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Palladium-Catalyzed Weakly Coordinating Lactone-Directed C−H Bond Functionalization of 3-Arylcoumarins: Synthesis of Bioactive Coumestan Derivatives

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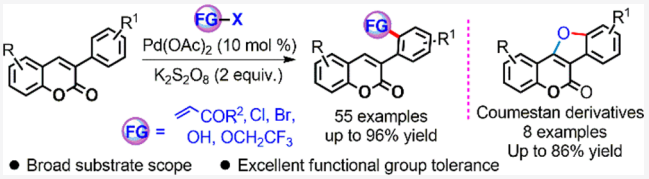
ABSTRACT: A palladium-catalyzed highly regioselective *ortho*-selective C−H functionalization of 3-arylcoumarins has been developed. The method utilizes the weakly coordinating lactone as a directing group. The versatility of the strategy is highlighted by developing methodologies for alkenylation, halogenation, fluoroalkoxylation, and hydroxylation. Different functional groups were well tolerated, and functionalized coumarins were obtained in moderate to high yields. The method also showed good selectivity for monofunctionalization versus difunctionalization. The generated *ortho*-hydroxy derivatives were cyclized in the presence of DDQ, thus developing a simple and fast method for the synthesis of bioactive coumestan from 3-arylcoumarins.

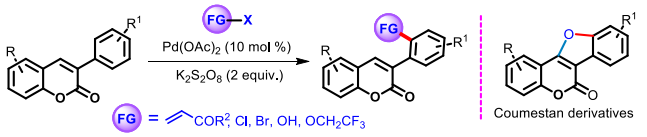


INTRODUCTION

Transition-metal-catalyzed direct C−H bond functionalization has emerged as one of the most elegant approaches for the synthesis of synthetic building blocks from simple substrates as well as late-stage functionalization.[1] In this approach, substrate-directed functionalization through *ortho*-C−H bond activation continues to be an area of intense interest for synthetic organic chemists as it offers step- and atom-economic, cost-effective, green, and sustainable methodology to construct complex molecules.[2] Most commonly strong coordinating functionalities (nitrogen-, sulfur-, or phosphorus-containing groups) are used as directing groups (DGs) in these transition-metal-catalyzed C−H functionalization reactions.[3] The intermediate metallacycle of these strongly coordinating groups are thermodynamically stable and are less reactive in the subsequent functionalization step and, thus, impede the efficacy and versatility of the process. To facilitate the reaction at a faster rate and improve selectivity, weakly coordinating groups (oxygen-containing groups) have gained importance in directed C−H functionalization reactions.[4] A large number of weak coordinating groups such as Weinreb amides,[5] ketone,[6] carbamates,[7] oxazolidinone,[8] carboxylic acids,[9] and esters[10] have been explored as DGs for C−H functionalization. However, there are very few examples in literature utilizing the weak coordinating feature of lactones.[11]

On the other hand, a coumarin (2*H*-chromen-2-one) skeleton is present in many biologically active agents, drug molecules, and natural products.[12] 3-Arylcoumarins contain an aromatic ring neighboring to the lactone group that makes them a potential substrate for the directed C−H bond activation. We were intrigued by the potential yet unraveled role of the lactone group in coumarins as a weak coordinating group in C−H bond functionalization reactions. Regioselective C−H functionalization of this key scaffold might open a new avenue in drug discovery. As part of our research program toward the development of new methods for the synthesis and functionalization of heterocyclic compounds,[13] we herein report a lactone-directed, Pd-catalyzed C(sp^2)−H bond functionalization of 3-arylcoumarins (Scheme 1). Moreover, this method has provided direct access to coumestan derivatives in a short synthetic path under mild reaction conditions.

Scheme 1. Pd-Catalyzed C(sp^2)−H Bond Functionalization of 3-Arylcoumarins



RESULTS AND DISCUSSION

We began our investigation to optimize the reaction conditions by selecting 3-phenyl-2*H*-chromen-2-one (**1a**) and methyl acrylate (**2a**) as model substrates. Initially, the reaction of **1a** (0.23 mmol) and **2a** (0.90 mmol) in the presence of $Pd(OAc)_2$ (10 mol %), $K_2S_2O_8$ (2 equiv) in trifluoroacetic acid (TFA) and

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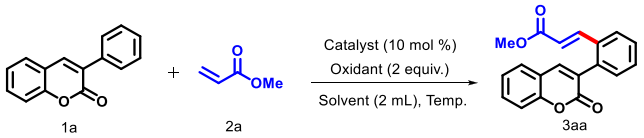
Table 1. Optimization of the Reaction Conditions for *ortho*-Alkenylation[a]



entry	catalyst	oxidant	solvent	T (°C)	yield (%)[b]
1	$Pd(OAc)_2$	$K_2S_2O_8$	TFA/HFIP (1:9)	90	39
2	$Pd(OAc)_2$		TFA/HFIP (1:9)	90	NR
3		$K_2S_2O_8$	TFA/HFIP (1:9)	90	NR
4	$Pd(OAc)_2$	$K_2S_2O_8$	HFIP	90	NR
5	$Pd(OAc)_2$	$K_2S_2O_8$	TFA	90	41
6	$Pd(OAc)_2$	$K_2S_2O_8$	AcOH	90	35
7	$Pd(OAc)_2$	$K_2S_2O_8$	PivOH	90	27
8	$Pd(OAc)_2$	$K_2S_2O_8$	TfOH	90	26
9	$Pd(OAc)_2$	$K_2S_2O_8$	TFAA	90	39
10	$Pd(OAc)_2$	$K_2S_2O_8$	TFA/TFAA (1:1)	90	45
11	$Pd(OAc)_2$	$K_2S_2O_8$	TFA/TFAA (3:1)	90	52
12	$Pd(OAc)_2$	$K_2S_2O_8$	TFA/TFAA (6:1)	90	68
13	$Pd(OAc)_2$	$K_2S_2O_8$	TFA/TFAA (9:1)	90	88
14	$Pd(OAc)_2$	$K_2S_2O_8$	TFA/TFAA (9:1)	80	66
15	$Pd(OAc)_2$	$K_2S_2O_8$	TFA/TFAA (9:1)	70	56
16	$Pd(OAc)_2$	$K_2S_2O_8$	TFA/TFAA (9:1)	110	61
17	$Pd(OAc)_2$	IBD	TFA/TFAA (9:1)	90	52
18	$Pd(OAc)_2$	TBHP	TFA/TFAA (9:1)	90	48
19	$Pd(OAc)_2$	MnO_2	TFA/TFAA (9:1)	90	32
20	$Pd(OAc)_2$	$Cu(OAc)_2$	TFA/TFAA (9:1)	90	45
21	$Pd(OAc)_2$	AgOAc	TFA/TFAA (9:1)	90	46
22	$Pd(OAc)_2$	$AgNO_3$	TFA/TFAA (9:1)	90	31
23	$Pd(OAc)_2$	$Na_2S_2O_8$	TFA/TFAA (9:1)	90	61
24	$Pd(OAc)_2$	$(NH_4)_2S_2O_8$	TFA/TFAA (9:1)	90	64
25	$PdCl_2$	$K_2S_2O_8$	TFA/TFAA (9:1)	90	52
26	$Pd(PPh)_3Cl_2$	$K_2S_2O_8$	TFA/TFAA (9:1)	90	41
27	$Pd(CH_3CN)_2Cl_2$	$K_2S_2O_8$	TFA/TFAA (9:1)	90	56
28	$Pd_2(dba)_3$	$K_2S_2O_8$	TFA/TFAA (9:1)	90	59
29	Ru(*p*-cymene)$_2Cl_2$	$K_2S_2O_8$	TFA/TFAA (9:1)	90	NR
30	$Co(OAc)_2{\cdot}4H_2O$	$K_2S_2O_8$	TFA/TFAA (9:1)	90	NR
31	$Mn(OAc)_2{\cdot}4H_2O$	$K_2S_2O_8$	TFA/TFAA (9:1)	90	NR

