*-chromen-2-one (4a). White solid (28.3 mg, 88%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60–7.50 (m, 1H), 7.39 (d, J = 8.1 Hz, 1H), 7.26 (td, J = 13.9, 6.7 Hz, 4H), 7.01 (d, J = 8.7 Hz, 2H), 3.87 (s, 3H), 2.42 (t, J = 7.2 Hz, 2H), 1.49 (dq, J = 14.6, 7.3 Hz, 2H), 0.73 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.13, 160.69, 158.70, 153.47, 151.16, 132.48, 130.44, 128.01, 124.54, 124.49, 119.71, 117.10, 114.28, 55.44, 45.55, 16.64, 13.47. HRMS (ESI-TOF) m/z calcd for $C_{20}H_{19}O_4$ $[M + H]^+$ 323.1278, found 323.1280.

3-Butyryl-4-(*p*-tolyl)-2*H*-chromen-2-one (4b). White solid (21.4 mg, 70%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58–7.53 (m, 1H), 7.38 (d, J = 8.3 Hz, 1H), 7.29 (d, J = 7.8 Hz, 2H), 7.26 (dd, J = 8.0, 1.5 Hz, 1H), 7.20 (t, J = 8.0 Hz, 3H), 2.46–2.41 (m, 5H), 1.52–1.43 (m, 2H), 0.72 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.98, 158.70, 153.44, 151.62, 139.85, 132.52, 129.53, 129.47, 128.76, 128.09, 127.93, 124.56, 119.63, 117.05, 45.55, 21.43, 16.62, 13.42. HRMS (ESI-TOF) m/z calcd for $C_{20}H_{19}O_3$ $[M + H]^+$ 307.1329, found 307.1334.

4-([1,1′-Biphenyl]-4-yl)-3-butyryl-2*H*-chromen-2-one (4c). White solid (25.1 mg, 68%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, J = 8.3 Hz, 2H), 7.64 (d, J = 7.2 Hz, 2H), 7.61–7.57 (m, 1H), 7.49 (t, J = 7.6 Hz, 2H), 7.41 (t, J = 8.6 Hz, 4H), 7.32 (dd, J = 8.0, 1.4 Hz, 1H), 7.24 (t, J = 7.7 Hz, 1H), 2.50 (t, J = 7.1 Hz, 2H), 1.54–1.47 (m, 2H), 0.73 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.92, 158.66, 153.48, 151.25, 142.59, 139.92, 132.68, 131.34, 129.39, 129.05, 128.08, 127.42, 127.19, 124.70, 119.49, 117.15, 45.61, 29.75, 16.63, 13.43. HRMS (ESI-TOF) m/z calcd for $C_{25}H_{21}O_4$ $[M + H]^+$ 369.1485, found 369.1487.

4-(4-Bromophenyl)-3-butyryl-2*H*-chromen-2-one (4d). White solid (27.5 mg, 74%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, J = 8.3 Hz, 2H), 7.56 (t, J = 7.1 Hz, 1H), 7.37 (d, J = 8.3 Hz, 1H), 7.24–7.11 (m, 4H), 2.50 (t, J = 7.2 Hz, 2H), 1.48 (dq, J = 14.7, 7.4 Hz, 2H), 0.73 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.55, 158.45, 153.39, 150.46, 132.88, 132.05, 131.39, 130.45, 128.15, 127.81, 124.80, 124.12, 119.16, 117.16, 45.53, 16.64, 13.44. HRMS (ESI-TOF) m/z calcd for $C_{19}H_{16}BrO_3$ $[M + H]^+$ 371.0277, found 371.0280.

