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可见光诱导 4-色满酮合成: 醋酸碘苯促进的 α-酮酸与邻-烯丙氧基芳醛的自由基串联环化反应

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摘要 报道了在可见光照射下, 通过醋酸碘苯(PIDA)促进的 α-酮酸与邻-烯丙氧基芳醛的自由基串联环化反应, 高效构建了含有 1,4-二酮片段的 4-色满酮衍生物. 该反应在温和的条件下即可进行, 如室温、蓝色 LED 灯照射、无需光氧化还原催化剂等. 在最优的反应条件下, 可以中等到好的产率得到目标杂环化合物.
关键词 可见光; 4-色满酮; 自由基; 串联反应

Visible Light-Induced 4-Chromanones Synthesis: Radical Cascade Cyclization of α-Oxocarboxylic Acids with *o*-(Allyloxy)arylaldehydes Promoted by Phenyliodine(III) Diacetate

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Abstract An efficient and sustainable visible light-promoted cascade radical cyclization of α-oxocarboxylic acids with *o*-(allyloxy)arylaldehydes towards the construction of 1,4-diketone containing chromanone derivatives has been developed. The reaction occurred under mild reactions, *e.g.* room temperature, blue LED irradiation, photoredox catalyst free, and provided the final heterocycles in moderate to good yields.
Keywords visible light; 4-chromanone; radical; cascade reaction

1 Introduction

4-Chromanones are privileged structural motifs which can be found in numerous bioactive molecules and natural products, and many of them show pronounced biological activities such as antioxidant, antitumor, antidiabetic, anti-angiogenic, antiallergic, antiviral, and anti-inflammatory properties.[1] On the other hand, the 1,4-diketones are versatile synthetic building blocks, leading to the formation of various biologically important carbocycles and heterocycles, such as pyrrole, furan and thiophene derivatives.[2] Driven by their rich biological activities and synthetic utilities, there is no doubt that significant effects have been devoted to the development of robust methods for the synthesis of these two compounds in synthetic organic chemistry. Generally, 4-chromanone scaffold can be achieved through intramolecular *oxo*-Michael addition,[3] intramolecular Stetter reactions promoted by *N*-heterocyclic carbene (NHC)[4] or cascade radical cyclization strategy.[5] And the acyl radical triggered Michael-types addition process is one of the most powerful synthetic approach to access 1,4-diketone structures.[6] Despite these advances, methods towards the synthesis of structure **A**, which containing both 4-chromanone and 1,4-diketone fragments, are still rare. Note that, the combination of the two key fragments into one molecule may obtain structurally diverse chemicals endowed with novel or amplified bioactivities and applications.

The first approach to the construction of **A** is NHC-mediated intramolecular Stetter reactions, which have been

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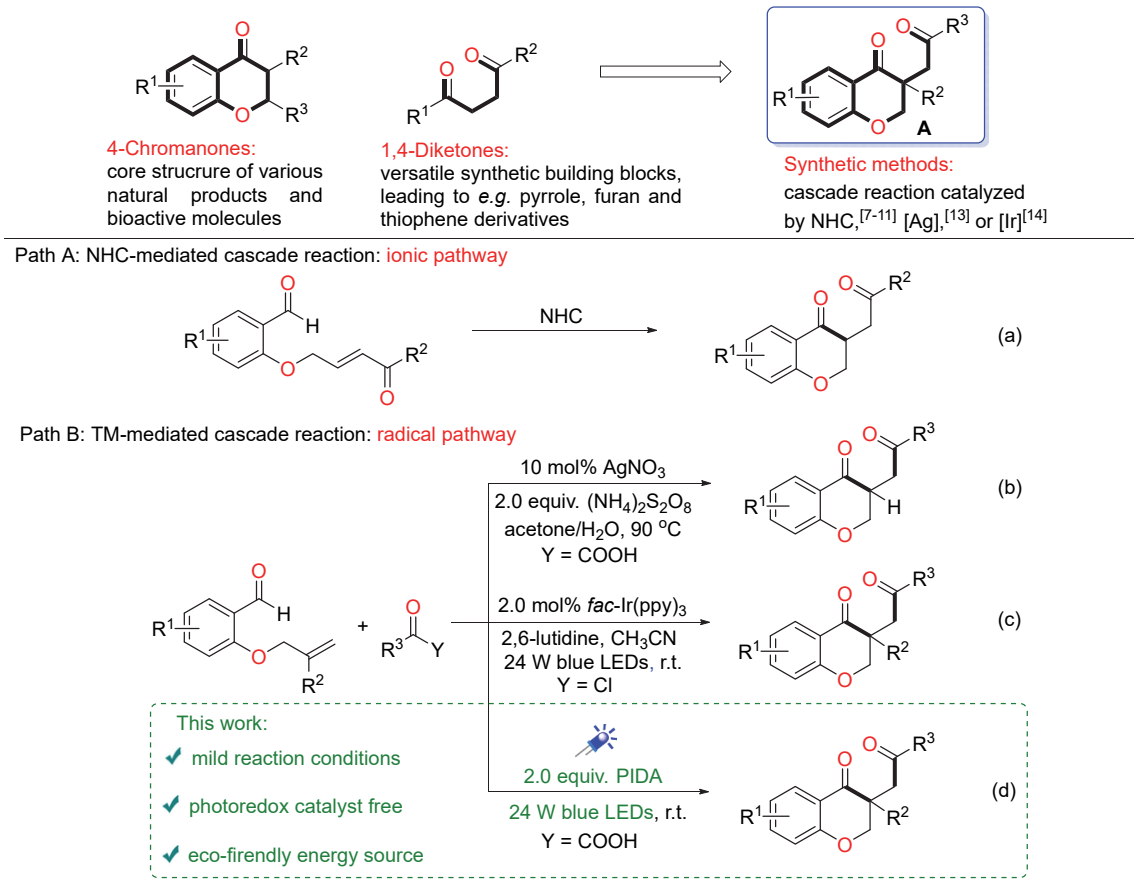
well developed by Enders,[7] Bach,[8] Miller,[9] Rovis[10] and Glorius *et al.*[11] in the past several years (Scheme 1a). In contrast to those ionic reaction processes, acyl-radical triggered cascade cyclization of *o*-(allyloxy)-arylaldehydes provided an alternative approach to access the target molecule.[12] In 2017, Wu *et al.*[13] reported a silver nitrate catalyzed cascade cyclization of acyl radical with *o*-(allyloxy)arylaldehydes by using *α*-oxocarboxylic acids as the acyl radical precursors (Scheme 1b). Although the approach is efficient, limitations still remain, such as high reaction temperature and the requirement transition-metal salt as radical initiator. Recently, our group developed a visible light-promoted cascade radical cyclization of aroyl chlorides with *o*-(allyloxy)arylaldehydes at room temperature, leading to the corresponding heterocyclic compound **A** in moderate to good yields (Scheme 1c).[14] However, transition-metal photoredox catalyst *fac*-Ir(ppy)$_3$ (ppy = 2-phenylpyridine) is required to run the process. It is still an important objective to discover novel and efficient approaches to synthesize 4-chromanone derivative **A**, especially under transition-metal-free reaction conditions.

