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Cyanomethylation and Cyclization of Aryl Alkynoates with Acetonitrile under Transition-Metal-Free Conditions: Synthesis of 3-Cyanomethylated Coumarins

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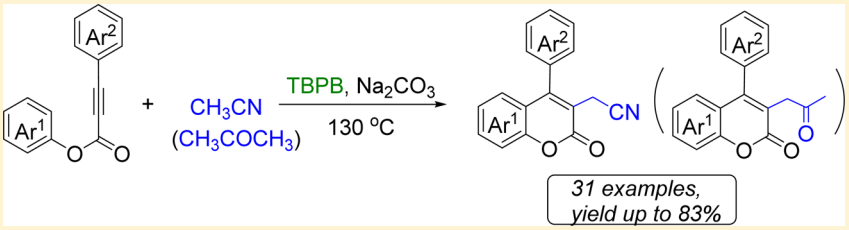
Supporting Information



ABSTRACT: Cyanomethylated coumarins were synthesized via cyanomethylation and cyclization of aryl alkynoates using cheap and available reagent acetonitrile as the cyanomethyl source in the presence of TBPB (*tert*-butyl peroxybenzoate) under transition-metal-free conditions. For the substrates with various substituents on benzene ring, the reaction proceeded smoothly to give the corresponding products in moderate to good yields. The resulting products could be simply converted into some other related coumarin derivatives.

The cyano group exists in a number of natural products and pharmaceuticals.[1] It is also an important structural motif in organic synthesis because this group can be easily converted into other functional groups such as carboxylic acids, esters, amides, amines, aldehydes, tetrazoles, and ketones.[2] In addition, the C−CN bond activation provided new chances for the synthesis of various functional molecules.[3] Thus, much effort has been directed toward the preparation of nitriles. Except virulent potassium cyanide or sodium cyanide, several compounds such as TMSCN,[4] *N*-cyanosuccinimide,[5] *N*-cyano-*N*-phenyl-*p*-methylbenzenesulfonamide (NCTS),[6] etc. were employed as cyano sources. Moreover, a series of cyanation methods were developed by using inert acetonitrile as the cyanating reagent via C−CN bond cleavage.[7] Except for direct cyanation, cyanoalkylation provided another synthetically useful protocol for the synthesis of nitriles.[8] As a cheap and available cyano-containing compound, the synthetic use of acetonitrile via the methyl C (sp^3)−H bond activation has aroused much attention in recent years. Especially, the cyanomethylation of activated alkenes have been well studied, and a cyanomethyl radical was believed to be involved in these tandem reaction processes.[9] It will be valuable to further develop the application of this reagent in the synthesis of the useful cyano-containing compounds from the viewpoint of perfect atom economy.

The addition of radicals to a carbon−carbon triple bond can form the highly reactive vinyl radicals. The sequential additions of these vinyl radicals to other π-systems provide the opportunity to construct new carbon−carbon bonds, especially to produce cyclic compounds. By this strategy, a series of coumarin derivatives, a class of very important heterocyclic compounds in pharmaceuticals as well as in fluorescent materials,[10] were synthesized via the addition of several radicals to aryl alkynoates, in which diselenides,[11] Togni's reagent (trifluoromethylation reagent),[12] dialkyl H-phosphonates,[13] sulfonylhydrazides,[14] sulfinic acids,[15] α-keto acids,[16] ethyl bromodifluoroacetate,[17] NIS,[18] and 2,4-diones[19] were employed as the radical sources. In continuation of our study on the covalent bond activation of inert solvents and their application in organic synthesis,[20] in this work, we selected acetonitrile as the cyanomethyl source, through a peroxide promoted C−H bond activation and addition to the carbon−carbon triple bond of aryl alkynoates, followed by cyclization to synthesize 3-cyanomethylated coumarins.

In our initial study, phenyl 3-phenylpropiolate (**1a**) was chosen as a model substrate to react with acetonitrile for the optimization of reaction conditions (Table 1). We were pleased to find that peroxide could obviously promote the transformation. In the presence of 1 equiv TBPB (*tert*-butyl peroxybenzoate) and without any transition-metal catalyst, a cyanomethylated and cyclized product 2-(2-oxo-4-phenyl-2*H*-chromen-3-yl)acetonitrile (**2a**) was obtained in 30% yield at 120 °C under a N_2 atmosphere after 16 h (entry 1). Increasing TBPB to 2.0 equiv resulted in a higher yield of 45% (entry 2); while the addition of 3.0 equiv TBPB did not further improve the yield of the product (entry 3). Several other peroxides such

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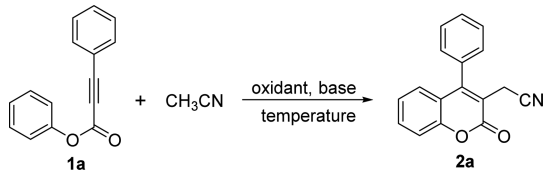
Table 1. Optimization of Reaction Conditions[a]



1a 2a

entry	oxidant (equiv)	base (equiv)	temp (°C)	yield (%)
1	TBPB (1)	–	120	30
2	TBPB (2)	–	120	45
3	TBPB (3)	–	120	42
4	DTBP (2)	–	120	<5
5	TBHP (2)	–	120	<5
6	BPO (2)	–	120	12
7	DCP (2)	–	120	15
8	TBPB (2)	–	130	60
9	TBPB (2)	–	100	16
10	TBPB (2)	KOAc (2)	130	65
11	TBPB (2)	K_2HPO_4 (2)	130	73
12	TBPB (2)	$NaHCO_3$ (2)	130	75
13	TBPB (2)	Na_2CO_3 (2)	130	83
14	TBPB (2)	NaOH (2)	130	80
15[b]	TBPB (2)	Na_2CO_3 (2)	130	78

[a]Unless otherwise specified, the reactions were carried out in the presence of **1a** (0.3 mmol), oxidant, base, and CH_3CN (2 mL) under a N_2 atmosphere for 16 h. [b]In an air atmosphere.

as DTBP (di-*tert*-butyl peroxide), TBHP (*tert*-butyl hydroperoxide), BPO (benzoyl peroxide), and DCP (dicumyl peroxide) were then screened, and all of them showed very low efficiency for this reaction (entries 4–7). Raising the reaction temperature to 130 °C enhanced the yield to 62%, but at 100 °C, only a low yield of 16% was obtained (entries 8, 9). The presence of a base proved to be beneficial for the reaction. Thus, a series of bases were tested, and Na_2CO_3 gave the best result (entries 10–14). When 2 equiv Na_2CO_3 were added, the yield of **2a** could be increased to 83% (entry 14). In addition, if the reaction took place in an air atmosphere, little decrease in the yield occurred (entry 15).