3-Butyryl-4-(4-fluorophenyl)-2*H*-chromen-2-one (4e). White solid (13.6 mg, 44%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62–7.56 (m, 1H), 7.41 (d, J = 8.3 Hz, 1H), 7.31 (dd, J = 8.6, 5.2 Hz, 2H), 7.25–7.17 (m, 4H), 2.49 (t, J = 7.2 Hz, 2H), 1.53–1.45 (m, 2H), 0.74 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.73, 164.36, 162.36, 158.54, 153.42, 150.52, 132.78, 130.94, 130.87, 128.41, 127.81, 124.74, 119.45, 117.21, 116.16, 115.98, 45.56, 16.59, 13.42. HRMS (ESI-TOF) m/z calcd for $C_{19}H_{16}FO_3$ $[M + H]^+$ 311.1078, found 311.1081.

Methyl 4-(3-butyryl-2-oxo-2*H*-chromen-4-yl)benzoate (4f). White solid (21.0 mg, 60%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, J = 8.3 Hz, 2H), 7.60–7.55 (m, 1H), 7.39 (dd, J = 7.7, 5.4 Hz, 3H), 7.23–7.17 (m, 1H), 7.10 (dd, J = 8.0, 1.3 Hz, 1H), 3.95 (s, 3H), 2.52 (t, J = 7.2 Hz, 2H), 1.50–1.43 (m, 2H), 0.72 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.38, 166.26, 158.44, 153.41, 150.80, 137.14, 132.95, 131.28, 129.91, 128.92, 128.09, 127.82, 124.83, 119.08, 117.20, 52.49, 45.54, 16.61, 13.43. HRMS (ESI-TOF) m/z calcd for $C_{21}H_{19}O_5$ $[M + H]^+$ 351.1227, found 351.1229.

3-Butyryl-4-(4-chlorophenyl)-2*H*-chromen-2-one (4g). White solid (21.5 mg, 66%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (t, J = 5.8 Hz, 1H), 7.48 (d, J = 6.7 Hz, 1H), 7.41 (d, J = 6.6 Hz, 1H), 7.25 (ddt, J = 21.4, 14.6, 5.3 Hz, 5H), 2.50 (dt, J = 11.6, 5.7 Hz, 2H), 1.49 (dt, J = 5.8, 5.3 Hz, 2H), 0.75 (dt, J = 7.8, 5.9 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.59, 158.50, 153.42, 150.46, 135.96, 132.85, 130.88, 130.23, 129.12, 127.81, 124.77, 119.27, 117.21, 116.15, 115.98, 45.57, 16.64, 13.43. HRMS (ESI-TOF) m/z calcd for $C_{19}H_{16}ClO_3$ $[M + H]^+$ 327.0782, found 327.0787.

3-Butyryl-4-(4-(trifluoromethyl)phenyl)-2*H*-chromen-2-one (4h). White solid (14.1 mg, 39%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, J = 8.0 Hz, 2H), 7.60 (ddd, J = 8.6, 7.3, 1.5 Hz, 1H), 7.45 (d, J = 8.0 Hz, 2H), 7.43 (dd, J = 8.3, 0.8 Hz, 1H), 7.25–7.20 (m, 1H), 7.08 (dd, J = 8.0, 1.4 Hz, 1H), 2.56 (t, J = 7.2 Hz, 2H), 1.50 (dd, J = 14.6, 7.3 Hz, 2H), 0.74 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.29, 158.40, 153.44, 150.40, 136.33, 133.04, 129.30, 128.32, 127.75, 125.75, 125.72, 124.88, 119.09, 117.26, 45.54, 29.73, 16.64, 13.36. HRMS (ESI-TOF) m/z calcd for $C_{20}H_{16}F_3O_4$ $[M + H]^+$ 361.1046, found 361.1049.

3-Butyryl-4-(*m*-tolyl)-2*H*-chromen-2-one (4i). White solid (21.7 mg, 71%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (ddd, J = 8.7, 3.2, 1.6 Hz, 1H), 7.37 (dd, J = 8.2, 2.1 Hz, 1H), 7.31–7.23 (m, 3H), 7.20 (t, J = 7.5 Hz, 3H), 2.46–2.38 (m, 5H), 1.54–1.40 (m, 2H), 0.72 (td, J = 7.4, 1.7 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.01, 158.70, 153.43, 151.63, 139.86, 132.54, 129.48, 128.76, 128.09, 127.90, 124.58, 119.61, 117.04, 45.54, 21.43, 16.61, 13.42. HRMS (ESI-TOF) m/z calcd for $C_{20}H_{19}O_3$ $[M + H]^+$ 307.1329, found 307.1335.

