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Note

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Regioselective Palladium-Catalyzed Decarboxylative Cross-Coupling Reaction of Alkenyl Acids with Coumarins: Synthesis of 3-Styrylcoumarin Compounds

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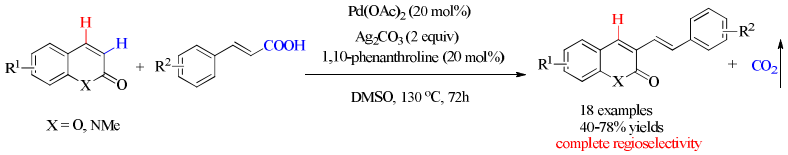


ABSTRACT: A novel and efficient protocol for the regioselective synthesis of 3-styrylcoumarins from readily available cinnamic acids and coumarins is presented. The reaction proceeds *via* a decarboxylative cross-coupling mediated by catalytic amount of $Pd(OAc)_2$, Ag_2CO_3 as an oxidant, and 1,10-phenanthroline as a ligand. A plausible reaction mechanism for this process is depicted, and the resulting 3-styrylcoumarins show excellent fluorescence quantum yields.

Decarboxylative coupling reactions have become a powerful tool for regioselective C-C and C-heteroatom bonds formation,[1] thus providing new protocols for Heck-type reactions,[2] oxidative arylations,[3] redox-neutral cross-coupling reactions,[4] and allylations.[5] Among those, alkenyl acids act as cross-coupling components by a metal-promoted decarboxylation process and are used in construction of C-C,[6] C-N,[7] C-S,[8] and C-P[9] bonds because of their stable, low cost, diversity, ready availability, and the nontoxic byproduct (CO_2). From environmental and economic perspectives, the development of organic synthesis using inexpensive and stable material such as alkenyl acids would be of significant importance.

Coumarins constitute a major class of naturally occurring compounds and

privileged medicinal scaffolds, have been extensively investigated regard to their pharmacological activity[10] and outstanding optical properties[11]. Due to effective fluorophores characterized by high fluorescence quantum yields,[12] several coumarins have been shown to exhibit their photophysical properties.[13-18] The challenge is how to effectively increase the spectroscopic bands intensity of coumarin derivatives. A best solution is extending the conjugated π-electron system, yielding coumarin derivatives with greater intensity. Recently, various synthetic approaches have been reported to synthesize 3-styrylcoumarins in the literature.[19] For example, Heck cross-coupling reaction between 3-bromocoumarin and olefins,[19a] 3-vinyl coumarins and aryl halides,[19b] coumarin-3-carboxylic acid and olefins,[19c] coumarins and alkenes,[19d] are a few prominent methods of synthesizing 3-styryl coumarins (Scheme 1). In light of the literature precedences[1-19] and continuation of our efforts in the development of transition-metal-catalyzed C-H functionalization,[20] we thought it would be of interest to develop a method by a decarboxylative cross-coupling reaction of α,β-unsaturated carboxylic acids using coumarins. Herein, we disclose an efficient, economic route for rapid synthesis of 3-styrylcoumarins *via* palladium-catalyzed decarboxylative coupling of cinnamic acids employing coumarins.

Scheme 1. Reported Methods for the Synthesis of 3-Styrylcoumarins

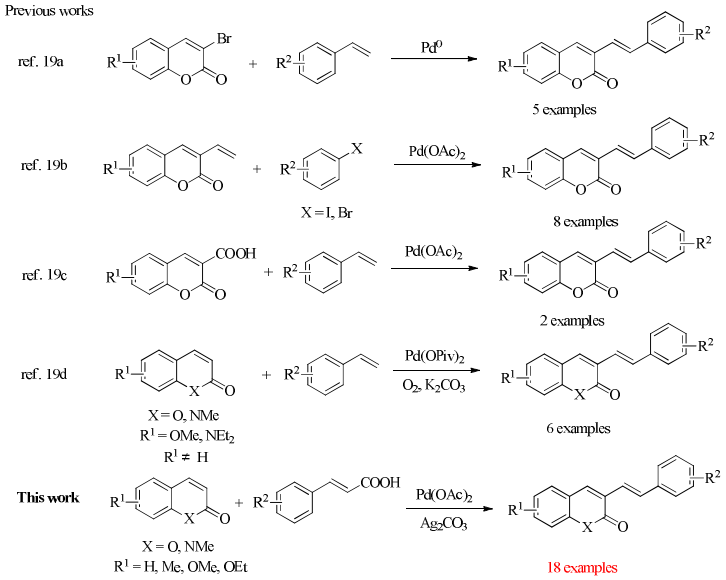
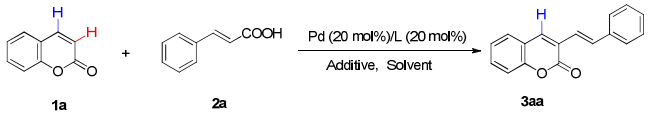


