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Silver-Mediated Radical Cyclization of Alkynoates and α-Keto Acids Leading to Coumarins via Cascade Double C−C Bond Formation

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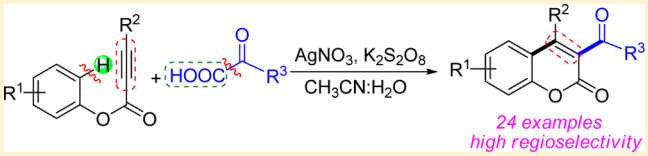
Supporting Information

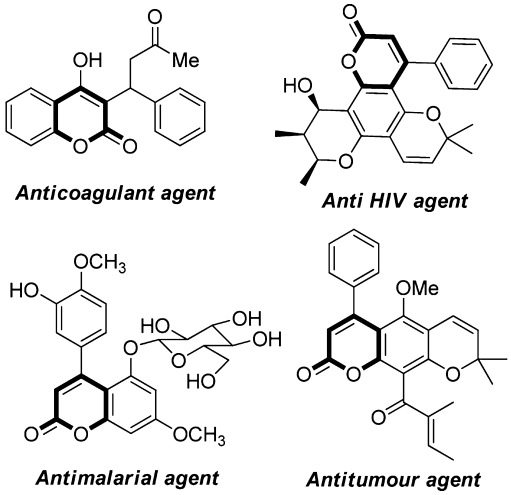
ABSTRACT: A novel and convenient silver-mediated radical cyclization method for the synthesis of coumarin derivatives via the direct difunctionalization of alkynoates with α-keto acids through double C−C bond formation under mild conditions has been developed. This new method is highly efficient and practical, and the starting materials are readily prepared. The present method should provide a useful strategy for the construction of coumarin motifs.



INTRODUCTION

The coumarin nucleus is a key core structure that widely occurs in natural products and biological molecules, and it is also widely used in materials chemistry.[1] Importantly, coumarin derivatives are well documented as therapeutic agents and possess a variety of pharmacological properties, such as antitumor,[2] antimalarial,[3] anticoagulant,[4] antimicrobial,[5] and anti-HIV properties[6] (Scheme 1). Thus, development of novel and efficient methods for construction of these compounds will be great value for the screening of novel biologically active molecules. The conventional methods for the preparation of coumarins typically involve three approaches, including the Pechmann reaction,[7] the Wittig reaction,[8] and the Knoevenagel condensation.[9] In 2008, Gabriele and co-workers developed a palladium-catalyzed dicarbonylation process to construct coumarins using 2-(1-hydroxyprop-2-ynyl)phenols as substrates.[10] Despite these methods having had various levels of success, the harshness of strong acid conditions and the not easily available precursors could limit their wide applications. Therefore, more effective processes are needed. Transition-metal-catalyzed transformations are useful tools in organic chemistry. Recently, Heck cross-couplings,[11] Suzuki cross-couplings,[12] and Pd-catalyzed site-selective cross-coupling reactions[13] have emerged as attractive methods for the synthesis of coumarin derivatives. However, challenges still remain, but it is still highly desirable to develop new strategies to prepare functionalized coumarins that utilize inexpensive substrates and proceed under mild conditions.

Scheme 1. Some Representative Compounds Containing the Coumarin Motif



As one of the promising synthesis strategies, direct difunctionalization of alkynes has attracted considerable attention because of its high efficiency in the cascade formation of carbon−carbon or carbon−heteroatom bonds. In this field, some excellent difunctionalization reactions such as halosulfonylation,[14] *ipso*-carboacylation,[15] arylphosphorylation,[16] and oxyvinylcyclization[17] have been significantly disclosed. Also, as a valuable functional group, the carbonyl functionality is widely used in organic chemistry. Consequently, the introduction of a carbonyl group into the organic framework strongly attracts synthetic chemists.[18] Nevertheless, until now, very few strategies for the fabrication of carbonyl compounds have been developed via the difunctionalization of alkynes.[15a,c,d] In addition, recent years have witnessed significant efforts devoted to the development of decarboxylative reactions using carboxylic acids as the coupling partners, owing to that those substrates are readily available and stable, and besides that, CO_2 is the sole waste product from the transformation.[19] For example, Jafarpour and co-workers developed an elegant work for the synthesis of coumarins via palladium-catalyzed decarboxylative arylation and alkenylation of coumarin-3-carboxylic acids.[20] Among all the carboxylic acids, α-keto

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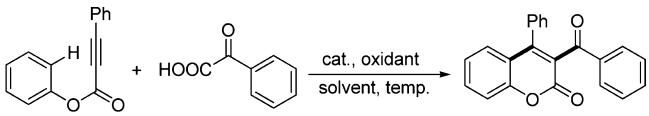
acids have emerged as appealing coupling partners in decarboxylative reactions. In 2008, Gooβen and co-workers first reported a Cu/Pd-catalyzed decarboxylative cross-coupling of α-keto carboxylate salts with aryl bromides to afford diaryl ketones.[21] Since then, the α-keto acid decarboxylative reaction has been extensively studied.[22] Meanwhile, α-keto acid decarboxylative reactions via radical pathways have also been widely explored, such as difunctionalization of activated alkenes,[23] acylfluorination of styrenes,[24] and acyloxylation of the sp^3 C−H bond.[25] Inspired and encouraged by these excellent works and with our interest in heterocycles synthesis via radical pathways,[26] we herein describe a new silver-mediated direct carbonylation of alkynes with α-keto acids toward 3-carbonylated coumarins under mild conditions.

