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Palladium-Catalyzed Carbonylation of Coumarin C(sp^2)–H Bonds: A New Entry to Arylcoumarin Ketones

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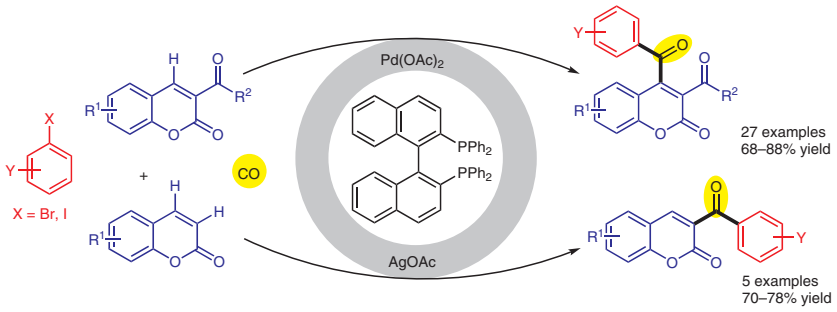

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Abstract A facile and efficient palladium-catalyzed carbonylation of coumarins involving two C–C bond formations has been developed. The C–H bond oxidative functionalization proceeds through aroylation with insertion of carbon monoxide to give arylcoumarin ketones. The reaction conditions, employing ambient pressures of CO gas as C1 feedstock, dramatically improve the generality of the carbonylation of aryl halides.

Key words Pd catalysis, carbonylation, arylcoumarin ketones, aryl halides, carbon monoxide.

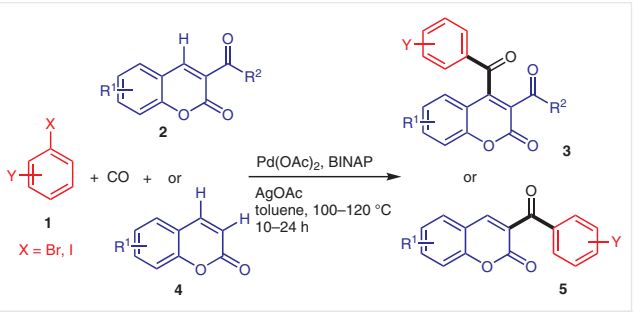
The coumarin core is a key structural motif and an essential component for the preparation of a wide range of natural products and pharmaceutically active substances.[1] The coumarin molecule has been shown to possess unique biological activity such as antitumor,[2] anticancer,[3] anti-HIV,[4] anti-inflammatory,[5] antibacterial,[6] vasorelaxant,[7] antiviral,[8] enzymatic inhibitors,[9] anti-inflammatory,[10] antimicrobial,[11] anti-Alzheimer's[12] and anti-malarial activities.[13]

The construction of C–C bonds has been recognized as one of the basic yet crucial elements to synthesize a variety of organic compounds.[14] In this respect, increased attention has been paid to the development of novel and efficient approaches towards C–C bond formation.[15] Over the last few decades, transition-metal-catalyzed reactions have emerged as one of the most promising and rapidly expanding fields for the construction of C–C bonds,[16] in which the palladium-catalyzed variants have been particularly prominent.[17] It is worth noting that palladium-catalyzed reactions have experienced a tremendous surge in development for the assembly of a wide range of important molecules and densely functionalized heterocycles in agricultural, pharmaceutical, and natural product chemistry from relatively simple starting compounds.

Carbonylation of organic compounds with CO as readily available C1 feedstock has continued to be an effective strategy in both scientific research and chemical industries. Indeed, this system has proven to provide a practical carbonyl source for the preparation of carboxylic acid derivatives, aldehydes, and ketones, which are important synthetic intermediates in organic synthesis and are indispensable for applications in advanced materials, dyes, pharmaceuticals, agrochemicals, and other industrial products.[18]

Palladium-catalyzed carbonylation reactions, via C–X (X= I, Br, H, etc.) activation and functionalization with carbon monoxide has emerged as an important approach to construct more-functionalized organic molecules.[19] The archetype for today's Pd-catalyzed carbonylations is the well-known 'Wacker Process', which was developed in the late 1950s for the synthesis of acetaldehyde from ethylene in the presence of Pd(II) and Cu(II) salts. Utilization of aryl halides[20] or pseudoaryl halides (aryl triflates,[21] tosylates,[22] phosphates,[23] and other reagents[24]) as electrophilic coupling partners in palladium-catalyzed carbonylation reactions remain in great demand. We have recently reported an alternative route to construct 3- and 4-aroylcoumarin via oxidative cross-dehydrogenative coupling reactions.[25] Herein, we report the first general and efficient protocol for the carbonylation of coumarins with aryl halides, leading to

arylcoumarin ketones as the principal reaction products, using palladium catalyst under CO at atmospheric pressure (Scheme 1).



Scheme 1 Pd-catalyzed carbonylation of coumarins with aryl halides

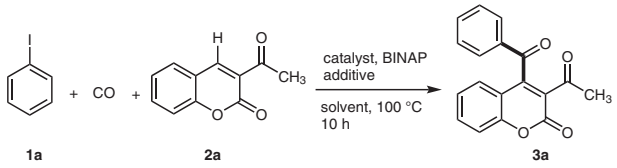
We began our study by investigating the Pd-catalyzed carbonylation of iodobenzene **1a** and 3-acetyl-2*H*-chromen-2-one **2a** under 1 atm CO. For the construction of **3a**, several parameters, such as catalysts, additives, solvents, and ligands were screened. Firstly, different additives such as a variety of potassium salts (e.g., K_2CO_3, KOH, K_3PO_4, and *t*-BuOK), Ag salts (e.g., AgOAc, and Ag_2O), 1,4-BQ, $K_2S_2O_8$, and $Mn(OAc)_2$ were examined. Screening of the additives showed that AgOAc is the best choice of additive and gave the desired carbonylation product **3a** in 87% yield (Table 1, entry 5). Other additives such as K_3PO_4, 1,4-BQ, and $Mn(OAc)_2$ exhibited less reactivity, providing **3a** in 36, 5, and 40% yields, respectively. Furthermore, K_2CO_3, KOH, Ag_2O, and $K_2S_2O_8$ were totally ineffective to this reaction (entries 1–3 and 7–8). Subsequently, we evaluated the effect of various palladium catalysts. No desired product **3a** was detected when $PdCl_2$ was used as the catalyst instead of $Pd(OAc)_2$ (entry 10).

