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# Transition Metal-Free Cross-Dehydrogenative Coupling Reaction of Coumarins with Acetonitrile or Acetone

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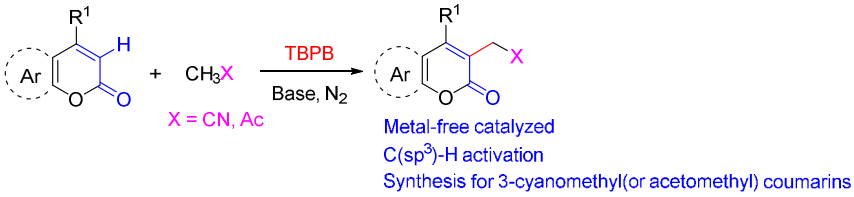
*Supporting Information*




**ABSTRACT:** A transition metal-free cross-dehydrogenative coupling of coumarins with acetonitrile or acetone has been established. A series of coumarins were subjected to reaction with acetonitrile or acetone in the presence of *tert*-butyl benzoperoxoate (TBPB) and potassium fluoride (KF) for direct synthesis 3-cyanomethyl (or acetomethyl) coumarins. The method exhibits good functional group tolerance and desired products were obtained in moderate to good yields. Meanwhile, a radical pathway was proposed to describe the cross-dehydrogenative coupling of coumarins with acetonitrile.

## INTRODUCTION

Direct cross-dehydrogenative-coupling reactions via transformations of C-H bond into other bonds have established as effective and robust methods for the preparation of valuable fragments of pharmaceuticals and intermediates of natural products.[1] Among them, the oxidative C-H activation of acetonitrile and acetone has been received extensively attention because these groups not only play an important role in bioactive molecules[2], pharmaceuticals[3], and specialty chemicals[4], but also it can be good approaches toward other valuable synthons[5]. As a consequence, the development of novel and effective strategies to realize C-H activation of acetonitrile and acetone leading to useful structures usually remains to be extremely attractive and significant.[6] Previously, various 2-cyanomethylation of olefins with acetonitrile were described via metal-catalyzed di-functionalization leading to organocyanides.[7] Very recently, Rao[8] reported iron-catalyzed cross-dehydrogenative coupling of acetonitrile with 2-phenylimidazo[1,2-a] pyridine, and iron-catalyzed 2-cyanomethylation of indoles and pyrroles were developed by Guo[9] group.

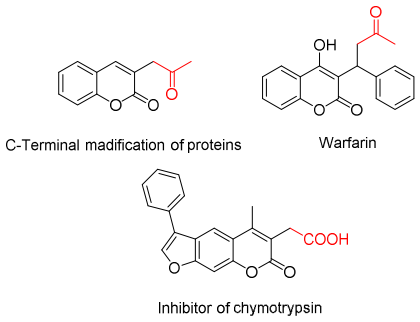
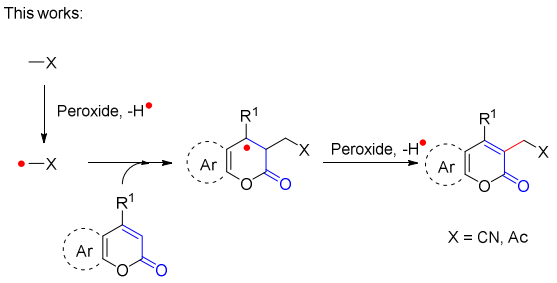



**Figure 1**. Representative bioactive coumarins.

Coumarins and chalcones possessing α,β-unsaturated ketonic fragment in their structures have widely emerged as natural products[10], fluorescent materials[11] and bioactive molecules (Figure 1).[12] Therefore, it is greatly challengable and significant for molecular modification of coumarins and chalcones.[13] In recent years, various metal-catalyzed cross-dehydrogenative-coupling reactions for coumarins and chalcones have been described[14-15], for example, Jafarpour and other research groups[14] reported the metal-catalyzed regioselective C-3 alkylation of coumarins and Prof. Huang[15a] has realized the copper-catalyzed dehydrogenative coupling of methylarylenes with α, β-unsaturated ketones. On the basis of the fact that the 3-cyanomethylation (or 3-acetmethyl) of coumarins and chalcones have not yet been reported, herein, we described a nonmetal-catalyzed cross-dehydrogenative-coupling reaction of coumarins with acetonitrile or acetone via direct oxidative $Csp^3$-H activation. (**Scheme 1**).