With the optimized conditions in hand, we then examined the reaction of various alkynoates with CH_3CN (Table 2). Aryl phenylpropiolates with a variety of substituents on the aromatic ring (phenoxy ring) were first employed as the reactants. It was interesting that the ester migration might occur in these reaction processes and the position of C–O bond in the products was not the same as that in the substrates, which was consistent with the previous related reports.[16b,18,19] For example, when the substrates with a substituent on the *para*-position of the phenoxy ring were used, the 7-position substituted coumarin derivatives were obtained (**2b–2l**). The reactions of the substrates with electron-donating groups such as alkyl, alkoxy, or phenyl on the aromatic rings gave moderate to good yields (**2b–2h**), and the presence of electron-withdrawing groups such as halogen or trifluoromethyl led to a small decrease in the yields (**2i–2l**). A 3,5-dimethyl substituted substrate (**1m**) also gave the corresponding product (**2m**) in 79% yield. For the *meta*-chloro substituted reactant (**1n**), a mixture of the products $\mathbf{2n^1}$ and $\mathbf{2n^2}$ was separated from the reaction mixture in a ratio of **2:1**. However, from *o*-tolyl phenylpropiolate (**1p**), we almost did not obtain the desired product, which was obviously due to the steric hindrance. We next investigated the influence of the substituent directly bonded to the carbon–carbon triple bond. As shown in Table 2, alkynes having either an electron-deficient or electron-rich aromatic ring gave the corresponding coumarins in moderate yields (**2q–2z**), and the electronic effect of the substituent here was not evident. When an alkyl group directly bonded to the carbon–carbon triple bond, however, no desired coumarin derivative (**2aa**) was obtained.

The structures of **2h** and **2u** were further confirmed by single crystal X-ray diffraction analysis (see Supporting Information).[21]

We further explored the scope of this tandem cyclization by using acetone instead of acetonitrile. Under the same reaction conditions, 3-(2-oxopropyl) substituted coumarins **3** were obtained in satisfactory yields (Scheme 1).

As mentioned before, the cyano group is an important motif which can be converted into various functional groups. We then decided to use this intramolecular cyclization in the synthesis of other functionalized coumarins by the conversion of the cyano group (Scheme 2). First, by dissolving the cyanomethylated product 2-(2-oxo-4-phenyl-2*H*-chromen-3-yl)acetonitrile (**2a**) in methanol, in the presence of H_2SO_4, **2a** could be converted into methyl 2-(2-oxo-4-phenyl-2*H*-chromen-3-yl)acetate (**4a**) after heating the mixture for 24 h. In addition, **2a** could be easily hydrolyzed to generate 2-(2-oxo-4-phenyl-2*H*-chromen-3-yl)acetamide (**5a**) in the presence of H_2O_2 and K_2CO_3.

In order to understand the details of the reaction mechanism, some control experiments were carried out, as shown in Scheme 3. The reaction was completely inhibited when 4 equiv of radical scavenger TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy) or BHT (2,6-di-*tert*-butyl-4-methylphenol) was added under the standard reaction conditions. These results indicated that this reaction might proceed via a radical pathway.

Based on the above results and the previous related reports,[11–19] a possible reaction mechanism was proposed in Scheme 4. Initially, TBPB decomposed into the *tert*-butoxy and benzoyloxy radical at high temperature. These radicals abstracted a hydrogen radical from CH_3CN to generate the cyanomethyl radical which added to alkynoate (**1b**) to produce the alkenyl radical **A**. The radical intermediate **A** underwent an intramolecular spirocyclization to give the spiro-radical intermediate **B**. The ester migration then took place via a carboxyl radical **C** to generate the coumarin radical **D**. **D** was finally oxidized to a carbocation followed by deprotonation to yield the product **2b**.

In summary, we have developed a novel tandem oxidative cyclization reaction for the preparation of cyanomethylated coumarins using cheap and available acetonitrile as the cyanomethyl source by means of metal-free catalysis. The reaction was found to tolerate a wide range of functional groups. Furthermore, as an important precursor, the cyano group can be converted into various functional groups. The convenient and efficient pathway for the synthesis of functionalized coumarins will have significant value in synthetic and pharmaceutical chemistry.