Further screening of the catalyst revealed that $Pd(OAc)_2$ was a more effective catalyst for direct carbonylation reaction than $Pd(OPiv)_2$, $PdCl_2(PPh_3)_2$, and $Pd(dba)_2$ (Table 1, entry 11–13). Next, the effect of different solvents such as *o*-xylene, CH_3CN, PhCl, 1,4-dioxane, and DMSO on the efficiency of the reaction was tested. However, carrying out the reaction in *o*-xylene, CH_3CN, PhCl, and DMSO led to a decrease in the yield of **3a**, and in 1,4-dioxane **3a** was not detected (entries 14–18). The importance of the palladium, BINAP, and the AgOAc source was clearly demonstrated because the reaction simply fails in the absence of one of them (entries 19–21). It is worth noting that the yield dropped greatly after the use of PPh_3, PCy_3, and 1,10-phenanthroline instead of BINAP (entries 22–24).

With the optimized reaction conditions in hand, we next focused on the substrate scope of the carbonylation of 3-substituted coumarins with aryl halides to determine the potential and general applicability of this reaction. The results are summarized in Scheme 2. Various iodobenzenes with electronically neutral and electron-donating groups, such as *p*-methyl, *p*-isopropyl, and *o*-, *m*- and *p*-methoxy on the benzene ring gave the desired product **3a–f** in 75–88% yield. The 1-chloro-4-iodobenzene also underwent the reaction and produced the corresponding product **3g** with a yield of 75%. Furthermore, when a heteroaryl iodide such as 2-iodothiophene was used as substrate, the desired product **3h** was obtained in 80% yield after 12 h.

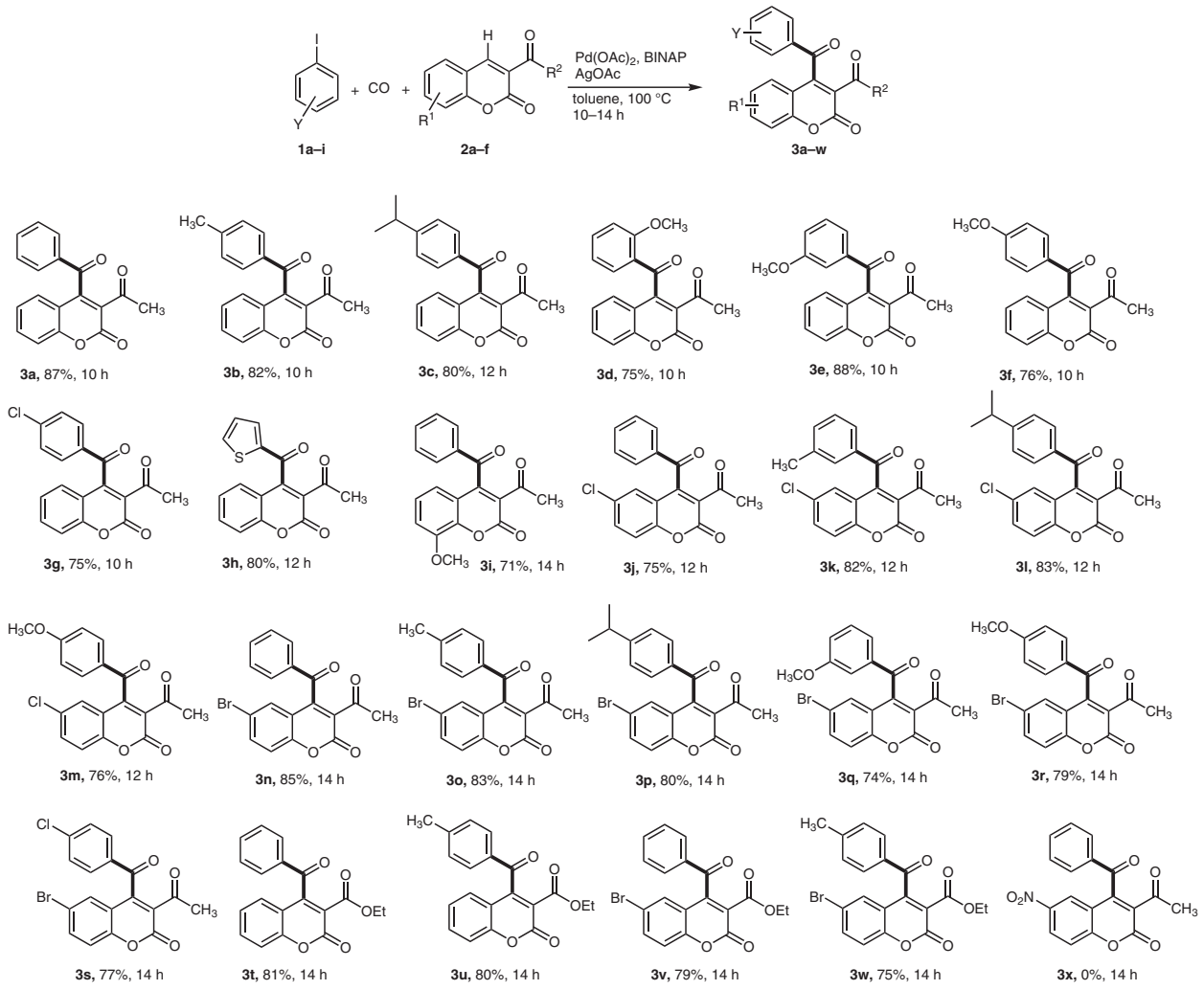
The effect of various substituents on 3-acetylcoumarins was then examined. Generally, coumarins possessing either an electron-donating substituent (8-OMe) or an electron-withdrawing substituent (6-Cl and 6-Br) were well tolerat-

Table 1 Optimization of Reaction Conditions[a]



Entry	[Pd]	Additive	Solvent	Yield (%)[b]
1	$Pd(OAc)_2$	K_2CO_3	$PhCH_3$	n.d.
2	$Pd(OAc)_2$	KOH	$PhCH_3$	n.d.
3	$Pd(OAc)_2$	*t*-BuOK	$PhCH_3$	n.d.
4	$Pd(OAc)_2$	K_3PO_4	$PhCH_3$	36
5	$Pd(OAc)_2$	AgOAc	$PhCH_3$	87
6	$Pd(OAc)_2$	1,4-BQ	$PhCH_3$	5
7	$Pd(OAc)_2$	Ag_2O	$PhCH_3$	n.d.
8	$Pd(OAc)_2$	$K_2S_2O_8$	$PhCH_3$	n.d.
9	$Pd(OAc)_2$	$Mn(OAc)_2$	$PhCH_3$	40
10	$PdCl_2$	AgOAc	$PhCH_3$	n.d.
11	$Pd(OPiv)_2$	AgOAc	$PhCH_3$	58
12	$PdCl_2(PPh_3)_2$	AgOAc	$PhCH_3$	25
13	$Pd(dba)_2$	AgOAc	$PhCH_3$	33
14	$Pd(OAc)_2$	AgOAc	*o*-xylene	15
15	$Pd(OAc)_2$	AgOAc	CH_3CN	trace
16	$Pd(OAc)_2$	AgOAc	PhCl	54
17	$Pd(OAc)_2$	AgOAc	1,4-Dioxane	n.d.
18	$Pd(OAc)_2$	AgOAc	DMSO	70
19	–	AgOAc	$PhCH_3$	n.d.
20	$Pd(OAc)_2$	–	$PhCH_3$	n.d.
21[c]	$Pd(OAc)_2$	AgOAc	$PhCH_3$	n.d.
22[d]	$Pd(OAc)_2$	AgOAc	$PhCH_3$	18
23[e]	$Pd(OAc)_2$	AgOAc	$PhCH_3$	25
24[f]	$Pd(OAc)_2$	AgOAc	$PhCH_3$	<5