[a]Reaction conditions: **1a** (0.23 mmol), **2a** (0.90 mmol), catalyst (10 mol %), oxidant (2 equiv), solvent (2 mL), T = 70−110 °C for 3 h. [b]Isolated yields after column chromatography.

hexafluoroisopropanol (HFIP) mixture (2 mL, 1:9 v/v) for 3 h gave methyl 3-(2-(2-oxo-2*H*-chromen-3-yl)phenyl)acrylate (**3aa**) in 39% yield. The molecular structure of **3aa** was elucidated with the help of ^{1}H NMR, ^{13}C{^{1}H} NMR, HRMS, and single-crystal X-ray analysis (CCDC no. 1989999). In the absence of either oxidant or palladium catalyst, the reaction did not proceed (Table 1, entries 2 and 3). Next, we examined the effect of various solvents on the yield of **3aa** employing $Pd(OAc)_2$ as the catalyst and $K_2S_2O_8$ as an oxidant under standard conditions (Table 1, entries 4−13). Switching the solvent from TFA/HFIP mixture to pure HFIP was unfruitful. Among all screened solvents mixture of TFA and trifluoroacetic anhydride (TFAA) in 9:1 (v/v) ratio provided the highest yield (88%) of **3aa** (Table 1, entry 13). Further, no improvement in the yield of **3aa** was observed by changing the reaction temperature (Table 1, entries 14−16). The yield of the product did not improve on varying the oxidizing agent from $K_2S_2O_8$ to IBD, TBHP, MnO_2, $Cu(OAc)_2$, AgOAc, $AgNO_3$, $Na_2S_2O_8$, and $(NH_4)_2S_2O_8$ (Table 1, entries 17−24). In order to improve the yield of **3aa**, the model reaction was also carried out with different catalysts (Table 1, entries 25−31). Moderate yields (41−59%) of **3aa** were obtained from $PdCl_2$, $Pd(PPh)_3Cl_2$, $Pd(CH_3CN)_2Cl_2$, and $Pd_2(dba)_3$, while no product formation was observed using Ru(*p*-cymene)$_2Cl_2$, $Co(OAc)_2{\cdot}4H_2O$, and $Mn(OAc)_2{\cdot}4H_2O$ as the catalyst. On the basis of these studies, we conclude that the optimal reaction condition for the alkenylation of 3-phenylcoumarin (**1a**) using methyl acrylate (**2a**) involves $Pd(OAc)_2$ (10 mol %) and $K_2S_2O_8$ (2 equiv) in a mixture of TFA and TFAA (2 mL, 9:1 v/v) at 90 °C for 3 h (Table 1, entry 13).

The scope and limitations of the alkenylation protocol are outlined in Table 2. The reaction of **1a** with ethyl, octadecyl, cyclohexyl, and phenyl acrylates (**2b−e**) afforded corresponding alkenylated products **3ab−ae** in moderate to good yields (45−76%). Unfortunately, *tert*-butyl acrylate, acrylamide, and vinyl acetate failed to produce the desired product under the optimized conditions. Next, the scope for 3-arylcoumarins with a substituent on both the C3-phenyl ring and the benzene ring of a coumarin scaffold (**1b−h**) was evaluated, and to our satisfaction, corresponding alkenylated products (**3ba−hd**) were obtained in moderate to high yields (44−90%). Interestingly, better yields of alkenylated products were