EXPERIMENTAL SECTION

General. All reactions were run in a sealed tube with a Teflon lined cap under ambient N_2. Chemicals were commercially available from chemical suppliers and were used without purification. Solvents were dried in a standard manner. Aryl phenylpropiolates were prepared according to the literature procedures.[22] The NMR spectra were recorded at 400 MHz (^{1}H) and 100 MHz (^{13}C) in $CDCl_3$ or DMSO-d_6 using TMS as an internal standard. The following abbreviations

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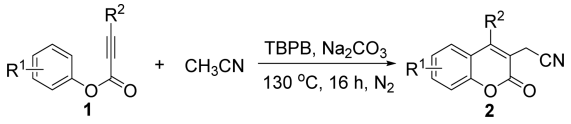
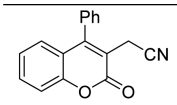
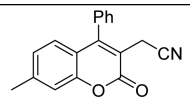
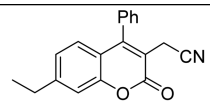
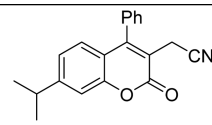
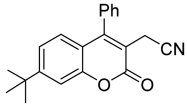
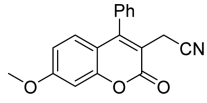
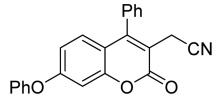
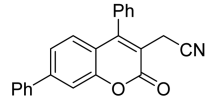
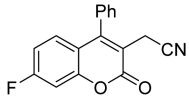
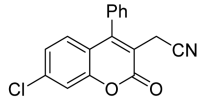
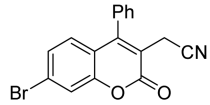
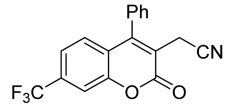
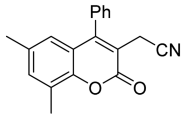
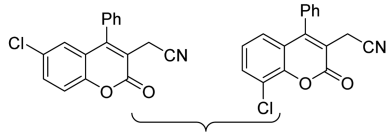
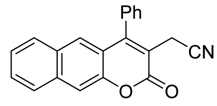
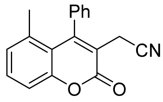
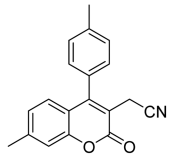
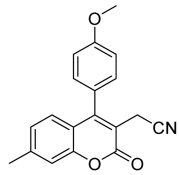
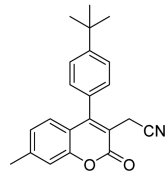
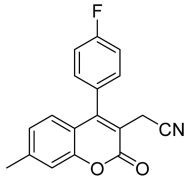
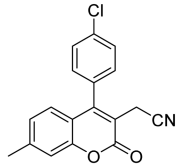
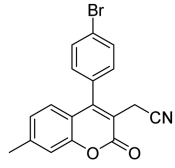
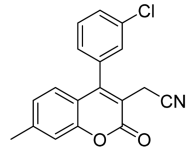
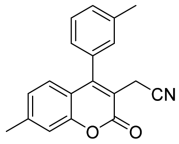
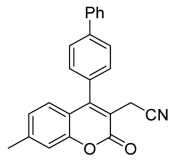
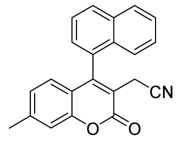
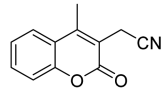
Table 2. Cyclization of Various Alkynoates with Acetonitrile[a]



 **2a**, 83%	 **2b**, 82%	 **2c**, 78%	 **2d**, 70%
 **2e**, 73%	 **2f**, 76%	 **2g**, 70%	 **2h**, 72%
 **2i**, 65%	 **2j**, 70%	 **2k**, 68%	 **2l**, 65%
 **2m**, 79%	 **2n**[1]+**2n**[2], 72% (2:1)		 **2o**, 76%
 **2p**, trace	 **2q**, 55%	 **2r**, 64%	 **2s**, 60%
 **2t**, 68%	 **2u**, 65%	 **2v**, 62%	 **2w**, 63%
 **2x**, 50%	 **2y**, 64%	 **2z**, 63%	 **2aa**, 0%

[a]Reaction conditions: **1** (0.3 mmol), TBPB (2 equiv), Na_2CO_3 (2 equiv) in CH_3CN (2 mL) at 130 °C under a N_2 atmosphere for 16 h.

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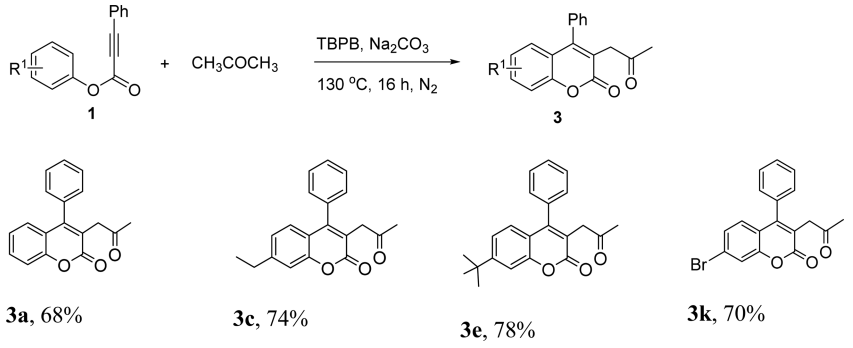
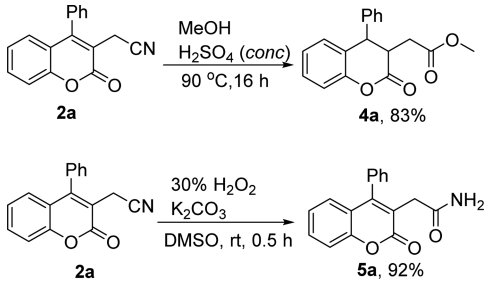
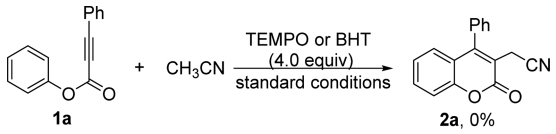
Scheme 1. Cyclization of Alkynoates with Acetone



Scheme 2. Transformation of Cyanomethylated Coumarin



Scheme 3. Control Experiments



were used to explain the multiplicities: s = singlet, d = doublet, dd = doublet of doublet, t = triplet, dt = doublet of triplet, td = triplet of doublet, q = quartet, m = multiplet, ddd = doublet of doublet of doublet. Melting points are uncorrected. Q-TOF was used for the HRMS measurements.