[a] Reaction conditions: **1a** (0.33 mmol), **2a** (0.3 mmol), catalyst (10 mol %), BINAP (10 mol%), additive (2 equiv), solvent (2 mL), CO (1 atm), at 100 °C for 10 h in a sealed reaction tube.
[b] Isolated yield.
[c] Reaction was carried out in the absence of BINAP.
[d] 20 mol% PPh_3 was used instead of BINAP.
[e] 20 mol% PCy_3 was used instead of BINAP.
[f] 10 mol% 1,10-phenanthroline was used instead of BINAP.



Scheme 2 Carbonylation of aryliodides with a range of 3-acetyl coumarins. *Reaction conditions*: **1** (0.33 mmol), **2** (0.3 mmol), $Pd(OAc)_2$ (10 mol %), BINAP (10 mol%), AgOAc (2 equiv), toluene (2 mL), CO (1 atm), at 100 °C for 10–14 h in a sealed reaction tube. Isolated yields are given.

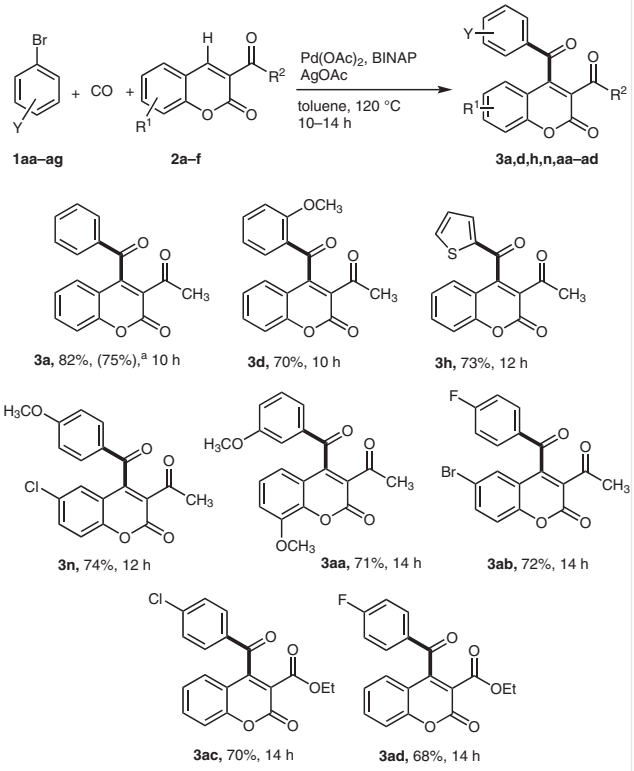
ed, affording the corresponding products **3i–s** in 71–85% yields after 12–14 h. Furthermore, this methodology is compatible with the reaction of ethyl 2-oxo-2*H*-chromene-3-carboxylate and ethyl 6-bromo-2-oxo-2*H*-chromene-3-carboxylate with iodobenzene derivatives and gave the desired products **3t–w** after 14 h in 75–81% yields. Unfortunately, the electron-deficient coumarin bearing a nitro group was not tolerated under the carbonylation reaction conditions (**3x**).

Application of this carbonylation approach using 3-acetyl coumarins was then performed with a range of aryl bromides (Scheme 3). Aryl iodides required a temperature of 100 °C, whereas aryl bromides required a temperature of 120 °C for complete conversion. Gratifyingly, 2-bromoanisole as less hindered compound can be reacted successfully in carbonylation reaction (**3d**).

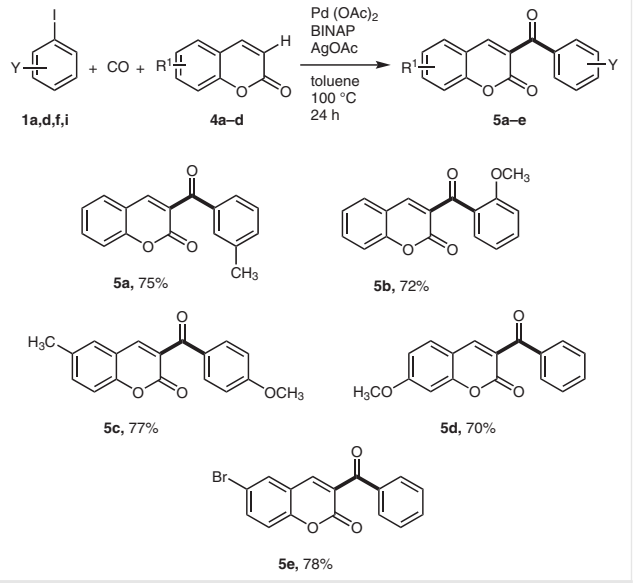
We further explored the scope of this carbonylation by using simple coumarins **4a–d** instead of 3-substituted coumarins. Under the same reaction conditions for 24 h, 3-aroylcoumarins **5a–e** were obtained in satisfactory yields through C3 regioselective carbonylation reaction (Scheme 4).

The gram-scale reaction of 3-acetyl-4-benzoyl coumarin **3a** was achieved in 69% yield by using 10 mol% $Pd(OAc)_2$, AgOAc (2 equiv), CO (1 atm), and toluene at 100 °C for 24 h (Scheme 5).

A possible mechanism for the Pd-catalyzed carbonylation of 3-acetylcoumarin **2a** in the presence of iodobenzene **1a** is outlined in Scheme 6. The reaction started with Pd(0), which undergoes oxidative addition with iodobenzene **1a** to give organopalladium species **A**, which undergoes coordination of CO into the palladium to generate coordinate complex **B**. The insertion of carbon monoxide into the Pd–C

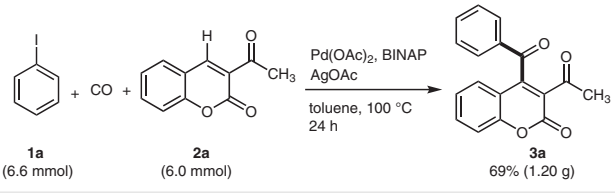


Scheme 3 Carbonylation of aryl bromides with a range of 3-acetyl coumarins. Reaction condition: **1** (0.33 mmol), **2** (0.3 mmol), $Pd(OAc)_2$ (10 mol %), BINAP (10 mol%), AgOAc (2 equiv), toluene (2 mL), CO (1 atm), at 120 °C for 10–14 h in a sealed reaction tube. Isolated yields are given. [a] Reaction was carried out at 100 °C for 10 h.