As our ongoing research interests devoted to the development of heterocycle-oriented methodologies,[15] we describe herein a transition-metal-free approach to the synthesis of 4-chromanone derivative **A** through a visible light-induced cascade radical cyclization[16] of *α*-oxocarboxylic acids with *o*-(allyloxy)arylaldehydes (Scheme 1d). Note that, photoredox catalyst was not required and the reaction was promoted by cheap and mild phenyliodine (III) diacetate (PIDA).[17]

2 Results and discussion

Our investigation started with the reaction of 2-(allyloxy)benzaldehyde **1a** with 2-*oxo*-2-phenylacetic acid **2a** in the presence of 2.0 equiv. of PIDA at room temperature. As the results shown in Table 1, to our delight, the desired 4-chromanone product **3a** could be afforded in 26% isolated yield when the reaction was performed in CH_3CN under the irradiation with 24 W blue LEDs for 24 h (Table 1, Entry 1). Encouraged by this preliminary result, other reaction paraments were screened in order to further improve the reaction yield. It was found that conversion efficiency strongly depended on the reaction medias used. Replacement CH_3CN to other commonly used solvents, such as 1,2-dichloroethane (DCE), EtOAc, tetrahydrofuran (THF) and toluene, no better result was obtained (Table 1, Entries 2～5). Only trace amount of **3aa** was observed when high polar solvent *N*,*N*-dimethylformamide (DMF) or dimethyl sulfoxide (DMSO) was involved (Table 1, Entries 6, 7). No product was detected when the reaction was performed in protic solvents, such as MeOH or H_2O (Table 1, Entries 8, 9). Delightfully, when the ratio of **1a**/**2a** was changed to 1∶4, the yield of **3a** was improved to 62% and reduced the react-

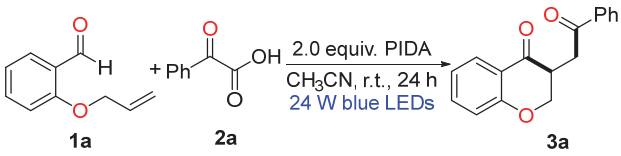


Scheme 1 Methods for the synthesis of 4-chromanone containing 1,4-diketone skeleton

ion time to 12 h (Table 1, Entry 10). It was noticed that further prolonged the reaction time could not improve the reaction yield (Table 1, Entry 11). Only trace amount of **3a** was detected when the reaction was performed in air (Table 1, Entry 12). Control experiments revealed that both phenyliodine(III) diacetate and blue LEDs irradiation played a critical rule for the 4-chromanone product **3a** formation (Table 1, Entries 13 and 14).

With the optimal reaction conditions in hand, the substrate scope for this transition-metal-free 4-chromanone synthesis reaction was explored (Table 2). Firstly, the R^1 substituents anchoring in the phenyl ring of *o*-(allyloxy)-arylaldehydes were investigated. As shown in Table 2, a wide range of *o*-(allyloxy)arylaldehydes bearing both electron-donating group (Me, OMe) and electron-withdrawing group (F, Cl, Br) at C(5) or C(3) positions could smoothly react with 2-*oxo*-2-phenylacetic acid, affording the corresponding products **3a**～**3g** in moderate to good yields. Moreover, the 3,5-disubstituted substrates also worked to provide the desired heterocycles **3h** and **3i**, albeit with relatively low yields. It is worth noting that the method could be efficiently applied to the synthesis of 4-chromanones bearing an important quaternary carbon center. For instance, the reaction of 2-((2-methylallyl)oxy)benzaldehyde with 2-*oxo*-2-phenylacetic acid under the optimal reaction

Table 1 Reaction optimization between **1a** and **2a**[a]