**Scheme 1. Metal-Transition-Free Catalyzed Cross-Dehydrogenative Coupling Reaction of Coumarins with Acetonitrile or Acetone.**




## RESULTS AND DISCUSSION

Initially, our research began with the cyanomethylation for synthesis of **3aa** using coumarin (0.20 mmol) **1a** and acetonitrile (5 mL) **2a** to conduct model reaction in the presence of various oxidants (2.5 equiv.) and nitrogen ($N_2$) at 110 □ for 16 h (Table 1, entries 1-4). The desired product **3aa** was obtained in 36 % yield when *tert*-butyl benzoperoxoate (TBPB) was employed as radical initiator and in these cases either low yields were gain or no reaction occurred for other radical initiators such as TBHP, DTBP, DCP. To improve the yield of **3aa**, different bases were employed as additives and inorganic bases ($Na_2CO_3$, KF $NaHCO_3$) exhibiting more health effect than organic bases ($NEt_3$, DBU) for synthesis of **3aa** (Table 1, 5-9). Among them the yield of **3aa** was increased to 67 % when KF (1.0 equiv.) was selected as an additive, but no desired product was obtained when NaOH was selected as an additive (Table 1, entry 10). To our delight, the yield of **3aa** was improved to 78 % when the amount of acetonitrile was increased to 10 mL (Table 1, entry 11). However, cyanomethylation of coumarin **1a** was conducted when 10 % mol $FeCl_2$ was added in the reaction system showed a downtrend in yield of **3aa** (Table 1, entry 12), and the desired product **3aa** was not detected with employment of 10 % mol $Cu(OAc)_2$ as catalyst (Table 1, entry 13). Likewise, the use of 1.5 equiv. or 3.5 equiv. of TBPB showed an obvious downtrend in yield of **3aa** (Table 1, entries 12-15).

**Table 1. Optimization of the Reaction Conditions**[a]

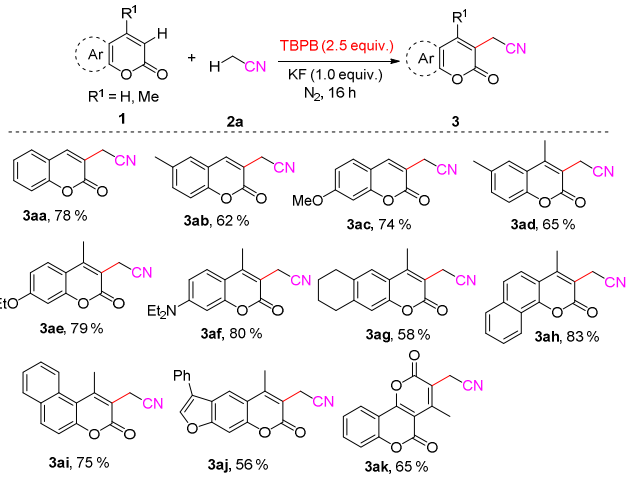

**1a** **2a** **3aa**

| entry | Oxidants (equiv.) | Base (equiv.) | Catalyst (% mol) | Yield[b] (%) |
|---|---|---|---|---|
| 1 | TBHP(2.5) | - | - | N.R. |
| 2 | DTBP(2.5) | - | - | trace |
| 3 | DCP (2.5) | - | - | 21 |
| 4 | TBPB (2.5) | - | - | 37 |
| 5 | TBPB (2.5) | $NEt_3$ | - | 23 |
| 6 | TBPB (2.5) | DBU | - | trace |
| 7 | TBPB (2.5) | $Na_2CO_3$ | - | 61 |
| 8 | TBPB (2.5) | $NaHCO_3$ | - | 43 |
| 9 | TBPB (2.5) | KF | - | 67 |
| 10 | TBPB (2.5) | NaOH | - | trace |
| 11 | TBPB (2.5) | KF | - | **78**[c] |
| 12 | TBPB (2.5) | KF | $FeCl_2$(10) | 72 |
| 13 | TBPB (2.5) | KF | $Cu(OAc)_2$(10) | trace |
| 14 | TBPB (1.5) | KF | - | 52 |
| 15 | TBPB (3.5) | KF | - | 71 |

[a]Reaction conditions: **1a** (0.20 mmol), **2a** (5 mL), base (1.0 equiv.), under $N_2$, 110 □, 16 h, isolated yields. [c]**2a** (10 mL).

With the optimized conditions in hand, cyanomethylation of various coumarins were explored and the result was summarized in **Scheme 2**. Cyanomethylation of coumarins bearing various groups (e.g., Me, OMe, OEt, $NEt_2$) were realized to form 3-cyanomethylcoumarins in moderate to good yields (**3aa-3ag**, 78-58 %). Then, two benzo-coumarins and a furocoumarin as substrates were used to conduct cyanomethylation reaction leading to desired products in moderate good yields (**3ah-3aj**, 83-56 %). Surprisingly, the desired product was obtained in good yield for cyanomethylation of 4-methyl-2H,5H-pyrano[3,2-c] chromene-2,5-dione with structure of dilactone (**3ak**, 65 %).