General Experimental Procedure for the Synthesis of Cyanomethylated Coumarins. Aryl alkynoate (**1**) (0.3 mmol), Na_2CO_3 (0.6 mmol), and TBPB (0.6 mmol) were added in CH_3CN (2 mL) under a N_2 atmosphere. The solution was stirred at 130 °C for 16 h. After completion of the reaction, the resulting solution was cooled to room temperature and diluted with EtOAc (15 mL) and then washed with brine. The organic layer was dried over anhydrous Mg_2SO_4, filtered, and concentrated in *vacuo*. The residue was purified by silica gel chromatography using hexane/ethyl acetate (5:1) to afford the pure product (**2**).

3-(2-Oxopropyl) substituted coumarins (**3a**, **3c**, **3e**, and **3k**) were synthesized using the same procedures in acetone.

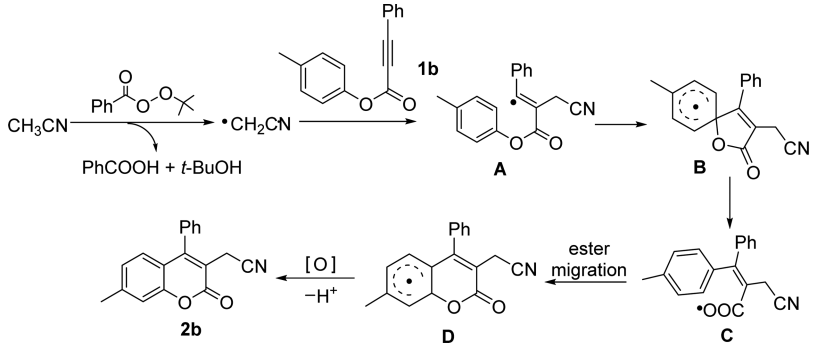
*Preparation of Methyl 2-(2-Oxo-4-phenyl-2H-chromen-3-yl)-acetate (**4a**).* To a solution of 2-(2-oxo-4-phenyl-2*H*-chromen-3-yl)acetonitrile (**2a**, 130.5 mg, 0.5 mmol) in MeOH (4 mL) in a sealed tube were added H_2O (4 drops) and H_2SO_4 (conc., 1.5 mL). The reaction mixture was heated at 90 °C for 24 h. After cooling to room temperature, the reaction mixture was slowly quenched with saturated aqueous $NaHCO_3$ to pH 8 and extracted with DCM (10 mL × 3). The combined organic phases were washed with brine (15 mL), dried over anhydrous Na_2SO_4, and concentrated in *vacuo*. The residue was purified by silica gel chromatography using hexane/ethyl acetate (5:1) to afford the pure product **4a**.

*Preparation of 2-(2-Oxo-4-phenyl-2H-chromen-3-yl)acetamide (**5a**).* To a stirred solution of 2-(2-oxo-4-phenyl-2*H*-chromen-3-yl)acetonitrile (**2a**, 130.5 mg, 0.5 mmol) in DMSO (2 mL) were added 30% H_2O_2 (0.5 mL) and K_2CO_3 (69.1 mg, 0.5 mmol) at 0 °C. Then the reaction mixture was stirred at room temperature for 0.5 h. After completion of the reaction, the reaction mixture was diluted with H_2O (15 mL) and extracted with EtOAc (15 mL × 3). The combined organic phases were washed with brine (15 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by silica gel chromatography using hexane/ethyl acetate (5:1) to afford the pure product **5a**.

*2-(2-Oxo-4-phenyl-2H-chromen-3-yl)acetonitrile (**2a**).* Yellow solid (65.0 mg, 83% yield); mp 134−135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63−7.57 (m, 4H), 7.43 (d, J = 8.2 Hz, 1H), 7.35 (dd, J = 7.6, 1.6 Hz, 2H), 7.25−7.21 (m, 1H), 7.10 (dd, J = 8.0, 1.4 Hz, 1H), 3.45 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 154.6, 153.1, 132.9, 132.5, 129.9, 129.5, 128.0, 124.7, 119.8, 117.0, 116.4, 116.3, 17.5; HRMS (ESI) m/z calcd for $C_{17}H_{12}NO_2$ $[M + H]^+$ 262.0863, found 262.0865.

*2-(7-Methyl-2-oxo-4-phenyl-2H-chromen-3-yl)acetonitrile (**2b**).* Yellow solid (67.7 mg, 82% yield); mp 98−100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64−7.58 (m, 3H), 7.34−7.32 (m, 2H), 7.23 (s, 1H), 7.04−7.02 (m, 1H), 6.97 (d, J = 8.1 Hz, 1H), 3.42 (s, 2H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 154.6, 153.1, 144.0,

Scheme 4. Plausible Reaction Mechanism



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133.1, 129.7, 129.4, 128.0, 127.6, 125.9, 117.4, 117.1, 116.6, 115.0, 21.7, 17.4; HRMS (ESI) m/z calcd for $C_{18}H_{14}NO_2$ $[M + H]^+$ 276.1019, found 276.1020.

2-(7-Ethyl-2-oxo-4-phenyl-2H-chromen-3-yl)acetonitrile (**2c**). Yellow solid (67.6 mg, 78% yield); mp 75−77 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64−7.56 (m, 3H), 7.35−7.32 (m, 2H), 7.26 (d, J = 1.2 Hz, 1H), 7.06 (dd, J = 8.2, 1.6 Hz, 1H), 7.00 (d, J = 8.2 Hz, 1H), 3.43 (s, 2H), 2.76 (q, J = 7.6 Hz, 2H), 1.28 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 154.6, 153.3, 150.2, 133.1, 129.7, 129.4, 128.0, 127.8, 124.7, 117.6, 116.6, 115.9, 115.0, 28.9, 17.5, 15.1; HRMS (ESI) m/z calcd for $C_{19}H_{16}NO_2$ $[M + H]^+$ 290.1176, found 290.1173.

