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Indium-catalyzed oxidative cross-dehydrogenative coupling of chromenes with 1,3-dicarbonyls and aryl rings†

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An effective indium-catalyzed oxidative cross-dehydrogenative coupling of electronically varied chromenes with 1,3-dicarbonyl compounds and aryl rings has been established. Both the C–H alkylation and arylation proceed smoothly at room temperature to afford diverse α-substituted chromene compounds in up to 91% yields. Besides these two types of C–H components, simple ketones like cyclohexanones also prove to be well tolerated.

Introduction

Alkyl and aryl substituted chromans are present in a number of biologically active natural products and synthetic pharmaceuticals possessing antioxidative, antipsychotic, antibacterial, antifungal, antiviral, and anticancer activities (Fig. 1).[1] The nucleophilic addition of carbon-centered reagents to chromene-based oxocarbenium ions represents an efficient and powerful approach to access the substructures.[2] In these reactions, oxocarbenium intermediates are typically generated *in situ* through the acid-mediated collapse of the corresponding acetals. However, the substrate preparation suffers from extra and unproductive steps and reagents.[3] On the other hand, the direct oxidative cross-dehydrogenative coupling (CDC) of chromenes with readily available C–H components provides excellent opportunities to synthesize the target simply by connecting two C–H bonds with a minimal amount of intermediary refunctionalizations and with high atom economy.[4,5] Over the past several years, the oxidative CDC reaction involving the isochroman type substrate has received much attention, with several reaction systems well developed.[6] However, the direct C–H functionalization of chromenes remains relatively unexplored. The Floreancig group developed an oxidative coupling of chromenes with diverse allylic silanes and enolsilanes in high efficiency.[7] Very recently, we reported

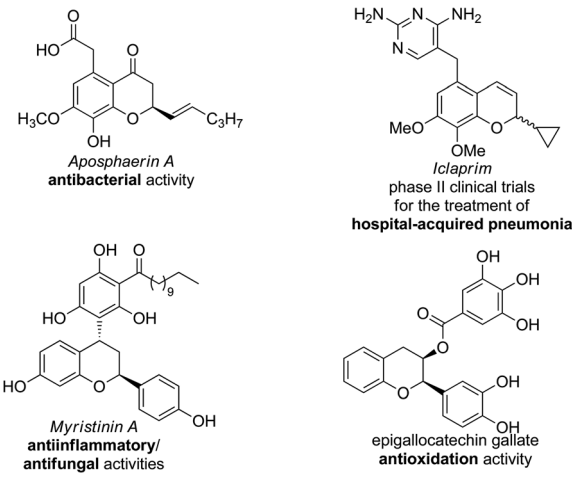

Fig. 1 Representative α-substituted chromans.

a trityl ion-mediated oxidative C–H arylation of chromenes employing nucleophilic potassium aryltrifluoroborate salts as coupling components.[8] Huang and coworkers disclosed a proline-catalyzed oxidative CDC of the unsubstituted 2*H*-chromene with aldehydes.[9] Albeit the above three pioneer studies, the C–H functionalization of electronically varied chromenes with dicarbonyls and aryl rings has not been established to date. Herein, we reported our recent efforts on the oxidative CDC reaction of chromenes using 1,3-dicarbonyls and aryl rings as coupling partners.

Results and discussion

Initially, the oxidative CDC of chromene **1a** with diisopropyl malonate **2a** was selected as the model reaction for optimiz-

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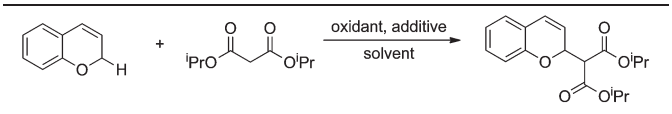
Table 1 Reaction condition optimization[a]