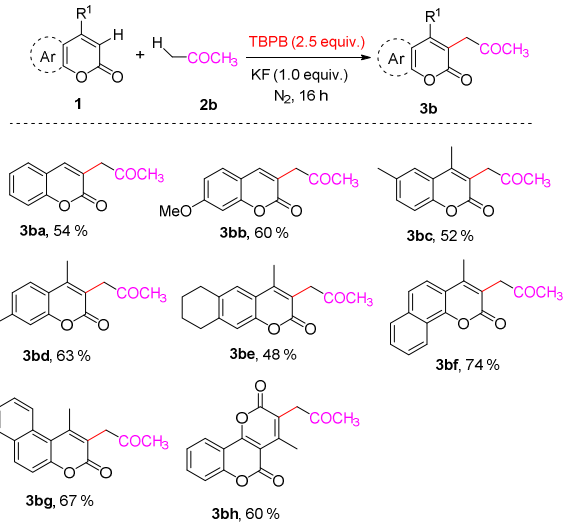
**Scheme 2. 3-Cyanomethylation of Various Coumarins**[a]




[a]Reaction conditions: **1a** (0.20 mmol), **2a** (10 mL), KF (1.0 equiv.), TBPB (2.5 equiv.) under $N_2$, 16 h, isolated yields.

Next, the 3-acetmethylation of coumarins was investigated, and a series of desired products were isolated in moderated to good yields, as shown in **Scheme 3**. Among them, the target products were obtained in moderated yields for 3-acetmethylation of coumarins with methyl, methoxy, ethoxy, cyclohexyl groups on the benzene (**3ba-3be**, 54-48 %). Similarly, the 3-cyanomethylation, 3-acetmethylation of benzocoumarin and 4-methyl-2H,5H-pyrano[3,2-c] chromene-2,5-dione also work well and the corresponding products were obtained in good yields (**3bf-3bh**, 74-72 %).

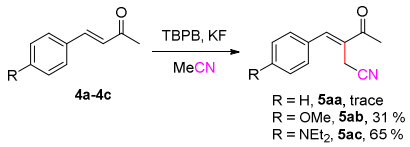
**Scheme 3. 3-Acetmethylation of Various Coumarins**[a]




[a]Reaction conditions: **1** (0.20 mmol), **2b** (10 mL), KF (1.0 equiv.), TBPB (2.5 equiv.) under $N_2$, 110 □, 16 h, isolated yields.

To further extend substrates scope, cyanomethylation of α, β-unsaturated ketones were carried out (**Scheme 4**). (E)-4-phenylbut-3-en-2-one derivatives were also tested as substrates and the desired products were obtained in moderate yields (**5ab-5ac**, 31-58%) for substrates **4b** and **4c** with electron-donating groups (OMe, and $NEt_2$) on the benzene ring, however, no desired product was obtained for **4a** without electron-donating group on the benzene ring.

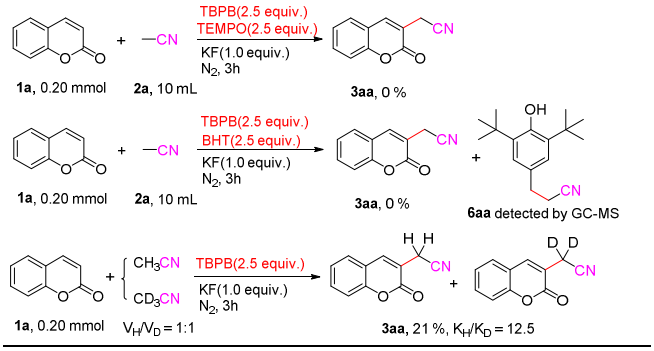
**Scheme 4. 3-Cyanomethylation of α, β-Unsaturated Ketones**




[a]Reaction conditions: **4a-4c** (0.20 mmol), MeCN (10 mL), KF (1.0 equiv.), TBPB (2.5 equiv.) under $N_2$, 110 □, 6 h, isolated yields.

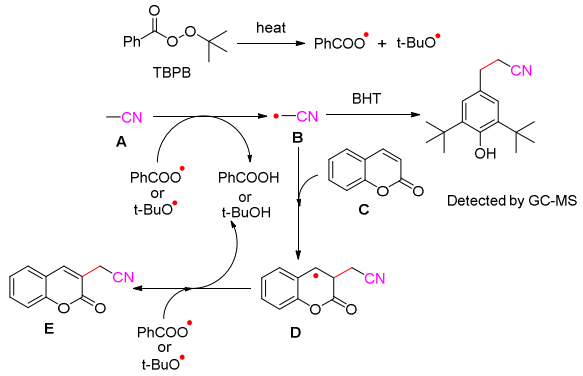
Some control experiments were carried out to investigate the reaction mechanism (**Scheme 5**). Two different radical scavenger, 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) and 2,6-di-tert-butyl-4-methylphenol (BHT) were introduced into cyanomethylation of coumarin under optimized conditions for 3 h and the result shown that the 3-cyanomethylation was inhibited (**(a)-(b)**) and compound **6aa** was detected by GC-MS. Therefore, a single-electron-transfer (SET) pathway was considered and cyanomethyl radical might act as intermediate. Meanwhile, a kinetic isotope effect (KIE) was described via an intermolecular competition experiment between $CH_3CN$ and $CD_3CN$ and the $K_H/K_D$ radio was 12.5 (**(c)**), the KIE experiment suggested that the cleavage of C($sp^3$)-H might be the radio-dominant step for this reaction system.