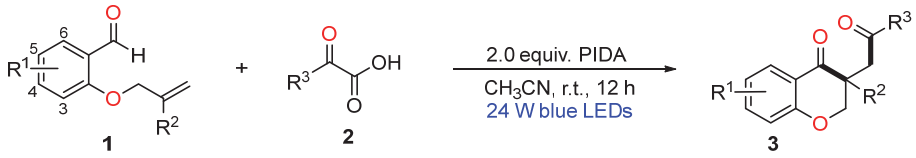


1a **2a** **3a**

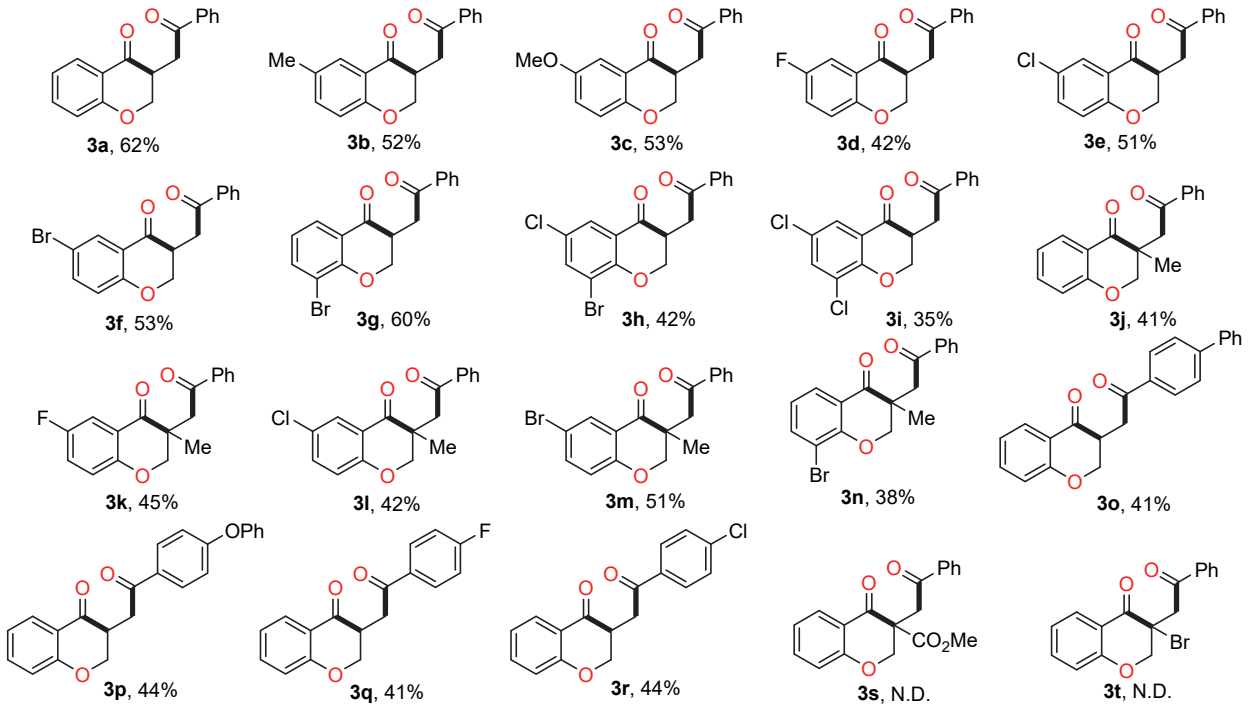
Entry	Deviation from standard conditions	Yield[b]/%
1	None	26
2	DCE instead of CH_3CN	21
3	EtOAc instead of CH_3CN	25
4	THF instead of CH_3CN	12
5	Toluene instead of CH_3CN	9
6	DMF instead of CH_3CN	Trace
7	DMSO instead of CH_3CN	Trace
8	MeOH instead of CH_3CN	0
9	H_2O instead of CH_3CN	0
10	**1a**∶**2a**=1∶4, 12 h	**62**
11	**1a**∶**2a**=1∶4, 24 h	61
12[c]	**1a**∶**2a**=1∶4, 12 h	Trace
13	Without PIDA	0
14	Without blue LEDs	0

[a] Reaction conditions: **1a** (0.1 mmol) and **2a** (0.2 mmol) in the indicated solvent (1.0 mL), irradiation by 24 W blue LEDs at room temperature for 24 h under argon atmosphere. [b] Isolated yield. [c] The reaction was performed in air.

Table 2 Substrate scope of *o*-(allyloxy)arylaldehydes and *α*-oxocarboxylic acids



1 **2** **3**

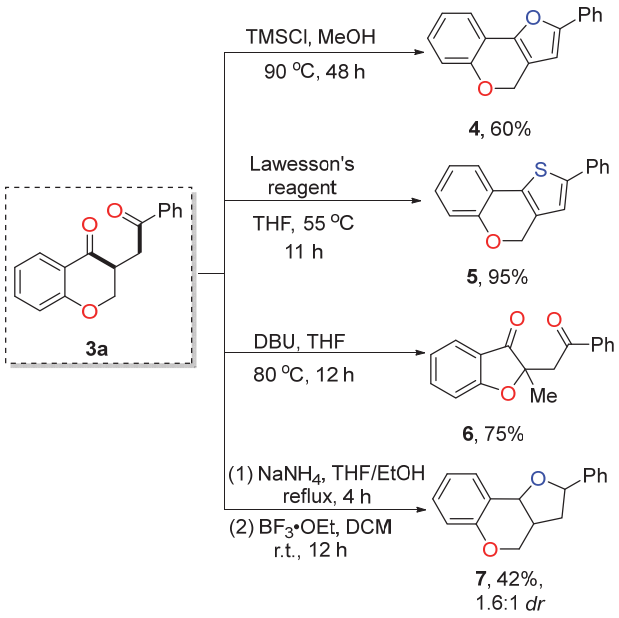


[a] **1** (0.1 mmol), **2** (0.4 mmol), CH_3CN (1.0 mL), irradiation by 24 W blue LEDs at room temperature for 12 h under argon atmosphere. [b] Isolated yield.