2-(7-Isopropyl-2-oxo-4-phenyl-2H-chromen-3-yl)acetonitrile (**2d**). Yellow oil (63.7 mg, 70% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64−7.58 (m, 3H), 7.35−7.33 (m, 2H), 7.29 (d, J = 1.6 Hz, 1H), 7.10 (dd, J = 8.3, 1.7 Hz, 1H), 7.01 (d, J = 8.2 Hz, 1H), 3.43 (s, 2H), 3.05−2.98 (m, 1H), 1.29 (d, J = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 154.9, 154.6, 153.3, 133.1, 129.7, 129.4, 128.0, 127.8, 123.4, 117.7, 116.6, 115.0, 114.6, 34.2, 23.6, 17.4; HRMS (ESI) m/z calcd for $C_{20}H_{18}NO_2$ $[M + H]^+$ 304.1332, found 304.1334.

2-(7-tert-Butyl-2-oxo-4-phenyl-2H-chromen-3-yl)acetonitrile (**2e**). Yellow oil (69.5 mg, 73% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63−7.56 (m, 3H), 7.43 (d, J = 1.8 Hz, 1H), 7.34 (dd, J = 7.8, 1.7 Hz, 2H), 7.26 (dd, J = 8.5, 1.9 Hz, 1H), 7.03 (d, J = 8.4 Hz, 1H), 3.44 (s, 2H), 1.36 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 157.2, 154.5, 153.1, 133.1, 129.8, 129.4, 128.0, 127.5, 122.3, 117.4, 116.6, 115.2, 113.7, 35.3, 31.0, 17.4; HRMS (ESI) m/z calcd for $C_{21}H_{20}NO_2$ $[M + H]^+$ 318.1489, found 318.1492.

2-(7-Methoxy-2-oxo-4-phenyl-2H-chromen-3-yl)acetonitrile (**2f**). Yellow oil (66.4 mg, 76% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63−7.57 (m, 3H), 7.33 (dd, J = 7.8, 1.7 Hz, 2H), 6.99 (d, J = 8.9 Hz, 1H), 6.91 (d, J = 2.5 Hz, 1H), 6.78 (dd, J = 8.9, 2.5 Hz, 1H), 3.90 (s, 3H), 3.40 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 160.7, 154.9, 154.7, 133.2, 129.7, 129.4, 128.9, 127.9, 116.7, 113.4, 112.9, 112.7, 100.8, 55.9, 17.3; HRMS (ESI) m/z calcd for $C_{18}H_{14}NO_3$ $[M + H]^+$ 292.0968, found 292.0966.

2-(2-Oxo-7-phenoxy-4-phenyl-2H-chromen-3-yl)acetonitrile (**2g**). Yellow oil (74.2 mg, 70% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69−7.54 (m, 3H), 7.48−7.40 (m, 2H), 7.34 (dd, J = 7.7, 1.7 Hz, 2H), 7.27−7.23 (m, 1H), 7.10 (dd, J = 8.6, 1.0 Hz, 2H), 7.03 (d, J = 8.9 Hz, 1H), 6.92 (d, J = 2.4 Hz, 1H), 6.85 (dd, J = 8.9, 2.4 Hz, 1H), 3.41 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.9, 160.4, 154.8, 154.5, 133.0, 130.3, 129.8, 129.5, 129.3, 127.9, 125.3, 120.4, 116.6, 114.8, 114.6, 113.6, 104.9, 17.4; HRMS (ESI) m/z calcd for $C_{23}H_{16}NO_3$ $[M + H]^+$ 354.1125, found 354.1125.

2-(2-Oxo-4,7-diphenyl-2H-chromen-3-yl)acetonitrile (**2h**). Yellow solid (72.8 mg, 72% yield); mp 133−135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68−7.62 (m, 6H), 7.53−7.45 (m, 4H), 7.38 (dd, J = 7.8, 1.6 Hz, 2H), 7.17 (d, J = 8.3 Hz, 1H), 3.47 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 154.4, 153.4, 145.6, 138.7, 132.9, 129.9, 129.5, 129.2, 128.8, 128.3, 128.0, 127.2, 123.5, 118.7, 116.5, 115.8, 115.0, 17.6; HRMS (ESI) m/z calcd for $C_{23}H_{16}NO_2$ $[M + H]^+$ 338.1176, found 338.1178.

2-(7-Fluoro-2-oxo-4-phenyl-2H-chromen-3-yl)acetonitrile (**2i**). Yellow solid (54.4 mg, 65% yield); mp 159−160 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65−7.58 (m, 3H), 7.33 (dd, J = 7.7, 1.7 Hz, 2H), 7.15−7.08 (m, 2H), 6.98−6.93 (m, 1H), 3.42 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6 (d, J = 256.6 Hz), 160.0, 154.2 (d, J = 13.0 Hz), 154.2 (d, J = 1.0 Hz), 132.7, 130.1, 130.0 (d, J = 10.3 Hz), 129.9, 129.6, 127.9, 116.6 (d, J = 2.8 Hz), 116.3, 115.2 (d, J = 3.0 Hz), 112.8 (d, J = 22.6 Hz), 104.5 (d, J = 25.8 Hz), 17.5; HRMS (ESI) m/z calcd for $C_{17}H_{11}FNO_2$ $[M + H]^+$ 280.0768, found 280.0771.

2-(7-Chloro-2-oxo-4-phenyl-2H-chromen-3-yl)acetonitrile (**2j**). Yellow solid (62.0 mg, 70% yield); mp 140−141 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66−7.60 (m, 3H), 7.42 (d, J = 1.9 Hz, 1H), 7.34−7.32 (m, 2H), 7.19 (dd, J = 8.6, 2.0 Hz, 1H), 7.05 (d, J = 19.5 Hz, 1H), 3.43 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 154.0, 153.2, 138.5, 132.5, 130.1, 129.6, 128.9, 127.9, 125.3, 118.5, 117.2, 116.3, 116.2, 17.5; HRMS (ESI) m/z calcd for $C_{17}H_{11}ClNO_2$ $[M + H]^+$ 296.0473, found 296.0472.