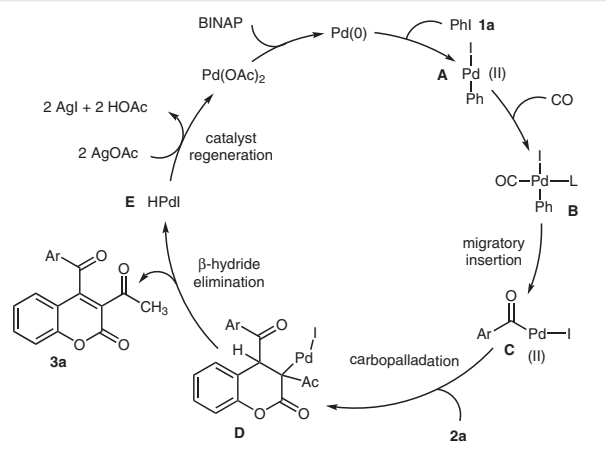


Scheme 4 Reaction scope of 3-aroylcoumarin derivatives. *Reaction conditions*: **1a** (6.6 mmol), **2a** (6 mmol), $Pd(OAc)_2$ (10 mol%), BINAP (10 mol%), AgOAc (2 equiv), a balloon filled with CO in toluene (30 mL) at 100 °C for 24 h. Isolated yields are given.

bond furnishes an acylpalladium complex **C**. Next, carbonyl palladation at the β-position of 3-acetylcoumarin **2a** through migratory insertion occurs, leading to the formation of the intermediate **D**. Product **3a** is released through β-hydride elimination, generating the H–Pd(II)–I species **E**. Silver acetate then serves as a halophile agent in the catalyst regeneration step.[26] Eventually, a reductive elimination by the BINAP at the $Pd(OAc)_2$ affords the active catalyst Pd(0).



Scheme 5 *Reaction conditions*: **1a** (6.6 mmol), **2a** (6 mmol), $Pd(OAc)_2$ (10 mol%), BINAP (10 mol%), AgOAc (2 equiv), a balloon filled with CO in toluene (30 mL) at 100 °C for 24 h.



Scheme 6 Possible mechanism of Pd-catalyzed carbonylation reaction

In summary, we have demonstrated a new and efficient method for the preparation of 4-aroylcoumarin and 3-aroylcoumarin derivatives. The palladium-catalyzed direct carbonylation allows for the transformation of aryl iodides and aryl bromides into the corresponding arylcoumarin ketones under atmospheric CO pressure. Reactions proceed in toluene solvent in the presence of AgOAc as a driving force through carbonylation of iodo/bromo arenes and coumarins via one C–I and C–H bond cleavage, and two C–C bond formation processes. The reaction tolerates a variety of aroylcoumarin substrates and proceeds in good yields.

All reactions were carried out in an oven-dried Schlenk tube under a carbon monoxide atmosphere with a balloon. 3-Substituted coumarins were synthesized according to reported procedures.[27] Toluene

was dried and distilled from Na under vacuum. All chemicals were purchased from Merck (Germany) and were used without further purification. Melting points were measured with an Electrothermal 9100 apparatus and are uncorrected. FTIR spectra were obtained with a Unicom Galaxy Series FTIR 5000 spectrophotometer. ^{1}H and ^{13}C NMR spectra were measured ($CDCl_3$ solution with TMS as an internal standard) with Bruker DRX-500 AVANCE (at 500.1 and 125.8 MHz, resp.), Bruker DRX-400 AVANCE III (at 400.1 and 100.6 MHz, resp.), instruments. Elemental analyses for C and H were performed with an ECS 4010 CHNSO analyzer. Chromatography columns were prepared from Merck silica gel 230–240 meshes.

Synthesis of 3-Substituted 4-Aroylcoumarins (3); General Procedure

In an oven-dried Schlenk tube equipped with a stir bar, 3-substituted coumarin **2** (0.3 mmol), iodoaren **1** (0.33 mmol), $Pd(OAc)_2$ (10 mol%, 0.0067 g), BINAP (10 mol%, 0.0186 g), and AgOAc (0.6 mmol, 0.1 g), a balloon filled with CO (1 atm) was connected to the Schlenk tube by the side tube and the system was purged three times. Toluene (2 mL) was then added to the tube by using a syringe. The Schlenk tube was heated at 100 °C for 10 h. When the reaction was complete (detected by TLC), the mixture was cooled to r.t., and the reaction was quenched with H_2O (10 mL) and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and evaporated in vacuum. The residue was purified by column chromatography on silica gel to afford the corresponding product **3**.

3-Acetyl-4-benzoyl-2*H*-chromen-2-one (3a)[28a]

Isolated yield: 0.076 g (87%); pale-yellow solid; m.p. 180–182 °C [lit.[28a] 182–183 °C].

IR (KBr): 3080, 3009, 2975, 2921, 1718, 1671, 1599, 1552, 1468, 1350, 1185, 745 cm^{-1}.

^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.87 (dd, *J* = 7.15, 1.3 Hz, 2 H), 7.63–7.65 (m, 2 H), 7.45–7.53 (m, 3 H), 7.23–7.29 (m, 2 H), 2.68 (s, 3 H).

3-Acetyl-4-(4-methylbenzoyl)-2*H*-chromen-2-one (3b)[28a]

Isolated yield: 0.075 g (82%); light-yellow solid; m.p. 194–196 °C [lit.[28a] 199–200 °C].

IR (KBr): = 3107, 3075, 2949, 2846, 1716, 1672, 1597, 1534, 1467, 1253, 1174, 1020, 766, 731, 574 cm^{-1}.

^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 8.1 Hz, 2 H), 7.67 (ddd, *J* = 8.6, 7.2, 1.6 Hz, 1 H), 7.45 (d, *J* = 8.0 Hz, 1 H), 7.30–7.32 (m, 3 H), 7.24 (td, *J* = 7.6, 0.8 Hz, 1 H), 2.67 (s, 3 H, CH_3), 2.44 (s, 3 H, CH_3),

3-Acetyl-4-(4-isopropylbenzoyl)-2*H*-chromen-2-one (3c)[25b]

Isolated yield: 0.080 g (80%); white solid; m.p. 186–189 °C [lit.[25b] 188–190 °C].

IR (KBr): = 3073, 2966, 2871, 1662, 1607, 1547, 1267, 106, 769 cm^{-1}.

^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.79 (d, *J* = 8.3 Hz, 2 H), 7.68 (ddd, *J* = 8.6, 7.4, 1.5 Hz, 1 H), 7.46 (d, *J* = 8.3 Hz, 1 H), 7.35 (d, *J* = 8.4 Hz, 2 H), 7.32 (dd, *J* = 8.0, 1.5 Hz, 1 H), 2.99 (m, *J* = 6.9 Hz, 1 H), 7.25 (m, 1 H), 2.68 (s, 3 H, CH_3), 1.29 (d, *J* = 6.9 Hz, 6 H, 2 × CH_3).