conditions afforded **3j** in 41% isolated yield. Incorporation of fluoro, chloro and bromo substituents at different positions did not apparently influence the reaction yield, affording the corresponding products **3k**～**3n** in moderate yields. Then, the R^3 substituents on the aryl ring of *α*-oxocarboxylic acids **2** were further examined, and the corresponding products **3o**～**3r** containing various substituents, including aryl, ether and halogen substituents, could be obtained in moderate to good yields. The reactivity of **1** bearing other R^2 substituents was also tested. Unfortunately, both R^2 ester or halogen substituted alkenes could not act as suitable radical acceptor (**3s** and **3t**). The relatively low yields in some cases might be due to the formation un-known by-products.

Considering the high synthetic value of 1,4-diketone motifs in final chromanone products,[2] some represented synthetic transformations were conducted by using **3a** as examples. In our previous investigations,[14] we found that **3a** could be efficiently transferred to polycyclic pyrrole **4** and thiophene **5** in good yield. Moreover, a DBU (1,5-dizzabicyclo[5.4.0]undecen-5-ene)-mediated ring contraction afforded benzofuranone **6** in 75% yield. Treatment of **3a** under reductive conditions, followed by a BF_3•OEt promoted intramolecular cyclization, provided **7** in moderate yield and diastereoselectivity.

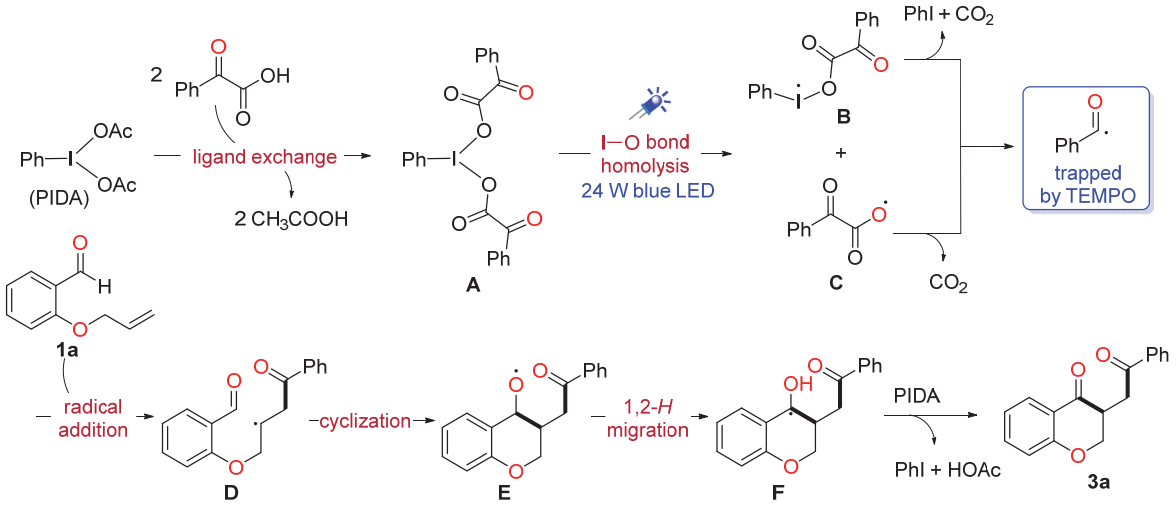
A plausible reaction mechanism was proposed in Scheme 3 to explain this visible light-promoted chromanone formation process. Initially, ligand exchange of PIDA with 2-*oxo*-2-phenylacetic acid afforded a hypervalent iodine(III) species **A**.[18] Then, I—O bond homolysis of **A** under visible light irradiation gave two radical intermediate and **C**. Note that, both of those two radical intermediates could further fragment to give the key acyl radical. It is worth noting that the exitance of acyl radical species in the reaction system was further proved by control experiment results (see supporting information). The addition of acyl radical to the C=C bond of *o*-(allyloxy)arylaldehyde provided carbon centered radical species **D**, which subsequently underwent intramolecular radical cyclization to give oxygen-centered radical intermediate **E**.[13-14] Finally, 1,2-H migration/oxidative deprotonation of **E** afforded the final chromanone products.



Scheme 2 Synthetic transformations of **3a**

3 Conclusions

In conclusion, we have developed an efficient visible light promoted cascade radical cyclization of *α*-oxocarboxylic acids with *o*-(allyloxy)arylaldehydes, leading to a wide range of 1,4-diketone containing chromanone derivatives in moderate to good yields. Compared with reported processes, photoredox catalysts or other types of transition metals were not required to run the reaction. The I—O bond homolysis of *in-situ* formed photo-sensitive iodine(III) specie was considered as the key intermediate to generate acyl radical. In addition, the successful transformation of



Scheme 3 Plausible reaction mechanism for 4-chromanones synthesis

the final product to other biologically important polycyclic heterocycles further demonstrated the approach valuable and attractive. The application of this method in the synthesis of other types important heterocycles is currently underway in our laboratory.

4 Experimental section

4.1 Instruments and reagents

All reactions involving air- or moisture-sensitive reagents or intermediates were carried out in pre-heated glassware under an argon atmosphere using standard Schlenk techniques. THF was freshly distilled from Na under argon. All other solvents and reagents were purified according to standard procedures or were used as received from chemical suppliers. The starting materials were synthesized according to literature procedures.