**Scheme 5. Control Experiments and Kinetic Isotope Effect (KIE) Study.**




Based on the above experimental results and the previous literature studies[8, 9, 13d], a plausible mechanism for cyanomethylation of coumarins has been proposed in **Scheme 6**. Initially, the benzoate radical and *tert*-butoxy radical were produced by the thermal hemolytic cleavage of TBPB. Next, cyanomethyl radical **B** emerged by single-electron-transfer of acetonitrile **A** with benzoate radical or *tert*-butoxy radical releasing benzoic acid or *tert*-butanol. The cyanomethyl radical attacks the carbon-carbon double bond of coumarin **C** leading to intermediate **D**, which is suggested that direct oxidation by benzoate radical or *tert*-butoxy radical and deprotonation to produce desired product **E**.

**Scheme 6. Plausible Mechanism**




## CONCLUSION

In summary, we have descried a novel dehydrogenative coupling reaction of coumarins with acetonitrile via direct C($sp^3$)-H activation of acetonitrile toward 3-cyanomethyl-coumarins. The method exhibits good functional group tolerance and 3-cyanomethyl-coumarins were obtained in moderate to good yields. Meanwhile, 3-acetomethyl coumarins were obtained in moderate yields when acetonitrile was replaced by acetone. Thus, we provided an efficient and novel method for synthesis of cyanomethyl (or acetomethyl)-substituted coumarins and a radical pathway was put forward to describe the oxidative C-H activation of acetonitrile.

## EXPERIMENTAL SECTION

**General Information**. The NMR spectra were recorded 400 MHz ($^1$H) or 600 MHz ($^1$H) and 100 MHz ($^{13}$C{$^1$H} NMR) or 150 MHz ($^{13}$C{$^1$H} NMR) in $CDCl_3$ using tetramethylsilane as an internal reference. NMR multiplicities are abbreviated as follows: s = singlet, d = doublet, m = multiplet, br = broad signal. Chemical shifts (δ) and coupling constants (J) were expressed in ppm and Hz, respectively. Coumarins **1d**, **1g**, **1h**, **1i**, **1g**, **1k**, and α, β-unsaturated ketones **4a**, **4b**, **4c** were prepared according to the literature procedure[16]. The rest of

chemicals were purchased from the Sinopharm Chemical Reagent Co., Adamas, Aladdin and TCI used as received. Q-TOF were used for the HRMS and GC-MS measurement. HRMS (ESI) data were obtained using electron spray ionization and GC-MS data were obtained using electron impact ionization.

**General procedure for the 3-cyanomethylation of coumarins with acetonitrile**. Coumarins **1** (0.2 mmol), KF (0.2 mmol, 11.6 mg), TBPB (0.5 mmol), and acetonitrile **2a** (10 mL) were mixed and stirred at 110 □ in a sealed tube under $N_2$ for 16 h. After completion of the reaction, the reaction mixture was cooled to room temperature, and diluted with dichloromethane (5 × 3 mL), the organic layers were combined, washed with sat. aq. $Na_2CO_3$ (10 mL), dried ($Na_2SO_4$), and concentrated in vacuo. The residue was purified by column chromatography using 10- 20 % ethyl acetate in petroleum as an eluent to get target compounds.

**General procedure for the 3-acetomethylation of coumarins with acetone**. Coumarins **1** (0.2 mmol), KF (0.2 mmol, 11.6 mg), TBPB (0.5 mmol), and acetone **2b** (10 mL) were mixed and stirred at 110 □ in a sealed tube under $N_2$ for 16 h. After completion of the reaction, the reaction mixture was cooled to room temperature, and diluted with dichloromethane (5 × 3 mL), the organic layers were combined, washed with sat. aq. $Na_2CO_3$ (10 mL), dried ($Na_2SO_4$), and concentrated in vacuo. The residue was purified by column chromatography using 20 % ethyl acetate in petroleum as an eluent to get target compounds.

**General procedure for the 3-cyanomethylation of α, β-unsaturated ketones with acetonitrile**. α, β-unsaturated ketones **4a-4c** (0.2 mmol), KF (0.2 mmol, 11.6 mg), TBPB (0.5 mmol), and acetonitrile **2a** (10 mL) were mixed and stirred at 110 □ in sealed tube under $N_2$ for 6 h. After completion of the reaction, the reaction mixture was cooled to room temperature, and diluted with dichloromethane (5 × 3 mL), the organic layers were combined, washed with sat. aq. $Na_2CO_3$ (10 mL), dried ($Na_2SO_4$), and concentrated in vacuo. The residue was purified by column chromatography using 5-10 % ethyl acetate in petroleum as an eluent to get target compounds.

*2-(2-oxo-2H-chromen-3-yl)-acetonitrile* ***(3aa)***: Purified by using a flash column chromatography (28.9 mg, 78 %); white solid; mp: 155-156 □. $^1$H NMR (400 MHz, Chloroform-d) δ (ppm)7.94 (s, 1H), 7.57 (td, J = 8.2, 7.7, 2.7 Hz, 2H), 7.39 – 7.31 (m, 2H), 3.70 (s, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, Chloroform-d) δ (ppm) 160.1, 153.3, 140.6, 132.3, 128.0, 125.0, 118.7, 118.4, 116.7, 116.1, 19.6. HRMS (ESI-TOF) m/z: [M+H] $^+$ Calcd for $C_{11}H_8NO_2$ 186.0550; Found 186.0547.