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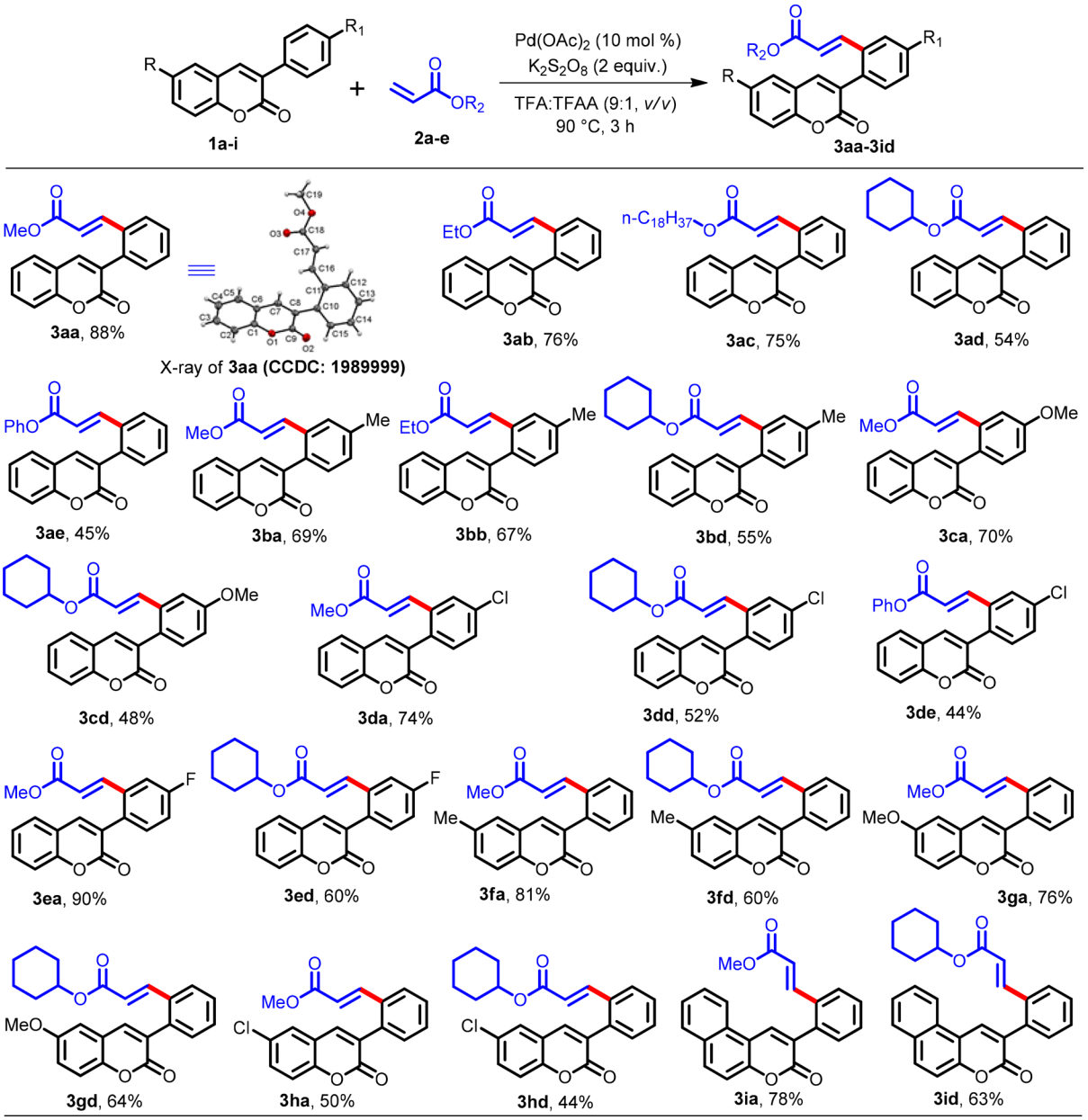
Table 2. ***ortho*-Alkenylation of 3-Arylcoumarins**[a,b]



[a]Reaction condition: **1** (0.23 mmol), **2** (0.90 mmol), $Pd(OAc)_2$ (10 mol %), $K_2S_2O_8$ (2 equiv), TFA/TFAA (2 mL, 9:1 v/v), 90 °C, 3 h. [b]Yields for isolated products.

obtained from 3-arylcoumarins having C3-phenyl substituted with deactivating groups (compare **3ea** and **3ba** vs **3ca**). Pleasingly, 2-phenyl-3*H*-benzo[*f*]-chromen-3-one (**1i**) also reacted with **2a** and **2d** under optimized conditions to furnish corresponding alkenylated products **3ia** and **3id** in 78% and 63% yields, respectively. It is noteworthy that, in the case of low yields, we isolated an unreacted substrate, while, in some cases, traces of byproducts were formed possibly by double *ortho*-functionalization, which could not be isolated in enough quantities to characterize.

After successful implementation of the *ortho*-selective C−H alkenylation of 3-arylcoumarins, we studied their halogenation with slight modification in the reaction conditions (Table 3). The reaction of **1a** with *N*-bromosuccinimide (NBS, **4a**) using $Pd(OAc)_2$ (10 mol %) as the catalyst, $K_2S_2O_8$ (2 equiv) as anoxidant, and TfOH (2 equiv) as the acidic additive in 1,2-dichloroethane (DCE) at 80 °C for 24 h afforded 3-(2-bromophenyl)-2*H*-chromen-2-one (**5aa**) in 73% yield. Various functional groups such as chloro, fluoro, methyl, and methoxy on both the C3-phenyl ring and benzene ring of the coumarin scaffold were well tolerated, and the corresponding brominated compounds (**5ba**−**ia**) were obtained in good yields. Further, the use of *N*-chlorosuccinimide (NCS, **4b**) also resulted in *ortho*-chlorinated products (**5ab**−**ib**) in good to excellent yields. The molecular structure of **5ab** was confirmed by single-crystal X-ray analysis (CCDC no. 2071538). Interestingly, the protocol could introduce a halo substituent at the *meta*-position to *ortho*-directing groups.

The incorporation of a fluorine atom in organic molecules imparts enhanced bioavailability and metabolic stability, and