Chromatography: Analytical thin layer chromatography was performed using Qingdao Puke Parting Materials Co. silica gel plates (Silica gel 60 F254). Visualization was by ultraviolet fluorescence (λ=254 nm) and/or staining with phosphomolybdic acid or potassium permanganate ($KMnO_4$). Flash column chromatography was performed using 200～300 mesh silica gel.

^1H NMR and ^{13}C NMR spectra were recorded on a Bruker AVII 400 and JEOL JNM ECZ400R at 300 K, respectively. Spectra were calibrated relative to solvent residual proton and carbon chemical shift: $CHCl_3$ (δ 7.26 for ^1H NMR and δ 77.0 for ^{13}C NMR).

4.2 General procedure and spectral data of 3

A flame-dried Schlenk-tube equipped with a magnetic stir bar was charged with **1a** (1.0 equiv., 0.1 mmol), PIDA (4.0 equiv., 0.4 mmol) in 1.0 mL of CH_3CN was added **2a** (4.0 equiv., 0.4 mmol) under a nitrogen atmosphere. The reaction mixture was then stirred under the irradiation with 24W blue LEDs for 12 h. The solvent was then removed under reduced pressure with the aid of a rotary evaporator. The crude residue was purified by silica gel column chromatography to afford pure product **3a** as a yellow solid in 62% yield.

3-(2-*oxo*-2-Phenylethyl)chroman-4-one (**3a**):[13] Light yellow oil, ^1H NMR (400 MHz, $CDCl_3$, 300 K) δ: 8.00～7.95 (m, 2H), 7.90 (dd, J=7.9, 1.5 Hz, 1H), 7.60～7.53 (m, 1H), 7.49～7.44 (m, 3H), 7.05～6.94 (m, 2H), 4.64 (dd, J=11.1 Hz, 5.3, 1H), 4.30 (t, J=11.4 Hz, 1H), 3.70 (dd, J=18.0 Hz, 3.8, 1H), 3.62～3.55 (m, 1H), 3.01 (dd, J=18.0 Hz, 8.2, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 300 K) δ: 196.9, 193.3, 161.7, 136.3, 135.9, 133.3, 128.6, 128.0, 127.3, 121.3, 120.5, 117.8, 70.3, 41.7, 34.2.

6-Methyl-3-(2-*oxo*-2-phenylethyl)chroman-4-one (**3b**):[13] Light yellow oil, ^1H NMR (400 MHz, $CDCl_3$, 300 K) δ: 8.03～7.98 (m, 2H), 7.72～7.69 (m, 1H), 7.62～7.56 (m, 1H), 7.51～7.45 (m, 2H), 7.33～7.28 (m, 1H), 6.89 (d, J=8.4 Hz, 1H), 4.62 (dd, J=11.1, 5.2 Hz, 1H), 4.28 (t, J=11.3 Hz, 1H), 3.71 (dd, J=18.0, 3.7 Hz, 1H), 3.63～3.52 (m, 1H), 3.03 (dd, J=18.0, 8.4 Hz, 1H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 300 K) δ: 197.1, 193.7, 159.9, 137.01, 136.5, 133.4, 130.9, 128.7, 128.1, 126.9, 120.2, 117.7, 70.4, 41.9, 34.4, 20.4.

6-Methoxy-3-(2-*oxo*-2-phenylethyl)chroman-4-one (**3c**):[14] Light yellow oil, ^1H NMR (400 MHz, $CDCl_3$, 300 K) δ: 8.03～7.98 (m, 2H), 7.62～7.56 (m, 1H), 7.50～7.47 (m, 2H), 7.34 (d, J=3.2 Hz, 1H), 7.11 (dd, J=9.0, 3.2 Hz, 1H), 6.93 (d, J=9.0 Hz, 1H), 4.60 (dd, J=11.1, 5.2 Hz, 1H), 4.29 (t, J=11.3 Hz, 1H), 3.80 (s, 3H), 3.68 (dd, J=18.0, 3.8 Hz, 1H), 3.61～3.52 (m, 1H), 3.05 (dd, J=18.0, 8.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 300 K) δ: 197.0, 193.6, 156.6, 154.1, 136.4, 133.4, 128.7, 128.1, 125.2, 120.4, 119.2, 107.7, 70.5, 55.8, 41.9, 34.5.

6-Fluoro-3-(2-*oxo*-2-phenylethyl)chroman-4-one (**3d**):[14] Light yellow solid, m.p. 127～129 ℃ (lit.[14] m.p. 129～130 ℃); ^1H NMR (400 MHz, $CDCl_3$, 300 K) δ: 8.04～7.96 (m, 2H), 7.63～7.53 (m, 2H), 7.48 (t, J=7.7 Hz, 2H), 7.24～7.19 (m, 1H), 6.99～6.94 (m, 1H), 4.67～4.60 (m, 1H), 4.35～4.26 (m, 1H), 3.74～3.65 (m, 1H), 3.62～3.54 (m, 1H), 3.05 (dd, J=18.1, 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 300 K) δ: 196.7, 192.7, 158.1, 157.3 (d, J=240.5 Hz), 136.3, 133.5, 128.7, 128.1, 123.5 (d, J=24.5 Hz), 119.5 (d, J=7.3 Hz), 112.3 (d, J=23.1 Hz), 70.6, 41.7, 34.3.