*2-(6-methyl-2-oxo-2H-chromen-3-yl)-acetonitrile* ***(3ab)***: Purified by using a flash column chromatography (24.7 mg, 62 %); white solid; mp: 123-124 □. $^1$H NMR (400 MHz, Chloroform-d) δ (ppm) 7.87 (d, J = 1.7 Hz, 1H), 7.39 – 7.30 (m, 2H), 7.27 – 7.22 (m, 1H), 3.68 (s, 2H), 2.42 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, Chloroform-d) δ (ppm) 160.3, 151.5, 140.5, 134.8, 133.3, 127.8, 118.5, 118.1, 116.4, 116.1, 20.8, 19.6. HRMS (ESI-TOF) m/z: [M+H] $^+$ Calcd for $C_{12}H_{10}NO_2$ 200.0706; Found 200.0705.

*2-(7-methoxy-2-oxo-2H-chromen-3-yl)-acetonitrile* ***(3ac)***: Purified by using a flash column chromatography (31.8 mg, 74 %); white solid; mp: 159-160 □. $^1$HNMR (400 MHz, Chloroform-d) δ (ppm) 7.84 (s, 1H), 7.42 (d, J = 8.7 Hz, 1H), 6.88 (dd, J = 8.7, 2.5 Hz, 1H), 6.82 (d, J = 2.5 Hz, 1H), 3.87 (s, 3H), 3.64 (s, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, Chloroform-d) δ (ppm) δ 163.1, 160.4, 155.2, 140.7, 128.9, 116.3, 114.8, 113.2, 112.0, 100.7, 55.9, 19.3. HRMS (ESI-TOF) m/z: [M+H] $^+$ Calcd for $C_{12}H_{10}NO_3$ 216.0655, Found 216.0656.

*2-(4,6-dimethyl-2-oxo-2H-chromen-3-yl)-acetonitrile* ***(3ad)***: Purified by using a flash column chromatography (27.7 mg, 65 %); white solid; mp: 157-158 □. $^1$H NMR (400 MHz, Chloroform-d) δ (ppm) 7.45 – 7.41 (m, 1H), 7.36 (dd, J = 8.4, 2.0 Hz, 1H), 7.22 (d, J = 8.4 Hz, 1H), 3.77 (s, 2H), 2.53 (s, 3H), 2.43 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, Chloroform-d) δ (ppm) 160.4, 150.5, 150.5, 134.4, 133.4, 124.8, 119.3, 116.8, 116.3, 115.6, 21.1, 15.8, 15.6. HRMS (ESI-TOF) m/z: [M+H] $^+$ Calcd for $C_{13}H_{12}NO_2$ 214.0863; Found 214.0864.

*2-(7-ethoxy-4-methyl-2-oxo-2H-chromen-3-yl)-acetonitrile* ***(3ae)***: Purified by using a flash column chromatography (38.43 mg, 79 %); white solid; mp: 144-145 □. $^1$H NMR (400 MHz, Chloroform-d) δ (ppm) 7.53 (d, J = 8.9 Hz, 1H), 6.86 (dd, J = 8.9, 2.5 Hz, 1H), 6.76 (d, J = 2.5 Hz, 1H), 4.08 (q, J = 7.0 Hz, 2H), 3.72 (s, 2H), 2.49 (s, 3H), 1.43 (t, J = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, Chloroform-d) δ (ppm) 162.4, 160.7, 154.2, 150.7, 126.0, 116.6, 113.3, 113.0, 112.2, 101.2, 64.3, 15.6, 15.5, 14.5. HRMS (ESI-TOF) m/z: [M+H] $^+$ Calcd for $C_{14}H_{14}NO_3$ 244.0968; Found: 244.0969.

*2-(7-(diethylamino)-4-methyl-2-oxo-2H-chromen-3-yl)-acetonitrile* ***(3af)***: Purified by using a flash column chromatography (43.2 mg, 80 %); yellow solid; mp: 83-84 □.$^1$H NMR (400 MHz, Chloroform-d) δ (ppm) 7.41 (d, J = 9.1 Hz, 1H), 6.59 (dd, J = 9.1, 2.6 Hz, 1H), 6.45 (d, J = 2.6 Hz, 1H), 3.69 (s, 2H), 3.40 (q, J = 7.1 Hz, 4H), 2.43 (s, 3H), 1.19 (t, J = 7.1 Hz, 6H). $^{13}C\{^1H\}$ NMR (100 MHz, Chloroform-d) δ (ppm)161.5, 155.0, 151.0, 150.9, 126.0, 117.1, 109.0, 108.6, 108.4, 97.3, 44.7, 15.5, 15.2, 12.4. HRMS (ESI-TOF) m/z: [M+H] $^+$ Calcd for $C_{16}H_{19}N_2O_2$ 271.1441; Found: 271.1443.