3-Butyryl-4-(3-methoxyphenyl)-2*H*-chromen-2-one (4j). White solid (22.5 mg, 70%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.60 (ddd, J = 8.6, 7.3, 1.6 Hz, 1H), 7.43 (dd, J = 12.8, 5.1 Hz, 2H), 7.32 (dd, J = 8.0, 1.5 Hz, 1H), 7.25 (t, J = 7.1 Hz, 1H), 7.09–7.03 (m, 1H), 6.91 (t, J = 6.8 Hz, 1H), 6.90–6.85 (m, 1H), 3.86 (s, 3H), 2.50 (q, J = 7.0 Hz, 2H), 1.53 (dd, J = 14.6, 7.3 Hz, 2H), 0.76 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.77, 159.71, 158.62, 153.41, 151.19, 133.70, 132.63, 130.01, 128.06, 124.66, 121.04, 119.36, 117.04, 115.29, 114.50, 55.45, 45.50, 16.57, 13.40. HRMS (ESI-TOF) m/z calcd for $C_{20}H_{19}O_4$ $[M + H]^+$ 323.1278, found 323.1280.

3-Butyryl-7-methyl-4-phenyl-2*H*-chromen-2-one (4k). White solid (22.3 mg, 73%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.49–7.43

(m, 3H), 7.29 (dd, J = 6.4, 2.9 Hz, 2H), 7.19 (s, 1H), 7.08 (d, J = 8.1 Hz, 1H), 7.01 (d, J = 8.2 Hz, 1H), 2.44 (s, 3H), 2.43 (d, J = 7.2 Hz, 2H), 1.50–1.39 (m, 2H), 0.69 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.99, 158.90, 153.55, 151.63, 144.15, 132.78, 129.58, 128.78, 128.73, 127.75, 126.94, 125.86, 117.21, 45.60, 21.73, 16.61, 13.40. HRMS (ESI-TOF) m/z calcd for $C_{20}H_{19}O_3$ $[M + H]^+$ 307.1329, found 307.1335.

7-(*tert*-Butyl)-3-butyryl-4-phenyl-2*H*-chromen-2-one (4l). White solid (24.4 mg, 70%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50–7.45 (m, 3H), 7.40 (d, J = 1.7 Hz, 1H), 7.30 (dd, J = 6.5, 2.9 Hz, 2H), 7.24 (dd, J = 8.5, 1.7 Hz, 1H), 7.14 (d, J = 8.4 Hz, 1H), 2.44 (t, J = 7.1 Hz, 2H), 1.46 (h, J = 7.3 Hz, 2H), 1.34 (s, 9H), 0.70 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.98, 159.01, 157.38, 153.51, 151.53, 132.79, 129.57, 128.77, 128.71, 127.61, 127.09, 122.21, 116.97, 113.85, 45.60, 35.34, 31.01, 16.64, 13.41. HRMS (ESI-TOF) m/z calcd for $C_{23}H_{25}O_3$ $[M + H]^+$ 349.1798, found 349.1802.

3-Butyryl-7-methoxy-4-phenyl-2*H*-chromen-2-one (4m). White solid (28.9 mg, 90%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56–7.38 (m, 3H), 7.28 (dd, J = 6.7, 2.9 Hz, 2H), 7.10 (d, J = 8.9 Hz, 1H), 6.87 (d, J = 2.5 Hz, 1H), 6.76 (dd, J = 8.9, 2.5 Hz, 1H), 3.88 (s, 3H), 2.45 (t, J = 7.2 Hz, 2H), 1.46 (dq, J = 14.6, 7.3 Hz, 2H), 0.70 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.04, 163.50, 159.06, 155.36, 152.15, 133.03, 129.53, 129.18, 128.70, 124.76, 112.91, 100.84, 55.94, 45.66, 16.72, 13.43. HRMS (ESI-TOF) m/z calcd for $C_{20}H_{19}O_4$ $[M + H]^+$ 323.1278, found 323.1280.