6-Chloro-3-(2-*oxo*-2-phenylethyl)chroman-4-one (**3e**):[13] Light yellow solid, m.p. 113～114 (lit.[13] m.p. 115～116 ℃); ^1H NMR (400 MHz, $CDCl_3$, 300 K) δ: 8.03～7.95 (m, 3H), 7.62～7.52 (m, 2H), 7.51～7.45 (m, 2H), 6.92 (dd, J=22.1, 8.8 Hz, 1H), 4.65 (dd, J=11.2, 5.4 Hz, 1H), 4.36～4.25 (m, 1H), 3.69 (dd, J=18.1, 3.7 Hz, 1H), 3.61～3.54 (m, 1H), 3.04 (dd, J=18.1, 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 300 K) δ: 195.7, 191.3, 159.3, 135.3, 134.8, 132.5, 127.7, 127.1, 126.0, 125.7, 120.4, 118.6, 69.5, 40.6, 33.2.

6-Bromo-3-(2-*oxo*-2-phenylethyl)chroman-4-one (**3f**):[13] Light yellow solid, ^1H NMR (400 MHz, $CDCl_3$, 300 K) δ: 8.02～7.98 (m, 3H), 7.62～7.54 (m, 2H), 7.52～7.45 (m, 2H), 6.90 (d, J=8.8 Hz, 1H), 4.65 (dd, J=11.1, 5.4 Hz, 1H), 4.31 (dd, J=11.9, 11.2 Hz, 1H), 3.70 (dd, J=18.1, 3.7 Hz, 1H), 3.64～3.49 (m, 1H), 3.05 (dd, J=18.1, 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 300 K) δ: 196.7, 192.2, 160.7, 138.6, 136.3, 133.6, 129.8, 128.7, 128.1, 120.0, 70.5, 41.6, 34.2.

8-Bromo-3-(2-*oxo*-2-phenylethyl)chroman-4-one (**3g**):[14] Light yellow solid, m.p. 111～113 ℃ (lit.[14] m.p. 114～115 ℃); ^1H NMR (400 MHz, $CDCl_3$, 300 K) δ: 8.03～7.96 (m, 2H), 7.88 (dd, J=7.8, 1.7 Hz, 1H), 7.75 (dd, J=7.8, 1.6 Hz, 1H), 7.63～7.57 (m, 1H), 7.49 (t, J=7.6 Hz, 2H), 6.94 (t, J=7.8 Hz, 1H), 4.79 (dd, J=11.1, 5.3 Hz, 1H), 4.43 (t, J=11.4 Hz, 1H), 3.74～3.58 (m, 2H), 3.15～3.03 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 300 K) δ: 196.6, 192.6, 158.1, 139.2, 136.3, 133.5, 128.7, 128.1, 126.8, 122.2, 121.9, 111.5, 70.9, 41.5, 34.3.

8-Bromo-6-chloro-3-(2-*oxo*-2-phenylethyl)chroman-4-one (**3h**). Light yellow solid, m.p. 147～149 ℃; ^1H NMR (400 MHz, $CDCl_3$, 300 K) δ: 7.99 (dd, J=8.4, 1.3 Hz, 2H), 7.85 (d, J=2.6 Hz, 1H), 7.73 (d, J=2.6 Hz, 1H), 7.63～7.58 (m, 1H), 7.52～7.46 (m, 2H), 4.78 (dd, J=11.1, 5.4

Hz, 1H), 4.42 (dd, *J*=11.9, 11.1 Hz, 1H), 3.67 (dd, *J*=17.9, 3.7 Hz, 1H), 3.63～3.57 (m, 1H), 3.11 (dd, *J*=17.9, 7.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 300 K) *δ*: 196.3, 191.6, 156.9, 138.5, 136.2, 133.6, 128.8, 128.1, 127.2, 126.2, 122.1, 112.4, 71.0, 41.3, 34.2. HRMS (ESI) calcd for $C_{17}H_{13}BrClO_3$ $[M+H]^+$ 378.9737, found 378.9727.

6,8-Dichloro-3-(2-*oxo*-2-phenylethyl)chroman-4-one (**3i**):[13] Light yellow solid, m.p. 139～140 ℃ (lit.[13] m.p. 136～138 ℃); ^{1}H NMR (400 MHz, $CDCl_3$, 300 K) *δ*: 7.99 (dd, *J*=8.4, 1.4 Hz, 2H), 7.79 (d, *J*=2.6 Hz, 1H), 7.63～7.55 (m, 2H), 7.51～7.46 (m, 2H), 4.78 (dd, *J*=11.1, 5.3 Hz, 1H), 4.46～4.37 (m, 1H), 3.72～3.56 (m, 2H), 3.11 (dd, *J*=17.9, 7.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 300 K) *δ*: 196.3, 191.5, 156.0, 136.2, 135.5, 133.6, 128.7, 128.1, 126.7, 125.4, 123.8, 122.2, 71.0, 41.4, 34.2.

3-Methyl-3-(2-*oxo*-2-phenylethyl)chroman-4-one (**3j**):[13] Light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$, 300 K) *δ*: 7.97～7.94 (m, 3H), 7.59～7.54 (m, 1H), 7.49～7.43 (m, 3H), 7.07～7.03 (m, 1H), 6.98 (dd, *J*=8.3, 1.0 Hz, 1H), 4.86 (d, *J*=11.2 Hz, 1H), 4.24 (d, *J*=11.2 Hz, 1H), 3.59 (d, *J*=17.7 Hz, 1H), 3.18 (d, *J*=17.7 Hz, 1H), 1.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 300 K) *δ*: 197.1, 196.0, 161.2, 136.9, 135.7, 133.4, 128.6, 128.1, 128.0, 121.6, 119.8, 117.8, 74.3, 44.2, 41.8, 19.9.