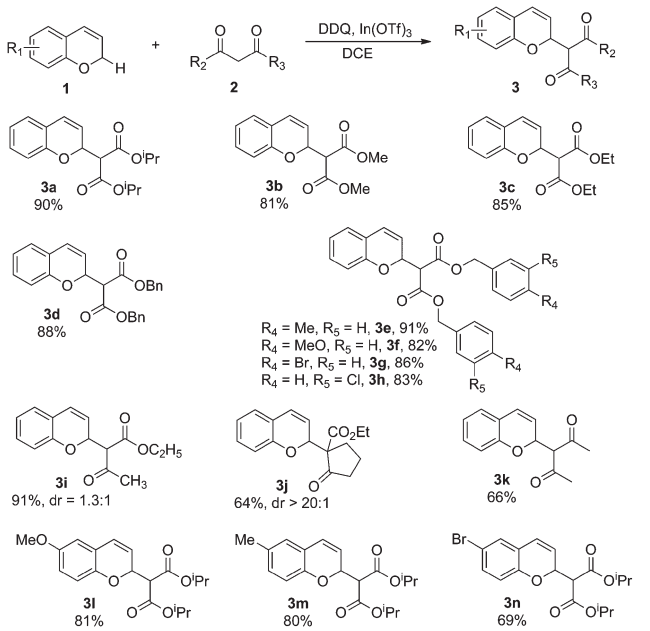


Entry	Oxidant	Additive	Solvent	Yield[b] (%)
1	DDQ	—	CH_2Cl_2	<5
2	DDQ	CuI	CH_2Cl_2	35
3	DDQ	CuBr	CH_2Cl_2	22
4	DDQ	CuCl	CH_2Cl_2	31
5	DDQ	$CuCl_2$	CH_2Cl_2	16
6	DDQ	$Cu(OAc)_2$	CH_2Cl_2	43
7	DDQ	CuOTf	CH_2Cl_2	55
8	DDQ	$Cu(OTf)_2$	CH_2Cl_2	65
9	DDQ	$Fe(OTf)_2$	CH_2Cl_2	50
10	DDQ	$Zn(OTf)_2$	CH_2Cl_2	46
11	DDQ	$In(OTf)_3$	CH_2Cl_2	79
12	DDQ	AgOTf	CH_2Cl_2	<5
13	DDQ	$Bi(OTf)_3$	CH_2Cl_2	<5
14	DDQ	$Mg(OTf)_2$	CH_2Cl_2	<5
15[c]	DDQ	$In(OTf)_3$	CH_2Cl_2	60
16[d]	DDQ	$In(OTf)_3$	CH_2Cl_2	70
17[e]	DDQ	$In(OTf)_3$	CH_2Cl_2	66
18	$PhI(OAc)_2$	$In(OTf)_3$	CH_2Cl_2	8
19	$Na_2S_2O_8$	$In(OTf)_3$	CH_2Cl_2	<5
20	CAN	$In(OTf)_3$	CH_2Cl_2	<5
21	MnO_2	$In(OTf)_3$	CH_2Cl_2	<5
22	TBHP/$CuBr_2$	$In(OTf)_3$	CH_2Cl_2	<5
23	DDQ	$In(OTf)_3$	DCE	90
24	DDQ	$In(OTf)_3$	$CHCl_3$	28
25	DDQ	$In(OTf)_3$	CH_3NO_2	63
26	DDQ	$In(OTf)_3$	Toluene	46
27	DDQ	$In(OTf)_3$	$PhCF_3$	50
28	DDQ	$In(OTf)_3$	EtOAc	56
29	DDQ	$In(OTf)_3$	Hexane	33
30	DDQ	$In(OTf)_3$	CH_3CN	<5

[a] General conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), DDQ (0.2 mmol), additive (10 mol%), and solvent (3.0 mL) at room temperature for 5 h, unless stated otherwise. [b] Isolated yield. [c] 5 mol% $In(OTf)_3$ employed. [d] 15 mol% $In(OTf)_3$ employed. [e] 20 mol% $In(OTf)_3$ employed.

ation (Table 1). No reaction was observed when 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) was employed as the oxidant without any additive (entry 1, Table 1). Therefore, a variety of metal additives were applied to the CDC reaction in CH_2Cl_2. Delightedly, copper salts effected the coupling, with $Cu(OTf)_2$ affording the best yields (entries 2–8, Table 1). Next, an extensive investigation on different metal sources bearing a triflate counteranion revealed 10 mol% of $In(OTf)_3$ as the ideal choice (entries 9–17). Other oxidants that are effective in promoting the oxidative CDC reaction of isochromans including PhI$(OAc)_2$, $Na_2S_2O_8$, CAN (cerium ammonium nitrate), MnO_2, and *tert*-butyl hydroperoxide (TBHP)/$CuBr_2$ failed to effect the model reaction (entries 18–22). The reaction was found to be highly dependent on the solvent choice, and 1,2-dichloroethane was identified as the optimal candidate (entries 23–30).

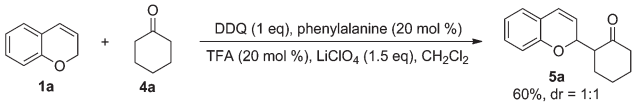
With the optimized reaction conditions in hand, the scope of 1,3-dicarbonyl components was investigated (Scheme 1). Commonly encountered symmetric 1,3-diesters were found to be well compatible with the oxidation system in good to excellent yields (**3a–3h**). β-Keto esters proved to be suitable coupling partners for the reaction, with **3i** and **3j** bearing a quaternary carbon accessed. 1,3-Diketone moieties were also tolerated, as demonstrated by the formation of **3k**. The substituent effect of the chromene component was next explored. Chromenes bearing electron-donating as well as -withdrawing substituents were well compatible with the oxidative CDC reaction in good yields (**3l–3n**). Notably, bromine was well tolerated for further diversifications and manipulations.



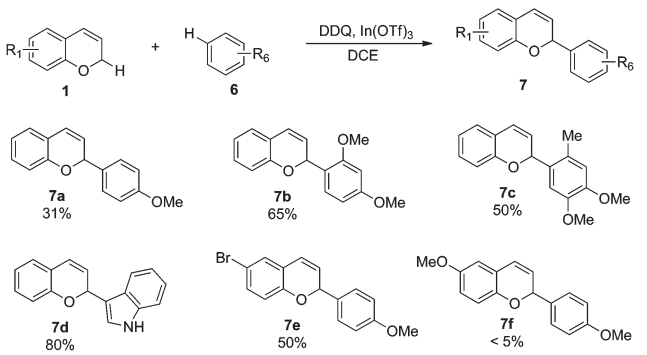
Scheme 1 The scope of CDC reactions of chromenes and 1,3-dicarbonyl compounds.