2-(7-Bromo-2-oxo-4-phenyl-2H-chromen-3-yl)acetonitrile (**2k**). Yellow solid (69.2 mg, 68% yield); mp 105−107 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65−7.59 (m, 4H), 7.36−7.32 (m,3H), 6.96 (d, J = 8.6 Hz, 1H), 3.43 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 154.0, 153.1, 132.4, 130.1, 129.6, 129.0, 128.1, 127.9, 126.6, 120.2, 118.9, 116.5, 116.1, 17.6; HRMS (ESI) m/z calcd for $C_{17}H_{11}BrNO_2$ $[M + H]^+$ 339.9968, found 339.9969.

2-(7-(Trifluoromethyl)-2-oxo-4-phenyl-2H-chromen-3-yl)-acetonitrile (**2l**). Yellow oil (64.2 mg, 65% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69−7.61 (m, 4H), 7.46 (dd, J = 8.3, 1.2 Hz, 1H), 7.35 (dd, J = 7.6, 1.9 Hz, 2H), 7.25 (d, J = 8.3 Hz, 1H), 3.48 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 153.5, 152.7, 134.0 (q, J = 33.8 Hz), 132.1, 130.3, 129.7, 128.9, 127.9, 124.5, 123.0 (q, J = 274.6 Hz), 121.2 (q, J = 3.5 Hz), 118.6, 115.9, 114.4 (q, J = 3.9 Hz), 17.7; HRMS (ESI) m/z calcd for $C_{18}H_{11}F_3NO_2$ $[M + H]^+$ 330.0736, found 330.0733.

2-(6,8-Dimethyl-2-oxo-4-phenyl-2H-chromen-3-yl)acetonitrile (**2m**). Yellow solid (68.6 mg, 79% yield); mp 142−144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64−7.56 (m, 3H), 7.32 (dd, J = 7.7, 1.5 Hz, 2H), 7.25 (s, 1H), 6.69 (s, 1H), 3.42 (s, 2H), 2.48 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 154.9, 149.6, 135.0, 133.8, 133.4, 129.7, 129.4, 127.9, 126.1, 125.3, 119.3, 116.6, 115.7, 20.8, 17.5, 15.5; HRMS (ESI) m/z calcd for $C_{19}H_{16}NO_2$ $[M + H]^+$ 290.1176, found 290.1179.

2-(6-Chloro-2-oxo-4-phenyl-2H-chromen-3-yl)acetonitrile (**2n^1**) *and 2-(8-Chloro-2-oxo-4-phenyl-2H-chromen-3-yl)acetonitrile* (**2n^2**). Yellow oil (63.7 mg, 72% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66−7.60 (m, 5.20H), 7.53 (dd, J = 8.8, 2.5 Hz, 1.15H), 7.39−7.33 (m, 4.34H), 7.18−7.14 (m, 0.57H), 7.05 (d, J = 2.4 Hz, 0.92H), 7.01 (dd, J = 8.1, 1.5 Hz, 0.47H), 3.45 (s, 1H), 3.44 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 159.2, 154.3, 153.5, 151.4, 148.8, 132.8, 132.6, 132.5, 132.2, 130.2, 130.2, 130.1, 129.7, 129.6, 127.9, 127.9, 127.2, 126.6, 124.7, 122.0, 121.3, 121.0, 118.5, 117.5, 117.1, 116.1, 17.6, 17.6; HRMS (ESI) m/z calcd for $C_{17}H_{11}ClNO_2$ $[M + H]^+$ 296.0473, found 296.0470.

2-(2-Oxo-4-phenyl-2H-benzo[g]chromen-3-yl)acetonitrile (**2o**). Yellow solid (70.9 mg, 76% yield); mp 150−151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 7.86 (s, 1H), 7.70−7.58 (m, 6H), 7.39−7.38 (m, 2H), 7.06 (d, J = 8.8 Hz, 1H), 3.50 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 155.5, 150.4, 135.0, 133.3, 129.8, 129.5, 129.3, 128.0, 127.8, 127.5, 124.5, 122.9, 122.8, 122.6, 116.5, 115.6, 115.0, 21.1; HRMS (ESI) m/z calcd for $C_{21}H_{14}NO_2$ $[M + H]^+$ 312.1019, found 312.1016.

2-(7-Methyl-2-oxo-4-p-tolyl-2H-chromen-3-yl)acetonitrile (**2q**). Yellow oil (47.7 mg, 55% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, J = 7.7 Hz, 2H), 7.21 (d, J = 7.8 Hz, 3H), 7.04−6.99 (m, 2H), 3.44 (s, 2H), 2.49 (s, 3H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 154.9, 153.1, 143.9, 139.9, 130.1, 130.0, 127.9, 127.7, 125.8, 117.6, 117.1, 116.7, 114.9, 21.7, 21.4, 17.5; HRMS (ESI) m/z calcd for $C_{19}H_{16}NO_2$ $[M + H]^+$ 290.1176, found 290.1178.

2-(4-(4-Methoxyphenyl)-7-methyl-2-oxo-2H-chromen-3-yl)-acetonitrile (**2r**). Yellow oil (58.6 mg, 64% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, J = 8.5 Hz, 2H), 7.20 (s, 1H), 7.11 (d, J = 8.6 Hz, 2H), 7.03 (s, 2H), 3.92 (s, 3H), 3.45 (s, 2H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 160.6, 154.6, 153.1, 143.9, 129.5, 127.7, 125.8, 125.0, 117.7, 117.1, 116.8, 115.0, 114.8, 55.5, 21.7, 17.5; HRMS (ESI) m/z calcd for $C_{19}H_{16}NO_3$ $[M + H]^+$ 306.1125, found 306.1127.