RESULTS AND DISCUSSION

Initially, phenyl 3-phenylpropiolate (**1a**) and 2-oxo-2-phenylacetic acid (**2a**) were chosen as the model substrates to optimize reaction conditions including the catalysts, oxidants, and solvents under nitrogen atmosphere. As shown in Table 1,

Table 1. Silver-Mediated Synthesis of 3-Benzoyl-4-phenyl-2*H*-chromen-2-one via Cascade Reaction of Phenyl 3-Phenylpropiolate with 2-Oxo-2-phenylacetic Acid: Optimization of the Catalysis Conditions[a]



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

entry	catalyst	oxidant	solvent	yield[b] (%)
1	$AgNO_3$	$Na_2S_2O_8$	CH_3CN/H_2O	57
2	$AgNO_3$	$(NH_4)_2S_2O_8$	CH_3CN/H_2O	40
3	$AgNO_3$	TBHP	CH_3CN/H_2O	20
4	$AgNO_3$	O_2	CH_3CN/H_2O	trace
5	**$AgNO_3$**	**$K_2S_2O_8$**	**CH_3CN/H_2O**	**75**
6	Ag_2O	$K_2S_2O_8$	CH_3CN/H_2O	44
7	Ag_2CO_3	$K_2S_2O_8$	CH_3CN/H_2O	46
8	AgOAc	$K_2S_2O_8$	CH_3CN/H_2O	49
9	none	$K_2S_2O_8$	CH_3CN/H_2O	16
10	$AgNO_3$	$K_2S_2O_8$	$DMSO/H_2O$	31
11	$AgNO_3$	$K_2S_2O_8$	H_2O	trace
12	$AgNO_3$	$K_2S_2O_8$	DMF/H_2O	32
13	$AgNO_3$	$K_2S_2O_8$	CH_3CN/H_2O	38[c]
14	$AgNO_3$	$K_2S_2O_8$	CH_3CN/H_2O	58[d]
15	$AgNO_3$	$K_2S_2O_8$	CH_3CN/H_2O	76[e]
17	$AgNO_3$	$K_2S_2O_8$	CH_3CN/H_2O	39[f]
18	$AgNO_3$	$K_2S_2O_8$	CH_3CN/H_2O	56[g]

[a]Reaction conditions: under nitrogen atmosphere, **1a** (0.3 mmol), **2a** (0.6 mmol), catalyst (0.3 mmol), oxidant (4.0 equiv), solvent (2 mL), CH_3CN/H_2O (v_1/v_2 = 1:1), 60 °C, and reaction time (24 h). TBHP = *tert*-butyl hydroperoxide solution 5.5 M in decane. [b]Isolated yield. [c]Reaction temperature (30 °C). [d]Reaction temperature (50 °C). [e]Reaction temperature (70 °C). [f]$AgNO_3$ (0.06 mmol). [g]$AgNO_3$ (0.18 mmol).

five oxidants, $Na_2S_2O_8$, $K_2S_2O_8$, $(NH_4)_2S_2O_8$, TBHP, and O_2, were investigated at 60 °C by using 1.0 equiv of $AgNO_3$ (relative to amount of **2a**) in 2 mL of CH_3CN/H_2O (v_1/v_2 = 1:1), and $K_2S_2O_8$ gave the highest yield (75%) (entries 1−5, Table 1). Furthermore, the silver salts, including $AgNO_3$, Ag_2O, Ag_2CO_3, and AgOAc, were tested in CH_3CN/H_2O (entries 5−8, Table 1) using $K_2S_2O_8$ as the oxidant at 60 °C, and $AgNO_3$ was found to be the most effective catalyst (entries 5−9, Table 1). We attempted to use different solvents, and CH_3CN/H_2O was superior to the others (compare entries 5 and 10−12, Table 1). Various reaction temperatures were attempted (entries 5, 13, and 14, Table 1), and 60 °C was found to be suitable for this reaction (entry 5, Table 1). Notably, elevated temperature did not obviously enahance the yield (entry 15, Table 1). Additionally, the amount of $AgNO_3$ was rationally changed (compare entries 5, 17, and 18, Table 1), and 1.0 equiv of $AgNO_3$ provided the highest yield. After the optimization process for catalysts, oxidants, solvents, and temperature, the various coumarin derivatives were synthesized under our standard conditions: 1.0 equiv of $AgNO_3$ as the promoter, 4.0 equiv of $K_2S_2O_8$ as the oxidant, and 2 mL of CH_3CN/H_2O (v_1/v_2 = 1:1) as the solvent at 60 °C under nitrogen atmosphere.