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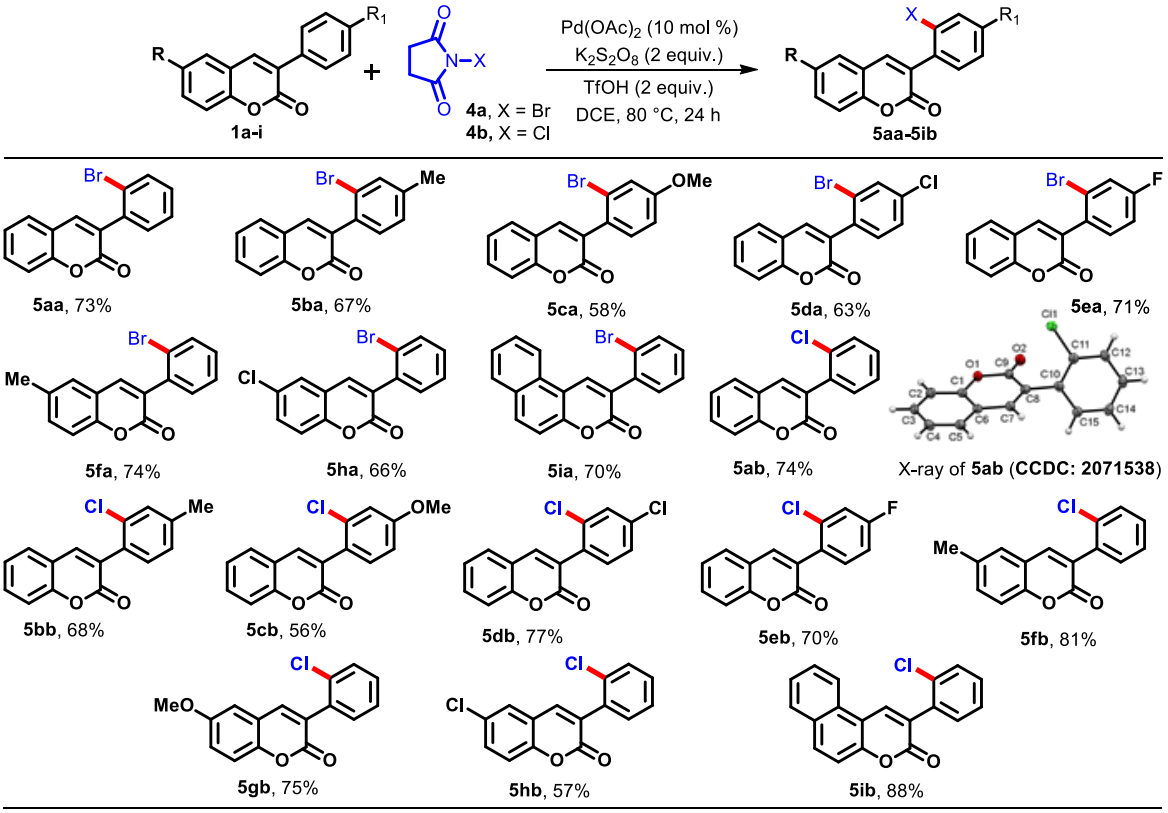
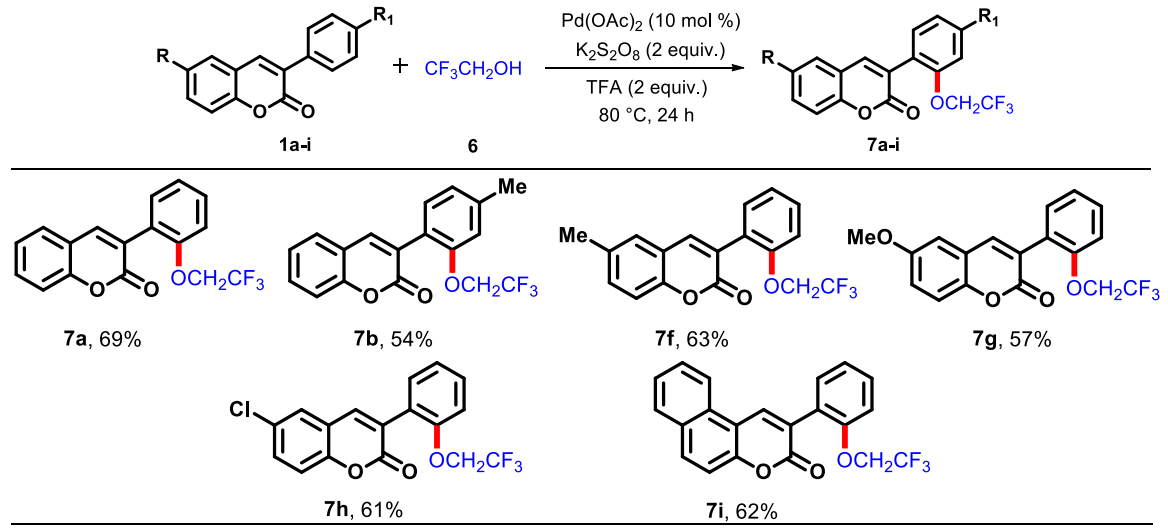
Table 3. *ortho*-Halogenation of 3-Arylcoumarins[a,b]



[a]Reaction condition: **1** (0.23 mmol), **4** (0.25 mmol), $Pd(OAc)_2$ (10 mol %), $K_2S_2O_8$ (2 equiv), TfOH (0.45 mmol), DCE (2 mL), 80 °C, 24 h. [b]Yields for isolated products.

Table 4. *ortho*-Trifluoroethoxylation of 3-Arylcoumarins[a,b]



[a]Reaction condition: **1** (0.23 mmol), $Pd(OAc)_2$ (10 mol %), $K_2S_2O_8$ (2 equiv), TFA (0.45 mmol), TFE (**6**, 2 mL), 80 °C, 24 h. [b]Yields for isolated products.

thus, fluorine-containing compounds continue to receive considerable attention in pharmaceuticals and agrochemicals.[14] We decided to explore direct C−H fluoroalkoxylation of 3-arylcoumarins. To our satisfaction, the reaction of **1a** with trifluoroethanol (TFE, **6**) using $Pd(OAc)_2$ (10 mol %) as the catalyst, $K_2S_2O_8$ (2 equiv) as the oxidant, and TFA (2 equiv) as the acidic additive at 80 °C for 24 h afforded 3-(2-(2,2,2-trifluoroethoxy)phenyl)-2*H*-chromen-2-one (**7a**) in 69% yield. Similarly, the reaction of 3-arylcoumarins (**1b**−**e**) bearing substituents on both C3-phenyl ring as well as on the benzene ring of the coumarin scaffold reacted with TFE to afford the corresponding *ortho*-trifluoroethoxylated products (**7b**−**i**) in moderate to good yields (54−63%) as shown in Table 4. The

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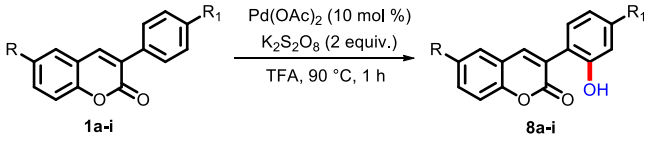
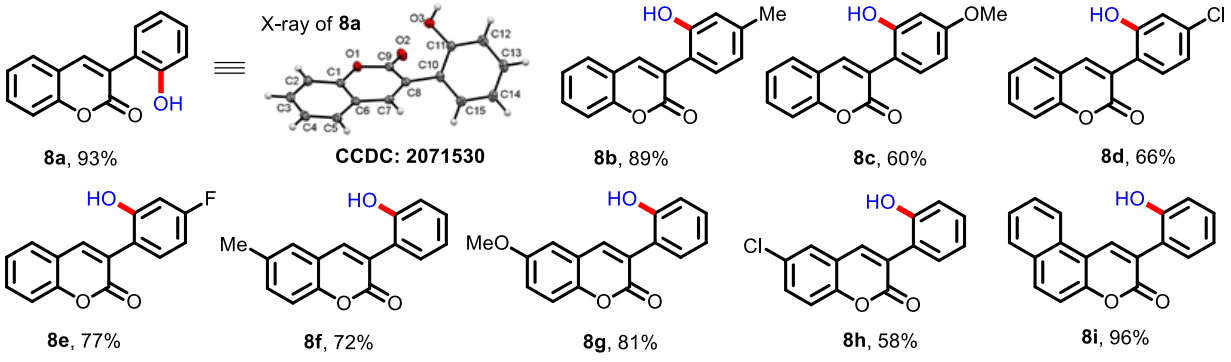
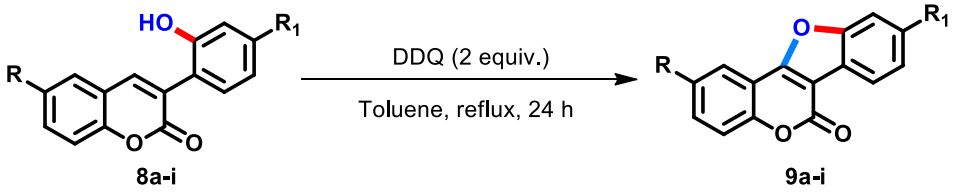
Table 5. *ortho*-Hydroxylation of 3-Arylcoumarins[a,b]