2-(4-(4-tert-Butylphenyl)-7-methyl-2-oxo-2H-chromen-3-yl)-acetonitrile (**2s**). Yellow solid (59.6 mg, 60% yield); mp 210−211 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62−7.60 (m, 2H), 7.28−7.24 (m, 3H), 7.03 (d, J = 0.8 Hz, 2H), 3.44 (s, 2H), 2.48 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7, 154.9, 153.1, 153.0, 143.9, 130.0, 127.8, 127.8, 126.3, 125.8, 117.6, 117.1, 116.9, 114.9, 35.0, 31.3, 21.7, 17.6; HRMS (ESI) m/z calcd for $C_{22}H_{22}NO_2$ $[M + H]^+$ 332.1645, found 332.1647.

2-(4-(4-Fluorophenyl)-7-methyl-2-oxo-2H-chromen-3-yl)-acetonitrile (**2t**). Yellow solid (59.8 mg, 68% yield); mp 127−128 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37−7.30 (m, 4H), 7.24 (s, 1H), 7.07−7.04 (m, 1H), 6.95 (d, J = 8.2 Hz, 1H), 3.44 (s, 2H), 2.48 (s,

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3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3 (d, J = 249.2 Hz), 160.4, 153.7, 153.1, 144.2, 130.1 (d, J = 8.4 Hz), 129.8 (d, J = 16.0 Hz), 128.9 (d, J = 3.6 Hz), 127.4, 126.1, 117.4, 117.2, 116.8 (d, J = 22.0 Hz), 115.9 (d, J = 115.0 Hz), 21.7, 17.4; HRMS (ESI) m/z calcd for $C_{18}H_{13}FNO_2$ $[M + H]^+$ 294.0925, found 294.0924.

*2-(4-(4-Chlorophenyl)-7-methyl-2-oxo-2H-chromen-3-yl)-acetonitrile (**2u**).* Yellow solid (60.3 mg, 65% yield); mp 145−146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 8.3 Hz, 2H), 7.30 (d, J = 8.4 Hz, 2H), 7.22 (s, 1H), 7.06−7.04 (m, 1H), 6.94 (d, J = 8.1 Hz, 1H), 3.42 (s, 2H), 2.47 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 153.4, 153.1, 144.3, 136.1, 131.4, 129.8, 129.5, 127.3, 126.0, 117.2, 117.1, 116.4, 115.3, 21.7, 17.4; HRMS (ESI) m/z calcd for $C_{18}H_{13}ClNO_2$ $[M + H]^+$ 310.0629, found 310.0628.

*2-(4-(4-Bromophenyl)-7-methyl-2-oxo-2H-chromen-3-yl)-acetonitrile (**2v**).* Yellow solid (65.7 mg, 62% yield); mp 124−125 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77−7.75 (m, 2H), 7.24−7.22 (m, 3H), 7.06−7.04 (m, 1H), 6.94 (d, J = 8.2 Hz, 1H), 3.43 (s, 2H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 153.4, 153.1, 144.3, 132.7, 131.8, 129.7, 127.3, 126.1, 124.2, 117.2, 117.0, 116.4, 115.1, 21.7, 17.4; HRMS (ESI) m/z calcd for $C_{18}H_{13}BrNO_2$ $[M + H]^+$ 354.0124, found 354.0123.

*2-(4-(3-Chlorophenyl)-7-methyl-2-oxo-2H-chromen-3-yl)-acetonitrile (**2w**).* Yellow solid (58.4 mg, 63% yield); mp 119−120 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 3.9 Hz, 2H), 7.33 (s, 1H), 7.29−7.24 (m, 2H), 7.06 (d, J = 8.1 Hz, 1H), 6.95−6.92 (m, 1H), 3.52−3.36 (m, 2H), 2.48 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 153.1, 153.0, 144.4, 135.6, 134.7, 130.9, 130.1, 128.0, 127.3, 126.3, 126.1, 117.2, 117.0, 116.3, 115.3, 21.7, 17.4; HRMS (ESI) m/z calcd for $C_{18}H_{13}ClNO_2$ $[M + H]^+$ 310.0629, found 310.0626.

*2-(7-Methyl-2-oxo-4-m-tolyl-2H-chromen-3-yl)acetonitrile (**2x**).* Yellow oil (43.4 mg, 50% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50−7.47 (m, 1H), 7.38 (d, J = 7.9 Hz, 1H), 7.22 (s, 1H), 7.12−7.10 (m, 2H), 7.04−6.98 (m, 2H), 3.42 (s, 2H), 2.47 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 154.9, 153.1, 143.9, 139.3, 133.0, 130.5, 129.3, 128.4, 127.7, 125.9, 125.0, 117.5, 117.0, 116.7, 114.8, 21.7, 21.5, 17.5; HRMS (ESI) m/z calcd for $C_{19}H_{16}NO_2$ $[M + H]^+$ 290.1176, found 290.1177.

*2-(4-([1,1′-Biphenyl]-4-yl)-7-methyl-2-oxo-2H-chromen-3-yl)-acetonitrile (**2y**).* Yellow solid (67.4 mg, 64% yield); mp 110−111 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, J = 8.3 Hz, 2H), 7.71 (dd, J = 5.2, 3.3 Hz, 2H), 7.54 (dd, J = 10.2, 4.8 Hz, 2H), 7.45−7.41 (m, 3H), 7.28 (d, J = 7.3 Hz, 1H), 7.07 (s, 2H), 3.50 (s, 2H), 2.50 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 154.4, 153.2, 144.1, 142.7, 139.8, 131.8, 129.1, 128.5, 128.1, 128.0, 127.6, 127.2, 125.9, 117.4, 117.2, 116.7, 115.1, 21.7, 17.6; HRMS (ESI) m/z calcd for $C_{24}H_{18}NO_2$ $[M + H]^+$ 352.1332, found 352.1330.