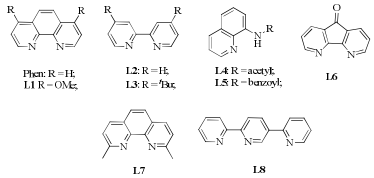
Table 1. Reaction Conditions Optimization[a]



1a 2a 3aa

entry	catalyst	ligand	additive[c]	solvent	yield (%)[b]
1	$Pd(OAc)_2$	–	AgOAc	DMSO	10
2	$Pd(OAc)_2$	Phen	AgOAc	DMSO	40
3	$PdCl_2$	Phen	AgOAc	DMSO	36
4	$Pd(acac)_2$	Phen	AgOAc	DMSO	30
5	$Pd(dba)_2$	Phen	AgOAc	DMSO	22
6	$Pd(OAc)_2$	Phen	Ag_2CO_3	DMSO	47
7	$Pd(OAc)_2$	Phen	Ag_2O	DMSO	42
8	$Pd(OAc)_2$	Phen	AgOTf	DMSO	39
9	$Pd(OAc)_2$	**L1**	Ag_2CO_3	DMSO	32
10	$Pd(OAc)_2$	**L2**	Ag_2CO_3	DMSO	17
11	$Pd(OAc)_2$	**L3**	Ag_2CO_3	DMSO	12
12	$Pd(OAc)_2$	**L4**	Ag_2CO_3	DMSO	14
13	$Pd(OAc)_2$	**L5**	Ag_2CO_3	DMSO	11
14	$Pd(OAc)_2$	**L6**	Ag_2CO_3	DMSO	15
15	$Pd(OAc)_2$	**L7**	Ag_2CO_3	DMSO	34
16	$Pd(OAc)_2$	**L8**	Ag_2CO_3	DMSO	41
17	$Pd(OAc)_2$	Phen	Ag_2CO_3	PhCl	14
18	$Pd(OAc)_2$	Phen	Ag_2CO_3	DMF	31
19	$Pd(OAc)_2$	Phen	Ag_2CO_3	Dioxane	0
20	$Pd(OAc)_2$	Phen	Ag_2CO_3	DCE	0
21	$Pd(OAc)_2$	Phen	Ag_2CO_3	CH_3CN	0
22[d]	**$Pd(OAc)_2$**	**Phen**	**Ag_2CO_3**	**DMSO**	**69**
23[e]	$Pd(OAc)_2$	Phen	Ag_2CO_3	DMSO	70
24[f]	$Pd(OAc)_2$	Phen	Ag_2CO_3	DMSO	43

[a]All reactions were carried out under the following conditions: coumarin **1a** (0.3 mmol), **2a** (0.2 mmol), Pd catalyst (20 mol %), ligand (20 mol %) in different solvents (2 mL) at 130 °C for 72 h. [b]Isolated yield based on **2a**. [c]2.0 Equivalents. [d] Sealed tube . [e]140 °C. [f] The reaction was carried out using 15 mol % $Pd(OAc)_2$.