With the optimum reaction conditions in hand, we investigated the scope of substrates for the silver-mediated radical cyclization of substituted alkynoates (**1**) with α-keto acids (**2**) leading to coumarin derivatives (**3**). As shown in Table 2, the tested substrates afforded moderate to good yields. For the substituted α-keto acids which bear an electron-withdrawing group, such as −Cl and −Br (Table 2, **3d**, **3h**, **3o**, and **3t**), could give slight good yields as compared to the α-keto acids with the electron-donating substituents (Table 2, **3g**, **3n**, and **3r**). For the substituted alkynoates, the electron-withdrawing as well as electron-donating substituents did not significantly affect the catalytic activity. With a strong electron-withdrawing substituent (CF_3) on the phenoxy ring, the corresponding products (**3q−t**) were obtained in good yield. However, alkynoates containing a NO_2 group did not work in the reaction. The steric hindrance in the α-keto acids did not significantly affect the catalytic efficiency (Table 2, **3b** and **3r**). Although aromatic α-keto acids showed high reactivity, unfortunately, aliphatic ones were poor substrates. If aliphatic α-keto acids such as 2-oxopropanoic acid and 3,3-dimethyl-2-oxobutanoic acid were used as the substrates under the optimal reaction conditions, only a trace of product was obtained (Table 2, **3u** and **3v**). As expected, the *meta*-substituent of the phenoxy ring gave two regioselective products (**3aa**/**3aa′**). Unfortunately, alkylpropiolates such as methylpropiolate were not tolerated in the transformation (**3ab**).The silver-mediated domino reactions could tolerate some functional groups such as alkyl group, C−Cl bonds, C−Br bonds, and C−CF_3 bonds, which could be used for further modifications at the substituted positions. The structure of **3a** was unambiguously confirmed by X-ray crystallographic analysis (Figure 1, see the Supporting Information).

According to the previous report, acyl radicals were easily generated from the Ag(I)/$K_2S_2O_8$ system,[26] which implies that the transformation should proceed through a free-radical mechanism. As shown in Scheme 2, when 2.0 equiv of TEMPO (2,2,6,6-tetramethylpiperidin-1-yloxy, a well-known radical inhibitor) was added under the standard reaction conditions, the formation of **2a** was completely inhibited as expected. In addition, another radical scavenger such as BHT (butylated hydroxytoluene) was also proven to inhibit the transformation. Furthermore, the cyclization product **4a** was not obtained when **1a** was performed only under the standard conditions.

On the basis of the preliminary results discussed above, a possible mechanism for the silver-mediated radical cyclization

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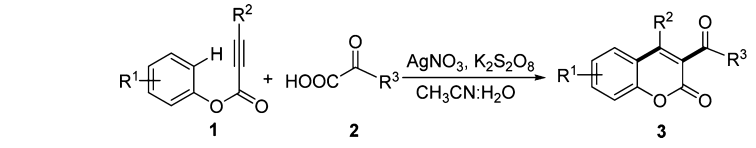
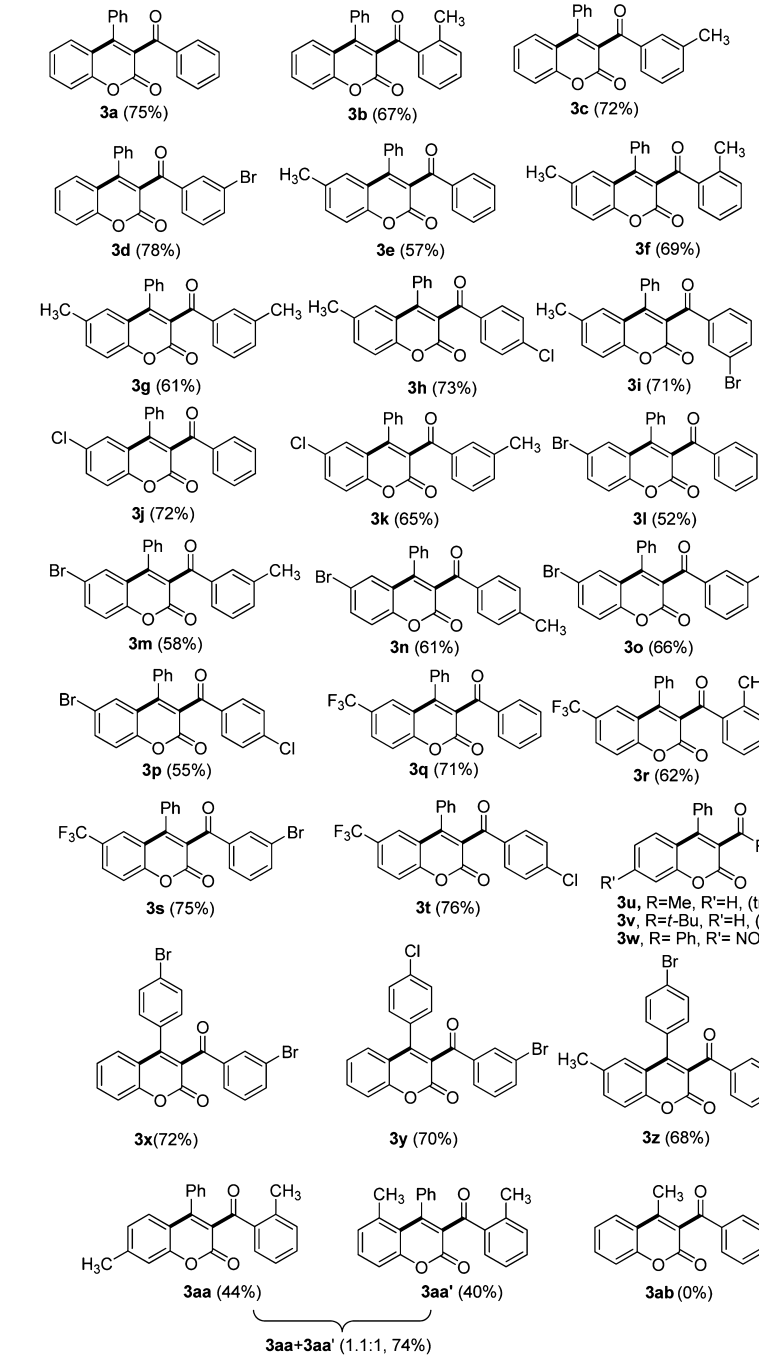
Table 2. Silver-Mediated Synthesis of Coumarin Derivatives via Radical Cyclization of Alkynoates with α-Keto Acids[a−c]