3-Acetyl-4-(2-methoxybenzoyl)-2*H*-chromen-2-one (3d)

Isolated yield: 0.072 g (75%); white solid; m.p. 185–186 °C.

IR (KBr): = 3068, 2949, 2847, 1743, 1677, 1659, 1594, 1546, 1283, 1253, 1002, 764 cm^{-1}.

^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 8.22 (dd, *J* = 7.8, 1.4 Hz, 1 H), 7.59–7.66 (m, 2 H), 7.43 (d, *J* = 8.3 Hz, 1 H), 7.29 (dd, *J* = 8.1, 1.1 Hz, 1 H), 7.17–7.23 (m, 2 H), 6.93 (d, *J* = 8.3 Hz, 1 H), 3.50 (s, 3 H, OCH_3), 2.66 (s, 3 H, CH_3).

^{13}C NMR (125.8 MHz, $CDCl_3$): δ = 196.5, 191.4, 161.1, 159.7, 159.6, 154.7, 136.0, 134.2, 130.4, 127.6, 125.3, 124.9, 121.6, 118.9, 117.2, 117.0, 112.5, 55.7, 30.9.

Anal. Calcd for $C_{19}H_{15}O_5$: C, 70.80; H, 4.38; Found: C, 70.64, H, 4.29.

3-Acetyl-4-(3-methoxybenzoyl)-2*H*-chromen-2-one (3e)[25b]

Isolated yield: 0.085 g (88%); pale-yellow solid; m.p. 120–122 °C [lit.[25b] 120–121 °C].

IR (KBr): 3080, 3041, 2969, 2835, 1740, 1681, 1594, 1539, 1266, 1041, 764 cm^{-1}.

^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.68 (ddd, *J* = 8.5, 7.3, 1.6 Hz, 1 H), 7.53 (s, 1 H), 7.45 (d, *J* = 8.3 Hz, 1 H), 7.36 (t, *J* = 7.8 Hz, 1 H), 7.23–7.31 (m, 3 H), 7.18 (ddd, *J* = 8.1, 2.2, 0.65 Hz, 1 H), 3.89 (s, 3 H, OCH_3), 2.68 (s, 3 H, CH_3).

3-Acetyl-4-(4-methoxybenzoyl)-2*H*-chromen-2-one (3f)[25b]

Isolated yield: 0.073 g (76%); pale-yellow solid; m.p. 150–152 °C [lit.[25b] 154–155 °C].

IR (KBr): 3093, 3010, 2978, 2923, 1722, 1670, 1608, 1535, 1245, 1179, 1008, 762 cm^{-1}.

^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 8.5 Hz), 7.67 (td, *J* = 8.5, 1.5 Hz, 1 H), 7.46 (d, *J* = 8.0 Hz, 1 H), 7.32 (dd, *J* = 8.0, 1.5 Hz), 7.24 (td, *J* = 7.6, 0.7 Hz, 1 H), 3.90 (s, 3 H, OCH_3), 2.67 (s, 3 H, CH_3).

3-Acetyl-4-(4-chlorobenzoyl)-2*H*-chromen-2-one (3g)[28a]

Isolated yield: 0.073 g (75%); yellow solid; m.p. 236–237 °C [lit.[28a] 239–240 °C].

IR (KBr): 3087, 2921, 1739, 1676, 1585, 1538, 1360, 1230, 1004, 759 cm^{-1}.

^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 8.5 Hz, 2 H), 7.69–7.73 (m, 1 H), 7.49 (d, *J* = 8.6 Hz, 2 H), 7.47 (d, *J* = 8.0 Hz, 1 H), 7.27 (d, *J* = 4.1 Hz, 2 H), 2.70 (s, 3 H, CH_3).

3-Acetyl-4-(thiophene-2-carbonyl)-2*H*-chromen-2-one (3h)[28a]

Isolated yield: 0.071 g (80%); pale-yellow solid; m.p. 150–153 °C [lit. 158–159 °C].

IR (KBr): 3093, 2927, 1725, 1690, 162, 1539, 1413, 1263, 1227, 1026, 765 cm^{-1}.

^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.82 (dd, *J* = 4.9, 1.0 Hz, 1 H), 7.70 (ddd, *J* = 8.6, 7.3, 1.6 Hz, 1 H), 7.42–7.47 (m, 3 H), 7.29 (td, *J* = 7.19, 1 Hz, 1 H), 7.14 (dd, *J* = 4.8, 3.9 Hz, 1 H), 2.69 (s, 3 H, CH_3).

3-Acetyl-4-benzoyl-8-methoxy-2*H*-chromen-2-one (3i)[25b]

Isolated yield: 0.068 g (71%); yellow solid; m.p. 190–192 °C [lit. 188–190 °C].

IR (KBr): 3083, 3048, 2945, 2842, 1732, 1684, 1672, 1542, 1467, 1281, 1249, 941, 76, 716 cm^{-1}.

^{1}H NMR (400.1 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 7.4 Hz, 2 H), 7.64 (t, *J* = 7.4 Hz, 1 H), 7.51 (t, *J* = 7.7 Hz, 2 H), 7.22 (dd, *J* = 8.1, 1.3 Hz, 1 H), 7.17 (t, *J* = 8.0 Hz, 1 H), 6.85 (dd, *J* = 7.7, 1.1 Hz, 1 H), 4.03 (s, 3 H, OCH_3), 2.69 (s, 3 H, CH_3).

3-Acetyl-4-benzoyl-6-chloro-2*H*-chromen-2-one (3j)[25b]

Isolated yield: 0.073 g (75%); white solid; m.p. 187–189 °C [lit.[25b] 186–188 °C].

IR (KBr): 3065, 2977, 2881, 1720, 1677, 1590, 1426, 1269, 772 cm^{-1}.

^1H NMR (500.1 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 8.9 Hz, 2 H), 7.72 (t, *J* = 7.1 Hz, 1 H), 7.68 (dd, *J* = 8.8, 2.3 Hz, 1 H), 7.59 (t, *J* = 7.7 Hz, 2 H), 7.47 (d, *J* = 8.8 Hz, 1 H), 7.31 (d, *J* = 2.3 Hz, 1 H), 2.72 (s, 3 H).

3-Acetyl-6-chloro-4-(3-methylbenzoyl)-2*H*-chromen-2-one(3k)[25b]

Isolated yield: 0.084 g (82%); pale-yellow solid; m.p. 186–188 °C [lit.[25b] 192–194 °C].

IR (KBr): 3082, 2981, 2885, 1718, 1672, 1585, 1436, 1273, 780 cm^{-1}.