The high efficiency of the CDC with 1,3-dicarbonyl components prompted us to explore the possibility of employing simple ketones as nucleophilic partners (Scheme 2). In the presence of phenylalanine (20 mol%), TFA (20 mol%), $LiClO_4$ (1.5 equiv.), and DDQ (1.0 equiv.), the oxidative CDC reaction of **1a** with cyclohexanone (**4a**) proceeded smoothly at room temperature delivering **5a** in 60% yield with a dr of 1 : 1.

α-Aryl substituted chromans are key building blocks in numerous biologically active natural products and synthetic pharmaceuticals. The existing approaches rely on the nucleophilic attack of organoboranes onto cyclic oxocarbenium intermediates. While high efficiency was achieved, the preparation of these boronate nucleophiles requires extra steps. Employing aryl rings instead of the corresponding aryl boronates would be an attractive solution to the issue of atoms as



Scheme 2 Oxidative CDC reaction of chromene with cyclohexanone.



Scheme 3 The scope of CDC reactions of chromenes with aryl rings.

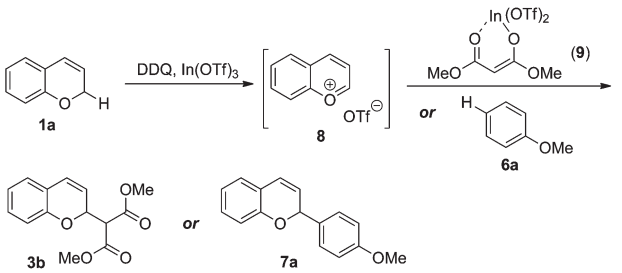


Fig. 2 A proposed mechanism for the $In(OTf)_3$-catalyzed CDC reaction.

well as step economy. Therefore, we next examined the CDC reaction of chromenes with aryl rings under the optimized reaction conditions (Scheme 3). Aryls bearing electron-donating substituents served as suitable nucleophilic partners delivering **7a–7c**. The heteroaryl moiety (**6d**) was also tolerated with the C–H functionalization process. With respect to the chromene partner, the electron-deficient moiety was tolerated providing **7e** in modest yield, though no reactivity was observed for the electron-rich one (**7f**).

According to the pioneering study of Li, a plausible mechanism for the indium-catalyzed oxidative CDC of chromenes was proposed in Fig. 2.[6c] In the presence of $In(OTf)_3$, DDQ promoted the C–H oxidation of chromene **1a** to provide oxocarbenium intermediate **8**. $In(OTf)_3$ activated the dicarbonyl compound giving **9** for the subsequent nucleophilic addition process to afford **3b**. The arylation of **8** with **6a** generated **7a**.

Conclusions

In summary, we have developed an indium-catalyzed oxidative C–H alkylation and arylation of chromenes promoted by DDQ and a catalytic amount of $In(OTf)_3$. The scope of nucleophilic components for the CDC is broad, with a wide range of dicarbonyl compounds and aryl rings well tolerated. The simple ketone like cyclohexanone also serves as an effective coupling partner. The scope with respect to chromenes is also broad, with electron-donating and -withdrawing substituents well tolerated. The mild conditions endowed good functional group compatibility, with bromine and ester tolerated for further manipulation.

Experimental

Proton (^{1}H NMR) and carbon (^{13}C NMR) nuclear magnetic resonance spectra were recorded at 300, 400, or 600 MHz and 75, 100, or 151 MHz, respectively. The chemical shifts are given in parts per million (ppm) on the delta (δ) scale. The solvent peak was used as a reference value, for ^{1}H NMR: $CDCl_3$ = 7.27 ppm, for ^{13}C NMR: $CDCl_3$ = 77.23 ppm. Analytical TLC was performed on precoated silica gel GF254 plates. HRMS were carried out using an Orbitrap analyzer.

General procedure for the oxidative CDC reaction of chromenes

To the solution of **1a** (26.4 mg, 0.2 mmol) and **2a** (56.4 mg, 0.3 mmol) in DCE (3.0 mL) was added DDQ (45.4 mg, 0.2 mmol) followed by $In(OTf)_3$ (11.2 mg, 0.02 mmol). The reaction mixture was stirred at room temperature for 5 h. Then it was quenched with sat. aqueous $NaHCO_3$ solution in an ice-bath and extracted twice with CH_2Cl_2. The combined organic layers were washed with brine, dried over anhydrous $MgSO_4$ and concentrated *in vacuo*. The residue was purified by chromatography on silica gel to yield the desired **3a** in 90% yield (57.2 mg).