[a]Reaction conditions: under nitrogen atmosphere, substituted alkynoates (0.3 mmol), α-keto acids (0.6 mmol), $AgNO_3$(0.3 mmol), $K_2S_2O_8$ (1.2 mmol), CH_3CN/H_2O (v_1/v_2 = 1:1) (2.0 mL), 60 °C. [b]Isolated yield. [c]Reaction time (24 h).

reactions for the synthesis of coumarin derivatives is suggested in Scheme 3. First, an acyl radical (**A**) is generated from α-keto acids (**2**) by Ag(I)/$K_2S_2O_8$ with release of one molecular CO_2.[27] Selectivie addition of the acyl radical (**A**) to the alkynoates (**1**) gives the vinyl radical (**B**) stabilized by the phenyl group. Subsequently, the vinyl radical (**B**) undergoes an intramolecular cyclization to generate radical intermediate **C**. Finally, an Ag(II)-mediated hydrogen abstraction of radical intermediate **C** takes place, releasing the product **3**, H^+, and Ag(I).

In summary, a novel and useful protocol has been developed for the synthesis of coumarin derivatives via silver-mediated

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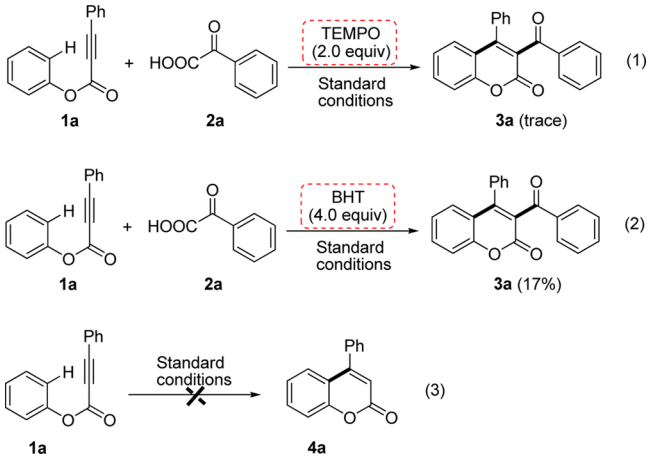
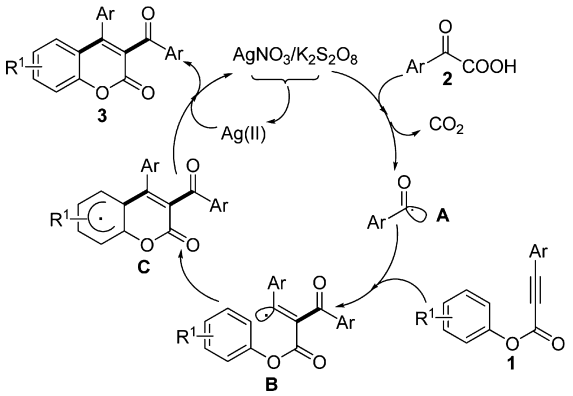
Scheme 2. Control Experiments



Scheme 3. Proposed Mechanism for the Direct Transformation



tandem radical cyclization of readily prepared alkynoates and α-keto acids. A series of potentially biological coumarin frameworks could be conveniently and efficiently obtained in moderate to good yields with excellent functional group tolerance. The easy and efficient method for the synthesis of coumarin compounds should attract much attention in synthetic and pharmaceutical chemistry.

EXPERIMENTAL SECTION

General Methods. All commercially available reagent-grade chemicals were purchased from chemical suppliers and used as received without further purification unless otherwise stated. Alkynoates were prepared according to previous literatures.[28] All solvents were dried according to standard procedures. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on a 400 MHz spectrometer with TMS as internal standard (400 MHz ^{1}H, 100 MHz ^{13}C) at room temperature, the chemical shifts (δ) were expressed in ppm, and J values were given in hertz. The following abbreviations are used to indicate the multiplicity: singlet (s), doublet (d), triplet (t), and multiplet (m). All first-order splitting patterns were assigned on the basis of the appearance of the multiplet. Splitting patterns that could not be easily interpreted were designated as multiplet (m). Mass analyses and HRMS were obtained by ESI on a TOF mass analyzer. Column chromatography was performed on silica gel (200−300 mesh).

General Experimental Procedures. A 25 mL Schlenk tube equipped with a magnetic stirring bar was charged with $AgNO_3$ (51 mg, 0.3 mmol), potassium persulfate (324 mg, 1.2 mmol), substituted various alkynoates (**1**) (0.3 mmol), and α-keto acids (**2**) (0.6 mmol). The tube was evacuated twice and backfilled with nitrogen, and 2 mL of CH_3CN/H_2O (v_1/v_2 = 1:1) was added to the tube under nitrogen atmosphere. The tube was sealed with a balloon, and then the mixture was allowed to stir under nitrogen atmosphere at 60 °C for 24 h. After completion of the reaction, the resulting solution was cooled to room temperature, and the solvent was removed with the aid of a rotary evaporator. The residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate as eluent to provide the desired product (**3**).