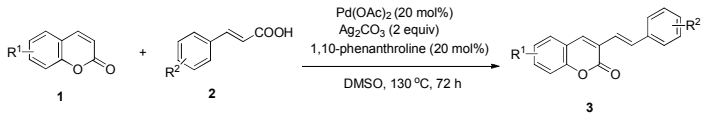


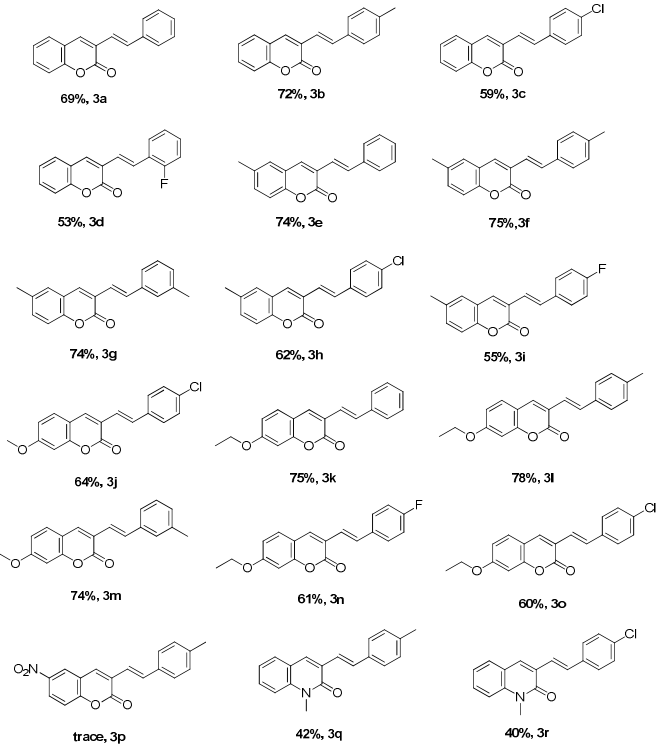
Our initial experiments showed that using $Pd(OAc)_2$/AgOAc/DMSO as catalytic system, the C3-olefination of coumarin occurred with complete regioselectivity giving a low isolated yield (10%) (Table 1, entry 1). Addition of 20 mol% 1,10-phenanthroline increased the yield to 40% (Table 1, entry 2). In the presence of 1,10-phenanthroline, a series of palladium catalysts were screened and did not display better catalytic activity except $PdCl_2$ showing the similar activity as that of $Pd(OAc)_2$ (Table 1, entries 3, 4 and 5; Table S1, Supporting Information). Among the additives examined, Ag_2CO_3 provided the best result (Table 1, entries 6-8; Table S1, Supporting Information). Some other N,N-ligands **L1-L8** were also evaluated, while these ligands did produce active catalyst systems, the yields were inferior to that obtained with 1,10-phenanthroline (Table 1, entries 9-16; Table S2, Supporting Information). The solvent also affected the coupling reaction of coumarin and alkenyl acid. No product was found with dioxane, DCE, or CH_3CN as solvent, and only poor yields were obtained when other solvents such as PhCl, DMF were employed (Table 1, entries 17−21), where DMSO turned out to be the most appropriate (Table S3, Supporting Information). When in the sealed tube, the yield of **3a** enhanced from 40% to 69% (Table 1, entry 22), but no obvious improvement in the yield could be obtained as the temperature was increased to 140 °C (Table 1, entry 22 *vs.* 23). A very slow reaction rate and low yield were observed when the catalytic amount of $Pd(OAc)_2$ decreased from 20 to 15 mol % (Table 1, entry 22 *vs.* 24). The above investigations revealed that the $Pd(OAc)_2/Ag_2CO_3$/phen/DMSO system is the best combination for promoting the olefination.

With the optimized reaction conditions established, we started to investigate the scope and limitation of this reaction, and the results are summarized in Table 2. It was observed that a range of selected coumarin derivatives and cinnamic acids were compatible with the reaction conditions, resulting in the formation of the desired products in moderate to good yields with completely regioselectivity. Cinnamic acids featuring electron-donating or neutral groups at phenyl ring provided somewhat higher yields of the olefination products than did those bearing electron-withdrawing groups (**3a-b** *vs.* **3c-d** and **3e-g** *vs.***3h-i**). Gratifyingly, moderate to good reaction

yields (55-78%) were obtained when courmarins were substituted by electron-donating groups such as -Me, -OMe, -OEt at the C-6 or C-7 position even in a shorter time (**3e-o**). The crystallization of compound **3g** from ethanol gave a single crystal suitable for X-ray analysis. It illustrates the molecular structure of the substituted 3-styrylcoumarin **3g** (see Suporting Information pp S29). Unfortunately, coumarin possessing an electron-withdrawing group such as -NO_2 at the C-6 position gave the desired product **3p** in poor yield. The electron-withdrawing group presumably is not conducive to the intermediate **II** formation (see Scheme 3). We further investigated additional substrates and were pleased to observe that quinolinones also worked well in the optimized system, leading to the formation of **3q** and **3r**.