6-Fluoro-3-methyl-3-(2-*oxo*-2-phenylethyl)chroman-4-one (**3k**): Light yellow solid, m.p. 89～91 ℃; ^{1}H NMR (400 MHz, $CDCl_3$, 300 K) *δ*: 7.97～7.91 (m, 2H), 7.61～7.56 (m, 2H), 7.47～7.43 (m, 2H), 7.25～7.18 (m, 1H), 6.97 (dd, *J*=9.0, 4.2 Hz, 1H), 4.84 (d, *J*=11.2 Hz, 1H), 4.20 (d, *J*=11.1 Hz, 1H), 3.63 (d, *J*=17.8 Hz, 1H), 3.16 (d, *J*=17.8 Hz, 1H), 1.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 300 K) *δ*: 196.8, 195.3, 157.5 (d, *J*=240.4 Hz), 157.4, 136.7, 133.5, 133.1, 128.4 (d, *J*=55.0 Hz), 128.1, 123.2 (d, *J*=24.5 Hz), 120.4, 119.4 (d, *J*=7.4 Hz), 112.9 (d, *J*=23.1 Hz), 74.5, 44.0, 42.1, 20.1. HRMS (ESI) calcd for $C_{18}H_{16}FO_3$ $[M+H]^+$ 299.1083, found 299.1075.

6-Chloro-3-methyl-3-(2-*oxo*-2-phenylethyl)chroman-4-one (**3l**): Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, 300 K) *δ*: 7.97～7.92 (m, 2H), 7.90 (d, *J*=2.7 Hz, 1H), 7.61～7.55 (m, 1H), 7.49～7.40 (m, 3H), 6.95 (d, *J*=8.9 Hz, 1H), 4.85 (d, *J*=11.2 Hz, 1H), 4.22 (d, *J*=11.2 Hz, 1H), 3.63 (d, *J*=17.9 Hz, 1H), 3.16 (d, *J*=17.9 Hz, 1H), 1.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 300 K) *δ*: 196.8, 194.9, 159.6, 136.7, 135.5, 133.5, 128.7, 128.1, 127.3, 127.1, 120.7, 119.5, 74.4, 44.0, 42.1, 20.1. HRMS (ESI) calcd for $C_{18}H_{16}ClO_3$ $[M+H]^+$ 315.0788, found 315.0780.

6-Bromo-3-methyl-3-(2-*oxo*-2-phenylethyl)chroman-4-one (**3m**): Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, 300 K) *δ*: 8.05 (d, *J*=2.5 Hz, 1H), 7.96～7.91 (m, 2H), 7.60～7.54 (m, 2H), 7.49～7.43 (m, 2H), 6.89 (d, *J*=8.8 Hz, 1H), 4.85 (d, *J*=11.2 Hz, 1H), 4.22 (d, *J*=11.2 Hz, 1H), 3.63 (d, *J*=17.8 Hz, 1H), 3.15 (d, *J*=17.8 Hz, 1H), 1.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 300 K) *δ*: 196.8, 194.7, 160.0, 138.3, 136.7, 133.5, 130.4, 128.6, 128.1, 121.2, 119.9, 114.3, 74.4, 43.9, 42.1, 20.1.; HRMS (ESI) calcd for $C_{18}H_{16}BrO_3$ $[M+H]^+$ 359.0283, found 359.0275.

8-Bromo-3-methyl-3-(2-*oxo*-2-phenylethyl)chroman-4-one (**3n**):[14] Light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$, 300 K) *δ*: 7.74 (dd, *J*=7.8, 1.7 Hz, 1H), 7.60～7.55 (m, 1H), 7.48～7.43 (m, 2H), 6.95 (t, *J*=7.8 Hz, 1H), 4.95 (d, *J*=11.1 Hz, 1H), 4.35 (d, *J*=11.2 Hz, 1H), 3.69 (d, *J*=17.9 Hz, 1H), 3.16 (d, *J*=17.9 Hz, 1H), 1.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, 300 K) *δ*: 196.7, 195.2, 157.5, 138.9, 136.7, 133.5, 128.6, 128.1, 127.4, 122.4, 121.2, 111.4, 75.0, 43.9, 42.3, 20.3.

3-(2-([1,1'-Biphenyl]-4-yl)-2-oxoethyl)chroman-4-one (**3o**):[13] Light yellow solid, m.p. 87～88 ℃ (lit.[13] m.p. 85～86 ℃); ^{1}H NMR (400 MHz, $CDCl_3$, 300 K) *δ*: 8.08 (d, *J*=8.4 Hz, 2H), 7.92 (dd, *J*=7.9, 1.7 Hz, 1H), 7.70 (d, *J*=8.4 Hz, 2H), 7.65～7.61 (m, 2H), 7.47 (t, *J*=7.5 Hz, 3H), 7.44～7.38 (m, 1H), 7.07～6.97 (m, 2H), 4.67 (dd, *J*=11.1, 5.3 Hz, 1H), 4.33 (t, *J*=11.4 Hz, 1H), 3.74 (dd, *J*=17.9, 3.8 Hz, 1H), 3.65～3.59 (m, 1H), 3.05 (dd, *J*=17.9, 8.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 300 K) *δ*: 196.6, 193.5, 161.9, 146.1, 139.7, 136.0, 135.1, 129.0, 128.7, 128.3, 127.4, 127.3, 127.3, 121.5, 120.6, 117.9, 70.4, 41.9, 34.4.