*3-Benzoyl-4-phenyl-2H-chromen-2-one (**3a**).* Compound **3a** was obtained in 75% yield (74 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (20:1); mp 100−101 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.81 (d, 2H, J = 8.0 Hz), 7.66−7.62 (m, 1H), 7.50 (t, 2H, J = 8.0 Hz), 7.38−7.35 (m, 5H), 7.30−7.27 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 192.1, 158.8, 153.8, 153.0, 136.3, 133.8, 132.7, 132.3, 129.5, 129.3, 128.7, 128.6, 128.0, 126.0, 124.7, 119.5, 117.2; HRMS m/z calcd for $C_{22}H_{14}O_3$ [M + Na]$^+$ 349.0841, found 349.0827.

*3-(2-Methylbenzoyl)-4-phenyl-2H-chromen-2-one (**3b**).* Compound **3b** was obtained in 67% yield (68 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (30:1); mp 177−179 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.64−7.58 (m, 2H), 7.48 (d, 2H, J = 8.0 Hz), 7.36−7.32 (m, 4H), 7.26−7.23 (m, 4H), 7.17−7.12 (m, 2H), 2.41 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 193.8, 158.8, 153.7, 152.3, 140.2, 136.0, 132.6, 132.5, 132.4, 132.0, 131.1, 129.3, 128.6, 128.5, 127.9, 127.5, 125.5, 124.6, 119.6, 117.2, 21.3; HRMS m/z calcd for $C_{23}H_{16}O_3$ [M + Na]$^+$ 363.0997, found 363.0996.

*3-(3-Methylbenzoyl)-4-phenyl-2H-chromen-2-one (**3c**).* Compound **3c** was obtained in 72% yield (73 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (20:1); mp 154−156 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.72 (d, 2H, J = 8.0 Hz), 7.65−7.61 (m, 1H), 7.48 (d, 1H, J = 8.0 Hz), 7.37−7.35 (m, 3H), 7.18 (d, 1H, J = 8.0 Hz), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 191.7, 158.6, 153.7, 152.7, 144.9, 133.8, 132.6, 132.4, 129.4, 129.3, 128.7, 128.6, 128.0, 126.2, 124.6, 119.5, 117.2, 21.8; HRMS m/z calcd for $C_{23}H_{16}O_3$ [M + Na]$^+$ 363.0997, found 363.0996.

*3-(3-Bromobenzoyl)-4-phenyl-2H-chromen-2-one (**3d**).* Compound **3d** was obtained in 78% yield (95 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (20:1); mp 150−152 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.91 (s, 1H), 7.43 (d, 1H, J = 8.0 Hz), 7.66−7.63 (m, 2H), 7.50 (d, 1H, J = 8.0 Hz), 7.40−7.36 (m, 3H), 7.34−7.24 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 190.6, 158.5, 153.8, 153.5, 138.0, 136.5, 132.9, 132.2, 132.0, 130.1, 129.7, 128.7, 128.1, 127.7, 125.3, 124.7, 122.9, 119.3, 117.3; HRMS m/z calcd for $C_{22}H_{13}BrO_3$ [M + Na]$^+$ 426.9946, 428.9925, found 426.9947, 428.9925.

*3-Benzoyl-6-methyl-4-phenyl-2H-chromen-2-one (**3e**).* Compound **3e** was obtained in 57% yield (58 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (20:1); mp 167−169 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.81 (d, 2H, J = 8.0 Hz), 7.51 (t, 1H, J = 8.0 Hz), 7.40−7.33 (m, 5H), 7.29−7.26 (m, 3H), 7.19 (d, 1H, J = 8.0 Hz), 7.08 (d, 1H, J = 8.0 Hz), 7.51 (t, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 192.4, 159.1, 153.9, 153.1, 144.3, 133.7, 132.6, 129.4, 129.3, 128.7, 128.6, 128.5, 127.7, 125.9, 117.3, 117.0, 21.7; HRMS m/z calcd for $C_{23}H_{16}O_3$ [M + Na]$^+$ 363.0997, found 363.0992.

*3-Benzoyl-6-methyl-4-phenyl-2H-chromen-2-one (**3f**).* Compound **3f** was obtained in 69% yield (73 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (30:1); mp 131−132 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.57 (d, 1H, J = 8.0 Hz), 7.34−7.28 (m, 5H), 7.23−7.20 (m, 2H), 7.16−7.11 (m, 3H), 7.05 (d, 1H, J = 8.0 Hz), 2.50 (s, 3H), 2.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 194.0, 159.0, 153.8, 152.5, 144.1, 140.1, 132.7, 132.3, 131.9, 131.0, 129.2, 128.5, 128.4, 127.7, 125.8, 125.5, 117.3, 117.2, 21.7, 21.2; HRMS m/z calcd for $C_{24}H_{18}O_3$ [M + Na]$^+$ 377.1154, found 377.1149.

*6-Methyl-3-(2-methylbenzoyl)-4-phenyl-2H-chromen-2-one (**3g**).* Compound **3g** was obtained in 61% yield (65 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (20:1); mp 124−126 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.63−7.60 (m,

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2H), 7.36−7.32 (m, 4H), 7.29−7.24 (m, 4H), 7.19 (d, 1H, J = 8.0 Hz), 7.08 (d, 1H, J = 8.0 Hz), 2.51 (s, 3H), 2.34 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 192.5, 159.1, 153.9, 153.0, 144.2, 134.6, 129.6, 129.4, 128.7, 128.5, 128.4, 127.7, 126.7, 125.9, 117.3, 117.1, 21.7, 21.3; HRMS m/z calcd for $C_{24}H_{18}O_3$ $[M + Na]^+$ 377.1154, found 377.1149.