3-Butyryl-7-fluoro-4-phenyl-2*H*-chromen-2-one (4n). White solid (16.7 mg, 54%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54–7.45 (m, 3H), 7.29 (dd, J = 6.6, 2.9 Hz, 2H), 7.21 (dd, J = 8.9, 6.0 Hz, 1H), 7.12 (dd, J = 8.8, 2.4 Hz, 1H), 6.98–6.91 (m, 1H), 2.43 (t, J = 7.1 Hz, 2H), 1.52–1.41 (m, 2H), 0.70 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.48, 165.94, 163.90, 158.34, 154.66, 154.55, 151.14, 132.37, 129.97, 129.87, 128.91, 128.71, 126.90, 116.27, 112.89, 112.71, 104.70, 104.50, 45.55, 16.57, 13.37. HRMS (ESI-TOF) m/z calcd for $C_{19}H_{16}FO_3$ $[M + H]^+$ 311.1078, found 311.1081.

3-Butyryl-7-chloro-4-phenyl-2*H*-chromen-2-one (4o). White solid (16.3 mg, 50%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52–7.47 (m, 3H), 7.40 (d, J = 1.7 Hz, 1H), 7.28 (dd, J = 6.6, 2.9 Hz, 2H), 7.17 (dt, J = 16.4, 5.2 Hz, 2H), 2.43 (t, J = 7.1 Hz, 2H), 1.46 (dd, J = 14.6, 7.3 Hz, 2H), 0.69 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.38, 158.04, 153.63, 150.84, 138.68, 132.12, 129.92, 128.94, 128.72, 125.24, 118.18, 117.31, 45.50, 16.53, 13.36. HRMS (ESI-TOF) m/z calcd for $C_{19}H_{16}ClO_3$ $[M + H]^+$ 327.0782, found 327.0784.

3-Butyryl-4-phenyl-2*H*-benzo[*g*]chromen-2-one (4p). White solid (22.9 mg, 67%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.60–8.52 (m, 1H), 7.83 (dd, J = 5.2, 3.6 Hz, 1H), 7.65 (pd, J = 6.3, 1.1 Hz, 2H), 7.56 (d, J = 8.8 Hz, 1H), 7.54–7.48 (m, 3H), 7.35 (dt, J = 6.0, 3.2 Hz, 2H), 7.16 (d, J = 8.8 Hz, 1H), 2.50 (t, J = 7.1 Hz, 2H), 1.54–1.44 (m, 2H), 0.72 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.99, 158.66, 152.58, 150.88, 135.11, 133.01, 129.65, 129.34, 128.84, 127.80, 127.46, 127.33, 124.42, 122.94, 122.82, 122.76, 114.67, 77.39, 77.14, 76.88, 76.21, 45.60, 16.66, 13.45. HRMS (ESI-TOF) m/z calcd for $C_{23}H_{19}O_3$ $[M + H]^+$ 343.1329, found 343.1332.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

1 (*a*) L. Santana, E. Uriarte, F. Roleira, N. Milhazes and F. Borges, *Curr. Med. Chem.*, 2004, **11**, 3239; (*b*) F. Borges, F. Roleira, N. Milhazes, L. Santana and E. Uriarte, *Curr. Med. Chem.*, 2005, **12**, 887; (*c*) M. E. Riveiro, K. N. De and A. Moglioni, *Curr. Med. Chem.*, 2010, **17**, 1325; (*d*) X. M. Peng, G. L. V. Damu and C. H. Zhou, *Curr. Pharm. Des.*, 2013, **19**, 3884; (*e*) F. G. Medina, J. G. Marrero, M. Macias-Alonso, M. C. González, I. Córdova-Guerrero, A. G. Teissier Garcia and S. Osegueda-Robles, *Nat. Prod. Rep.*, 2015, **32**, 1472.

