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Iron-catalyzed regioselective direct coupling of aromatic aldehydes with coumarins leading to 3-aroyl coumarins

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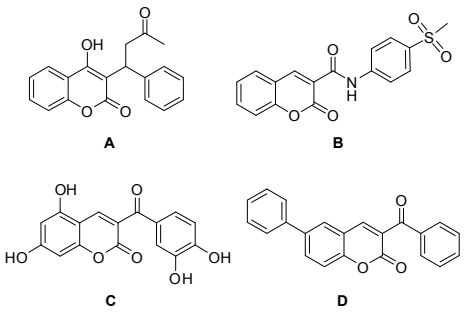
An efficient protocol for iron-catalyzed cross-coupling of coumarins with aromatic aldehydes has been developed. The various 3-aroyl coumarins were selectively afforded in moderate yields. Some notable features of this protocol are high efficiency, wide functional group tolerance, commercially available and cheap aromatic aldehydes and coumarins as starting materials. Furthermore, this reaction conditions were also applicable to N-methyl quinolinones, affording the corresponding 3-aroyl quinolinone derivatives in good yields.

Introduction

Coumarins are significant natural products, which display wide and interesting pharmacological properties such as anti-breast cancer,[1] anti-HIV,[2] anti-Alzheimer,[3] vasorelaxant and platelet antiaggregatory activities.[4] Coumarin derivatives containing carbonyl groups have proven to be a useful skeleton in organic synthesis as a valuable building block and in pharmaceuticals due to its biological and physical properties.[5] In particular, 3-carbonyl coumarin represents an important structural element in anticoagulant agent (A),[6] monoamine oxidase (MAO)-B inhibitor (B),[7] antioxidant (C)[8] and α-glucosidase antihyperglycemic inhibitor (D)[9] (Scheme 1). Moreover, 3-aroyl coumarin derivatives also exhibited characteristics of triplet sensitizers.[5c] Thus, the development of novel and efficient methods for construction of this kind of compound will be great value for the screening of novel functional active molecules.



Scheme 1 Several examples illustrating the importance of 3-carbonyl coumarins

Traditional procedures to synthesize 3-aroyl coumarins involved the Knoevenagel condensation of substituted salicylaldehydes with β-ketoesters in the presence of piperidine in acetonitrile, or using alkaline protease from *Bacillus Licheniformis* as a catalyst.[10] Prakash Rao's group reported a method toward 3-aroyl coumarins by the condensation of α-aroylketene dithioacetals (AKDTAs) and 2-hydroxybenzaldehydes in the presence of catalytic amount of piperidine (Scheme 2, a).[11] Transition metal-free cross-coupling has been employed as an environmentally friendly and alternative approach to replace the metal catalyzed/mediated transformations.[12] Recently, Wu's group described a metal-free TBAB-mediated oxidative tandem coupling of alkynoates with aldehydes for selective synthesis of 3-acylcoumarins (Scheme 2, b).[13] Wang's group used carboxylic acids as the coupling partners, to react with alkynoates by a silver-mediated catalyst to obtain 3-aroyl coumarins (Scheme 2, c).[14] Duan's group also reported a synthetic method for preparation of monosubstituted and polysubstituted coumarins by a silver-catalyzed decarboxylative acylation reactions using α-oxocarboxylic acids as acyl sources (Scheme 2, d).[15] Despite these methods having had various levels of success, some problems exist with these procedures, such as: (1) requirement of complicated starting materials, which are not commercially available or are expensive, and (2) a narrow scope of substrates. Therefore, developing a general and applicable strategy for a variety of 3-aroyl coumarins is still desirable. Recently, transition metal-catalyzed oxidative acylations of inactive sp^2 C-H bonds with aldehydes as acyl surrogates were reported.[16] Guided by recent studies on base promoted hemolytic aromatic substitution (BHAS) using aromatic aldehydes as *C*-radical precursors,[17] we decided to investigate the modular synthesis of 3-aroyl coumarins by BHAS. Herein, we disclose an efficient,

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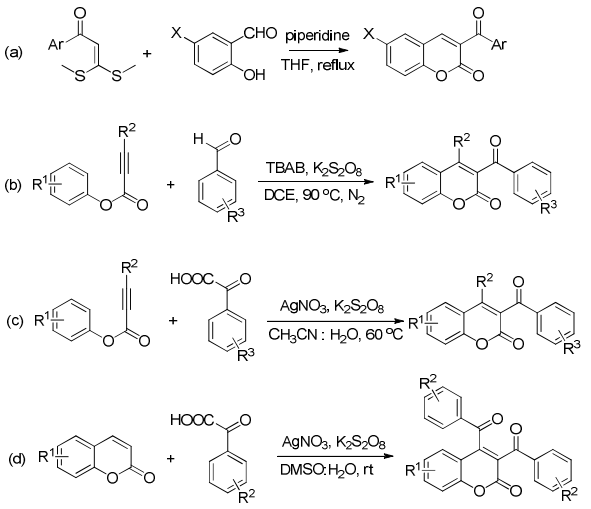
practical procedure to synthesize various 3-aroyl coumarins *via* iron-catalyzed cross-coupling radical reactions of commercially available aromatic dehydes with coumarins (Scheme 2, e).

Previous works:



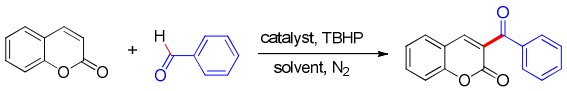
This work:

Scheme 2

Results and discussion

We initiated our investigation with the reaction of coumarin **1a** with benzaldehyde **2a** as a model reaction to identify the optimal reaction conditions. Several parameters, such as catalyst sources, the quantity of catalyst and oxidant *t*-butylhydroperoxide (TBHP), solvents and reaction temperature were screened. The results are listed in Table 1. The initial reaction was conducted in chlorobenzene using a 4-fold excess of benzaldehyde and 3.0 equiv of TBHP in the presence of $Cu(OAc)_2$ as the catalyst (10 mol %) at 120 °C under a nitrogen for 12 h., which led to disappointing result (Table 1, entry 1). A variety of Cu and Fe salts (*e.g.* $CuCl_2$, CuCl, CuI, $Fe(NO_3)_3$, $FeCl_3$, and $FeCl_2$) were tested (Table 1, entries 2-7), Cu salts were not efficient catalysts. Pleasingly, $FeCl_2$ was clearly the ideal choice for this reaction, **3aa** was formed in 46% yield (Table 1, entry 7). Bu_4NI has been successfully used in radical chemistry recently,[18] But Bu_4NI turned out to be an inefficient catalyst in this reaction (Table 1, entry 8). With the optimal catalyst in hand we also varied the amount of catalyst and found 10 mol % to be the ideal loading (Table 1, entries 7, 9-11). A variety of solvents (*e.g.* CH_3CN, DMSO, Dioxane, $ClCH_2CH_2Cl$, and DMF) were tested (Table 1, entries 7, 12-16), chlorobenzene was clearly the best choice for this catalytic system (Table 1, entries 7). To our delight, the yield was improved to 54 % when the amount of TBHP was changed to 4.0 eq, which indicated that the TBHP played an important role in this reaction (Table 1, entries 7, 17-19). Slightly lower yield (49%) was achieved upon lowering the amount of benzaldehyde to 3.0 equiv. However, the product yields dramatically dropped to 23% and 7% if 2.0 equiv and 1.0 equiv of benzaldehyde were used under otherwise identical conditions (Table 1, entries 20-22). Various reaction temperatures were also examined, and 120 °C was found to be the best choice. In the absence of nitrogen, the yield of **3aa** was decreased to 36% (Table 1, entries 23). Additionally, a controlled experimental showed that the yield of **3aa** was only 10% without the catalyst (Table 1, entries 24).