Table 2. Direct C3-Olefination of the Coumarins with Various Cinnamic Acid Derivatives[a,b]



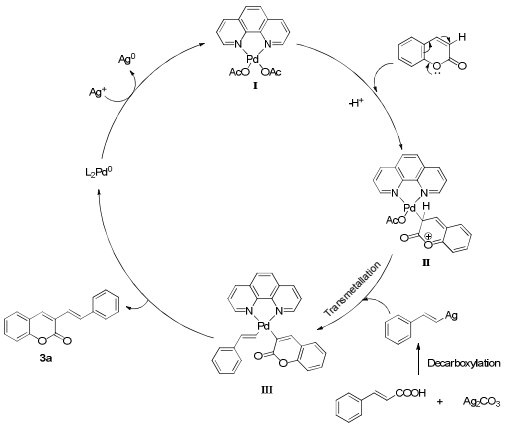


[a]Reaction conditions: **1** (0.3 mmol), **2** (0.2 mmol), $Pd(OAc)_2$ (20 mol % to **2**), Ag_2CO_3 (2 equiv to **2**), 1,10-phenanthroline (20 mol % to **2**), DMSO (2 mL) , at 130 °C, sealed tube, 72 h. [b]Average isolated yield based on **2.**

To investigate the reaction mechanism, control experiment was conducted (Scheme 2). A 67% yield of **3a** was smoothly obtained in the presence of the radical scavenger butyleret hydroxytoluen (BHT) (eq (1)), which could indicate that free radical pathway is not involved. On the basis of these data, we proposed a mechanism for the present reaction pathway (Scheme 3).[21] Electrophilic palladation of coumarin at the C3 position with the Pd-ligand species was favorable due to the more nucleophilic 3-position, thereby affording the intermediate II. In parallel, the silver mediated decarboxylation of cinnamic acid **1a** affords alkenyl–silver specie. Alkenyl silver would then transfer the alkenyl group to intermediate II under formation of silver derivates by transmetallation to give the intermediate III. Finally, the desired product **3a** would be released, regenerating the initial palladation species and resuming the catalytic cycle.

Scheme 2. Mechanistic Investigations for the Decarboxylative Cross-Coupling Reaction.

Scheme 3. Plausible Mechanism.



Absorption and emission properties, as well as fluorescence quantum yields (Φ_F) of the synthesized coumarins derivatives **3** are summarized in Table 3. A change of less than 8 nm for λ_{max} was observed among **3e**, **3f**, **3g**, **3h**, **3i** by simply modifying the substituents at the benzene ring moiety position (Table 3, entries 5-9). In comparison with **3a** and **3b**, a longer wavelength of the absorption maximum peak (λ_{max}) was obtained upon the introduction of electron-donating groups such as ethoxy at the C-7 position (Table 3, entry 3 *vs.* 1; entry 4 *vs.* 2). All of these compounds exhibited excellent fluorescence, regardless of the electron-donating or withdrawing ability of the substituents. The fluorescence quantum yield (Φ_F) remained in the range of 0.39-0.92. Obviously, the introduction of electron-donating groups into 3-styrylcoumarin derivatives showed a better fluorescence quantum yields than electron-withdrawing groups.

Table 3. Photophysical Properties of 3-Styrylcoumarin Derivatives 3.

entry	compounds	λ_{max} [a] [nm]	λ_{em} [b] [nm]	Φ_F [c]
1	**3a**	349	440	0.67
2	**3b**	354	447	0.76
3	**3k**	358	444	0.83
4	**3l**	365	452	0.92
5	**3e**	349	444	0.81
6	**3f**	354	448	0.88
7	**3g**	351	443	0.87
8	**3h**	354	440	0.39
9	**3i**	346	442	0.52
10	**3j**	346	450	0.79
11	**3m**	355	446	0.86
12	**3n**	360	442	0.82
13	**3o**	350	443	0.75

[a]Absorption maxima in acetonitrile (longest wavelength transition). [b]Maxima of the corrected emission spectra in acetonitrile. [c]Determined by quinine sulfate (Φ_F = 0.55, excited at 347 nm) as a standard.