Characterization data for the products in Scheme 1

Diisopropyl 2-(2*H*-chromen-2-yl)malonate (3a). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.12 (td, J = 8.0, 1.4 Hz, 1H), 6.99 (dd, J = 7.4, 1.2 Hz, 1H), 6.88 (td, J = 7.4, 0.6 Hz, 1H), 6.75 (d, J = 8.1 Hz, 1H), 6.49 (d, J = 9.9 Hz, 1H), 5.90 (dd, J = 9.9, 4.0 Hz, 1H), 5.48 (ddd, J = 9.3, 3.9, 0.7 Hz, 1H), 5.14 (dt, J = 12.5, 6.2 Hz, 1H), 5.06 (dt, J = 12.5, 6.3 Hz, 1H), 3.80 (d, J = 9.3 Hz, 1H), 1.30–1.26 (m, 6H), 1.23 (dd, J = 6.2, 0.7 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 166.4, 166.1, 152.4, 129.7, 126.8, 125.4, 122.7, 121.8, 121.5, 116.7, 72.9, 69.5, 69.4, 57.6, 21.9, 21.8, 21.8, 21.7; IR ν_{max} 2986, 2920, 2845, 1740, 1480, 1456, 1358, 1270, 1202, 1148, 1113, 1011, 773 cm^{-1}; HRMS (EI) m/z [M + H]$^+$ calculated for $C_{18}H_{23}O_5$: 319.1540, found 319.1541.

Dimethyl 2-(2*H*-chromen-2-yl)malonate (3b). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.13 (t, J = 7.0 Hz, 1H), 7.00 (d, J = 6.7 Hz, 1H), 6.90 (d, J = 6.6 Hz, 1H), 6.76 (d, J = 7.5 Hz, 1H), 6.52 (d, J = 9.6 Hz, 1H), 5.96–5.84 (m, 1H), 5.58–5.45 (m, 1H), 3.90 (d, J = 9.1 Hz, 1H), 3.80 (s, 3H), 3.73 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 167.2, 166.8, 152.1, 129.9, 126.9, 125.7, 122.3, 122.0, 121.4, 116.7, 72.9, 56.7, 52.9, 52.8; IR ν_{max} 2986, 2919, 2845, 1738, 1433, 1459, 1270, 1202, 1145, 1111, 1011, 775, 694 cm^{-1}; HRMS (EI) m/z [M + H]$^+$ calculated for $C_{14}H_{15}O_5$: 263.0914, found 263.0917.

Diethyl 2-(2*H*-chromen-2-yl)malonate (3c). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.13 (t, J = 6.7 Hz, 1H), 6.99 (d, J = 6.9 Hz, 1H), 6.90 (d, J = 7.1 Hz, 1H), 6.75 (d, J = 7.8 Hz, 1H), 6.51 (d, J = 9.6 Hz, 1H), 5.98–5.82 (m, 1H), 5.56–5.44 (m, 1H),

4.31–4.15 (m, 4H), 3.86 (d, J = 9.0 Hz, 1H), 1.30 (t, J = 5.4 Hz, 3H), 1.24 (t, J = 5.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 166.8, 166.5, 152.2, 129.8, 126.9, 125.6, 122.5, 121.9, 121.4, 116.6, 72.9, 61.9, 61.9, 57.1, 14.3, 14.2; IR ν_{max} 2986, 2921, 2843, 1737, 1423, 1459, 1277, 1229, 1145, 1112, 1011, 775, 694 cm^{-1}; HRMS (EI) m/z [M + H]$^+$ calculated for $C_{16}H_{19}O_5$: 291.1227, found 291.1225.

Dibenzyl 2-(2*H*-chromen-2-yl)malonate (3d). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.37–7.33 (m, 8H), 7.30–7.26 (m, 2H), 7.08 (t, J = 7.2 Hz, 1H), 6.98 (d, J = 6.9 Hz, 1H), 6.88 (t, J = 7.3 Hz, 1H), 6.60 (d, J = 8.0 Hz, 1H), 6.48 (d, J = 9.9 Hz, 1H), 5.85 (dd, J = 9.8, 4.0 Hz, 1H), 5.56 (dd, J = 9.2, 3.9 Hz, 1H), 5.26–5.10 (m, 4H), 4.00 (d, J = 9.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 166.5, 166.2, 152.1, 135.5, 135.2, 129.8, 128.8, 128.7, 128.6, 128.6, 128.5, 128.3, 126.9, 125.7, 122.3, 122.0, 121.4, 116.7, 72.9, 67.5, 57.1; IR ν_{max} 2952, 2924, 2851, 1737, 1519, 1488, 1457, 1384, 1292, 1226, 1208, 1113, 962, 806, 748 cm^{-1}; HRMS (EI) m/z [M + H]$^+$ calculated for $C_{26}H_{23}O_5$: 415.1540, found 415.1542.