Table 1 Optimization of reaction conditions[a]

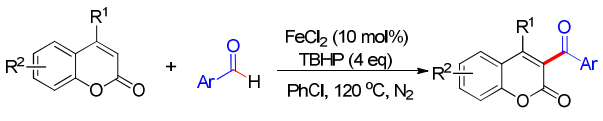


1a **2a** **3aa**

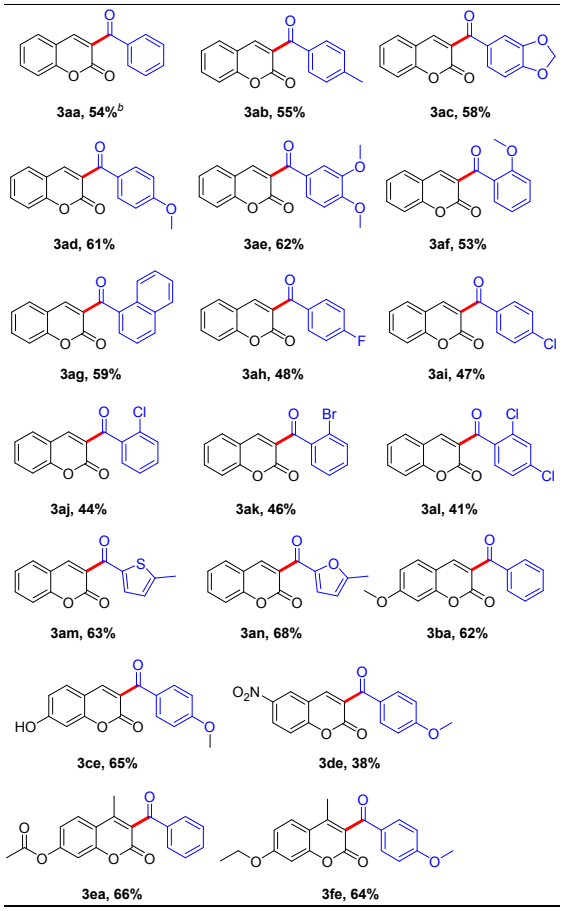
Entry	Catalyst (mol%)	TBHP (eq.)	Solvent	Temp (°C)	Yield[b] (%)
1	$Cu(OAc)_2$ (10)	3.0	PhCl	120	trace
2	$CuCl_2$ (10)	3.0	PhCl	120	11
3	CuCl (10)	3.0	PhCl	120	10
4	CuI (10)	3.0	PhCl	120	trace
5	$Fe(NO_3)_3$ (10)	3.0	PhCl	120	30
6	$FeCl_3$ (10)	3.0	PhCl	120	32
7	$FeCl_2$ (10)	3.0	PhCl	120	46
8	Bu_4NI (10)	3.0	PhCl	120	trace
9	$FeCl_2$ (5)	3.0	PhCl	120	21
10	$FeCl_2$ (15)	3.0	PhCl	120	34
11	$FeCl_2$ (20)	3.0	PhCl	120	35
12	$FeCl_2$ (10)	3.0	CH_3CN	90	10
13	$FeCl_2$ (10)	3.0	DMSO	120	trace
14	$FeCl_2$ (10)	3.0	Dioxane	90	trace
15	$FeCl_2$ (10)	3.0	DCE	90	18
16	$FeCl_2$ (10)	3.0	DMF	120	trace
17	$FeCl_2$ (10)	1.0	PhCl	120	trace
18	$FeCl_2$ (10)	2.0	PhCl	120	17
19	**$FeCl_2$ (10)**	**4.0**	**PhCl**	**120**	**54**
20[c]	$FeCl_2$ (10)	4.0	PhCl	120	49
21[d]	$FeCl_2$ (10)	4.0	PhCl	120	23
22[e]	$FeCl_2$ (10)	4.0	PhCl	120	7
23[f]	$FeCl_2$ (10)	4.0	PhCl	120	36
24[g]	/	4.0	PhCl	120	10

Reaction conditions: **1a** (0.25 mmol), **2a** (1.0 mmol), catalyst, and TBHP in solvent (2 mL) with stirring under nitrogen for 12 h.
[b] Isolated yield.
[c] 3.0 eq **2a** was used.
[d] 2.0 eq **2a** was used.
[e] 1.0 eq **2a** was used.
[f] Without nitrogen. [g] Without a catalyst.

Table 2 Synthesis of 3-aroyl coumarins from coumarins and aromatic aldehydes[a]



1a-c **2a-o** **3aa-fe**



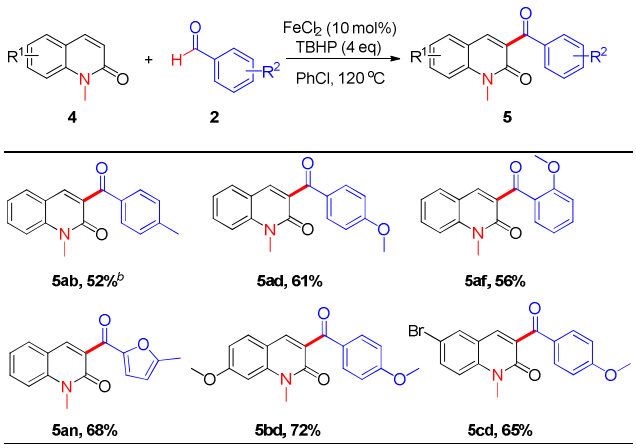
[a] Reaction conditions: coumarins (0.25 mmol), aromatic aldehydes (1.0 mmol), 10 mol % $FeCl_2$ and 4 eq TBHP in 2 mL PhCl solvent, 120 °C, under nitrogen for 12 h.
[b] Isolated yields.