In summary, we have successfully developed a flexible and rapid route to synthesize series of 3-styryl coumarins from cinnamic acids and coumarins *via* a palladium catalyzed decarboxylative cross-coupling reaction. 3-Styrylcoumarins were obtained in moderate to good yields and showed good fluorescence quantums. The current study provides a clue for the further development of new types fluorescent materials.

EXPERIMENTAL SECTION

The reaction mixture of coumarins **1** (0.3 mmol), alkenyl acid **2** (0.2 mmol), $Pd(OAc)_2$ (20 mol %), Ag_2CO_3 (2 equiv), 1,10-phenanthroline (20 mol %), DMSO (2 mL) was stirred at 130 ^oC for 72 h in sealed tube, and monitored periodically by TLC. Upon completion, the reaction mixture was diluted with water (30 mL) and extracted with ethyl acetate (3 × 30 mL). The combined organic layers were washed with water and brine, dried over Na_2SO_4 and filtered. The solvent was removed under vacuum. The residue was purified by flash column chromatography to afford **3**.

3-Styryl-chromen-2-one (3a): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 69% (34.2 mg) as a yellow solid: 161-163 ^oC (162-164 ^oC)[1]; ^1H NMR (500 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.63 (d, *J* = 16.3 Hz, 1H), 7.58-7.50 (m, 4H), 7.41-7.30 (m, 5H), 7.16 (d, *J* = 16.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.4, 152.8, 136.8, 133.6, 131.1, 128.7, 128.4, 127.6, 127.0, 124.9, 124.5, 122.0, 119.7, 116.4. HRAPCIMS calcd for $C_{17}H_{12}O_2$ $(M + H)^+$ 249.0916; found 249.0908.

Reference[1]: Gordo, J.; Avo, J.; Parola, A. J.; Lima, J. C.; Pereira, A.; Branco, P. S. *Org. Lett*., **2011**, *13*, 5112.

3-(2-p-Tolyl-vinyl)-chromen-2-one (3b): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 72% (37.7 mg) as a yellow solid: 147-149 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.49 (d, *J* = 16.3 Hz, 1H), 7.45-7.29 (m, 4H), 7.26-7.18 (m, 2H), 7.10 (d, *J* = 7.8 Hz, 2H), 7.02 (d, *J* = 16.3 Hz,

1H), 2.29 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.4, 152.7, 138.5, 136.2, 134.0, 133.6, 130.9, 129.5, 127.5, 126.9, 125.1, 124.5, 121.0, 119.7, 116.4, 21.3. HRAPCIMS calcd for $C_{18}H_{14}O_2$ $(M + H)^+$ 263.1072; found 263.1067.

3-[2-(4-Chloro-phenyl)-vinyl]-chromen-2-one (3c): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 59% (33.2 mg) as a yellow solid: 154-156 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.61 (d, J = 16.5 Hz, 1H), 7.56-7.45 (m, 4H), 7.37-7.28 (m, 4H), 7.11 (d, J = 16.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.2, 152.9, 137.3, 135.4, 134.1, 132.4, 131.3, 129.0, 128.1, 127.7, 124.7, 124.6, 122.7, 119.6, 116.5. HRAPCIMS calcd for $C_{17}H_{11}ClO_2$ $(M + H)^+$ 283.0526; found 283.0523.