Bis(4-methylbenzyl) 2-(2*H*-chromen-2-yl)malonate (3e). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.22 (d, J = 8.0 Hz, 2H), 7.19–7.11 (m, 6H), 7.10–7.04 (m, 1H), 6.97 (dd, J = 7.4, 1.4 Hz, 1H), 6.87 (td, J = 7.4, 0.7 Hz, 1H), 6.59 (d, J = 8.1 Hz, 1H), 6.47 (d, J = 9.9 Hz, 1H), 5.84 (dd, J = 9.8, 4.0 Hz, 1H), 5.52 (ddd, J = 9.3, 4.0, 0.7 Hz, 1H), 5.23–5.04 (m, 4H), 3.95 (d, J = 9.3 Hz, 1H), 2.37 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 166.6, 166.2, 152.1, 138.5, 138.4, 132.5, 132.3, 129.8, 129.4, 129.4, 128.6, 128.5, 126.8, 125.7, 122.4, 121.9, 121.4, 116.7, 72.9, 67.5, 57.1, 21.4; IR ν_{max} 2953, 2924, 2852, 1736, 1519, 1488, 1457, 1385, 1293, 1228, 1205, 1113, 960, 805, 748 cm^{-1}; HRMS (EI) m/z [M + H]$^+$ calculated for $C_{28}H_{27}O_5$: 443.1853, found 443.1853.

Bis(4-methoxybenzyl) 2-(2*H*-chromen-2-yl)malonate (3f). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.25 (d, J = 8.7 Hz, 2H), 7.20 (d, J = 8.6 Hz, 2H), 7.10–7.03 (m, 1H), 6.96 (dd, J = 7.2, 1.2 Hz, 1H), 6.90–6.81 (m, 5H), 6.57 (d, J = 8.0 Hz, 1H), 6.46 (d, J = 9.9 Hz, 1H), 5.81 (dd, J = 9.8, 4.0 Hz, 1H), 5.50 (dd, J = 9.2, 3.9 Hz, 1H), 5.19–5.02 (m, 4H), 3.92 (d, J = 9.3 Hz, 1H), 3.82 (s, 3H), 3.81 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 166.6, 166.3, 160.0, 159.9, 152.1, 130.4, 130.3, 129.8, 127.7, 127.4, 126.8, 125.7, 122.4, 121.9, 121.4, 116.7, 114.1, 114.1, 72.9, 67.4, 67.4, 57.1, 55.5, 55.5; IR ν_{max} 2955, 2924, 2852, 1737, 1520, 1488, 1450, 1364, 1293, 1228, 1202, 1113, 963, 805, 748, 695 cm^{-1}; HRMS (EI) m/z [M + H]$^+$ calculated for $C_{28}H_{27}O_7$: 475.1751, found 475.1755.

Bis(4-bromobenzyl) 2-(2*H*-chromen-2-yl)malonate (3g). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.52–7.42 (m, 4H), 7.18 (d, J = 8.3 Hz, 2H), 7.15–7.06 (m, 3H), 6.98 (dd, J = 7.4, 1.4 Hz, 1H), 6.89 (t, J = 7.3 Hz, 1H), 6.58 (d, J = 8.2 Hz, 1H), 6.48 (d, J = 9.9 Hz, 1H), 5.83 (dd, J = 9.8, 4.0 Hz, 1H), 5.57–5.47 (m, 1H), 5.17–5.01 (m, 4H), 3.97 (d, J = 9.1 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 166.3, 166.0, 152.0, 134.4, 134.1, 132.0, 131.9, 130.1, 130.0, 129.9, 126.9, 125.8, 122.8, 122.7, 122.1, 122.0, 121.2, 116.6, 72.8, 66.7, 66.7, 57.0; IR ν_{max} 2951, 2921, 2848, 1736, 1488, 1456, 1389, 1271, 1202, 1147, 1113, 1071, 800, 759 cm^{-1}; HRMS (EI) m/z [M + H]$^+$ calculated for $C_{26}H_{21}Br_2O_5$: 570.9750, found 570.9751.

Bis(3-chlorobenzyl) 2-(2*H*-chromen-2-yl)malonate (3h). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.34–7.26 (m, 6H), 7.21 (d, J = 7.2 Hz, 1H), 7.17–7.07 (m, 2H), 6.99 (d, J = 7.3 Hz, 1H), 6.90 (t, J = 7.4 Hz, 1H), 6.63 (d, J = 8.1 Hz, 1H), 6.51 (d, J = 9.8 Hz, 1H), 5.85 (dd, J = 9.8, 4.0 Hz, 1H), 5.55 (dd, J = 9.1, 3.9 Hz, 1H), 5.24–5.05 (m, 4H), 4.01 (d, J = 9.1 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 166.3, 166.0, 152.0, 137.4, 137.1, 134.7, 134.6, 130.1, 130.1, 130.0, 128.8, 128.8, 128.4, 128.3, 127.0, 126.4, 126.3, 125.9, 122.1, 122.0, 121.3, 116.7, 72.8, 66.6, 66.6, 57.0; IR ν_{max} 2954, 2922, 2848, 1736, 1489, 1457, 1386, 1270, 1204, 1137, 1111, 1071, 801, 760 cm^{-1}; HRMS (EI) m/z [M + H]$^+$ calculated for $C_{26}H_{21}Cl_2O_5$: 483.0761, found 483.0766.