With optimized conditions in hand (Table 1, entry 19) we next studied the scope and limitations of the 3-aroyl coumarins synthesis by firstly varying the aromatic aldehyde component in the reaction with coumarin **1a** (Table 2). The coupling of coumarin **1a** and aromatic aldehyde **2b-l** with electron-donating (CH_3, OCH_3, OCH_2CH_2O, etc) and electron-withdrawing groups (F, Cl, Br, etc) on the aromatic ring were found to be favored in the acylation reaction to afford regioselectively the correcponding products **3ab-al** in moderate to good yields. Moreover, aromatic aldehydes with electron-donating groups could give better yields than those with electron-withdrawing group. The result showed that electronic effects in the aldehyde component turned out to be weak. In addition, *ortho*-substituted benzaldehydes **2f, 2j-l** smoothly underwent this coupling reaction to generate the corresponding products **3af, 3aj-al** in moderate yield. Notably, a 59% yield of **3ag** was produced in the reaction of coumarin and α-naphthaldehyde **2g**. The steric hindrance of aromatic aldehyde did not obviously affect this transformation. It was gratifying to find that heterocyclic aromatic aldehydes **2m**, **2n** also reacted smoothly with coumarin, leading to the corresponding products **3am**, **3an** in good yields. Unfortunately, aliphatic aldehydes failed to deliver the desired products with the current catalytic system.

To further explore the substrate scope and limitations of this process, a broad range of coumarins **1b-f** were screened, as shown in Table 2. The coupling of benzaldehyde **2a** or **2e** and coumarins **1b-f** with electron-rich and electron-deficient groups (OH, OCH_3, OC_2H_5, $OCOCH_3$, NO_2) at the 6-position or 7-position were found to be favored in the acylation reaction to afford the corresponding products **3ba-fe** in moderate yields. Electronic effects in the coumarin structure turned out to be stronger, and a sharp decrease yield of 38% **3de** was afforded when coumarin **2d** with electron-deficient -NO_2 group was employed. Notably, the -OH and -$OCOCH_3$ moieties on the phenyl ring of coumarins were tolerated under these coupling conditions and offer versatile synthetic functionally for further elaboration. It is worthy of note that these standard reaction conditions were applied to 4-substituted coumarins, affording the corresponding products **3ea** and **3fe** in 66% and 64% yields, respectively. The results indicated that the steric hinderance of coumarins played a weak role in this reaction. Unfortunately, the yield of this reaction is typically 50-65% under the present reaction condition. After the reaction was finished, there were still some unreacted starting materials. The yield didn't increase obviously though the reaction time was increased. Moreover, there are few by-products made for this reaction, and no multiple substitutions were found.

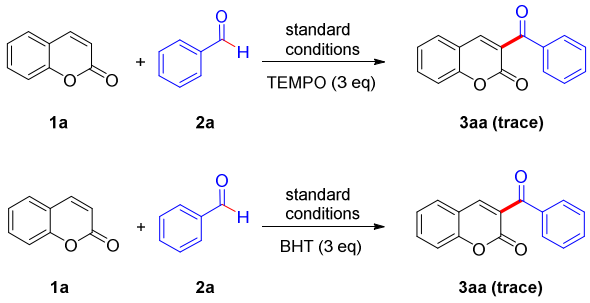
Finally, a series of *N*-methyl quinolinone derivatives was also investigated under the optimal conditions. As expected, the acyl groups were exclusively added to the 3-position of 2-quinolinone derivatives, affording dialkyl 2-quinolinone-3-yl phosphonates in 55-77% yields. Notably, the *N*-methyl 2-quinolinones were well tolerated, and they could react smoothly with aromatic aldehyde or heterocyclic aldehydes, producing the desired products. Moreover, *N*-methyl quinolinones with electron-rich (OCH_3) and electron-poor (Br) groups on the phenyl ring were tolerated under these coupling conditions. Unfortunately, 2-quinolinone derivatives failed to deliver the coupling products with the current catalytic system.

Table 3 Synthesis of 1-methyl-3-aroyl quinolinones from heteroarene **4** and aromatic aldehyde **2**[a]

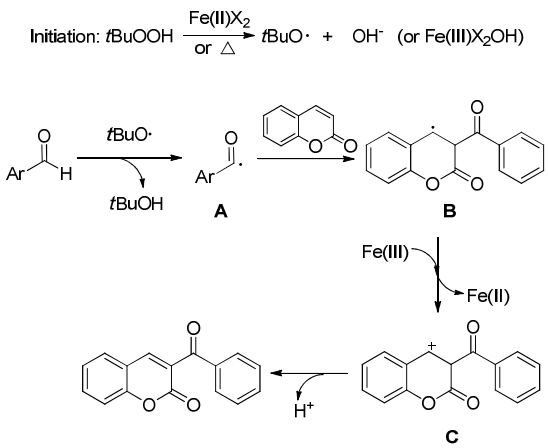


[a] Reaction conditions: *N*-methyl quinolinones (0.25 mmol), aromatic aldehydes (1.0 mmol), 10 mol % $FeCl_2$ and 4 eq TBHP in 2 mL PhCl solvent, 120 °C, under nitrogen for 12 h.
[b] Isolated yields.

To clarify the reaction mechanism, some controlled experiments were performed (Scheme 3). When the reaction of coumarin **1a** with benzaldehyde **2a** was carried out under the standard conditions by addition of 3 equivalents radical scavengers, such as TEMPO and BHT, the yields of the desired product **3aa** were decreased dramatically. These results indicated that the reaction might proceed *via* a radical pathway. Based on these results and previous studies,[16f,17d] a possible reaction mechanism was proposed as shown in Scheme 4. Initiation likely occurs by reducing *t*BuOOH with FeX_2 to give the *tert*-butoxyl radical along with an Fe(III) complex. The *tert*-butoxyl radical then abstracts the H-atom from the aldehyde to give acyl radical **A** which attacks selectively C3-position of coumarin to give the carbon radical **B** stabilized by the phenyl group. The radical **B** is stable because it could form four resonant structures, and the electron is dispersed to phenyl group. On the contrary, acyl radical **A** attacks C4-position of coumarin to give another carbon radical stabilized only by the adjacent carbonyl group. Subsequently, a single-electron transfer (SET) from **B** to Fe(III) would release the intermediate **C**, simultaneously Fe(III) was reduced into Fe(II). After that, the intermediate **C** loses a hydrogen, delivering the desired product.



Scheme 3 Controlled experiments



Scheme 4 Proposed reaction mechanism for C-3 arylation of coumarins

Experimental

General information

All reactions were carried out under a nitrogen atmosphere. Anhydrous solvents were obtained by standard procedure. All substrates were purchased from *J* & *K* Scientific Ltd. Used without further purification. Column chromatography was performed using 200-300 mesh silica with the indicated solvent system according to standard techniques. Analytical thin-layer chromatography (TLC) was performed on precoated, glass-backed silica gel plates. Visualization of the developed chromatogram was performed by UV absorbance (254 nm or 365 nm). Nuclear magnetic resonance spectra were recorded on Bruker Avance 400 MHz spectrometer. Chemical shifts for ^{1}H NMR spectra are recorded in parts per million from tetramethylsilane. Data were reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet an br = broad), coupling constant in Hz and integration. Chemical shifts for ^{13}C NMR spectra were recorded in parts per million from tetramethylsilane. High resolution mass spectra (HR MS) were obtained on Q-TOF using the ESI technique. IR spectra were recorded on Shimadazu IR-408 fourier transform infrared spectrophotometer using a thin film supported on KBr pellets. Melting points were measured on an XT4A microscopic apparatus and were uncorrected.