2 (*a*) A. Murakami, G.-X. Gao, M. Omura, M. Yano, C. Ito, H. Furukawa, D. Takahashi, K. Koshimizu and H. Ohigashi, *Bioorg. Med. Chem. Lett.*, 2000, **10**, 59; (*b*) Y. Shikishima, Y. Takaishi, G. Honda, M. Ito, Y. Takeda, O. K. Kodzhimatov, O. Ashurmetov and K. H. Lee, *Chem. Pharm. Bull.*, 2001, **49**, 877; (*c*) K. C. Fylaktakidou, D. J. Hadjipavlou-Litina, K. E. Litinas and D. N. Nicolaides, *Curr. Pharm. Des.*, 2004, **10**, 3813; (*d*) C. A. Kontogiorgis and D. J, *Bioorg. Med. Chem. Lett.*, 2004, **14**, 611; (*e*) D. A. Ostrov, J. A. Hernández Prada, P. E. Corsino, K. A. Finton, N. Le and T. C. Rowe, *Antimicrob. Agents Chemother*, 2007, **51**, 3688; (*f*) M. E. Riveiro, A. Moglioni, R. Vazquez, N. Gomez, G. Facorro, L. Piehl, E. R. De Celis, C. Shayo and C. Davio, *Bioorg. Med. Chem.*, 2008, **16**, 2665; (*g*) O. M. Abdelhafez, K. M. Amin, R. Z. Batran, T. J. Maher, S. A. Nada and S. Sethumadhavan, *Bioorg. Med. Chem.*, 2010, **18**, 3371; (*h*) D. Secci, S. Carradori, A. Bolasco, P. Chimenti, M. Yáñez, F. Ortuso and S. Alcaro, *Eur. J. Med. Chem.*, 2011, **46**, 4846; (*i*) S. Sandhu, Y. Bansal, O. Silakari and G. Bansal, *Bioorg. Med. Chem.*, 2014, **22**, 3806; (*j*) M. Z. Hassan, H. Osman, M. A. Ali and M. J. Ahsan, *Eur. J. Med. Chem.*, 2016, **123**, 236.

3 (*a*) Y.-R. Zhao, Q. Zheng, K. Dakin, K. Xu, M. L. Martinez and W.-H. Li, *J. Am. Chem. Soc.*, 2004, **126**, 4653;

(*b*) C. Murata, T. Masuda, Y. Kamochi, K. Todoroki, H. Yoshida, H. Nohta, M. Yamguchi and A. Takadate, *Chem. Pharm. Bull.*, 2005, **53**, 750; (*c*) J. A. Key, S. Koh, Q. K. Timerghazin, A. Brown and C. W. Cairo, *Dyes Pigm.*, 2009, **82**, 196; (*d*) S.-H. Zhou, J.-H. Jia, J. R. Gao, L. Han, Y.-J. Li and W.-J. Sheng, *Dyes Pigm.*, 2010, **86**, 123.

4 (*a*) M. C. Laufer, H. Hausmann and W. F. Hölderich, *J. Catal.*, 2003, **218**, 315; (*b*) M. K. Potdar, S. S. Mohile and M. M. Salunkhe, *Tetrahedron Lett.*, 2001, **42**, 9285; (*c*) G. P. Romanelli, D. Bennardi, D. M. Ruiz, G. Baronetti, H. J. Thomas and J. C. Autino, *Tetrahedron Lett.*, 2004, **45**, 8935; (*d*) H. Sharghi and M. Jokar, *Heterocycles*, 2007, **71**, 2721; (*e*) M. S. Manhas, S. N. Ganguly, S. Mukherjee, A. K. Jain and A. K. Bose, *Tetrahedron Lett.*, 2006, **47**, 2423; (*f*) G. V. M. Sharma, J. Janardhan Reddy, P. Sree Lakshmi and P. Radha Krishna, *Tetrahedron Lett.*, 2005, **46**, 6119; (*g*) B. Tyagi, M. K. Mishra and R. V. Jasra, *J. Mol. Catal. A: Chem.*, 2007, **276**, 47.