*2-(7-Methyl-4-(naphthalen-2-yl)-2-oxo-2H-chromen-3-yl)-acetonitrile (**2z**).* Yellow oil (61.4 mg, 63% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 8.5 Hz, 1H), 8.01−7.94 (m, 2H), 7.85 (d, J = 0.7 Hz, 1H), 7.69−7.62 (m, 2H), 7.41 (dd, J = 8.4, 1.7 Hz, 1H), 7.28−7.27 (m, 1H), 7.04−6.99 (m, 2H), 3.51−3.42 (m, 2H), 2.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 154.7, 153.1, 144.1, 133.4, 133.0, 130.4, 130.2, 129.4, 128.5, 128.4, 128.0, 127.7, 127.6, 127.6, 127.4, 125.9, 125.0, 117.5, 117.2, 116.7, 115.2, 21.7, 17.6; HRMS (ESI) m/z calcd for $C_{22}H_{16}NO_2$ $[M + H]^+$ 326.1176, found 326.1176.

*3-(2-Oxopropyl)-4-phenyl-2H-chromen-2-one (**3a**).* Yellow solid (56.7 mg, 68% yield); mp 123−124 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54−7.49 (m, 4H), 7.40 (dd, J = 8.3, 1.0 Hz, 1H), 7.28−7.26 (m, 2H), 7.19−7.15 (m, 1H), 7.04 (dd, J = 8.0, 1.5 Hz, 1H), 3.52 (s, 2H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.8, 161.6, 153.0, 152.8, 134.2, 131.3, 129.1, 128.9, 128.1, 127.4, 124.2, 121.0, 120.4, 116.8, 43.1, 30.2; HRMS (ESI) m/z calcd for $C_{18}H_{15}O_3$ $[M + H]^+$ 279.1016, found 279.1011.

*7-Ethyl-3-(2-oxopropyl)-4-phenyl-2H-chromen-2-one (**3c**).* Yellow oil (68.0 mg, 74% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (dd, J = 5.1, 1.9 Hz, 3H), 7.27−7.23 (m, 3H), 7.00 (d, J = 1.6 Hz, 1H), 6.94 (d, J = 8.2 Hz, 1H), 3.49 (s, 2H), 2.74 (q, J = 7.6 Hz, 2H), 2.18 (s, 3H), 1.27 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.9, 161.9, 153.1, 148.7, 134.4, 129.0, 128.8, 128.1, 127.2, 124.2, 119.8, 118.2, 115.7, 43.0, 30.2, 28.8, 15.2; HRMS (ESI) m/z calcd for $C_{20}H_{19}O_3$ $[M + H]^+$ 307.1329, found 307.1329.

*7-tert-Butyl-3-(2-oxopropyl)-4-phenyl-2H-chromen-2-one (**3e**).* Yellow oil (78.2 mg, 78% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (dd, J = 5.0, 1.9 Hz, 3H), 7.41 (d, J = 1.9 Hz, 1H), 7.28−7.19 (m, 3H), 6.97 (d, J = 8.4 Hz, 1H), 3.50 (s, 2H), 2.18 (s, 3H), 1.35 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.9, 162.0, 155.7, 152.9, 152.9, 134.4, 129.0, 128.8, 128.1, 127.0, 121.7, 120.0, 118.0, 113.5, 43.0, 35.1, 31.1, 30.2; HRMS (ESI) m/z calcd for $C_{22}H_{23}O_3$ $[M + H]^+$ 335.1642, found 335.1640.

*7-Bromo-3-(2-oxopropyl)-4-phenyl-2H-chromen-2-one (**3k**).* Yellow solid (74.8 mg, 70% yield); mp 101−102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55−7.50 (m, 4H), 7.29−7.23 (m, 3H), 6.89 (d, J = 8.5 Hz, 1H), 3.49 (s, 2H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 204.5, 160.9, 153.0, 152.4, 133.7, 129.3, 129.1, 128.5, 128.0, 127.6, 125.1, 121.3, 119.9, 119.5, 43.1, 30.3; HRMS (ESI) m/z calcd for $C_{18}H_{14}BrO_3$ $[M + H]^+$ 357.0121, found 357.0120.

*Methyl 2-(2-Oxo-4-phenyl-2H-chromen-3-yl)acetate (**4a**).*[23] Yellow solid (122.0 mg, 83% yield); mp 115−116 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56−7.49 (m, 4H), 7.38 (dd, J = 8.3, 0.8 Hz, 1H), 7.30−7.28 (m, 2H), 7.19−7.14 (m, 1H), 7.05 (dd, J = 8.0, 1.5 Hz, 1H), 3.67 (s, 3H); 3.41 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 161.5, 153.0, 152.9, 134.0, 131.5, 129.2, 129.0, 128.2, 127.6, 124.3, 120.4, 120.2, 116.8, 52.2, 34.2.

*2-(2-Oxo-4-phenyl-2H-chromen-3-yl)acetamide (**5a**).* Yellow solid (128.4 mg, 92% yield); mp 89−90 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.61−7.54 (m, 4H), 7.47 (d, J = 8.3 Hz, 1H), 7.39 (s, 1H), 7.34 (d, J = 7.5 Hz, 2H), 7.27−7.23 (m, 1H), 6.95 (d, J = 8.1 Hz, 2H), 3.12 (s, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 171.2, 161.2, 152.7, 152.1, 134.4, 131.8, 129.4, 129.3, 128.6, 127.4, 124.9, 121.8, 120.6, 116.8, 35.6; HRMS (ESI) m/z calcd for $C_{17}H_{14}NO_3$ $[M + H]^+$ 280.0968, found 280.0970.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02155.

Copies of ^{1}H and ^{13}C NMR spectra for all products; crystal structures of **2h** and **2u** (PDF)
Crystallographic data for **2h** (CIF)
Crystallographic data for **2u** (CIF)

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Notes

The authors declare no competing financial interest.

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