General procedure for 3-benzoyl coumarin derivatives

In a 25 mL Schlenk tube, coumarins **1** (0.25 mmol), aromatic aldehydes **2** (1.0 mmol), TBHP (1.0 mmol) and $FeCl_2$ (0.025 mmol) were added and charged with Nitrogen (3 cycles). Chlorobenzene (2 mL) was then added, and the reaction mixture was heated in the oil bath at 120 °C for 12 h (monitored by TLC). After the reaction mixture had been cooled to room temperature, and the solvent was removed with the aid of a rotary evaporator. 2 mL ethylacetate was added to the residue. The solution was filtrated, and the filtrate was distilled under vacuum. The crude product was purified by silica gel column chromatography using ethylacetate/petroleum ether (1:5 to 2:1) as eluant to obtain the desired product **3**.

3-Benzoyl-2*H*-chromen-2-one (3aa)

Colorless crystal, mp 134-135 °C (134-136 °C[19]). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.06 (s, 1H), 7.87 (d, J_{H-H} = 7.2 Hz, 2H), 7.65 (td, J_{H-H} = 8.7 Hz, J_{H-H} = 1.5 Hz, 1H), 7.60 (dd, J_{H-H} = 7.9 Hz, J_{H-H} = 1.5 Hz, 1H), 7.48 (d, J_{H-H} = 7.9 Hz, 2H), 7.40 (t, J_{H-H} = 8.3 Hz, 1H), 7.35 (td, J_{H-H} = 7.8 Hz, J_{H-H} = 0.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 191.7 (C=O), 158.4 (C=O), 154.7, 145.4 (CH), 136.2, 133.8 (CH), 133.7 (CH), 129.6 (CH), 129.2 (CH), 128.6 (CH), 125.0 (CH), 118.2, 116.9 (CH). IR (KBr) ν(cm^{-1}): 1714, 1654 (C=O), 1608, 1565, 1448 (Ar-). ESI MS m/z: 251.0705 $[M + H]^+$ (calcd for $C_{16}H_{11}O_3^+$ 251.0703).

3-(4-methylbenzoyl)-2*H*-chromen-2-one (3ab)

Colorless crystal, mp 132-133 °C (132-134 °C[19]). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.05 (s, 1H), 7.78(d, J_{H-H} = 8.2 Hz, 2H), 7.63 (td, J_{H-H} = 8.7 Hz, J_{H-H} = 1.5 Hz, 1H), 7.60 (dd, J_{H-H} = 7.8 Hz, J_{H-H} = 1.5 Hz, 1H), 7.39 (d, J_{H-H} = 8.2 Hz, 2H), 7.32 (td, J_{H-H} = 8.2 Hz, J_{H-H} = 7.8 Hz, 1H), 7.27 (d, J_{H-H} = 8.0 Hz, 1H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 191.2

(C=O), 158.5 (C=O), 154.7, 145.1 (CH), 144.9, 133.6 (CH), 133.5, 129.8 (CH), 129.4 (CH), 129.2 (CH), 127.2, 124.9 (CH), 118.2, 116.9 (CH), 21.8 (CH_3). IR (KBr) ν(cm^{-1}): 1720, 1658 (C=O), 1608, 1567, 1455 (Ar-). ESI MS m/z: 265.1 $[M + H]^+$ (calcd for $C_{17}H_{13}O_3^+$ 265.0).

3-(Benzo[d][1,3]dioxole-5-carbonyl)-2*H*-chromen-2-one (3ac)

Slight yellow solid, mp 155-156 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.01 (s, 1H), 7.78(d, J_{H-H} = 8.2 Hz, 2H), 7.64 (td, J_{H-H} = 8.6 Hz, J_{H-H} = 1.5 Hz, 1H), 7.59 (dd, J_{H-H} = 7.7 Hz, J_{H-H} = 1.5 Hz, 1H), 7.44 (dd, J_{H-H} = 8.2 Hz, J_{H-H} = 1.5 Hz, 1H), 7.40-7.38 (m, 2H), 7.35 (t, J_{H-H} = 7.7 Hz, 1H), 6.84 (d, J_{H-H} = 8.1 Hz, 1H), 6.07 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 189.7 (C=O), 158.5 (C=O), 154.6, 152.7, 148.3, 144.6 (CH), 133.5 (CH), 130.7, 129.0 (CH), 127.4, 126.9 (CH), 124.9 (CH), 118.2, 116.9 (CH), 108.9 (CH), 108.0 (CH), 102.1 (CH_2). IR (KBr) ν(cm^{-1}): 1720 (C=O), 1606, 1488, 1440 (Ar-). HR MS m/z: 295.0603 $[M + H]^+$ (calcd for $C_{17}H_{11}O_5^+$ 295.0601).

3-(4-methoxybenzoyl)-2*H*-chromen-2-one (3ad)

White solid, mp 175-176 °C (174-175 °C[5c]). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.03 (s, 1H), 7.88(d, J_{H-H} = 8.8 Hz, 2H), 7.64 (td, J_{H-H} = 8.5 Hz, J_{H-H} = 1.3 Hz, 1H), 7.60 (dd, J_{H-H} = 7.7 Hz, J_{H-H} = 1.1 Hz, 1H), 7.40 (d, J_{H-H} = 8.2 Hz, 1H), 7.33 (t, J_{H-H} = 7.3 Hz, 1H), 6.95 (d, J_{H-H} = 8.8 Hz, 1H), 3.88 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 190.0 (C=O), 164.3, 158.6 (C=O), 154.6, 144.6 (CH), 133.4 (CH), 132.2 (CH), 129.0 (CH), 129.0, 127.6, 124.9 (CH), 118.3, 116.9 (CH), 113.9 (CH), 55.6 (OCH_3). IR (KBr) ν(cm^{-1}): 1714, 1646 (C=O), 1606, 1596, 1513 (Ar-). ESI MS m/z: 281.1 $[M + H]^+$ (calcd for $C_{17}H_{13}O_4^+$ 281.0).

3-(3,4-Dimethoxybenzoyl)-2*H*-chromen-2-one (3ae)

White solid, mp 193-194 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.02 (s, 1H), 7.66-7.55 (m, 3H), 7.42 (td, J_{H-H} = 8.8 Hz, J_{H-H} = 1.7 Hz, 2H), 7.36 (t, J_{H-H} = 7.5 Hz, 1H), 6.88 (d, J_{H-H} = 8.4 Hz, 1H), 3.96 (s, 3H), 3.95 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 190.0 (C=O), 158.6 (C=O), 154.6, 154.2, 149.3, 144.4 (CH), 133.3 (CH), 129.1, 128.9 (CH), 127.5, 125.5 (CH), 124.9 (CH), 118.2, 116.9 (CH), 110.9 (CH), 109.9 (CH), 56.2 (OCH_3), 56.1 (OCH_3). IR (KBr) ν(cm^{-1}): 1708, 1654 (C=O), 1592, 1581, 1515, 1454 (Ar-). HR MS m/z: 311.0916 $[M + H]^+$ (calcd for $C_{18}H_{15}O_5^+$ 311.0914).