*3-(4-Chlorobenzoyl)-6-methyl-4-phenyl-2H-chromen-2-one (**3h**).* Compound **3h** was obtained in 73% yield (82 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (30:1); mp 155−156 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.66 (t, 1H, J = 4.0 Hz), 7.68 (d, 1H, J = 8.0 Hz), 7.48 (d, 1H, J = 8.0 Hz), 7.38−7.35 (m, 3H), 7.34−7.25 (m, 4H), 7.19 (d, 1H, J = 8.0 Hz), 7.09 (d, 1H, J = 8.0 Hz), 2.52 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 191.1, 158.9, 153.9, 153.7, 144.6, 134.9, 133.6, 129.9, 129.6, 129.1, 128.6, 127.8, 127.3, 126.0, 117.4, 116.9, 21.7; HRMS m/z calcd for $C_{23}H_{15}ClO_3$ $[M + Na]^+$ 397.0607, found 397.0612.

*3-(3-Bromobenzoyl)-6-methyl-4-phenyl-2H-chromen-2-one (**3i**).* Compound **3i** was obtained in 73% yield (89 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (20:1); mp 147−149 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.91 (t, 1H, J = 4.0 Hz), 7.72 (d, 1H, J = 8.0 Hz), 7.63 (d, 1H, J = 8.0 Hz), 7.38−7.35 (m, 3H), 7.30−7.25 (m, 4H), 7.22 (d, 1H, J = 8.0 Hz), 7.09 (d, 1H, J = 8.0 Hz), 2.52 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 191.1, 158.9, 153.9, 153.8, 144.7, 136.5, 132.0, 130.1, 129.6, 128.6, 127.8, 126.0, 117.4, 116.9, 21.9; HRMS m/z calcd for $C_{23}H_{15}BrO_3$ $[M + Na]^+$ 441.0102, 443.0082, found 441.0111, 443.0076.

*3-Benzoyl-6-chloro-4-phenyl-2H-chromen-2-one (**3j**).* Compound **3i** was obtained in 72% yield (67 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (20:1); mp 148−150 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.79 (d, 2H, J = 8.0 Hz), 7.54−7.49 (m, 2H), 7.40−7.34 (m, 5H), 7.27−7.24 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 191.7, 158.2, 154.0, 152.4, 138.8, 136.1, 134.0, 132.0, 129.7, 129.3, 128.9, 128.7, 128.6, 125.9, 125.3, 118.1, 117.4; HRMS m/z calcd for $C_{22}H_{13}ClO_3$ $[M + Na]^+$ 383.0451, found 383.0449.

*3-Benzoyl-6-chloro-4-phenyl-2H-chromen-2-one (**3k**).* Compound **3k** was obtained in 65% yield (73 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (30:1); mp 142−144 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.56 (d, 2H, J = 8.0 Hz), 7.47 (d, 2H, J = 4.0 Hz), 7.37−7.30 (m, 4H), 7.22−7.19 (m, 4H), 7.15 (d, 2H, J = 8.0 Hz), 2.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 193.3, 158.2, 153.9, 151.7, 140.2, 138.7, 132.6, 132.0, 131.0, 129.5, 128.9, 128.6, 128.5, 125.6, 125.2, 118.3, 117.4, 21.3; HRMS m/z calcd for $C_{23}H_{15}ClO_3$ $[M + Na]^+$ 397.0607, found 397.0603.

*3-Benzoyl-6-bromo-4-phenyl-2H-chromen-2-one (**3l**).* Compound **3l** was obtained in 52% yield (63 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (20:1); mp 185−187 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.80 (d, 2H, J = 8.0 Hz), 7.65 (d, 2H, J = 4.0 Hz), 7.53 (t, 1H, J = 8.0 Hz), 7.40−7.35 (m, 6H), 7.27−7.25 (m, 2H), 7.17 (d, 2H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 191.7, 158.1, 153.9, 152.4, 136.1, 134.0, 131.9, 129.7, 129.2, 129.0, 128.7, 128.1, 126.9, 126.1, 120.4, 118.5; HRMS m/z calcd for $C_{22}H_{13}BrO_3$ $[M + Na]^+$ 426.9946, 428.9925, found 426.9941, 428.9927.

*6-Bromo-3-(3-methylbenzoyl)-4-phenyl-2H-chromen-2-one (**3m**).* Compound **3m** was obtained in 58% yield (73 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (20:1); mp 145−146 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.66 (d, 1H, J = 4.0 Hz), 7.61−7.58 (m, 2H), 7.41−7.34 (m, 5H), 7.29−7.25 (m, 3H), 7.17 (d, 2H, J = 8.0 Hz), 2.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 191.9, 158.1, 153.8, 152.3, 138.5, 134.8, 132.0, 129.7, 129.5, 129.0, 128.7, 128.5, 128.1, 126.7, 120.4, 118.5, 21.2; HRMS m/z calcd for $C_{23}H_{15}BrO_3$ $[M + Na]^+$ 441.0102, 443.0082, found 441.0113, 443.0081.