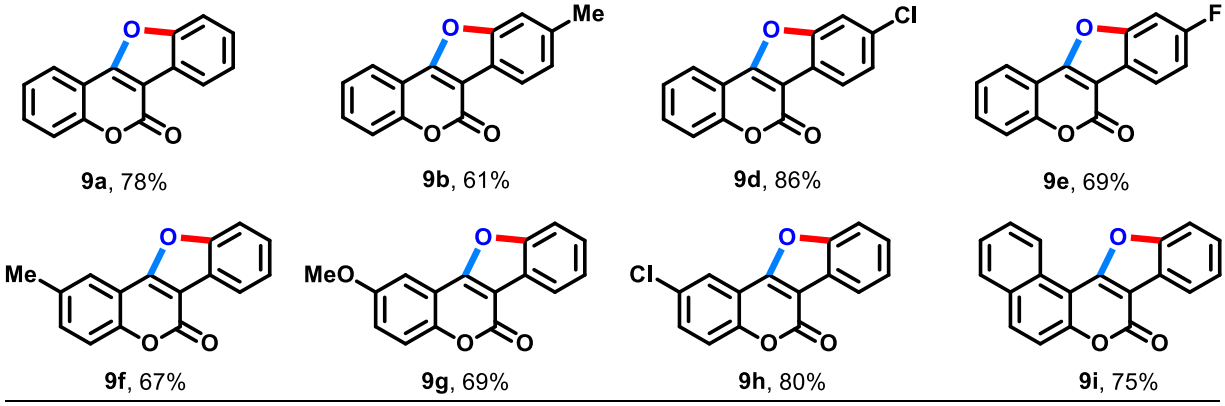




[a]Reaction conditions: **1** (0.23 mmol), $K_2S_2O_8$ (2 equiv), $Pd(OAc)_2$ (10 mol %), TFA (2 mL), 90 °C, 1 h. [b]Yields for isolated products.

Table 6. Synthesis of Coumestan Derivatives[a,b]





[a]Reaction condition: **8** (0.21 mmol), DDQ (2 equiv), toluene (2 mL), reflux, 24 h. [b]Yields for isolated products.

mechanism of the reaction is believed to involve a Pd(II)/Pd(IV) cycle.[15]

A hydroxyl group on 3-arylcoumarin moieties has been found in several natural products and pharmaceutically important compounds.[16] Also, several bioactive compounds can be achieved through the chemical transformation of a hydroxyl group. Thus, we examined *ortho*-hydroxylation of 2-arylcoumarins using TFA as an oxygen source.[17] The reaction of **1a** using $Pd(OAc)_2$ (10 mol %) as the catalyst, $K_2S_2O_8$ (2 equiv) as an oxidant in TFA at 90 °C for 1 h afforded 3-(2′-hydroxyphenyl)-coumarin (**8a**) in 93% yield. The structure of **8a**[18] was confirmed by NMR, HRMS and single-crystal X-ray diffraction analysis (CCDC no. 2071530). Hong et al. reported *ortho*-hydroxylation of 3-phenyl-2*H*-chromen-2-one to afford a mixture of 3-(2-hydroxyphenyl)-2*H*-chromen-2-one and 3-(2,6-dihydroxyphenyl)-2*H*-chromen-2-one in 71% and 25% yields, respectively, using monomeric [Ru(*p*-cymene)-$(CF_3CO_2)_2(H_2O)$] as the catalyst and $PhI(CF_3CO_2)_2$ as an oxidant.[11b] Next, various 3-arylcoumarins (**1b−i**) with different functional groups were subjected to the reaction under optimized conditions to afford the corresponding *ortho*-hydroxylated derivatives (**8b−i**) in good to excellent (58−96%) yields as indicated in Table 5. Notably, synthetically useful halo groups remained intact under these conditions, which can be used for further manipulations.

The furan-fused coumarin derivatives, coumestan, are widely found in nature and display a wide range of biological activities.[19] Due to their significant bioactivities, several synthetic methods have been developed for coumestan derivatives.[20] We, therefore, decided to cyclize the *ortho*-hydroxylated derivatives (**8**) to obtain coumestans **9**. Recently reported copper-catalyzed intramolecular cross-dehydrogen-