^1H NMR (500.1 MHz, $CDCl_3$): δ = 7.78 (s, 1 H), 7.68 (dd, *J* = 8.9, 2.4 Hz, 1 H), 7.65 (d, *J* = 7.7 Hz, 1 H), 7.54 (d, *J* = 7.5 Hz, 1 H), 7.47 (d, *J* = 8.9 Hz, 1 H), 7.45 (t, *J* = 7.6 Hz, 1 H), 7.31 (d, *J* = 2.3 Hz, 1 H), 2.72 (s, 3 H, CH_3), 2.50 (s, 3 H, CH_3).

3-Acetyl-6-chloro-4-(4-isopropylbenzoyl)-2*H*-chromen-2-one (3l)[25b]

Isolated yield: 0.092 g (83%); pale-yellow solid; m.p. 162–164 °C [lit.[25b] 162–164 °C].

IR (KBr): 3077, 2995, 2880, 1722, 1674, 1576, 1548, 1421, 1253, 765, 751 cm^{-1}.

^1H NMR (500.1 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 8.2 Hz, 2 H), 7.67 (dd, *J* = 8.8, 2.3 Hz, 1 H), 7.46 (d, *J* = 8.9 Hz, 1 H), 7.43 (d, *J* = 8.4 Hz, 2 H), 7.32 (d, *J* = 2.3 Hz, 1 H), 3.07 (sept, *J* = 6.9 Hz, 1 H), 2.72 (s, 3 H), 1.36 (d, *J* = 6.9 Hz, 6 H).

3-Acetyl-6-chloro-4-(4-methoxybenzoyl)-2*H*-chromen-2-one (3m)[25b]

Isolated yield: 0.081 g (76%); yellow solid; m.p. 199–201 °C [lit.[25b] 199–201 °C].

IR (KBr): 3091, 2995, 2888, 1732, 1670, 1573, 1532, 1449, 1281, 1266, 775 cm^{-1}.

^1H NMR (500.1 MHz, $CDCl_3$): δ = 7.89 (d, *J* = 8.4 Hz, 2 H), 7.66 (dd, *J* = 8.9, 2.4 Hz, 1 H), 7.46 (d, *J* = 8.9 Hz, 1 H), 7.32 (d, *J* = 2.3 Hz, 1 H), 7.05 (d, *J* = 8.9 Hz, 2 H), 3.97 (s, 3 H, CH_3), 2.71 (s, 3 H, CH_3).

3-Acetyl-4-benzoyl-6-bromo-2*H*-chromen-2-one (3n)

Isolated yield: 0.095 g (85%); light-yellow solid; m.p. 194–196 °C.

IR (KBr): 3044, 2978, 2877, 1735, 1724, 1676, 1601, 1554, 1233, 818, 728 cm^{-1}.

^1H NMR (400.1 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 7.2 Hz, 2 H), 7.75 (dd, *J* = 6.8, 2.2 Hz, 1 H), 7.67 (t, *J* = 7.5 Hz, 1 H), 7.53 (t, *J* = 7.8 Hz, 2 H), 7.38 (d, *J* = 2.2 Hz, 1 H), 7.34 (d, *J* = 8.9 Hz, 1 H), 2.65 (s, 3 H, CH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 191.6, 191.8, 157.0, 154.8, 152.4, 136.5, 134.0, 133.5, 129.3, 128.1, 127.4, 121.0, 117.7, 117.4, 117.0, 29.9.

Anal. Calcd for $C_{18}H_{11}BrO_4$: C, 58.25; H, 2.99; Found: C, 58.08, H, 3.10.

3-Acetyl-4-(4-methylbenzoyl)-6-bromo-2*H*-chromen-2-one (3o)[25b]

Isolated yield: 0.096 g (83%); pale-yellow solid; m.p. 180–182 °C [lit.[25b] 180–182 °C].

IR (KBr): 3052, 2981, 2876, 1732, 1719, 1675, 1614, 1553, 1228, 820, 725 cm^{-1}.

^1H NMR (400.1 MHz, $CDCl_3$): δ = 2.43 (s, 3 H, CH_3), 2.63 (s, 3 H, CH_3), 7.29–7.33 (m, *J* = 8.9 Hz, 3 H), 7.37 (d, *J* = 2.2 Hz, 1 H), 7.71–7.74 (m, 3 H).

3-Acetyl-6-bromo-4-(4-isopropylbenzoyl)-2*H*-chromen-2-one (3p)[25b]

Isolated yield: 0.099 g (80%); cream solid; m.p. 187–189 °C [lit.[25b] 188–190 °C].

IR (KBr): 3073, 2962, 2871, 1745, 1662, 1607, 1543, 1263, 1235, 1006, 828 cm^{-1}.

^1H NMR (400.1 MHz, $CDCl_3$): δ = 7.75–7.79 (m, 3 H), 7.41 (d, *J* = 2.2 Hz, 1 H), 7.38 (d, *J* = 8.4 Hz, 1 H), 7.36 (d, *J* = 8.9 Hz, 2 H), 3.0 (m, *J* = 6.9 Hz, 1 H), 2.67 (s, 3 H, CH_3), 1.3 (d, *J* = 6.9 Hz, 6 H, 2 × CH_3).

3-Acetyl-6-bromo-4-(3-methoxybenzoyl)-2*H*-chromen-2-one (3q)[25b]

Isolated yield: 0.089 g (74%); light-yellow solid; m.p. 169–171 °C [lit.[25b] 162–164 °C].

IR (KBr): 3045, 2923, 1749, 1678, 1603, 1547, 1231, 1010, 832, 773 cm^{-1}.

1 H NMR (400.1 MHz, $CDCl_3$): δ = 7.77 (dd, *J* = 8.8, 2.3 Hz, 1 H), 7.53 (br s, 1 H), 7.34–7.41 (m, 3 H), 7.26 (d, *J* = 7.6 Hz, 1 H), 7.21 (ddd, *J* = 8.3, 2.3, 0.7 Hz, 1 H), 3.92 (s, 3 H, OCH_3), 2.67 (s, 3 H, CH_3).

3-Acetyl-6-bromo-4-(4-methoxybenzoyl)-2*H*-chromen-2-one (3r)

Isolated yield: 0.095 g (79%); light-yellow solid; m.p. 171–172 °C.

IR (KBr): 3045, 2939, 2848, 1737, 1599, 1551, 1362, 1263, 1014, 832, 781 cm^{-1}.

^1H NMR (400.1 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 9.2 Hz, 2 H), 7.75 (dd, *J* = 8.8, 2.3 Hz, 1 H), 7.41 (d, *J* = 2.2 Hz, 1 H), 7.34 (d, *J* = 8.9 Hz, 1 H), 6.99 (d, *J* = 9.3 Hz, 2 H), 3.91 (s, 3 H, OCH_3), 2.65 (s, 3 H, CH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 194.8, 190.2, 163.7, 157.1, 154.5, 152.3, 136.3, 130.0, 129.4, 127.2, 121.4, 117.7, 117.5, 116.9, 113.5, 54.6, 29.9.