3-(2-methoxybenzoyl)-2*H*-chromen-2-one (3af)

White solid, mp 158-159 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.16 (s, 1H), 7.77 (dd, J_{H-H} = 7.6 Hz, J_{H-H} = 1.8 Hz, 1H), 7.63-7.59 (m, 2H), 7.52 (td, J_{H-H} = 7.8 Hz, J_{H-H} = 1.8 Hz, 1H), 7.37 (d, J_{H-H} = 8.2 Hz, 1H), 7.33 (td, J_{H-H} = 7.6 Hz, J_{H-H} = 0.9 Hz, 1H), 7.08 (td, J_{H-H} = 7.6 Hz, J_{H-H} = 0.7 Hz, 1H), 6.93 (d, J_{H-H} = 8.3, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 190.7 (C=O), 158.9, 158.7 (C=O), 154.7, 143.6 (CH), 134.4 (CH), 133.2 (CH), 130.7 (CH), 129.5 (CH), 129.4, 127.6, 124.7 (CH), 121.1 (CH), 118.7, 116.7 (CH), 111.4 (CH), 55.7 (OCH_3). IR (KBr) ν(cm^{-1}): 1718, 1660 (C=O), 1606, 1575, 1482, 1455 (Ar-). HR MS m/z: 281.0808 $[M + H]^+$ (calcd for $C_{17}H_{13}O_4^+$ 281.0808).

3-(1-naphthoyl)-2*H*-chromen-2-one (3ag)

Colorless crystal, mp 252-253 °C (above 200 °C[19]). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.54 (d, J_{H-H} = 8.4 Hz, 1H), 8.20 (s, 1H), 8.04 (d, J_{H-H} = 8.2 Hz, 1H), 7.92 (d, J_{H-H} = 7.6 Hz, 1H), 7.74 (dd, J_{H-H} = 7.2 Hz, J_{H-H} = 1.0 Hz, 1H), 7.67-7.56 (m, 4H), 7.48 (t, J_{H-H} = 7.5 Hz, 1H), 7.39 (d, J_{H-H} = 8.3 Hz, 2H), 7.34 (td, J_{H-H} = 7.6 Hz, J_{H-H} = 0.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 193.2 (C=O), 158.1 (C=O), 155.0, 146.7 (CH), 134.5, 134.0 (CH), 133.9, 133.3 (CH), 130.7, 129.6 (CH), 129.5 (CH), 128.6 (CH), 128.2 (CH), 127.5, 126.7 (CH), 125.4 (CH), 124.9 (CH), 124.3 (CH), 118.2, 116.9 (CH). IR (KBr) ν(cm^{-1}): 1737, 1658 (C=O), 1608, 1563, 1508, 1454 (Ar-). ESI MS m/z: 301.0855 $[M + H]^+$ (calcd for $C_{20}H_{13}O_3^+$ 301.0859).

3-(4-fluorobenzoyl)-2*H*-chromen-2-one (3ah)

Slight yellow solid, mp 167-168 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.12 (s, 1H), 7.93-7.90 (m, 2H), 7.66 (td, J_{H-H} = 8.6 Hz, J_{H-H} = 1.5 Hz, 1H), 7.61 (dd, J_{H-H} = 7.8 Hz, J_{H-H} = 1.4 Hz, 2H), 7.42 (d, J_{H-H} = 8.3 Hz, 1H), 7.37 (t, J_{H-H} = 7.6 Hz, 1H), 7.16 (t, J_{H-H} = 8.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 190.2 (C=O), 166.2 (d, J_{F-C} = 254.7 Hz), 158.5 (C=O), 154.8, 145.7 (CH), 133.8 (CH), 132.3 (d, J_{F-C} = 9.5 Hz, CH), 129.3 (CH), 126.8, 125.1 (CH), 118.2, 116.9 (CH), 115.8 (d, J_{F-C} = 22.1 Hz, CH). ^{19}F NMR (376 MHz, $CDCl_3$) δ: -103.5. IR (KBr) ν(cm^{-1}): 1709 (C=O), 1662 (C=O), 1610, 1597 (Ar-), 1244 (C-O), 1159 (C-F). HR MS m/z: 369.0604 $[M + H]^+$ (calcd for $C_{16}H_{10}FO_3^+$ 369.0608).

3-(4-chlorobenzoyl)-2*H*-chromen-2-one (3ai)

Colorless crystal, mp 205-206 °C (above 200 °C[19]). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.14 (s, 1H), 7.82(d, J_{H-H} = 8.5 Hz, 2H), 7.68 (t, J_{H-H} = 7.5 Hz, 1H), 7.62 (d, J_{H-H} = 7.7 Hz, 2H), 7.46 (d, J_{H-H} = 8.5 Hz, 1H), 7.42 (d, J_{H-H} = 8.5 Hz, 1H), 7.37 (t, J_{H-H} = 7.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 190.5 (C=O), 158.5 (C=O), 154.8, 146.1 (CH), 140.3, 134.6, 133.9 (CH), 130.9 (CH), 129.3 (CH), 128.9 (CH), 126.5, 125.1 (CH), 118.1, 117.0 (CH). IR (KBr) ν(cm^{-1}): 1712, 1680 (C=O), 1608, 1587, 1452 (Ar-), 1243 (C–O), 758 (C–Cl). ESI MS m/z: 285.1 $[M + H]^+$ (calcd for $C_{16}H_{10}ClO_3^+$ 285.0).

3-(2-chlorobenzoyl)-2*H*-chromen-2-one (3aj)

Slight yellow solid, mp 199-200 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.36 (s, 1H), 7.67-7.64 (m, 2H), 7.56 (d, J_{H-H} = 7.5 Hz, 1H), 7.45 (d, J_{H-H} = 6.2 Hz, 1H), 7.47-7.33 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 191.2 (C=O), 158.1 (C=O), 155.3, 147.1 (CH), 138.2, 134.3 (CH), 132.3 (CH), 131.6, 129.9 (CH), 129.9 (CH), 127.2 (CH), 126.2, 124.9 (CH), 118.4, 116.9 (CH). IR (KBr) ν(cm^{-1}): 1716, 1660 (C=O), 1608, 1563, 1452 (Ar-), 1224 (C–O), 757 (C–Cl). HR MS m/z: 285.0317 $[M + H]^+$ (calcd for $C_{16}H_{10}ClO_3^+$ 285.0313).