*2-(4-methyl-2-oxo-6,7,8,9-tetrahydro-2H-benzo[g]chromen-3-yl)-acetonitrile* ***(3ag)***: Purified by using a flash column chromatography (29.4 mg, 58 %); white solid; mp: 161-162 □. $^1$H NMR (400 MHz, Chloroform-d) δ (ppm) 7.32 (s, 1H), 7.02 (s, 1H), 3.76 (s, 2H), 2.88 – 2.80 (m, 4H), 2.51 (s, 3H), 1.82 (p, J = 3.3 Hz, 4H). $^{13}C\{^1H\}$ NMR (100 MHz, Chloroform-d) δ (ppm) 160.6, 150.5, 150.3, 143.1, 134.0, 124.7, 117.3, 116.6, 116.5, 114.5, 29.6, 29.0, 22.9, 22.5, 15.8, 15.5. HRMS (ESI-TOF) m/z: [M+H] $^+$ Calcd for $C_{16}H_{16}NO_2$ 254.1176; Found: 254.1180.

*2-(4-methyl-2-oxo-2H-benzo[h]chromen-3-yl)-acetonitrile* ***(3ah)***: Purified by using a flash column chromatography (41.4 mg, 83 %); white solid; mp: 194-195 □. $^1$H NMR (400 MHz, Chloroform-d) δ (ppm) 8.55 – 8.41 (m, 1H), 7.85 (dd, J = 6.8, 2.5 Hz, 1H), 7.72 – 7.53 (m, 4H), 3.80 (s, 2H), 2.59 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, Chloroform-d) δ (ppm) 160.2, 151.4, 149.6, 134.8, 129.0, 127.7, 127.4, 124.6, 122.8, 122.5, 120.3, 116.4, 115.0, 114.8, 16.1, 15.8. HRMS (ESI-TOF) m/z: [M+H] $^+$ Calcd for $C_{16}H_{12}NO_2$ 250.0863; Found: 250.0864.

*2-(1-methyl-3-oxo-3H-benzo[f]chromen-2-yl)-acetonitrile* ***(3ai)***: Purified by using a flash column chromatography (37.4 mg, 75 %); white solid; mp: 180-181 □. $^1$H NMR (400 MHz, Chloroform-d) δ (ppm) (ppm) 8.43 (d, J = 8.7 Hz, 1H), 7.97 (d, J = 8.9 Hz, 1H), 7.94 – 7.89 (m, 1H), 7.65 (ddd, J = 8.6, 6.7, 1.6 Hz, 1H), 7.60 – 7.54 (m, 1H), 7.41 (d, J = 8.9 Hz, 1H), 3.88 (s, 2H), 2.96 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, Chloroform-d) δ (ppm) 159.88, 153.1, 152.5, 134.3, 131.6, 129.8, 129.6, 127.9, 125.77, 125.2, 117.2, 116.3, 116.3, 114.8, 22.2, 16.3. HRMS (ESI-TOF) m/z: [M+H] $^+$ Calcd for $C_{16}H_{12}NO_2$ 250.0863; Found 250.0859.

*2-(5-methyl-7-oxo-3-phenyl-7H-furo[3,2-g]-chromen-6-yl)-acetonitrile* ***(3aj)***: Purified by using a flash column chromatography (35.3 mg, 56 %); white solid; dry distillation: 230 □. $^1$H NMR (400 MHz, Chloroform-d) δ (ppm) 7.72 (s, 1H), 7.58 (t, J = 7.5 Hz, 2H), 7.52 – 7.45 (m, 4H), 6.26 (s, 1H), 3.96 (s, 2H), 2.45 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, Chloroform-d) δ (ppm) 160.7, 155.6, 152.5, 152.2, 143.1, 129.7, 129.6, 128.8, 128.8, 125.1, 120.6, 117.2, 115.7, 114.7, 113.8, 100.0, 19.2, 16.6. HRMS (ESI-TOF) m/z: [M+H] $^+$ Calcd for $C_{20}H_{14}NO_3$ 316.0968; Found 316.0968.

*2-(4-methyl-2,5-dioxo-2H,5H-pyrano[3,2-c]-chromen-3-yl)-acetonitrile* ***(3ak)***: Purified by using a flash column chromatography (34.7 mg, 65 %); white solid; dry distillation: 246 □. $^1$H NMR (600 MHz, Chloroform-d) δ (ppm) 8.01 (dd, J = 8.0, 1.6 Hz, 1H), 7.65 – 7.60 (m, 1H), 7.33 (t, J = 7.6 Hz, 1H), 7.30 (d, J = 8.4 Hz, 1H), 3.67 (s, 2H), 2.70 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-d) δ (ppm) 161.2, 157.9, 157.9, 154.2, 153.2, 135.1, 125.3, 124.0, 116.9, 115.52, 115.50, 112.6, 103.7, 18.8, 15.7. HRMS (ESI-TOF) m/z: [M+H] $^+$ Calcd for $C_{15}H_{10}NO_4$ 268.0604; Found 268.0604.