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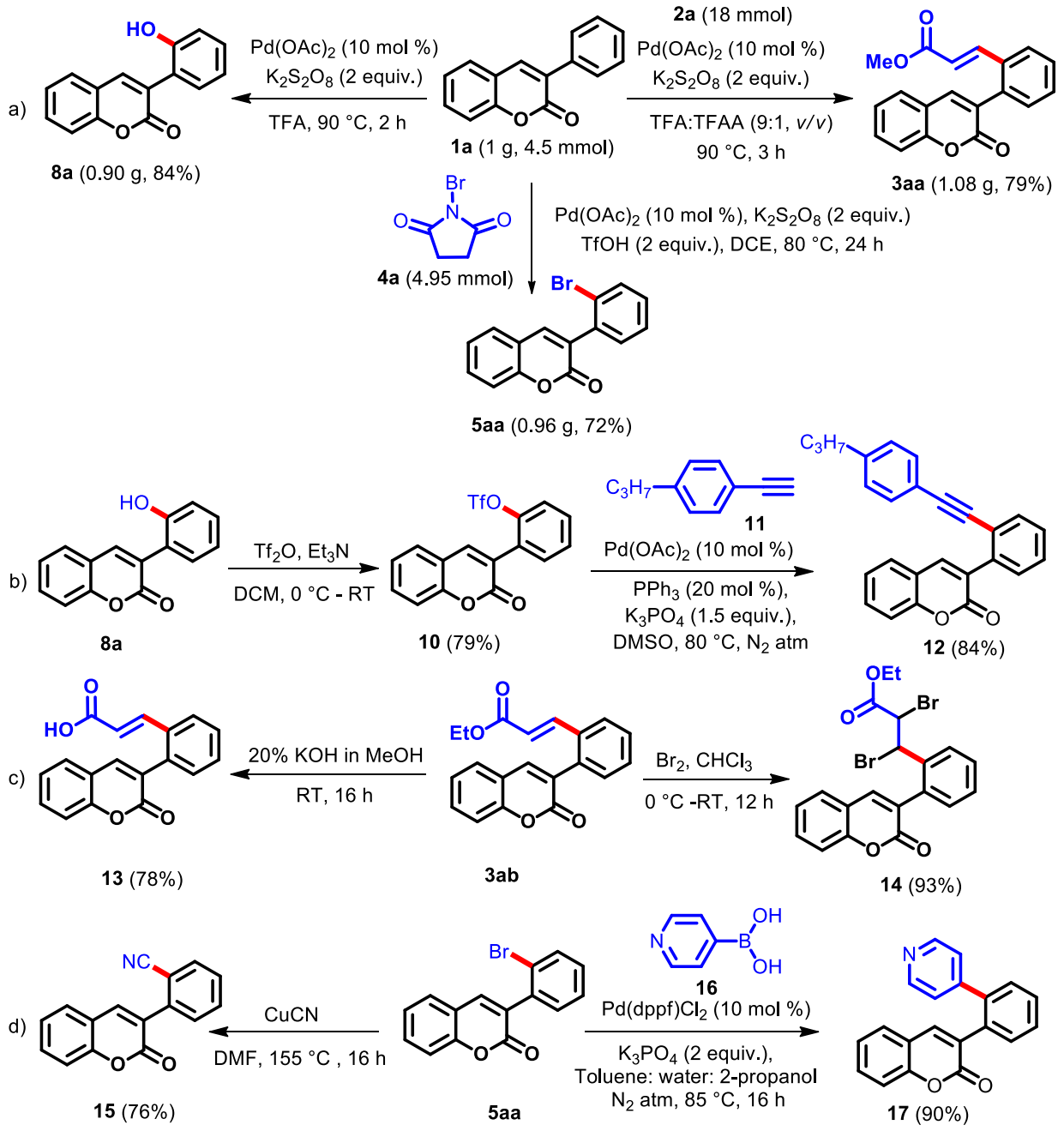
Scheme 2. Gram-Scale Synthesis and Synthetic Transformation of 3aa, 5aa, and 8a



ative coupling[20d] failed to produce the desired coumestans from 3-(2′-hydroxyaryl)coumarins in our hand. We then moved to DDQ-mediated oxidative cyclization in toluene.[21] Interestingly, various 3-(2′-hydroxyaryl)coumarins (**8**) containing substituents both on C3-phenyl ring as well as on benzene ring of coumarin scaffold afforded good yields of the corresponding coumestans (Table 6). Thus, the lactone-directed C−H functionalization protocol is successfully used to develop a simple and rapid method for the total synthesis of coumestans.

The scalability of the developed protocols was demonstrated by gram-scale alkenylation, bromination, and hydroxylation of **1a** (1 g, 4.5 mmol) (Scheme 2a). The desired products **3aa**, **5aa**, and **8a** were isolated in 79% (1.08 g), 72% (0.96 g), and 84% (0.90 g) yields, respectively. In addition, the synthetic utility of the *ortho*-functionalized 3-arylcoumarins was demonstrated by transforming the functional groups through synthetic manipulations. For instance, compound **8a** was transformed to compound **12** via sequential trifluoromethylsulfonylation and Sonogashira coupling (Scheme 2b). Product **3ab** could be easily hydrolyzed to give corresponding acid **13** in 78% yield, and bromination of **3ab** by adding bromine in $CHCl_3$ afforded dibromo compound **14** in 93% yield (Scheme 2c). Product **5aa** was converted to synthetically useful compounds **15** and **17** through copper-catalyzed cyanation and Suzuki coupling in 76% and 90% yields, respectively (Scheme 2d).

To gain insight into the reaction mechanism, we performed a few control experiments (Scheme 3). A competitive experiment between **1c** and **1e** for alkenylation with **2a** under optimized conditions gave corresponding products **3ca** and **3ea** in a 1:2.96 ratio (Scheme 3a). The result is incompatible with Friedel−