5 (*a*) J. R. Johnson, *The Perkin Reaction and Related Reactions*, ed. Scott E. Denmark, Wiley, Hoboken, 2011, ch. 8, pp. 210–265; (*b*) B. J. Donnelly, D. M. X. Donnelly and A. M. O'Sullivan, *Tetrahedron*, 1968, **24**, 2617.

6 (*a*) N. Cairns, L. M. Harwood and D. P. Astles, *J. Chem. Soc., Chem. Commun.*, 1986, 1264; (*b*) S. K. Chattopadhyay, T. Biswas and K. Neogi, *Chem. Lett.*, 2006, **35**, 376; (*c*) K. C. Majumdar, P. Debnath and P. K. Maji, *Tetrahedron Lett.*, 2007, **48**, 5265.

7 (*a*) F. Bigi, L. Chesini, R. Maggi and G. Sartori, *J. Org. Chem.*, 1999, **64**, 1033; (*b*) A.-M. Song, X.-B. Wang and K. S. Lam, *Tetrahedron Lett.*, 2003, **44**, 1755.

8 R. L. Shirner, *The Reformatsky Reaction*, ed. Scott E. Denmark, Wiley, Hoboken, 2011, ch. 1, pp. 1–37.

9 (*a*) S. Hesse and G. Kirsch, *Tetrahedron Lett.*, 2002, **43**, 1213; (*b*) Y. Takeuchi, N. Ueda, K. Uesugi, H. Abe, H. Nishioka and T. Harayama, *Heterocycles*, 2003, **59**, 217; (*c*) D. Maes, S. Vervisch, S. Debenedetti, C. Davio, S. Mangelinckx, N. Giubellina and N. De Kimpe, *Tetrahedron*, 2005, **61**, 2505; (*d*) J.-C. Tsai, S.-R. Li, M. Y. Chiang, L.-Y. Chen, P.-Y. Chen, Y.-F. Lo, C.-H. Wang, C.-N. Lin and E.-C. Wang, *J. Org. Chem.*, 2009, **74**, 8798.

10 (*a*) C. C. C. Johansson Seechurn, M. O. Kitching, T. J. Colacot and V. Snieckus, *Angew. Chem., Int. Ed.*, 2012, **51**, 5062, (*Angew. Chem.*, 2012, **124**, 5150); (*b*) Priyanka, R. K. Sharma and D. Katiyar, *Synthesis*, 2016, **48**, 2303; (*c*) J. Oyamada and T. Kitamura, *Tetrahedron*, 2006, **62**, 6918.

11 For selected Pd(II)-catalyzed synthesis of coumarins, see: (*a*) B. M. Trost and F. D. Toste, *J. Am. Chem. Soc.*, 1996, **118**, 6305; (*b*) C.-G. Jia, D.-G. Piao, J. Oyamada, W.-J. Lu, T. Kitamura and Y. Fujiwara, *Science*, 2000, **287**, 1992; (*c*) D. V. Kadnikov and R. C. Larock, *Org. Lett.*, 2000, **2**, 3643; (*d*) B. M. Trost, F. D. Toste and K. Greenman, *J. Am. Chem. Soc.*, 2003, **125**, 4518; (*e*) L. Zhang, T.-H. Meng, R.-H. Fan and J. Wu, *J. Org. Chem.*, 2007, **72**, 7279; (*f*) T. D. A. Fernandes, B. Gontijo Vaz, M. N. Eberlin, A. J. M. Silva and P. R. R. Costa, *J. Org. Chem.*, 2010, **75**, 7085; (*g*) J. Ferguson, F.-L. Zeng and H. Alper, *Org. Lett.*, 2012, **14**, 5602; (*h*) X.-F. Wu, L.-P. Wu, R. Jackstell, H. Neumann and M. Beller, *Chemistry*, 2013, **19**, 12245; (*i*) D. Kim, M. Min and S. Hong, *Chem. Commun.*, 2013, 4021; (*j*) U. Sharma, T. Naveen, A. Maji, S. Manna and D. Maiti, *Angew. Chem.*, 2013, **125**, 12901, (*Angew. Chem., Int. Ed.*, 2013, **52**, 12669); (*k*) M. Amézquita-Valencia and H. Alper, *Org. Lett.*, 2014, **16**, 5827.