*6-Bromo-3-(4-methylbenzoyl)-4-phenyl-2H-chromen-2-one (**3n**).* Compound **3n** was obtained in 61% yield (76 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (20:1); mp 203−204 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.70 (d, 2H, J = 8.0 Hz), 7.65 (s, 1H), 7.40−7.36 (m, 4H), 7.29−7.25 (m, 2H), 7.19−7.15 (m, 3H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 191.3, 158.2, 153.8, 152.1, 145.1, 133.7, 132.0, 129.7, 129.4, 128.9, 128.7, 128.6, 128.1, 126.7, 126.3, 120.4, 118.6, 21.8; HRMS m/z calcd for $C_{23}H_{15}BrO_3$ $[M + Na]^+$ 441.0102, 443.0082, found 441.0112, 443.0081.

*6-Bromo-3-(3-bromobenzoyl)-4-phenyl-2H-chromen-2-one (**3o**).* Compound **3o** was obtained in 66% yield (95 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (20:1); mp 138−140 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.89 (t, 1H, J = 2.0 Hz), 7.70 (d, 1H, J = 8.0 Hz), 7.67 (d, 1H, J = 4.0 Hz), 7.62 (d, 1H, J = 8.0 Hz), 7.42−7.36 (m, 4H), 7.26−7.22 (m, 3H), 7.18 (d, 1H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 190.4, 157.9, 153.9, 153.0, 137.8, 136.7, 131.9, 131.7, 130.2, 129.9, 129.4, 129.1, 128.8, 128.6, 128.3, 127.7, 127.2, 122.9, 120.5, 118.3; HRMS m/z calcd for $C_{22}H_{12}Br_2O_3$ $[M + Na]^+$ 504.9051, 506.9030, found 504.9049, 506.9033.

*6-Bromo-3-(4-chlorobenzoyl)-4-phenyl-2H-chromen-2-one (**3p**).* Compound **3p** was obtained in 55% yield (72 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (20:1); mp 164−166 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.74 (d, 2H, J = 8.0 Hz), 7.67 (d, 1H, J = 4.0 Hz), 7.43−7.35 (m, 6H), 7.26−7.23 (m, 2H), 7.17 (d, 1H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 190.5, 158.0, 153.9, 152.8, 140.5, 130.5, 129.9, 129.1, 129.0, 128.8, 128.6, 120.5, 118.4; HRMS m/z calcd for $C_{22}H_{12}BrClO_3$ $[M + Na]^+$ 460.9556, 462.9536, found 504.9049, 506.9033.

*3-Benzoyl-4-phenyl-6-(trifluoromethyl)-2H-chromen-2-one (**3q**).* Compound **3q** was obtained in 71% yield (84 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (20:1); mp 206−208 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.80 (d, 2H, J = 8.0 Hz), 7.74 (s, 1H), 7.52 (t, 2H, J = 8.0 Hz), 7.46−7.44 (m, 1H), 7.41−7.36 (m, 5H), 7.29−7.25 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 191.4, 157.9, 153.4, 151.7, 135.8, 134.1(q, ^2J = 32.3 Hz), 131.6, 129.9, 129.2 (q, ^1J = 271.2 Hz), 128.9, 128.8, 128.7, 128.6, 127.9, 121.1, 121.0, 114.6, 114.5, 114.4; HRMS m/z calcd for $C_{23}H_{13}F_3O_3$ $[M + Na]^+$ 417.0714, found 417.0716.

*3-(2-Methylbenzoyl)-4-phenyl-6-(trifluoromethyl)-2H-chromen-2-one (**3r**).* Compound **3r** was obtained in 62% yield (76 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (30:1); mp 111−113 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.73−7.30 (m, 3H), 7.52−7.44 (m, 2H), 7.40−7.37 (m, 3H), 7.30−7.26 (m, 2H), 7.19 (d, 2H, J = 8.0 Hz), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 190.9, 158.0, 153.3, 151.4, 145.3, 133.4 (q, ^2J = 33.0 Hz), 131.7, 129.5 (q, ^1J = 270.2 Hz), 128.8, 128.6, 127.9, 121.0, 114.6, 114.5, 21.8; HRMS m/z calcd for $C_{24}H_{15}F_3O_3$ $[M + Na]^+$ 431.0871, found 431.0874.

*3-(3-Bromobenzoyl)-4-phenyl-6-(trifluoromethyl)-2H-chromen-2-one (**3s**).* Compound **3r** was obtained in 75% yield (106 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (30:1); mp 176−178 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.90 (t, 1H, J = 2.0 Hz), 7.74 (s, 1H), 7.71 (d, 1H, J = 8.0 Hz), 7.66 (d, 1H, J = 8.0 Hz), 7.51−7.46 (m, 2H), 7.42−7.39 (m, 3H), 7.30−7.26 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 190.1, 157.7, 153.4, 152.3, 137.5, 136.9, 131.9, 131.4, 130.2, 130.1, 128.9 (q, ^1J = 270.0 Hz), 127.3, 123.0, 121.2, 114.7, 114.6; HRMS m/z calcd for $C_{24}H_{15}F_3O_3$ $[M + Na]^+$ 431.0871, found 431.0874.