3-(2-*oxo*-2-(4-Phenoxyphenyl)ethyl)chroman-4-one (**3p**): Light yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$, 300 K): *δ*: 8.00～7.95 (m, 2H), 7.90 (dd, *J*=7.9, 1.7 Hz, 1H), 7.50～7.45 (m, 1H), 7.41～7.37 (m, 2H), 7.23～7.17 (m, 1H), 7.08～7.04 (m, 2H), 7.02～6.96 (m, 4H), 4.63 (dd, *J*=11.1, 5.2 Hz, 1H), 4.30 (t, *J*=11.3 Hz, 1H), 3.66 (dd, *J*=17.7, 3.8 Hz, 1H), 3.62～3.53 (m, 1H), 2.97 (dd, *J*=17.7, 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 300 K) *δ*: 195.5, 193.5, 162.3, 161.8, 155.4, 136.0, 131.1, 130.4, 130.1, 127.4, 124.7, 121.4, 120.6, 120.2, 117.9, 117.3, 70.4, 41.9, 34.1. HRMS (ESI) calcd for $C_{23}H_{19}O_4$ $[M+H]^+$ 359.1283, found 359.1267.

3-(2-(4-fluorophenyl)-2-oxoethyl)chroman-4-one (**3q**):[13] Light yellow solid, m.p. 104～105 ℃ (lit.[13] m.p. 108～109 ℃); ^{1}H NMR (400 MHz, $CDCl_3$, 300 K) *δ*: 8.07～8.01 (m, 2H), 7.91 (dd, *J*=7.9, 1.7 Hz, 1H), 7.51～7.47 (m, 1H), 7.18～7.12 (m, 2H), 7.06～6.97 (m, 2H), 4.65 (dd, *J*=11.1, 5.3 Hz, 1H), 4.32 (t, *J*=11.4 Hz, 1H), 3.68 (dd, *J*=17.8, 3.9 Hz, 1H), 3.63 -3.56 (m, 1H), 2.98 (dd, *J*=17.9, 8.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 300 K) *δ*: 195.4, 193.3, 165.9(d, *J*=260 Hz), 161.8, 136.0, 132.9 (d, *J*=3.2 Hz), 130.8 (d, *J*=9.5 Hz), 127.3, 121.5, 120.6, 117.9, 115.8 (d, *J*=22 Hz), 70.3, 41.8, 34.2.

3-(2-(4-Chlorophenyl)-2-oxoethyl)chroman-4-one (**3r**):[13] Light yellow oil, ^{1}H NMR (400 MHz, $CDCl_3$, 300 K) *δ*: 7.96 (d, *J*=2.0 Hz, 1H), 7.94 (d, *J*=1.9 Hz, 1H), 7.91 (dd, *J*=7.9, 1.7 Hz, 1H), 7.52～7.44 (m, 3H), 7.06～6.98 (m, 2H), 4.65 (dd, *J*=11.1, 5.2 Hz, 1H), 4.32 (t, *J*=11.4 Hz, 1H), 3.67 (dd, *J*=17.8, 4.0 Hz, 1H), 3.64～3.55 (m, 1H), 2.98 (dd, *J*=17.8, 7.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 300 K) *δ*: 195.8, 193.3, 161.8, 139.9, 136.1, 134.8, 129.6, 129.0, 127.4, 121.5, 120.6, 117.9, 70.3, 41.9, 34.3.

4.3 Synthesis and spectral data of 7

To a solution of diketone **3a** (0.2 mmol, 53.3 mg) in THF/ethanol (2 mL, *V*∶*V*=1∶3), sodium borohydride (1 mmol, 37.8 mg) was added in portions and heated at reflux for 4 h. The reaction mixture was then poured into water (5

mL), extracted with ethyl acetate (5 mL×2) and dried (Na_2SO_4). The removal of solvent gave crude diol. Crude diol was dissolved in dry CH_2Cl_2 (2 mL), BF_3•OEt_2 (28.4 mg, 0.2 mmol) was added and stirred for 12 h. The reaction mixture was then poured into water (5 mL), extracted with CH_2Cl_2 (5 mL×2) and dried (Na_2SO_4). The removal of solvent *in vacuo* followed by column chromatographic purification afforded compound **7**[19] (21.2 mg, 42% yield, 1.6∶1 *dr*) as a colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, 300 K) δ: 7.47 (d, J=7.6 Hz, 2.6H), 7.39～7.21 (m, 15.6H), 7.02～6.95 (m, 2.6H), 6.91 (t, J=9.0 Hz, 2.6H), 5.09 (dd, J=11.7, 6.6 Hz, 2H), 5.05～4.94 (m, 1.6H), 4.80 (d, J=4.9 Hz, 1.6H), 4.21 (dd, J=11.0, 4.6 Hz, 1H), 4.13 (dd, J=10.8, 4.3 Hz, 1.6H), 3.98～3.81 (m, 1H), 3.73 (t, J=10.6 Hz, 1.6H), 2.86～2.72 (m, 1H), 2.74～2.59 (m, 3.2H), 2.42～2.20 (m, 2H), 1.55 (dd, J=10.0, 7.3 Hz, 2.6H); ^{13}C NMR (100 MHz, $CDCl_3$, 300 K) δ: 155.1, 154.9, 143.4, 141.9, 131.5, 131.0, 129.4, 129.3, 128.5, 128.4, 127.4, 127.3, 126.0, 125.6, 122.2, 121.4, 121.4, 121.1, 79.9, 74.0, 66.6, 66.0, 37.2, 37.0, 36.9, 36.4. HRMS (ESI) calcd for $C_{17}H_{17}O_2$ $[M+H]^+$ 253.1229, found 253.1225.

Supporting Information Copies of NMR spectra of products. The Supporting Information is available free of charge via the Internet at http://sioc-journal.cn.

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