3-[2-(4-Fluoro-phenyl)-vinyl]-chromen-2-one (3d): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 53% (28.2 mg) as a yellow solid: 145-148 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.70 (d, J = 16.5 Hz, 1H), 7.65-7.61 (m, 1H), 7.54-7.48 (m, 2H), 7.34 (d, J = 8.3 Hz, 1H), 7.31-7.26 (m, 2H), 7.25-7.19 (m, 1H), 7.15 (t, J = 7.6 Hz, 1H), 7.10-7.05 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.5 (d, $J_{(C\text{-}F)}$= 256.8 Hz), 160.4, 153.0, 137.1, 131.3, 129.8 (d, $J_{(C\text{-}F)}$ = 8.5 Hz), 127.7 (d, $J_{(C\text{-}F)}$ = 3.3 Hz), 127.5, 125.8 (d, $J_{(C\text{-}F)}$ = 3.7 Hz), 125.0, 124.8 (d, $J_{(C\text{-}F)}$ = 11.7 Hz), 124.6, 124.4 (d, J = 3.5 Hz), 124.2 (d, $J_{(C\text{-}F)}$ = 5.3 Hz), 119.6, 116.5, 115.9 (d, $J_{(C\text{-}F)}$ = 22.0 Hz). HRAPCIMS calcd for $C_{17}H_{11}FO_2$ $(M + H)^+$ 267.0821; found 267.0813.

6-Methyl-3-styryl-chromen-2-one (3e): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 74% (38.7 mg) as a yellow solid: 140-142 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.62 (d, J = 16.4 Hz, 1H), 7.59 -7.55 (m, 2H), 7.40 (t, J = 7.5 Hz, 2H), 7.33-7.24(m, 4H), 7.16 (d, J = 16.3 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.6, 151.0, 136.9, 134.2, 133.5, 132.2, 130.3, 128.8, 128.4, 127.5, 127.0, 124.8, 122.2, 119.5, 116.2, 20.8. HRAPCIMS calcd for $C_{18}H_{14}O_2$ $(M + H)^+$ 263.1072; found 263.1067.

6-Methyl-3-(2-p-tolyl-vinyl)-chromen-2-one (3f): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 75% (41.4 mg) as a yellow solid: 172-174 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (s, 1H),

7.57 (d, *J* = 16.4 Hz, 1H), 7.47 (d, *J* = 8.1 Hz, 2H), 7.31-7.28 (m, 2H), 7.24-7.19 (m, 3H), 7.11 (d, *J* = 16.3 Hz, 1H), 2.43 (s, 3H), 2.39 (s, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.7, 1510, 138.5, 136.4, 134.2, 132,1, 133.4, 132.1, 129.5 127.4, 126.9, 125.0, 121.2, 119.5, 116.1, 21.4, 20.8. HRAPCIMS calcd for $C_{19}H_{16}O_2$ $(M + H)^+$ 277.1229; found 277.1224.

6-Methyl-3-(2-m-tolyl-vinyl)-chromen-2-one (3g): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 74% (41.4 mg) as a yellow solid: 144-145 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.58 (d, *J* = 16.3 Hz, 1H), 7.41-7.36 (m, 2H), 7.32-7.25 (m, 4H), 7.18-7.13 (m, 2H), 2.44 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.7, 151.0, 138.3, 136.8, 136.6, 134.2, 133.5, 132.2, 129.3, 128.6, 127.6, 127.4, 124.9, 124.2, 121.9, 119.5, 116.1, 21.4, 20.8. HRAPCIMS calcd for $C_{19}H_{16}O_2$ $(M + H)^+$ 277.1229; found 277.1225.

3-[2-(4-Chloro-phenyl)-vinyl]-6-methyl-chromen-2-one (3h): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 62% (36.7 mg) as a yellow solid: 164-166 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.59 (d, *J* = 16.3 Hz, 1H), 7.48 (d, *J* = 8.1 Hz, 2H), 7.32 (dd, *J* = 24.8, 9.4 Hz, 4H), 7.24 (d, *J* = 8.3 Hz, 1H), 7.09 (d, *J* = 16.3 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.5, 151.0, 137.4, 135.4, 134.3, 134.0, 132.4, 132.2, 128.9, 128.1, 127.5, 124.5,122.9,119.3, 116.2, 20.8. HRAPCIMS calcd for $C_{18}H_{13}ClO_2$ $(M + H)^+$ 297.0682; found 297.0680.