*3-(3-Bromobenzoyl)-4-phenyl-6-(trifluoromethyl)-2H-chromen-2-one (**3t**).* Compound **3t** was obtained in 76% yield (98 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (20:1); mp 162−164 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.75−7.72 (m, 3H), 7.51−7.45 (m, 2H), 7.41−7.35 (m, 5H), 7.29−7.25 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 190.2, 157.8, 153.4, 152.0, 140.7, 134.2, 131.5, 130.5, 130.1, 129.1(q, ^1J = 270.0 Hz), 128.9, 128.6, 114.7, 114.6; HRMS m/z calcd for $C_{23}H_{12}ClF_3O_3$ $[M + Na]^+$ 451.0325, found 451.0320.

*3-(3-Bromobenzoyl)-4-(4-bromophenyl)-2H-chromen-2-one (**3x**).* Compound **3w** was obtained in 72% yield (104 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (20:1); mp 121−123 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.92 (s, 1H), 7.74 (d, 1H, J = 8.0 Hz), 7.69−7.64 (m, 2H), 7.52−7.48 (m, 3H), 7.32−7.25 (m, 3H), 7.17 (d, 2H, J = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz,

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J. Org. Chem. 2015, 80, 1550−1556

ppm) δ 190.5, 158.4, 153.8, 152.5, 137.8, 136.9, 133.3, 132.1, 132.0, 131.0, 130.4, 130.3, 127.8, 125.5, 125.0, 124.3, 123.1, 119.0, 117.4; HRMS *m/z* calcd for $C_{22}H_{12}Br_2O_3$ $[M + Na]^+$ 504.9051, 506.9030, found 504.9049, 506.9033.

*3-(3-Bromobenzoyl)-4-(4-chlorophenyl)-2H-chromen-2-one (**3y**).* Compound **3x** was obtained in 70% yield (92 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (20:1); mp 103−104 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.93 (s, 1H), 7.74 (d, 1H, *J* = 8.0 Hz), 7.69−7.64 (m, 2H), 7.49 (d, 1H, *J* = 8.0 Hz), 7.38 (d, 2H, *J* = 8.0 Hz), 7.31−7.26 (m, 3H), 7.23 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 190.6, 158.4, 153.8, 152.5, 137.8, 136.9, 136.1, 133.2, 132.0, 130.5, 130.4, 130.1, 128.1, 127.8, 125.6, 125.0, 123.1, 119.1, 117.4; HRMS *m/z* calcd for $C_{22}H_{12}BrClO_3$ $[M + Na]^+$ 460.9556, 462.9536, found 460.9551, 462.9532.

*3-(3-Bromobenzoyl)-4-(4-bromophenyl)-6-methyl-2H-chromen-2-one (**3z**).* Compound **3y** was obtained in 68% yield (101 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (20:1); mp 126−127 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.92 (s, 1H), 7.73 (d, 1H, *J* = 8.0 Hz), 7.67 (d, 1H, *J* = 8.0 Hz), 7.53 (d, 2H, *J* = 8.0 Hz), 7.30−7.26 (m, 2H), 7.16−7.11 (m, 4H), 2.52 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 190.7, 158.7, 153.9, 152.7, 144.9, 136.8, 136.7, 132.0, 131.2, 130.3, 130.2, 130.1, 127.7, 127.5, 126.2, 124.1, 123.0, 111.5, 116.5, 21.8; HRMS *m/z* calcd for $C_{23}H_{14}Br_2O_3$ $[M + Na]^+$ 518.9207, 520.9187, found 518.9201, 520.9185.

*7-Methyl-3-(2-methylbenzoyl)-4-phenyl-2H-chromen-2-one (**3aa**).* Compound **3aa** was obtained in 44% yield (47 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (50:1); mp 139−141 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.59 (d, 1H, *J* = 8.0 Hz), 7.42 (d, 1H, *J* = 8.0 Hz), 7.37−7.29 (m, 4H), 7.22−7.20 (m, 2H), 7.16−7.10 (m, 2H), 7.00 (s, 1H), 2.39 (s, 3H), 2.32 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 194.0, 159.1, 152.4, 151.8, 141.1, 136.1, 134.5, 133.7, 132.5, 132.4, 131.9, 131.1, 129.3, 128.5, 128.4, 127.9, 127.3, 125.5, 119.2, 116.9; HRMS *m/z* calcd for $C_{24}H_{18}O_3$ $[M + Na]^+$ 377.1154, found 377.1150.

*5-Methyl-3-(2-methylbenzoyl)-4-phenyl-2H-chromen-2-one (**3aa′**).* Compound **3aa** was obtained in 40% yield (43 mg) according to the general procedure: eluent petroleum ether/ethyl acetate (50:1); mp 131−133 °C; ^{1}H NMR ($CDCl_3$, 400 MHz, ppm) δ 7.59 (d, 1H, *J* = 8.0 Hz), 7.47 (d, 1H, *J* = 8.0 Hz), 7.34−7.28 (m, 4H), 7.22−7.20 (m, 2H), 7.16−7.07 (m, 4H), 2.39 (s, 3H), 2.32 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz, ppm) δ 194.0, 159.0, 152.0, 140.0, 136.1, 133.9, 132.8, 132.4, 132.0, 131.1, 129.2, 128.6, 128.4, 126.6, 125.7, 125.5, 124.0, 119.4, 21.3; HRMS *m/z* calcd for $C_{24}H_{18}O_3$ $[M + Na]^+$ 377.1154, found 377.1150.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra for all compounds and ORTEP structures of compound **3a**, spectroscopic data for **3a**; X-ray results (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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