*3-(2-oxopropyl)-2H-chromen-2-one* ***(3ba)***: Purified by using a flash column chromatography (21.8 mg, 54 %); white solid; mp: 88-89 □.$^1$H NMR (600 MHz, Chloroform-d) δ (ppm) 7.50 (s, 1H), 7.39 (ddd, J = 8.7, 7.3, 1.6 Hz, 1H), 7.35 (dd, J = 7.8, 1.6 Hz, 1H), 7.20 (d, J = 8.3 Hz, 1H), 7.16 (td, J = 7.6, 1.2 Hz, 1H), 3.58 (s, 2H), 2.21 (s, 3H). $^{13}C\{^1H\}$ NMR (150 MHz, Chloroform-d) δ (ppm) 204.2, 161.5, 153.5, 141.9, 131.3, 127.6, 124.5, 122.9, 119.2, 116.5, 44.5, 30.3. HRMS (ESI-TOF) m/z: [M+H] $^+$ Calcd for $C_{12}H_{11}O_3$ 203.0703; Found 203.0707.

*7-methoxy-3-(2-oxopropyl)-2H-chromen-2-one* ***(3bb)***: Purified by using a flash column chromatography (27.8 mg, 60 %); white solid;

mp: 97-98 □. $^1$H NMR (400 MHz, Chloroform-d) δ (ppm) 7.52 (s, 1H), 7.35 – 7.30 (m, 1H), 6.85 – 6.77 (m, 2H), 3.85 (d, J = 2.4 Hz, 3H), 3.62 (s, 2H), 2.28 (s, 3H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-d) δ (ppm) 204.6, 162.4, 161.8, 155.2, 142.0, 128.5, 119.1, 112.8, 112.6, 100.6, 55.7, 44.3, 30.2. HRMS (ESI-TOF) m/z: [M+H]$^+$ Calcd for $C_{13}H_{13}O_4$ 233.0808; Found 233.0805.

*4,6-dimethyl-3-(2-oxopropyl)-2H-chromen-2-one* ***(3bc)***: Purified by using a flash column chromatography (23.9 mg, 52 %); white solid; mp: 94-95 □. $^1$H NMR (400 MHz, Chloroform-d) δ (ppm) 7.38 (s, 1H), 7.29 (dd, J = 8.4, 2.1 Hz, 1H), 7.19 (d, J = 8.4 Hz, 1H), 3.81 (s, 2H), 2.40 (s, 3H), 2.32 (s, 3H), 2.27 (s, 3H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-d) δ (ppm) 204.3, 161.7, 150.4, 149.0, 133.8, 132.1, 124.6, 119.9, 119.8, 116.6, 42.2, 29.9, 21.0, 15.4. HRMS (ESI-TOF) m/z: [M+H]$^+$ Calcd for $C_{14}H_{15}O_3$ 231.1016; Found 231.1021.

*7-ethoxy-4-methyl-3-(2-oxopropyl)-2H-chromen-2-one* ***(3bd)***: Purified by using a flash column chromatography (32.8 mg, 63 %); white solid; mp: 124-125 □. $^1$H NMR (400 MHz, Chloroform-d) δ (ppm) 7.50 (d, J = 8.9 Hz, 1H), 6.84 (dd, J = 8.9, 2.5 Hz, 1H), 6.78 (d, J = 2.5 Hz, 1H), 4.07 (q, J = 7.0 Hz, 2H), 3.78 (s, 2H), 2.30 (s, 3H), 2.27 (s, 3H), 1.44 (t, J = 7.0 Hz, 3H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-d) δ (ppm) 204.7, 162.0, 161.6, 154.0, 149.4, 125.7, 116.5, 113.7, 112.8, 101.1, 64.1, 42.0, 29.9, 15.4, 14.5. HRMS (ESI-TOF) m/z: [M+H]$^+$ Calcd for $C_{15}H_{17}O_4$ 261.1121; Found 261.1124.

*4-methyl-3-(2-oxopropyl)-6,7,8,9-tetrahydro-2H-benzo[g]chrome n-2-one* ***(3be)***: Purified by using a flash column chromatography (25.9 mg, 48 %); white solid; mp: 117-118 □.$^1$H NMR (400 MHz, Chloroform-d) δ (ppm) 7.26 (s, 1H), 6.98 (s, 1H), 3.79 (s, 2H), 2.87 – 2.76 (m, 4H), 2.30 (s, 3H), 2.26 (s, 3H), 1.80 (p, J = 3.2 Hz, 4H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-d) δ (ppm) 204.5, 161.9, 150.3, 149.1, 141.7, 133.4, 124.6, 118.7, 118.0, 116.3, 42.2, 29.8, 29.5, 29.0, 23.0, 22.7, 15.3. HRMS (ESI-TOF) m/z: [M+H]$^+$ Calcd for $C_{17}H_{19}O_3$ 271.1329; Found: 271.1326.