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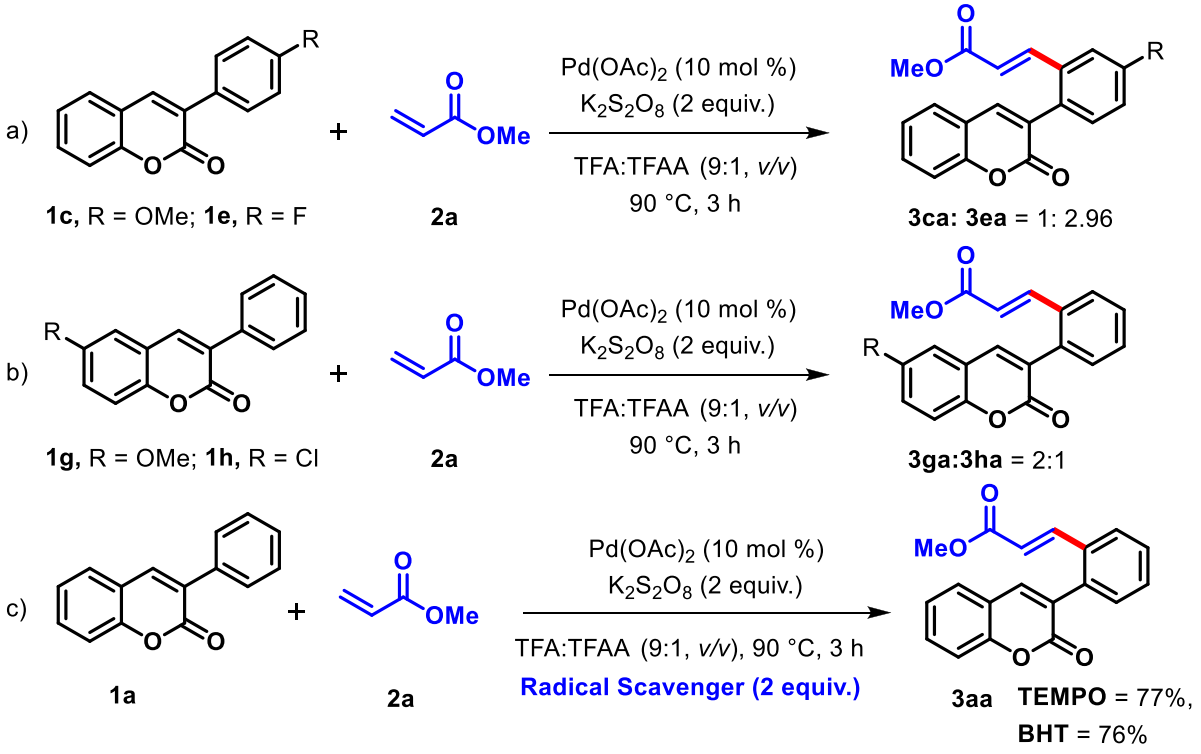
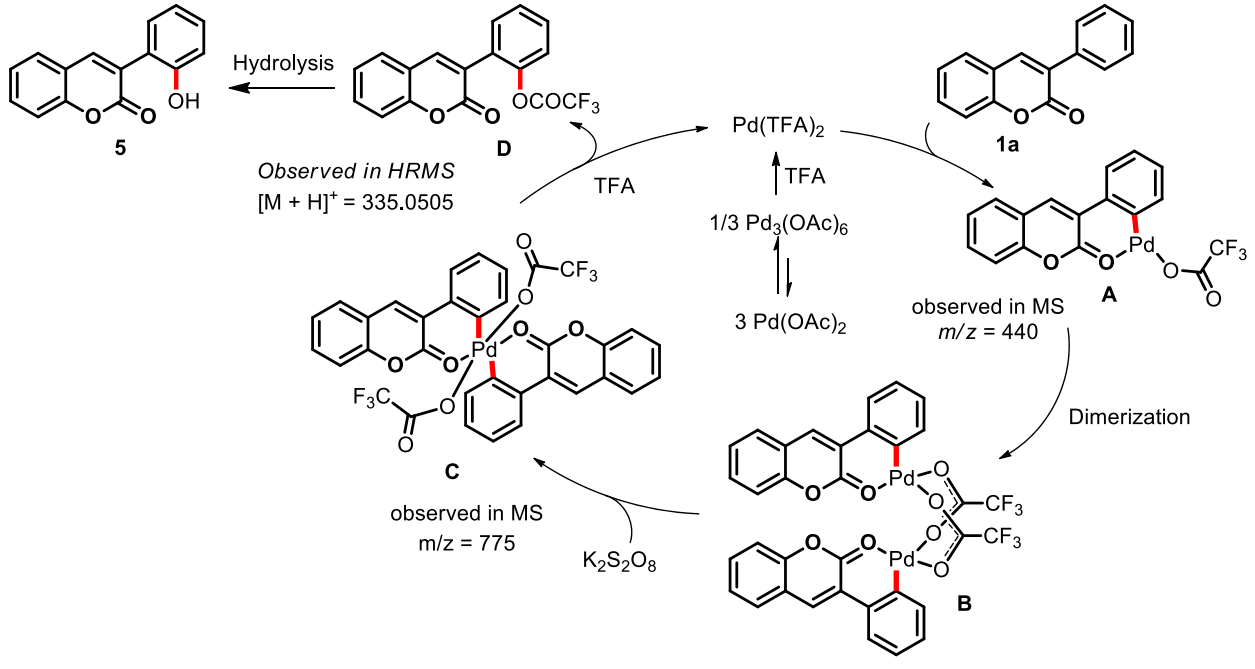
Scheme 3. Control Experiments



Scheme 4. Proposed Mechanism for *ortho*-Hydroxylation



Crafts-type electrophilic aromatic substitution (S_EAr) reactivity. Similarly, a competitive experiment between **1g** and **1h** produced corresponding products **3ga** and **3ha** in a 2:1 ratio (Scheme 3b). No significant reduction in the yield of **3aa** was observed when the reaction of **1a** with **2a** was performed in the presence of radical scavengers 2,2,6,6-tetramethylpiperidine-1-oxy (TEMPO) and butylated hydroxytoluene (BHT) under optimized conditions (Scheme 3c), ruling out the possibility of the radical mechanism.

On the basis of the experimental results and related literature,[6d,15,17b,c] it is proposed that the possible mechanism for the palladium-catalyzed weakly coordinating lactone-directed C−H bond functionalization of 3-arylcoumarins might involve a Pd(II)−Pd(IV) redox cycle. A proposed mechanism for hydroxylation of 3-arylcoumarins is shown in Scheme 4. Initially, lactone-directed C−H activation of **1a** generates palladacycle **A**, which then gets converted to cyclopalladium(II) dimeric intermediate **B**. Next, intermediate

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B in the presence of an external oxidant oxidizes to Pd(IV) intermediate **C**.[22] Finally, double reductive elimination from intermediate **C** provides trifluoroacetate intermediate **D**, which upon hydrolysis gets converted into a hydroxylated coumarin **5**. In the case of *ortho*-alkenylation, the reaction possibly proceeds through oxidative Heck reaction from intermediate **A** or **B**.[23]

CONCLUSIONS

In conclusion, a unified strategy is described for the palladium-catalyzed, weakly coordinating lactone-directed C−H bond functionalization of 3-arylcoumarins. The strategy allowed facile access to regioselective alkenylation, halogenation, fluoroalkoxylation, and hydroxylation. The reaction mechanism is proposed to involve oxidative palladium catalysis via a Pd(II)−Pd(IV) redox cycle. The developed protocol showed a broad substrate scope and afforded good to excellent yields of functionalized coumarins. The 3-(2′-hydroxyaryl)coumarins generated by the *ortho*-hydroxylation of 3-arylcoumarins were cyclized using DDQ to obtain coumestan derivatives in good yields. Given that the lactone functionality is present in a wide range of drug molecules and natural products, the developed method should allow their late-stage C−H functionalization under mild conditions.