3-(2-bromobenzoyl)-2*H*-chromen-2-one (3ak)

Slight yellow solid, mp 127-128 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.39 (s, 1H), 7.66 (t, J_{H-H} = 7.6 Hz, 2H), 7.60 (d, J_{H-H} = 7.9 Hz, 1H), 7.50 (dd, J_{H-H} = 7.6 Hz, J_{H-H} = 1.6 Hz, 1H), 7.44 (t, J_{H-H} = 7.4 Hz, 1H), 7.38-7.33 m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 191.8 (C=O), 157.9 (C=O), 155.4, 147.7 (CH), 140.3, 134.5 (CH), 133.1 (CH), 132.2 (CH), 130.0 (CH), 129.8 (CH), 127.6 (CH), 125.5, 125.0 (CH), 119.7, 118.4, 116.9 (CH). IR (KBr) ν(cm^{-1}): 1747, 1668 (C=O), 1606, 1558, 1454 (Ar-),

1234 (C–O), 759 (C–Br). HR MS m/z: 328.9812 $[M + H]^+$ (calcd for $C_{16}H_{10}BrO_3^+$ 328.9808).

3-(2,4-dichlorobenzoyl)-2*H*-chromen-2-one (3al)

Slight yellow solid, mp 158-159 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.41 (s, 1H), 7.70-7.66 (m, 2H), 7.52 (d, J_{H-H} = 8.3 Hz, 1H), 7.43-7.35 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 190.2 (C=O), 158.2 (C=O), 155.3, 147.4 (CH), 137.9, 136.7, 134.6 (CH), 132.5, 130.9 (CH), 130.0 (CH), 129.8 (CH), 127.6 (CH), 126.0, 125.1 (CH), 118.4, 117.0 (CH). IR (KBr) ν(cm^{-1}): 1722 (C=O), 1660 (C=O), 1608, 1556 (Ar-), 777 (C-Cl). HR MS m/z: 318.9927 $[M + H]^+$ (calcd for $C_{16}H_9Cl_2O_3^+$ 318.9923).

3-(5-methylthiophene-2-carbonyl)-2*H*-chromen-2-one (3am)

Slight yellow solid, mp 153-154 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.06 (s, 1H), 7.65 (td, J_{H-H} = 7.3 Hz, J_{H-H} = 1.2 Hz, 1H), 7.58 (d, J_{H-H} = 7.7 Hz, 1H), 7.54 (d, J_{H-H} = 3.8 Hz, 1H), 7.40 (d, J_{H-H} = 8.3 Hz, 1H), 7.34 (t, J_{H-H} = 7.5 Hz, 1H), 2.57 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 182.4 (C=O), 158.3 (C=O), 154.6, 152.4, 144.3 (CH), 140.6, 136.0 (CH), 133.5 (CH), 129.1 (CH), 127.2 (CH), 126.9, 124.9 (CH), 118.1, 116.9 (CH), 16.3 (CH_3). IR (KBr) ν(cm^{-1}): 2954, 2922 (-CH_3), 1720 (C=O), 1630 (C=O), 1603, 1566 (Ar-), 1250 (C-S). HR MS m/z: 271.0420 $[M + H]^+$ (calcd for $C_{15}H_{11}O_3S^+$ 271.0423).

3-(5-methylfuran-2-carbonyl)-2*H*-chromen-2-one (3an)

Slight yellow solid, mp 157-158 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.12 (s, 1H), 7.64 (t, J_{H-H} = 7.5 Hz, 2H), 7.60 (d, J_{H-H} = 7.8 Hz, 1H), 7.39 (d, J_{H-H} = 8.3 Hz, 1H), 7.33 (t, J_{H-H} = 7.6 Hz, 1H), 7.25 (d, J_{H-H} = 3.5 Hz, 1H), 6.24 (d, J_{H-H} = 3.4 Hz, 1H), 2.43 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 177.1 (C=O), 159.7 (C=O), 158.2, 154.6, 150.5, 145.0 (CH), 133.6 (CH), 129.2 (CH), 126.5, 124.9 (CH), 123.3 (CH), 118.2, 116.8 (CH), 109.7 (CH), 14.2 (CH_3). IR (KBr) ν(cm^{-1}): 1720, 1644 (C=O), 1606, 1567, 1508 (Ar-), 1211, 1174 (C–O). HR MS m/z: 255.0656 $[M + H]^+$ (calcd for $C_{15}H_{11}O_4^+$ 255.0652).

3-Benzoyl-7-methoxy-2*H*-chromen-2-one (3ba)

Slight yellow crystal, mp 153-154 °C (152-153 °C[5c]). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.07 (s, 1H), 7.85 (d, J_{H-H} = 7.5 Hz, 2H), 7.58 (t, J_{H-H} = 7.5 Hz, 1H), 7.50-7.44 (m, 3H), 6.90 (dd, J_{H-H} = 8.6 Hz, J_{H-H} = 2.3 Hz, 1H), 6.85 (d, J_{H-H} = 2.3 Hz, 1H), 3.90 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 191.9 (C=O), 164.6, 158.7 (C=O), 157.1, 146.4, 136.7, 133.4, 130.4, 129.5, 128.4, 122.8, 113.5, 111.8, 100.6, 56.0. IR (KBr) ν(cm^{-1}): 1707, 1657 (C=O), 1616, 1508, 1450 (Ar-), 1227 (C–O). ESI MS m/z: 281.2 $[M + H]^+$ (calcd for $C_{17}H_{13}O_4^+$ 281.0).

7-Hydroxy-3-(4-methoxybenzoyl)-2*H*-chromen-2-one (3ce)

Slight yellow crystal, mp 200-201 °C (190-191 °C[20]). ^{1}H NMR (400 MHz, DMSO) δ: 10.94 (s, 1H), 8.27 (s, 1H), 7.86 (dd, J_{H-H} = 6.8 Hz, J_{H-H} = 2.0 Hz, 2H), 7.68 (d, J_{H-H} = 8.5 Hz, 1H), 7.05 (dd, J_{H-H} = 6.8 Hz, J_{H-H} = 2.0 Hz, 2H),6.85 (dd, J_{H-H} = 8.5 Hz, J_{H-H} = 2.2 Hz, 1H), 6.79 (d, J_{H-H} = 2.2 Hz, 1H), 3.86 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ: 190.7 (C=O), 164.0, 163.4, 158.9 (C=O), 156.8, 146.2 (CH), 132.4 (CH), 131.7 (CH), 129.7, 122.2, 114.3 (CH), 114.2 (CH), 111.2, 102.5 (CH), 56.0 (CH_3). IR (KBr) ν(cm^{-1}): 3340 (-OH), 2924, 2843 (-CH_3), 1689, 1622 (C=O), 1601, 1564, 1454 (Ar-), 1230 (C–O). ESI MS m/z: 297.3 $[M + H]^+$ (calcd for $C_{17}H_{13}O_5^+$ 297.1).