Ethyl 2-(2*H*-chromen-2-yl)-3-oxobutanoate (3i). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.13 (t, J = 7.7 Hz, 1H), 6.99 (t, J = 6.0 Hz, 1H), 6.95–6.86 (m, 1H), 6.74 (d, J = 8.0 Hz, 1H), 6.49 (t, J = 10.1 Hz, 1H), 5.88–5.80 (m, 1H), 5.62–5.45 (m, 1H), 4.27 (q, J = 7.1 Hz, 1H), 4.21–4.16 (m, 1H), 4.04 (d, J = 9.4 Hz, 1H), 2.33 (s, 2H), 2.23 (s, 1H), 1.32–1.23 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 201.0, 200.5, 166.9, 166.5, 152.3, 152.0, 129.9, 129.8, 127.0, 126.9, 125.6, 125.4, 122.9, 122.7, 122.1, 121.9, 121.5, 121.5, 116.6, 116.5, 73.3, 73.0, 64.8, 63.5, 62.0, 61.8, 30.6, 30.5, 14.3, 14.2; IR ν_{max} 2987, 2918, 2845, 1742, 1717, 1487, 1456, 1356, 1272, 1222, 1149, 1113, 1019, 773 cm^{-1}; HRMS (EI) m/z [M + H]$^+$ calculated for $C_{15}H_{17}O_4$: 261.1121, found 261.1122.

Ethyl 1-(2*H*-chromen-2-yl)-2-oxocyclopentanecarboxylate (3j). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.07 (t, J = 7.7 Hz, 1H), 6.95–6.90 (m, 1H), 6.83 (t, J = 7.3 Hz, 1H), 6.63 (d, J = 7.9 Hz, 1H), 6.51–6.43 (m, 1H), 5.81 (s, 1H), 5.65 (dd, J = 10.0, 2.6 Hz, 1H), 4.28–4.15 (m, 2H), 2.58–2.41 (m, 3H), 2.40–2.31 (m, 1H), 2.06–1.95 (m, 2H), 1.27 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 212.5, 168.7, 153.5, 129.7, 126.9, 126.2, 121.9, 121.5, 120.6, 115.5, 77.9, 65.5, 61.9, 39.3, 28.3, 20.3, 14.2; IR ν_{max} 2988, 2919, 2845, 1744, 1716, 1480, 1446, 1358, 1277, 1204, 1148, 1113, 1011, 773, 754, 695 cm^{-1}; HRMS (EI) m/z [M + H]$^+$ calculated for $C_{17}H_{19}O_4$: 287.1278, found 287.1278.

3-(2*H*-Chromen-2-yl)pentane-2,4-dione (3k). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.14 (t, J = 7.0 Hz, 1H), 7.00 (d, J = 7.3 Hz, 1H), 6.91 (t, J = 7.3 Hz, 1H), 6.73 (d, J = 8.0 Hz, 1H), 6.48 (d, J = 9.7 Hz, 1H), 5.74 (dd, J = 9.8, 3.9 Hz, 1H), 5.61–5.55 (m, 1H), 4.28 (d, J = 9.7 Hz, 1H), 2.33 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 201.6, 201.2, 152.1, 130.0, 127.1, 125.7, 122.5, 122.2, 121.5, 116.6, 73.7, 73.1, 31.2, 29.6; IR ν_{max} 2937, 2859, 1707, 1483, 1457, 1385, 1230, 1205, 1128, 1113, 1013, 779, 754, 571 cm^{-1}; HRMS (EI) m/z [M + H]$^+$ calculated for $C_{14}H_{15}O_3$: 231.1016, found 231.1013.

Diisopropyl 2-(6-methoxy-2*H*-chromen-2-yl)malonate (3l). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 6.69 (s, 2H), 6.56 (s, 1H), 6.46 (d, J = 9.7 Hz, 1H), 5.99–5.89 (m, 1H), 5.46–5.37 (m, 1H), 5.17–5.10 (m, 1H), 5.07–5.01 (m, 1H), 3.82–3.76 (m, 4H), 1.29–1.26 (m, 6H), 1.24–1.21 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 166.4, 166.1, 154.6, 146.1, 125.5, 123.8, 122.2, 117.3, 115.0, 111.9, 72.8, 69.4, 69.4, 57.2, 56.0, 21.9, 21.8, 21.7; IR ν_{max} 2987, 2920, 2845, 1740, 1480, 1456, 1358, 1270, 1202, 1148, 1111, 1011, 773 cm^{-1}; HRMS (EI) m/z [M + H]$^+$ calculated for $C_{19}H_{25}O_6$: 349.1646, found 349.1648.

Diisopropyl 2-(6-methyl-2*H*-chromen-2-yl)malonate (3m). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 6.92 (d, J = 8.1 Hz, 1H), 6.80 (s, 1H), 6.65 (d, J = 8.1 Hz, 1H), 6.46 (d, J = 9.8 Hz, 1H), 5.90 (dd, J = 9.8, 4.0 Hz, 1H), 5.43 (dd, J = 9.1, 3.6 Hz, 1H), 5.14 (dt, J = 12.5, 6.3 Hz, 1H), 5.05 (dt, J = 12.5, 6.3 Hz, 1H), 3.79 (d, J = 9.5 Hz, 1H), 2.25 (s, 3H), 1.28 (t, J = 6.7 Hz, 6H), 1.22 (d, J = 6.2 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 166.4, 166.1, 150.1, 131.1, 130.2, 127.3, 125.6, 122.8, 121.4, 116.4, 72.8, 69.4, 69.4, 57.4, 21.9, 21.8, 21.7, 20.7; IR ν_{max} 2957, 2928, 2845, 1743, 1480, 1459, 1358, 1270, 1138, 1113, 1011, 773 cm^{-1}; HRMS (EI) m/z $[M + H]^+$ calculated for $C_{19}H_{25}O_5$: 333.1697, found 333.1694.