Anal. Calcd for $C_{19}H_{13}BrO_5$: C, 56.88; H, 3.27; Found: C, 56.66, H, 3.09.

3-Acetyl-6-bromo-4-(4-chlorobenzoyl)-2*H*-chromen-2-one (3s)[25b]

Isolated yield: 0.089 g (77%); yellow solid; m.p. 199–201 °C [lit.[25b] 197–200 °C].

IR (KBr): 3077, 2962, 2871, 1745, 1662, 1607, 1543, 1263, 1235, 1006, 828 cm^{-1}.

^1H NMR (400.1 MHz, $CDCl_3$): δ = 7.76–7.81 (m, 3 H), 7.51 (d, *J* = 8.7 Hz, 2 H), 7.35–7.37 (m, 2 H), 2.68 (s, 3 H, CH_3).

Ethyl 4-Benzoyl-2-oxo-2*H*-chromen-3-carboxylate (3t)[25b]

Isolated yield: 0.078 g (81%); white solid; m.p. 111–112 °C [lit. 111–112 °C].

IR (KBr): 3065, 2978, 2907, 1734, 1670, 1599, 1551, 1267, 1267, 1022, 713 cm^{-1}.

^1H NMR (400.1 MHz, $CDCl_3$): δ = 7.94 (dd, *J* = 8.4, 1.3 Hz, 2 H), 7.65–7.69 (m, 2 H), 7.54 (t, *J* = 8.1 Hz, 2 H), 7.45 (d, *J* = 8.6 Hz, 1 H), 7.24–7.30 (m, 2 H), 4.14 (q, *J* = 7.1 Hz, 2 H, OCH_2), 1.07 (t, *J* = 7.2 Hz, 3 H, CH_3).

Ethyl 4-(4-Methylbenzoyl)-2-oxo-2*H*-chromene-3-carboxylate (3u)[25b]

Isolated yield: 0.080 g (80%); white solid; m.p. 120–122 °C [lit.[25b] 121–123 °C].

IR (KBr): 3033, 2994, 2899, 1729, 1662, 1607, 1267, 1184, 1057, 1026, 761 cm^{-1}.

^1H NMR (400.1 MHz, $CDCl_3$): δ = 7.80 (d, *J* = 8.0 Hz, 2 H), 7.63 (ddd, *J* = 8.5, 1.6 Hz, 1 H), 7.42 (d, *J* = 8.3 Hz, 1 H), 7.31 (d, *J* = 8.0 Hz, 2 H), 7.26 (dd, *J* = 8.6, 1.5 Hz, 1 H), 7.21 (t, *J* = 7.7 Hz, 1 H), 4.12 (q, *J* = 7.1, 2 H, OCH_2), 2.44 (s, 3 H, CH_3), 1.06 (t, *J* = 7.1 Hz, 3 H, CH_3).

Ethyl 4-Benzoyl-6-bromo-2-oxo-2*H*-chromene-3-carboxylate (3v)

Isolated yield: 0.095 g (79%); cream solid; m.p. 138–140 °C.

IR (KBr): 3073, 2990, 2907, 1737, 1674, 1595, 1263, 1057, 820, 717 cm^{-1}.

^1H NMR (400.1 MHz, $CDCl_3$): δ = 7.90 (d, *J* = 7.3 Hz, 2 H), 7.67–7.74 (m, 2 H), 7.54 (t, *J* = 7.7 Hz, 2 H), 7.36 (d, *J* = 2.8 Hz, 1 H), 7.32 (dd, *J* = 8.9, 2.0 Hz, 1 H), 4.08 (q, *J* = 7.0 Hz, 2 H, OCH_2), 1.03 (t, *J* = 7.0 Hz, 3 H, CH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 190.2, 160.8, 154.7, 152.4, 152.0, 136.1, 134.0, 133.6, 128.6, 128.2, 128.0, 117.9, 117.4, 116.8, 61.5, 12.3.

Anal. Calcd for $C_{19}H_{13}BrO_5$: C, 56.88; H, 3.27; Found: C, 56.71, H, 3.42.

Ethyl 6-Bromo-4-(4-methylbenzoyl)-2-oxo-2*H*-chromene-3-carboxylate (3w)

Isolated yield: 0.093 g (75%); white solid; m.p. 140–141 °C.

IR (KBr): 3057, 2974, 2899, 1773, 1705, 1674, 1556, 1267, 1030, 820 cm^{-1}.

^1H NMR (400.1 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 8.0 Hz, 2 H), 7.74 (dd, *J* = 8.8, 2.3 Hz, 1 H), 7.32–7.39 (m, 4 H), 4.1 (q, *J* = 7.1 Hz, 2 H, OCH_2), 2.47 (s, 3 H, CH_3), 1.07 (t, *J* = 7.1 Hz, 3 H, CH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 189.8, 160.9, 154.8, 152.5, 152.1, 145.5, 136.0, 130.4, 129.0, 128.7, 128.3, 117.9, 117.5, 116.8, 61.4, 20.9, 12.4.

Anal. Calcd for $C_{20}H_{15}BrO_5$: C, 57.85; H, 3.64; Found: C, 57.98, H, 3.55.

3-Acetyl-8-methoxy-4-(3-methoxybenzoyl)-2*H*-chromen-2-one (3aa)[25b]

Isolated yield: 0.059 g (71%); pale-yellow solid; m.p. 174–176 °C [lit.[25b] 174–176 °C].

IR (KBr): 3085, 3018, 2943, 2844, 1733, 1674, 1599, 1476, 1275, 769, 729 cm^{-1}.

^1H NMR (400.1 MHz, $CDCl_3$): δ = 7.52 (s, 1 H), 7.35 (t, *J* = 7.9 Hz, 1 H), 7.28 (d, *J* = 7.6 Hz, 1 H), 7.14–7.22 (m, 3 H), 6.85 (dd, *J* = 7.8, 1.4 Hz, 1 H), 4.01 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3), 2.68 (s, 3 H, CH_3).

Ethyl 6-Bromo-4-(4-fluorobenzoyl)-2-oxo-2*H*-chromene-3-carboxylate (3ab)

Isolated yield: 0.084 g (72%); pale-orange solid; m.p. 184–186 °C.

IR (KBr): 3053, 2923, 1717, 1674, 1595, 1547, 1235, 1160, 852, 820, 761 cm^{-1}.