3-(4-methoxybenzoyl)-6-nitro-2H-chromen-2-one (3de)

Slight yellow crystal, mp 219-220 °C. ^{1}H NMR (400 MHz, DMSO) δ: 8.82 (d, J_{H-H} = 2.7 Hz, 1H), 8.51 (dd, J_{H-H} = 9.1 Hz, J_{H-H} = 2.7 Hz, 1H), 8.49 (s, 1H), 7.98 (dd, J_{H-H} = 7.0 Hz, J_{H-H} = 2.0 Hz, 2H), 7.72 (d, J_{H-H} = 9.1 Hz, 1H), 7.08(dd, J_{H-H} = 7.0 Hz, J_{H-H} = 2.0 Hz, 2H), 3.88 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ: 189.8 (C=O), 164.6, 158.1 (C=O), 157.7, 144.1, 143.5, 132.8, 129.0, 128.8, 128.0, 125.7, 119.2, 118.3, 114.6, 56.2. IR (KBr) ν(cm^{-1}): 1751, 1652 (C=O), 1614, 1596, 1571(Ar-), 1529, 1346 (-NO_2), 1257 (C–O). HR MS m/z: 326.0660 $[M + H]^+$ (calcd for $C_{17}H_{12}O_6^+$ 326.0659).

3-Benzoyl-4-methyl-2-oxo-2*H*-chromen-7-yl acetate (3ea)

Slight yellow solid, mp 114-115 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.91 (dd, J_{H-H} = 8.0 Hz, J_{H-H} = 0.8 Hz, 2H), 7.71 (d, J_{H-H} = 8.7 Hz, 1H), 7.61 (td, J_{H-H} = 7.4 Hz, J_{H-H} = 1.2 Hz, 1H), 7.47 (t, J_{H-H} = 8.0 Hz, 2H), 7.18 (d, J_{H-H} = 2.2 Hz, 1H), 7.14 (dd, J_{H-H} = 8.7 Hz, J_{H-H} = 2.2 Hz, 1H), 2.35 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 192.9 (C=O), 168.6, 158.4 (C=O), 153.7, 153.6, 149.7, 136.0, 134.3 (CH), 129.3 (CH), 129.0 (CH), 126.2 (CH), 125.3, 118.7 (CH), 117.4, 110.5 (CH), 21.1 (CH_3), 16.0 (CH_3). IR (KBr) ν(cm^{-1}): 3066, 2925 (-CH_3), 1768, 1720, 1670 (C=O), 1614, 1450 (Ar-), 1186 (C–O). HR MS m/z: 323.0916 $[M + H]^+$ (calcd for $C_{19}H_{15}O_5^+$ 323.0914).

7-Ethoxy-3-(4-methoxybenzoyl)-4-methyl-2*H*-chromen-2-one (3fe)

Slight yellow solid, mp 121-122 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.91 (dd, J_{H-H} = 9.7 Hz, J_{H-H} = 2.7 Hz, 1H), 7.58 (d, J_{H-H} = 8.9 Hz, 1H), 6.95-6.89 (m, 3H), 6.84 (d, J_{H-H} = 2.4 Hz, 1H), 4.11 (q, J_{H-H} = 7.0 Hz, 2H), 3.86 (s, 3H), 2.31 (s, 3H), 1.47 (t, J_{H-H} = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 191.9 (C=O), 164.4, 162.6, 159.2 (C=O), 154.9, 150.2, 131.9 (CH), 129.6, 126.2 (CH), 122.8, 114.2 (CH), 113.2 (CH), 112.9, 101.3 (CH), 64.3 (CH_2), 55.6 (OCH_3), 15.9 (CH_3), 14.5 (CH_3). IR (KBr) ν(cm^{-1}): 1714, 1660 (C=O), 1600, 1558 (Ar-), 1259 (C–O). HR MS m/z: 339.1229 $[M + H]^+$ (calcd for $C_{20}H_{19}O_5^+$ 339.1227).

General procedure for 3-benzoyl quinolin derivatives

In a 25 mL Schlenk tube, *N*-methyl quinolinones **4** (0.25 mmol), aromatic aldehyde **2** (1.0 mmol), TBHP (1.0 mmol) and $FeCl_2$ (0.025 mmol) were added and charged with Nitrogen (3 cycles). Chlorobenzene (2 mL) was then added, and the reaction mixture was heated in the oil bath at 120 °C for 12 h (monitored by TLC). After the reaction mixture had been cooled to room temperature, and the solvent was removed with the aid of a rotary evaporator. 2 mL ethylacetate was added to the residue. The solution was filtrated, and the filtrate was distilled under vacuum. The crude product was purified by silica gel column chromatography using ethylacetate/petroleum ether (1:5 to 2:1) as eluant to provide the desired products **5**.

1-Methyl-3-(4-methylbenzoyl)quinolin-2(1*H*)-one (5ab)

Slight yellow crystal, mp 143-144 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.94 (s, 1H), 7.78 (dd, J_{H-H} = 6.6 Hz, J_{H-H} = 1.6 Hz, 2H), 7.68-7.63 (m, 2H), 7.41 (d, J_{H-H} = 8.5 Hz, 1H), 7.28 (td, J_{H-H} = 7.9 Hz, J_{H-H} = 0.8 Hz, 1H), 7.24 (d, J_{H-H} = 7.9 Hz, 2H), 3.74 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 193.7 (C=O), 160.0 (C=O), 144.2, 140.8, 139.8 (CH), 134.5, 132.1 (CH), 131.8, 129.9 (CH), 129.7 (CH), 129.2 (CH), 122.6 (CH), 119.5, 114.3 (CH), 29.6 (CH_3), 21.8 (CH_3). IR (KBr) ν(cm^{-1}): 3054, 2923 (-CH_3), 1639 (C=O), 1589, 1571 (Ar-), 1290 (C–N). HR MS m/z: 278.1178 $[M + H]^+$ (calcd for $C_{18}H_{16}NO_2^+$ 278.1176).

3-(4-Methoxybenzoyl)-1-methylquinolin-2(1*H*)-one (5ad)

Slight yellow crystal, mp 165-166 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.91 (s, 1H), 7.87 (dd, J_{H-H} = 6.9 Hz, J_{H-H} = 4.8 Hz, 2H), 7.67-7.61 (m, 2H), 7.40 (d, J_{H-H} = 8.4 Hz, 1H), 7.27 (td, J_{H-H} = 7.8 Hz, J_{H-H} = 0.7 Hz, 1H), 6.91 (dd, J_{H-H} = 6.9 Hz, J_{H-H} = 2.0 Hz, 2H), 3.85 (s, 3H), 3.74 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 192.5 (C=O), 163.8, 160.0 (C=O), 140.7, 139.5 (CH), 132.1 (CH), 132.0 (CH), 129.9, 129.8 (CH), 122.6 (CH), 119.6, 114.3 (CH), 113.7 (CH), 55.5 (CH_3), 29.6 (CH_3). IR (KBr) ν(cm^{-1}): 2919, 2850 (-CH_3), 1650, 1639 (C=O), 1602, 1589, 1573 (Ar-), 1255 (C–N). HR MS m/z: 294.1126 $[M + H]^+$ (calcd for $C_{18}H_{16}NO_3^+$ 294.1125).