12 H. Tan, H.-J. Li, J.-W. Wang and L. Wang, *Chem. – Eur. J.*, 2015, **21**, 1904.

13 A. Seoane, N. Casanova, N. Quiñones, J. L. Mascareñas and M. Gulías, *J. Am. Chem. Soc.*, 2014, **136**, 834.

14 For selected Cu-catalyzed synthesis of coumarins, see: H.-J. Yuan, M. Wang, Y.-J. Liu and Q. Liu, *Adv. Synth. Catal.*, 2009, **351**, 112.

15 (*a*) D. L. Boger and R. J. Mathvink, *J. Am. Chem. Soc.*, 1990, **112**, 4008; (*b*) C. Chatgilialoglu, D. Crich, M. Komatsu and I. Ryu, *Chem. Rev.*, 1999, **99**, 1991; (*c*) S. Tang, P. Wang, H.-R. Li and A.-W. Lei, *Nat. Commun.*, 2016, **7**, 11676; (*d*) H. Yi, G.-T. Zhang, H.-M. Wang, Z.-Y. Huang, J. Wang, A. K. Singh and A.-W. Lei, *Chem. Rev.*, 2017, **117**, 9016; (*e*) H. Miyabe, *Eur. J. Org. Chem.*, 2017, 3302; (*f*) J. K. Matsui, S. B. Lang, D. R. Heitz and G. A. Molander, *ACS Catal.*, 2017, **7**, 2563; (*g*) S. Chaabouni, F. Simonet, A. François, S. Abid, C. Galaup and S. Chassaing, *Eur. J. Org. Chem.*, 2017, 271; (*h*) J. Twilton, C. Le, P. Zhang, M. H. Shaw, R. W. Evans and D. W. C. MacMillan, *Nat. Rev. Chem.*, 2017, **1**, 0052.

16 S.-Y. Ni, J. Zhou, H.-B. Mei and J.-L. Han, *Tetrahedron Lett.*, 2018, **59**, 1309.

17 For selected thermal controlled synthesis of coumarins, see: (*a*) X. Mi, C.-Y. Wang, M.-M. Huang, Y.-S. Wu and Y.-J. Wu, *J. Org. Chem.*, 2015, **80**, 148; (*b*) K.-L. Yan, D.-S. Yang, W. Wei, F. Wang, Y.-Y. Shuai, Q.-N. Li and H. Wang, *J. Org. Chem.*, 2015, **80**, 1550; (*c*) T. Liu, Q.-P. Ding, Q.-S. Zong and G.-Y.-S. Qiu, *Org. Chem. Front.*, 2015, **2**, 670; (*d*) Y.-W. Li, Y. Lu, G.-Y.-S. Qiu and Q.-P. Ding, *Org. Lett.*, 2014, **16**, 4240; (*e*) X. Mi, C.-Y. Wang, M.-M. Huang, J.-Y. Zhang, Y.-S. Wu and Y.-J. Wu, *Org. Lett.*, 2014, **16**, 3356; (*f*) W. Wei, J.-W. Wen, D.-S. Yang, M.-Y. Guo, Y.-Y. Wang, J.-M. You and H. Wang, *Chem. Commun.*, 2015, 768; (*g*) C.-D. Pan, R.-Z. Chen, W.-L. Sha and J.-T. Yu, *Org. Biomol. Chem.*, 2016, **14**, 9033; (*h*) G.-Y.-S. Qiu, T. Liu and Q.-P. Ding, *Org. Chem. Front.*, 2016, **3**, 510; (*i*) Y.-F. Zeng, D.-H. Tan, Y.-Y. Chen, W.-X. Lv, X.-G. Liu, Q.-J. Li and H.-G. Wang, *Org. Chem. Front.*, 2015, **2**, 1511; (*j*) T. Liu, Q.-P. Ding, G.-Y.-S. Qiu and J. Wu, *Tetrahedron*, 2016, **72**, 279; (*k*) W.-C. Gao, T. Liu, B. Zhang, X. Li, W.-L. Wei, Q. Liu, J. Tian and H.-H. Chang, *J. Org. Chem.*, 2016, **81**, 11297; (*l*) D.-Q. Zheng, J.-Y. Yu and J. Wu, *Angew. Chem., Int. Ed.*, 2016, **55**, 11925, (*Angew. Chem.*, 2016, **128**, 12104); (*m*) Y.-L. Yu, S.-Y. Zhuang, P. Liu and P.-P. Sun, *J. Org. Chem.*, 2016, **81**, 11489; (*n*) W.-Q. Wu,