^1H NMR (400.1 MHz, $CDCl_3$): δ = 7.90 (dd, *J* = 8.8, 5.3 Hz, 2 H), 7.78 (dd, *J* = 8.9, 2.2 Hz, 1 H), 7.35–7.37 (m, 2 H), 7.21 (dd, *J* = 8.6, 8.6 Hz, 2 H), 2.68 (s, 3 H, CH_3).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 194.7, 190.2, 165.5, 156.9, 154.4, 152.4, 136.7, 136.0, 131.1, 130.2 (d, $^3J_{C-F}$ = 9.7 Hz), 129.2, 117.9, 117.4, 117.1, 115.6 (d, $^2J_{C-F}$ = 22.3 Hz), 29.9.

Anal. Calcd for $C_{18}H_{10}BrFO_4$: C, 55.55; H, 2.59; Found: C, 55.28, H, 2.41.

Ethyl 4-(4-Clorobenzoyl)-2-oxo-2*H*-chromene-3-carboxylate (3ac)[25b]

Isolated yield: 0.075 g (70%); white solid; m.p. 137–139 °C [lit.[25b] 137–139 °C].

IR (KBr): 3053, 2990, 1737, 1674, 1559, 1275, 1022, 848, 773, 745 cm^{-1}.

^1H NMR (400.1 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 8.5 Hz, 2 H), 7.62–7.66 (m, 1 H), 7.48 (d, *J* = 8.5 Hz, 2 H), 7.42 (d, *J* = 8.5 Hz, 1 H), 7.19–7.22 (m, 2 H), 4.15 (q, *J* = 7.1 Hz, 2 H, OCH_2), 1.0 (t, *J* = 7.1 Hz, 3 H, CH_3).

Ethyl 4-(4-Fluorobenzoyl)-2-oxo-2*H*-chromene-3-carboxylate (3ad)

Isolated yield: 0.063 g (68%); white solid; m.p. 151–153 °C.

IR (KBr): 3057, 2986, 2915, 1736, 1721, 1678, 1595, 1555, 1373, 1026, 852, 777 cm^{-1}.

^1H NMR (400.1 MHz, $CDCl_3$): δ = 1.1 (t, *J* = 7.1 Hz, 3 H, CH_3), 4.17 (q, *J* = 7.1 Hz, 2 H, OCH_2), 7.20–7.26 (m, 4 H), 7.45 (d, *J* = 8.4 Hz, 1 H), 7.65–7.69 (m, 1 H), 7.98 (dd, *J* = 8.6, 5.3 Hz, 2 H).

^{13}C NMR (100.6 MHz, $CDCl_3$): δ = 189.5, 165.5 (d, $^1J_{C-F}$ = 258 Hz, C), 161.3, 155.3, 154.0, 153.3, 133.5, 130.8 (d, $^3J_{C-F}$ = 9.8 Hz, CH), 130.7, 130.7, 126.4, 124.1, 115.5 (d, $^2J_{C-F}$ = 22.2 Hz, CH), 116.3, 115.2, 61.4, 12.5.

Anal. Calcd for $C_{19}H_{13}FO_5$: C, 67.06; H, 3.85; Found: C, 66.91, H, 3.72.

3-(3-Methylbenzoyl)-2*H*-chromen-2-one (5a)[28b]

Isolated yield: 0.059 g (75%); white solid; m.p. 110–112 °C.

IR (KBr): 3041, 2930, 2855, 1731, 1650, 1612, 1567, 1242, 757 cm^{-1}.

^1H NMR (500.1 MHz, $CDCl_3$): δ = 8.09 (s, 1 H), 7.72 (s, 1 H), 7.68 (td, *J* = 8.6, 1.5 Hz, 2 H), 7.62 (dd, *J* = 7.8, 1.5 Hz, 1 H), 7.42–7.47 (m, 2 H), 7.35–7.41 (m, 2 H), 2.43 (s, 3 H, CH_3).

3-(2-Methoxybenzoyl)-2*H*-chromen-2-one (5b)[28c]

Isolated yield: 0.060 g (72%); white solid; m.p. 159–161 °C [lit.[28c] 158–159 °C].

IR (KBr): 3032, 2923, 2856, 1737, 1642, 1618, 1563, 1239, 1045, 745 cm^{-1}.

^1H NMR (300.1 MHz, $CDCl_3$): δ = 8.18 (s, 1 H), 7.78 (dd, *J* = 7.6, 1.6 Hz, 1 H), 7.57–7.71 (m, 2 H), 7.54 (td, *J* = 7.4, 1.8 Hz, 1 H), 7.28–7.45 (m, 2 H), 7.10 (t, *J* = 7.5 Hz, 1 H), 6.95 (d, *J* = 8.3 Hz, 1 H), 3.75 (s, 3 H, OCH_3).

3-(4-Methoxybenzoyl)-6-methyl-2*H*-chromen-2-one (5c)[28d]

Isolated yield: 0.068 g (77%); white solid; m.p. 206–207 °C.

IR (KBr): 3028, 2927, 2859, 1724, 1657, 1570, 1532, 1244, 1209, 738 cm^{-1}.

^1H NMR (500.1 MHz, $CDCl_3$): δ = 7.99 (s, 1 H), 7.89 (d, *J* = 8.8 Hz, 2 H), 7.45 (d, *J* = 8.5 Hz, 1 H), 7.38 (s, 1 H), 7.31 (d, *J* = 8.5 Hz, 1 H), 6.96 (d, *J* = 8.9 Hz, 2 H), 3.90 (s, 3 H, OCH_3), 2.45 (s, 3 H, CH_3).

3-Benzoyl-7-methoxy-2*H*-chromen-2-one (5d)[28e]

Isolated yield: 0.059 g (70%); white solid; m.p. 150–152 °C [lit. 152–153 °C].

IR (KBr): 3093, 2990, 2848, 1713, 1654, 1373, 1294, 1227, 867, 765 cm^{-1}.

^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 3.92 (s, 3 H, OCH_3), 6.86 (d, *J* = 2.3 Hz, 1 H), 6.91 (dd, *J* = 8.7, 2.4 Hz, 1 H), 7.48 (t, *J* = 7.8 Hz, 2 H), 7.50 (d, *J* = 8.7 Hz, 1 H), 7.60 (tt, *J* = 7.4, 1.2 Hz, 1 H), 7.85 (dd, *J* = 8.2, 1.1 Hz, 2 H), 8.09 (s, 1 H).

3-Benzoyl-6-bromo-2*H*-chromen-2-one (5e)[28f]

Isolated yield: 0.077 g (78%); white solid; m.p. 173–175 °C [lit. 177.8–178.7 °C].

IR (KBr): 3073, 1717, 1658, 1563, 1239, 828 cm^{-1}.

^{1}H NMR (500.1 MHz, $CDCl_3$): δ = 7.99 (s, 1 H), 7.87 (dd, *J* = 7.3, 1.2 Hz, 2 H), 7.70–7.76 (m, 2 H), 7.63 (t, *J* = 7.4 Hz, 1 H), 7.49 (t, *J* = 7.8 Hz, 2 H), 7.30 (d, *J* = 8.6 Hz, 1 H).

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0037-1610675.

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