3-(2-Methoxybenzoyl)-1-methylquinolin-2(1*H*)-one (5af)

Slight yellow crystal, mp 165-166 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.11 (s, 1H), 7.69 (td, J_{H-H} = 7.3 Hz, J_{H-H} = 1.6 Hz, 2H), 7.63 (td, J_{H-H} = 7.3 Hz, J_{H-H} = 1.6 Hz, 1H), 7.48 (td, J_{H-H} = 6.4 Hz, J_{H-H} = 1.8 Hz, 1H), 7.37 (d, J_{H-H} = 8.5 Hz, 1H), 7.27 (td, J_{H-H} = 7.8 Hz, J_{H-H} = 0.8 Hz, 1H), 7.05 (td, J_{H-H} = 7.5 Hz, J_{H-H} = 0.7 Hz, 1H), 6.91 (d, J_{H-H} = 8.2 Hz, 1H), 3.69 (s, 3H), 3.68 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 193.2 (C=O), 160.2, 158.6 (C=O), 141.0, 139.7 (CH), 133.5 (CH), 133.2, 132.1 (CH), 130.5 (CH), 130.3 (CH), 129.1, 122.4 (CH), 120.9 (CH), 119.8, 114.2 (CH), 111.4 (CH), 55.7 (CH_3), 29.4 (CH_3). IR (KBr) ν(cm^{-1}): 2922, 250 (-CH_3), 1643 (C=O), 1589, 1568, 1485, 1462 (Ar-), 1296 (C–N), 1250 (C–O). HR MS m/z: 294.1127 $[M + H]^+$ (calcd for $C_{18}H_{16}NO_3^+$ 294.1125).

1-Methyl-3-(5-methylfuran-2-carbonyl)quinolin-2(1*H*)-one (5an)

Slight yellow crystal, mp 114-116 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.97 (s, 1H), 7.67-7.62 (m, 2H), 7.40 (d, J_{H-H} = 8.4 Hz, 1H), 7.60 (dd, J_{H-H} = 7.8 Hz, J_{H-H} = 1.5 Hz, 1H), 7.39 (d, J_{H-H} = 8.2 Hz, 2H), 7.32 (td, J_{H-H} = 8.2 Hz, J_{H-H} = 7.8 Hz, 1H), 7.27 (d, J_{H-H} = 8.0 Hz, 1H), 2.42 (s, J_{H-H} = 2.43, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 191.2 (C=O), 158.5 (C=O), 154.7, 145.1 (CH), 144.9, 133.6 (CH), 133.5, 129.8 (CH), 129.4 (CH), 129.2 (CH), 127.2, 124.9 (CH), 118.2, 116.9 (CH), 21.8 (CH_3). IR (KBr) ν(cm^{-1}): 2922, 2852 (-CH_3), 1657, 1643 (C=O), 1591, 1512 (Ar-), 1292 (C-N), 1207 (C-O). HR MS m/z: 268.0967 $[M + H]^+$ (calcd for $C_{16}H_{14}NO_3^+$ 268.0968).

7-Methoxy-3-(4-methoxybenzoyl)-1-methylquinolin-2(1H)-one (5bd)

Slight yellow crystal, mp 179-181 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.90 (s, 1H), 7.86 (d, J_{H-H} = 8.9 Hz, 2H), 7.55 (d, J_{H-H} = 8.7 Hz, 1H), 6.92 (d, J_{H-H} = 8.9 Hz, 1H), 6.87 (dd, J_{H-H} = 8.6 Hz, J_{H-H} = 2.3 Hz, 1H), 6.81 (d, J_{H-H} = 2.3 Hz, 1H), 3.95 (s, 3H), 3.86 (s, 3H), 3.71 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 192.8 (C=O), 163.6, 163.1, 160.4 (C=O), 142.7, 140.1 (CH), 132.0 (CH), 131.5 (CH), 130.3, 128.5, 113.8, 113.6 (CH), 110.5 (CH), 98.5 (CH), 55.7 (CH_3), 55.4 (CH_3), 29.6 (CH_3). IR (KBr) ν(cm^{-1}): 2920, 2946 (-CH_3), 1655, 1645 (C=O), 1620, 1589, 1593 (Ar-), 1254 (C–N), 1236 (C-O). HR MS m/z: 324.1232 $[M + H]^+$ (calcd for $C_{19}H_{18}NO_4^+$ 324.1230).

6-Bromo-3-(4-methoxybenzoyl)-1-methylquinolin-2(1H)-one (5cd)

Slight yellow crystal, mp 182-183 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.84 (d, J_{H-H} = 8.9 Hz, 2H), 7.78 (s, 1H), 7.73(d, J_{H-H} = 2.2 Hz, 1H), 7.69 (dd, J_{H-H} = 8.6 Hz, J_{H-H} = 2.2 Hz, 1H), 7.28 (d, J_{H-H} = 8.6 Hz, 1H), 6.90 (d, J_{H-H} = 8.9 Hz, 1H), 3.85 (s, 3H), 3.71 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 191.9 (C=O), 164.0, 159.6 (C=O), 139.5, 137.9 (CH), 134.5 (CH), 133.2, 132.0 (CH), 131.7 (CH), 129.5, 121.0, 116.1 (CH), 115.3, 113.8 (CH), 55.5 (CH_3), 29.8 (CH_3). IR (KBr) ν(cm^{-1}): 2918, 2843 (-CH_3), 1658, 1637 (C=O), 1606, 1577, 1562 (Ar-), 1267 (C–N), 1178 (C-O), 810 (C-Br). HR MS m/z: 372.0233 $[M + H]^+$ (calcd for $C_{18}H_{15}BrNO_3^+$ 372.0230).

Conclusions

In conclusion, a novel, simple and efficient protocol for the synthesis of 3-aroyl coumarins via iron-catalyzed direct coupling of coumarins with aromatic aldehyde has been developed. Various 3-aroyl coumarins were obtained in moderate to good yields. The aroyl substituents were introduced into coumarins or other heteroarenes with complete regioselectivity at the 3-position.

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Graphic Abstract

Iron-catalyzed regioselective direct coupling of aromatic aldehydes with coumarins leading to 3-aroyl coumarins

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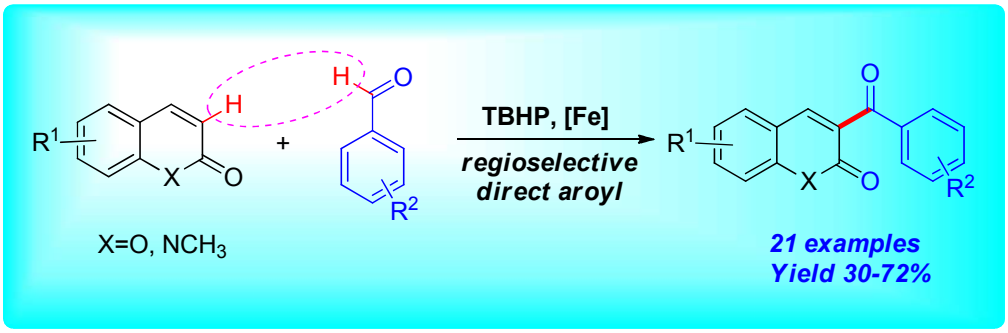

Iron-catalyzed direct radical acylation of coumarins with aromatic aldehydes to afford regioselectively 3-aroyl coumarin derivatives in moderate yields was described.