Y.-N. An, J.-X. Li, S.-R. Yang and H.-F. Jiang, *Org. Chem. Front.*, 2017, **4**, 1751.

18 For selected photonic energy induced synthesis of coumarins, see: (*a*) K. Kawaai, T. Yamaguchi, E. Yamaguchi, S. Endo, N. Tada, A. Ikari and A. Itoh, *J. Org. Chem.*, 2018, **83**, 1988; (*b*) S. Yang, H. Tan, W.-Q. Ji, X.-B. Zhang, P.-H. Li and L. Wang, *Adv. Synth. Catal.*, 2017, **359**, 443; (*c*) W.-C. Yang, S. Yang, P.-H. Li and L. Wang, *Chem. Commun.*, 2015, 7520; (*d*) W.-J. Fu, M. Zhu, G.-L. Zou, C. Xu, Z.-Q. Wang and B.-M. Ji, *J. Org. Chem.*, 2015, **80**, 4766; (*e*) S.-Y. Ni, J. Cao, H.-B. Mei, J.-L. Han, S.-H. Li and Y. Pan, *Green Chem.*, 2016, **18**, 3935; (*f*) S.-B. Fen, X.-G. Xie, W.-W. Zhang, L. Liu, Z.-L. Zhong, D.-Y. Xu and X.-G. She, *Org. Lett.*, 2016, **18**, 3846; (*g*) M. Zhu, W.-J. Fu, Z.-Q. Wang, C. Xu and B.-M. Ji, *Org. Biomol. Chem.*, 2017, **15**, 9057; (*h*) S.-B. Feng, J.-L. Li, Z.-M. Liu, H.-Y. Sun, H.-L. Shi, X.-L. Wang, X.-G. Xie and X.-G. She, *Org. Biomol. Chem.*, 2017, **15**, 8820; (*i*) Z.-K. Chen, N.-W. Liu, M. Bolte, H.-G. Ren and G. Manolikakes, *Green Chem.*, 2018, **20**, 3059.

19 (*a*) S. Massa, F. Corelli, M. Artico, A. Mai, R. Ragno, A. De Montis, A. G. Loi, S. Corrias, M. E. Marongiu and P. L. Colla, *J. Med. Chem.*, 1995, **38**, 803; (*b*) C. Ibis, A. F. Tuyun, Z. Ozsoy-Gunes, H. Bahar, M. V. Stasevych, R. Y. Musyanovych, O. Komarovska-Porokhnyavets and V. Novikov, *Eur. J. Med. Chem.*, 2011, **46**, 5861; (*c*) H. F. Motiwala, C. Fehl, S.-W. Li, E. Hirt, P. Porubsky and J. Aubé, *J. Am. Chem. Soc.*, 2013, **135**, 9000.

20 This crystal (**4k**) was deposited at the Cambridge Crystallographic Data Centre and assigned as CCDC 1841007† (https: //www.ccdc.cam.ac.uk/).

21 H. Sun, Y. Zhang, F. Guo, Y. Yan, C. Wan, Z. Zha and Z. Wang, *Eur. J. Org. Chem.*, 2012, 480.