3-[2-(4-Fluoro-phenyl)-vinyl]-6-methyl-chromen-2-one (3i): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 55% (30.8 mg) as a yellow solid: 144-145 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.57 (d, *J* = 16.3 Hz, 1H), 7.51 (dd, *J* = 8.1, 5.6 Hz, 2H), 7.30 (d, *J* = 8.7 Hz, 2H), 7.22 (d, *J* = 8.2 Hz, 1H), 7.05 (dd, *J* = 10.9, 6.1 Hz, 3H), 2.41 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.8 (d, $J_{(C-F)}$ = 247.0 Hz), 160.6, 151.0, 137.0, 134.2, 133.1 (d, $J_{(C-F)}$ = 3.7 Hz), 132.3, 131.4, 128.6 (d, $J_{(C-F)}$ = 8.0 Hz), 127.4, 124.6, 122.1,

119.4, 116.2, 115.8 (d, $J_{(C-F)}$ = 21.6 Hz), 20.8. HRAPCIMS calcd for $C_{18}H_{13}FO_2$ $(M + H)^+$ 281.0978; found 281.0976.

3-[2-(4-Chloro-phenyl)-vinyl]-7-methoxy-chromen-2-one (3j): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 64% (39.9 mg) as a yellow solid: 179-181 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.52 (d, *J* = 16.4 Hz, 1H), 7.44-7.40 (m, 3H), 7.32 (d, *J* = 8.5 Hz, 2H), 7.05 (d, *J* = 16.3 Hz, 1H), 6.88-6.82 (m, 2H), 3.88 (s, 3H);^{13}C NMR (125 MHz, $CDCl_3$) δ 162.7, 160.5,154.7,137.8, 135.7,133.8,131.1, 128.9, 128.7, 128.0, 123.0, 121.3,113.3,113.1, 100.5, 55.8. HRAPCIMS calcd for $C_{18}H_{13}ClO_3$ $(M + H)^+$ 313.0631; found 313.0627.

7-Ethoxy-3-styryl-chromen-2-one (3k): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 75% (43.8 mg) as a yellow solid: 147-148 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.56-7.53 (m, 3H), 7.42-7.29 (m, 3H), 7.30 (d, *J* = 7.4 Hz, 1H), 7.11 (d, *J* = 16.4 Hz, 1H), 6.86 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.82 (d, *J* = 2.1 Hz, 1H), 4.10 (q, *J* = 7.0 Hz, 2H), 1.47 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.9, 160.7, 154.7, 137.3, 137.1, 132.2, 128. 7, 128.6, 128.1, 126.8, 122.4,121.4, 113.3, 113.2, 100.9, 64.2, 14.6. HRAPCIMS calcd for $C_{19}H_{16}O_3$ $(M + H)^+$ 293.1178; found 293.1171.

7-Ethoxy-3-styryl-chromen-2-one (3l): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 78% (47.8 mg) as a yellow solid: 148-150 ^oC; ^1H NMR (500 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.49 (d, *J* = 16.3 Hz, 1H), 7.43 (d, *J* = 8.1 Hz, 2H), 7.39 (d, *J* = 8.6 Hz, 1H), 7.17 (d, *J* = 7.9 Hz, 2H), 7.06 (d, *J* = 16.3 Hz, 1H), 6.84 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.81 (d, *J* = 2.4 Hz, 1H), 4.09 (q, *J* = 7.0 Hz, 2H), 2.36 (s, 3H), 1.46 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.8, 160.8, 154.6, 138.2, 136.8, 134.3, 132.2, 129.5, 128.5, 126.8, 121.6, 121.3, 113.3,113.2, 100.9, 64.2, 21.3, 14.6. HRAPCIMS calcd for $C_{20}H_{18}O_3$ $(M + H)^+$ 307.1334; found 307.1332.

7-Ethoxy-3-(2-m-tolyl-vinyl)-chromen-2-one (3m): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 74% (45.2 mg) as a yellow solid: 138-140 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.51 (d, *J* = 16.3 Hz, 1H), 7.44-7.33 (m, 3H), 7.28 (d, *J* = 6.0 Hz, 1H), 7.12 (dd, *J* = 12.2, 4.0 Hz, 2H), 6.90-6.81 (m, 2H), 4.12 (q, *J* = 6.9 Hz, 2H), 2.40 (s, 3H), 1.49 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.8, 160.8, 154.6, 138.3, 137.0, 132.3, 129.0, 128.6, 128.5, 127.5, 124.1, 122.1, 121.5, 113.3, 113.2, 100.9, 64.2, 21.4, 14.6. HRAPCIMS calcd for $C_{20}H_{18}O_3$ $(M + H)^+$ 307.1334; found 307.1331.