*4-methyl-3-(2-oxopropyl)-2H-benzo[h]chromen-2-one* ***(3bf)***: Purified by using a flash column chromatography (39.4 mg, 74 %); white solid; mp: 165-166 □.$^1$H NMR (400 MHz, Chloroform-d) δ (ppm) 8.51 (dt, J = 7.1, 3.6 Hz, 1H), 7.87 – 7.78 (m, 1H), 7.65 (d, J = 8.8 Hz, 1H), 7.59 (tq, J = 7.7, 3.9 Hz, 3H), 3.86 (s, 2H), 2.40 (s, 3H), 2.31 (s, 3H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-d) δ (ppm) 204.4, 161.6, 150.1, 149.2, 134.4, 128.4, 127.5, 127.0, 124.1, 123.0, 122.4, 120.6, 119.3, 115.4, 42.2, 30.0, 16.0. HRMS (ESI-TOF) m/z: [M+H]$^+$ Calcd for $C_{17}H_{15}O_3$ 267.1016; Found 267.1019.

*1-methyl-2-(2-oxopropyl)-3H-benzo[f]chromen-3-one* ***(3bg)***: Purified by using a flash column chromatography (35.7 mg, 67 %); white solid; mp: 165-166 □. $^1$H NMR (600 MHz, Chloroform-d) δ (ppm) 8.32 (d, J = 8.6 Hz, 1H), 7.81 – 7.74 (m, 2H), 7.50 – 7.46 (m, 1H), 7.42 (d, J = 7.4 Hz, 1H), 7.28 (d, J = 8.8 Hz, 1H), 3.83 (s, 2H), 2.62 (s, 3H), 2.23 (s, 3H). $^{13}$C{$^1$H} NMR (150 MHz, Chloroform-d) δ (ppm) 204.3, 161.2, 152.6, 151.1, 133.0, 131.5, 129.7, 129.5, 127.3, 125.5, 125.3, 120.6, 117.2, 115.3, 42.7, 30.0, 22.0. HRMS (ESI-TOF) m/z: [M+H]$^+$ Calcd for $C_{17}H_{15}O_3$ 267.1016; Found 267.1017.

*4-methyl-3-(2-oxopropyl)-2H,5H-pyrano[3,2-c]-chromene-2,5-dione* ***(3bh)***: Purified by using a flash column chromatography (40.9 mg, 72 %); white solid; dry distillation: 250 □. $^1$H NMR (400 MHz, Chloroform-d) δ (ppm) 8.06 (dd, J = 8.1, 1.8 Hz, 1H), 7.64 (t, J = 7.9 Hz, 1H), 7.36 (q, J = 7.9 Hz, 2H), 3.82 (s, 2H), 2.54 (s, 3H), 2.30 (s, 3H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-d) δ (ppm) δ 203.2, 160.2, 159.1, 158.3, 152.9, 152.4, 134.3, 125.0, 123.8, 120.0, 116.7, 113.0, 104.1, 41.8, 29.9, 18.6. HRMS (ESI-TOF) m/z: [M+H]$^+$ Calcd for $C_{16}H_{13}O_5$ 285.0757; Found 285.0757.

*(E)-3-(4-methoxybenzylidene)-4-oxopentanenitrile* ***(5ab)***: Purified by using a flash column chromatography (13.3 mg, 31 %); clear liquid.$^1$H NMR (400 MHz, Chloroform-d) δ (ppm) 7.70 (s, 1H), 7.48 – 7.38 (m, 2H), 7.04 – 6.96 (m, 2H), 3.86 (s, 3H), 3.53 (s, 2H), 2.49 (s, 3H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-d) δ (ppm) 196.9, 161.1, 144.1, 131.5, 129.3, 126.1, 117.6, 114.6, 55.4, 25.2, 15.3. HRMS (ESI-TOF) m/z: [M+H]$^+$ Calcd for $C_{13}H_{14}NO_2$ 216.1019; Found 216.1011.

*(E)-4-(4-(diethylamino)-phenyl)-but-3-en-2-one* ***(5ac)***: Purified by using a flash column chromatography (33.3 mg, 65 %); yellow liquid.$^1$H NMR (400 MHz, Chloroform-d) δ (ppm) 7.61 (s, 1H), 7.42 – 7.37 (m, 2H), 6.74 – 6.68 (m, 2H), 3.61 (s, 2H), 3.42 (q, J = 7.1 Hz, 4H), 2.45 (s, 3H), 1.20 (t, J = 7.1 Hz, 6H). $^{13}$C{$^1$H} NMR (100 MHz, Chloroform-d) δ (ppm) 196.8, 149.3, 145.0, 132.5, 125.2, 120.1, 118.1, 111.4, 44.5, 25.0, 15.3, 12.5. HRMS (ESI-TOF) m/z: [M+H]$^+$ Calcd for $C_{16}H_{21}N_2O$ 257.1648; Found: 257.1654.

## ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.

$^1$H and $^{13}$C NMR spectra for the products (PDF)

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**Notes**

The authors declare no competing financial interest.

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