Diisopropyl 2-(6-bromo-2*H*-chromen-2-yl)malonate (3n). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.21 (d, J = 7.3 Hz, 1H), 7.11 (s, 1H), 6.63 (d, J = 8.2 Hz, 1H), 6.43 (d, J = 9.5 Hz, 1H), 6.02–5.93 (m, 1H), 5.48 (dd, J = 4.8, 3.8 Hz, 1H), 5.18–5.10 (m, 1H), 5.10–5.02 (m, 1H), 3.76 (d, J = 8.7 Hz, 1H), 1.27 (s, 6H), 1.23 (d, J = 5.5 Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 166.2, 165.9, 151.5, 132.3, 129.3, 124.4, 124.1, 123.3, 118.4, 113.9, 73.1, 69.6, 69.6, 57.5, 21.9, 21.8, 21.8, 21.7; IR ν_{max} 2988, 2920, 2845, 1742, 1480, 1456, 1348, 1202, 1148, 1112, 1011, 779 cm^{-1}; HRMS (EI) m/z $[M + H]^+$ calculated for $C_{18}H_{22}BrO_5$: 397.0645, found 397.0644.

2-(2*H*-Chromen-2-yl)cyclohexanone (5a). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.13–7.06 (m, 1H), 6.97–6.91 (m, 1H), 6.88–6.81 (m, 1H), 6.78 (d, J = 8.1 Hz, 0.5H), 6.72 (d, J = 8.1 Hz, 0.5H), 6.46–6.36 (m, 1H), 5.88–5.67 (m, 1H), 5.52–5.45 (m, 0.5H), 5.21–5.12 (m, 0.5H), 2.92–2.69 (m, 1H), 2.49–2.40 (m, 1.5H), 2.38–2.21 (m, 1.5H), 2.11–1.98 (m, 1.5H), 1.94–1.91 (m, 0.5H), 1.73–1.61 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 211.0, 210.8, 154.2, 153.3, 129.4, 126.8, 126.7, 125.7, 125.0, 124.1, 123.3, 121.4, 121.2, 116.2, 115.7, 74.2, 73.6, 56.1, 55.7, 42.9, 42.5, 29.9, 28.2, 27.9, 27.7, 24.9, 24.7; IR ν_{max} 3042, 2938, 2859, 1706, 1485, 1455, 1375, 1222, 1202, 1128, 1112, 1014, 754, 571 cm^{-1}; HRMS (EI) m/z $[M + H]^+$ calculated for $C_{15}H_{17}O_2$: 229.1223, found 229.1224.

Characterization data for the products in Scheme 2

2-(2*H*-Chromen-2-yl)cyclohexanone (5a). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.13–7.06 (m, 1H), 6.97–6.91 (m, 1H), 6.88–6.81 (m, 1H), 6.78 (d, J = 8.1 Hz, 0.5H), 6.72 (d, J = 8.1 Hz, 0.5H), 6.46–6.36 (m, 1H), 5.88–5.67 (m, 1H), 5.52–5.45 (m, 0.5H), 5.21–5.12 (m, 0.5H), 2.92–2.69 (m, 1H), 2.49–2.40 (m, 1.5H), 2.38–2.21 (m, 1.5H), 2.11–1.98 (m, 1.5H), 1.94–1.91 (m, 0.5H), 1.73–1.61 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 211.0, 210.8, 154.2, 153.3, 129.4, 126.8, 126.7, 125.7, 125.0, 124.1, 123.3, 121.4, 121.2, 116.2, 115.7, 74.2, 73.6, 56.1, 55.7, 42.9, 42.5, 29.9, 28.2, 27.9, 27.7, 24.9, 24.7; IR ν_{max} 3042, 2938, 2859, 1706, 1485, 1455, 1375, 1222, 1202, 1128, 1112, 1014, 754, 571 cm^{-1}; HRMS (EI) m/z $[M + H]^+$ calculated for $C_{15}H_{17}O_2$: 229.1223, found 229.1224.