7-Ethoxy-3-[2-(4-fluoro-phenyl)-vinyl]-chromen-2-one (3n): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 61% (37.8 mg) as a yellow solid: 118-120 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.52-7.49 (m, 2H), 7.41 (d, *J* = 8.5 Hz, 1H), 7.08-6.99 (m, 3H), 6.91-6.77 (m, 3H), 4.11 (q, 6.9 Hz, 2H), 1.47 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.6 (d, $J_{(C\text{-}F)}$ = 246.6 Hz), 161.9, 154.6, 137.4, 133.3 (d, $J_{(C\text{-}F)}$ = 3.3 Hz), 131.0, 128.6, 128.3 (d, $J_{(C\text{-}F)}$ = 8.0 Hz), 122.2, 121.2, 115.7 (d, $J_{(C\text{-}F)}$ = 21.6 Hz), 113.3, 113.2, 108.9, 100.9, 64.2, 14.5. HRAPCIMS calcd for $C_{19}H_{15}FO_3$ $(M + H)^+$ 311.1083; found 311.1067.

3-[2-(4-Chloro-phenyl)-vinyl]-7-ethoxy-chromen-2-one (3o): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 60% (39.1 mg) as a yellow solid: 118-120 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.50 (d, *J* = 16.4 Hz, 1H), 7.44 (d, *J* = 8.5 Hz, 2H), 7.39 (d, *J* = 8.6 Hz, 1H), 7.31 (d, *J* = 8.5 Hz, 2H), 7.03 (d, *J* = 16.3 Hz, 1H), 6.84 (dd, *J* = 8.6, 2.3 Hz, 1H), 6.80 (d, *J* = 2.3 Hz, 1H), 4.09 (q, *J* = 7.0 Hz, 2H), 1.45 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.1, 160.6, 154.7, 137.8, 135.7, 133.7, 130.9, 128.9, 128.7, 127.9, 123.1, 121.1, 113.4, 113.1, 100.9, 64.2, 14.6. HRAPCIMS calcd for $C_{19}H_{15}ClO_3$ $(M + H)^+$ 327.0788; found 327.0782.

6-Nitro-3-(2-p-tolyl-vinyl)-chromen-2-one (3p): HRAPCIMS calcd for $C_{18}H_{13}NO_4$ $(M + Na)^+$ 330.0742; found 330.0739.

1-Methyl-3-(2-p-tolyl-vinyl)-1H-quinolin-2-one (3q): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 42% (24.7 mg) as a yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.60 (d, *J* = 7.7 Hz, 1H), 7.56-7.45 (m, 4H), 7.40 -7.34 (m, 2H), 7.23 (d, *J* = 7.6 Hz, 1H), 7.17 (d, *J* = 7.8 Hz, 2H), 3.79 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.7, 139.0, 137.9, 134.8, 132.9, 131.7, 129.9, 129.4, 128.6, 128.2, 126.8, 122.5, 122.3, 120.9, 114.0, 29.9, 21.3. HRAPCIMS calcd for $C_{19}H_{17}NO$ $(M + H)^+$ 276.1388; found 276.1380.

3-[2-(4-Chloro-phenyl)-vinyl]-1-methyl-1H-quinolin-2-one (3r): Purified *via* flash column chromatography with 20% ethyl acetate/hexane, yielding 40% (23.6 mg) as a yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.55-7.48 (m, 4H), 7.39-7.29 (m, 5H), 3.79 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.6, 139.1, 136.0, 133.8, 133.5, 130.5, 130.3, 128.8, 128.,7, 128.4, 128.0, 124.3, 122.4, 120,7, 114.0, 29.7. HRAPCIMS calcd for $C_{18}H_{15}ClNO$ $(M + H)^+$ 296.0842; found 296.0834.

ASSOCIATED CONTENT

Supporting Information

Detailed experimental procedures and characterization of new compounds. This material is available free of charge *via* the Internet at http://pubs.acs.org.

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The authors declare no competing financial interest.

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