Characterization data for the substrates in Scheme 3

2-(4-Methoxyphenyl)-2*H*-chromene (7a). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.39 (d, J = 7.9 Hz, 2H), 7.10 (t, J = 7.8 Hz, 1H), 7.02 (d, J = 7.4 Hz, 1H), 6.93–6.85 (m, 3H), 6.76 (d, J = 8.1 Hz, 1H), 6.55 (d, J = 9.8 Hz, 1H), 5.88 (s, 1H), 5.79 (dd, J = 9.8, 3.0 Hz, 1H), 3.81 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ = 160.0, 153.3, 133.1, 129.6, 128.9, 126.7, 125.1, 124.2, 121.6, 121.3, 116.3, 114.2, 77.0, 55.5; IR ν_{max} 2930, 2837, 1610, 1586, 1513, 1485, 1457, 1304, 1268, 1250, 1227, 1205, 1175, 1111, 1037, 955, 932, 802, 756 cm^{-1}; HRMS (EI) m/z calcd for $C_{16}H_{15}O_2$: $[M + H]^+$ 239.1067, found 239.1068.

2-(2,4-Dimethoxyphenyl)-2*H*-chromene (7b). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.38 (d, J = 8.4 Hz, 1H), 7.13–7.07 (m, 1H), 7.00 (d, J = 7.3 Hz, 1H), 6.85 (t, J = 7.4 Hz, 1H), 6.78 (d, J = 8.1 Hz, 1H), 6.53–6.43 (m, 3H), 6.29 (dd, J = 3.2, 1.7 Hz, 1H), 5.76 (dd, J = 9.9, 3.6 Hz, 1H), 3.86 (s, 3H), 3.80 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 161.1, 157.5, 153.7, 129.4, 129.3, 126.6, 125.3, 123.7, 121.8, 121.6, 121.1, 116.2, 104.5, 98.9, 71.2, 55.8, 55.6; IR ν_{max} 2956, 2921, 2850, 1611, 1588, 1505, 1485, 1356, 1227, 1208, 1157, 1120, 1110, 1035, 955, 766 cm^{-1}; HRMS (EI) m/z $[M + H]^+$ calculated for $C_{17}H_{17}O_3$: 269.1172, found 269.1169.

2-(4,5-Dimethoxy-2-methylphenyl)-2*H*-chromene (7c). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.15–7.10 (m, 1H), 7.06–7.01 (m, 2H), 6.88 (t, J = 7.4 Hz, 1H), 6.80 (d, J = 8.0 Hz, 1H), 6.73 (s, 1H), 6.58 (dd, J = 9.9, 1.7 Hz, 1H), 6.15–6.07 (m, 1H), 5.75 (dd, J = 9.8, 2.9 Hz, 1H), 3.89 (s, 3H), 3.81 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 153.8, 148.9, 147.3, 130.6, 129.6, 128.6, 126.8, 125.2, 124.9, 121.7, 121.4, 116.2, 114.1, 111.5, 74.7, 56.2, 56.1, 18.8; IR ν_{max} 2957, 2927, 2850, 1611, 1589, 1505, 1485, 1356, 1227, 1208, 1157, 1120, 1111, 1035, 959, 756 cm^{-1}; HRMS (EI) m/z $[M + H]^+$ calculated for $C_{18}H_{19}O_3$: 283.1329, found 283.1330.

3-(2*H*-Chromen-2-yl)-1*H*-indole (7d). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 8.06 (s, 1H), 7.84 (d, J = 7.8 Hz, 1H), 7.36 (d, J = 8.0 Hz, 1H), 7.25–7.14 (m, 3H), 7.07 (d, J = 7.5 Hz, 2H), 6.88 (t, J = 7.4 Hz, 1H), 6.77 (d, J = 7.9 Hz, 1H), 6.63 (d, J = 9.8 Hz, 1H), 6.26 (d, J = 1.7 Hz, 1H), 5.98 (dd, J = 9.8, 3.6 Hz, 1H); ^{13}C NMR (101 MHz, $CDCl_3$) δ = 153.51, 136.7, 129.2, 126.5, 126.1, 124.6, 124.5, 124.0, 122.6, 122.0, 121.0, 120.1, 119.9, 116.4, 115.7, 111.3, 70.5; IR ν_{max} 3409, 2947, 2918, 2846, 1603, 1544, 1484, 1456, 1421, 1339, 1223, 1200, 1111, 1033, 1010, 938, 797, 744 cm^{-1}; HRMS (EI) m/z $[M + H]^+$ calculated for $C_{17}H_{14}NO$: 248.1070, found 248.1074.

6-Bromo-2-(4-methoxyphenyl)-2*H*-chromene (7e). ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.37 (t, J = 8.9 Hz, 2H), 7.15–6.86 (m, 5H), 6.72 (d, J = 8.1 Hz, 0.5H), 6.53 (d, J = 9.8 Hz, 0.5H), 5.91 (dd, J = 10.0, 3.4 Hz, 0.5H), 5.86 (d, J = 7.0 Hz, 1H), 5.83 (dd, J = 10.0, 3.4 Hz, 0.5H), 3.82 (s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$) δ 160.0, 154.3, 132.3, 130.0, 129.0, 127.6, 125.3, 124.3, 123.4, 119.6, 115.8, 114.2, 76.9, 55.5; IR ν_{max} 2923, 2835, 1610, 1594, 1558, 1513, 1481, 1445, 1304, 1247, 1208, 1174, 1035, 963, 820, 766 cm^{-1}; HRMS (EI) m/z calcd for $C_{16}H_{14}BrO_2$ $[M + H]^+$ 317.0172, found 317.0173.

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