EXPERIMENTAL SECTION

General Information. Unless otherwise stated, all commercially available materials were used without further purification. Palladium(II) acetate was purchased from Alfa Aesar. Potassium persulfate was bought from SD Fine Chemicals Ltd., India. All acrylates were obtained from TCI (India). Trifluoroacetic acid (TFA) was procured from Sigma-Aldrich. Trifluoroacetic anhydride (TFAA) and trifluoromethanesulfonic acid (triflic acid, TfOH) were received from Spectrochem, India. The 3-arylcoumarins (**1a**−**i**) were prepared by the reaction of salicylaldehyde and arylacetonitriles following literature procedures.[24] Acrylates (**2a**−**e**), NBS (**4a**), NCS (**4b**), and HFIP (**6**) are commercially available and were purchased from Spectrochem, India. All reactions were performed in a pressure tube under air with magnetic stirring. Column chromatography was performed on silica gel (100−200 mesh, Merck) using *n*-hexane and ethyl acetate as an eluent, and TLC was performed on Merck aluminum TLC sheets (silica gel 60 F_{254}). The ^{1}H NMR (400 MHz) and $^{13}C\{^1H\}$ NMR (100 MHz) spectra were recorded using $CDCl_3$ (TMS as an internal standard) or DMSO-d_6 as the solvent. Chemical shifts (δ) and coupling constants (J) are reported in parts per million (ppm) and hertz, respectively. The chemical multiplicities were reported as singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m) and their combinations as well. The $^{13}C\{^1H\}$ shifts were referenced at 77.6 ppm for $CDCl_3$ and 40.5 ppm for DMSO-d_6, respectively. High-resolution mass spectra (HRMS) were recorded in an electrospray ionization (ESI) mode on a Q-TOF LC-MS spectrometer. X-ray crystal structures were obtained with a Rigaku Oxford XtaLAB AFC12 (RINC): Kappa dual home/near diffractometer, and the thermal ellipsoids are drawn to the 50% probability level. Melting points were determined in open capillary tubes on an automated apparatus and were uncorrected.

Representative Procedure for *ortho*-Alkenylation (Method A). An oven-dried 10 mL round-bottom flask was charged with 3-phenyl-2*H*-chromen-2-one **1a** (0.23 mmol, 51 mg), methyl acrylate **2a** (0.9 mmol, 81 μL), $Pd(OAc)_2$ (10 mol %, 5.15 mg), $K_2S_2O_8$ (2 equiv, 124 mg), and TFA/TFAA (2 mL, 9:1 v/v). The reaction mixture was refluxed with stirring in an oil bath at 90 °C for 3 h. The reaction mixture was cooled to an ambient temperature, basified with aqueous $NaHCO_3$ solution (5 mL), and then extracted with ethyl acetate (3 × 5 mL). The combined organic layer was washed with water (2 × 5 mL) and dried over anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure. The resulting residue was purified by column chromatography over silica gel 60 (100−200 mesh size) using *n*-hexane/ethyl acetate as an eluting system to give 62 mg (88%) of **3aa**.

*Methyl (E)-3-(2-(2-Oxo-2H-chromen-3-yl)phenyl)acrylate (**3aa**).* The title compound **3aa** was synthesized following method A: R_f = 0.6; white solid (62 mg, 88%); mp = 168−170 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76−7.73 (m, 1H), 7.71 (d, J = 16.0 Hz, 1H), 7.67 (s, 1H), 7.63−7.59 (m, 1H), 7.55 (dd, J = 7.8, 1.4 Hz, 1H), 7.49−7.47 (m, 2H), 7.45−7.42 (m, 2H), 7.37−7.33 (m, 1H), 6.47 (d, J = 16.0 Hz, 1H), 3.76 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.0, 160.4, 154.0, 143.0, 142.4, 135.4, 133.7, 132.0, 130.8, 130.0, 129.2, 128.1, 127.5, 126.9, 124.7, 119.8, 119.1, 116.8, 51.7; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{19}H_{15}O_4^+$ 307.0965, found 307.0937.

*Ethyl (E)-3-(2-(2-Oxo-2H-chromen-3-yl)phenyl)acrylate (**3ab**).* The title compound **3ab** was synthesized following method A. The product was purified by using ethyl acetate/hexane (1.5:8.5 v/v) as an eluent: R_f = 0.7; white solid (56 mg, 76%); mp = 147−149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76−7.73 (m, 1H), 7.71 (d, J = 15.6 Hz, 1H), 7.66 (s, 1H), 7.63−7.58 (m, 1H), 7.55 (dd, J = 7.8, 1.4 Hz, 1H), 7.50−7.41 (m, 4H), 7.36−7.32 (m, 1H), 6.46 (d, J = 15.6 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 1.29 (t, J = 7.1 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.6, 160.4, 154.0, 143.1, 142.1, 135.3, 133.7, 132.0, 130.8, 129.9, 129.2, 128.1, 127.4, 126.9, 124.7, 120.2, 119.1, 116.7, 60.5, 14.3; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{20}H_{17}O_4^+$ 321.1121, found 321.1108.

*Octadecyl (E)-3-(2-(2-Oxo-2H-chromen-3-yl)phenyl)acrylate (**3ac**).* The title compound **3ac** was synthesized following method A. The product was purified by using ethyl acetate/hexane (1:9 v/v) as an eluent: R_f = 0.8; white solid (94 mg, 75%); mp = 95−97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78−7.75 (m, 1H), 7.71 (d, J = 15.6 Hz, 1H), 7.66 (s, 1H), 7.62−7.58 (m, 1H), 7.55 (dd, J = 7.8, 1.4 Hz, 1H), 7.49−7.45 (m, 3H), 7.43 (d, J = 8.4 Hz, 1H), 7.36−7.32 (m, 1H), 6.47 (d, J = 15.6 Hz, 1H), 4.15 (t, J = 6.7 Hz, 2H), 1.67−1.61 (m, 3H), 1.36−1.27 (m, 29H), 0.90 (t, J = 6.7 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.7, 160.4, 154.0, 143.0, 142.1, 135.3, 133.7, 131.9, 130.8, 129.9, 129.2, 128.1, 127.4, 126.9, 124.6, 120.2, 119.1, 116.8, 64.7, 31.9, 29.7, 29.7, 29.6, 29.5, 29.4, 29.3, 28.7, 25.9, 22.7, 14.1; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{36}H_{49}O_4^+$ 545.3625, found 545.3583.

*Cyclohexyl (E)-3-(2-(2-Oxo-2H-chromen-3-yl)phenyl)acrylate (**3ad**).* The title compound **3ad** was synthesized following method A. The product was purified by using ethyl acetate/hexane (2:8 v/v) as an eluent: R_f = 0.7; white solid (46 mg, 54%); mp = 150−152 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77−7.75 (m, 1H), 7.71 (d, J = 15.8 Hz, 1H), 7.66 (s, 1H), 7.62−7.58 (m, 1H), 7.55 (dd, J = 7.8, 1.5 Hz, 1H), 7.50−7.42 (m, 4H), 7.34 (t, J = 7.4 Hz, 1H), 6.46 (d, J = 15.8 Hz, 1H), 4.88−4.82 (m, 1H), 1.88−1.82 (m, 2H), 1.73−1.65 (m, 2H), 1.55−1.43 (m, 3H), 1.41−1.32 (m, 2H), 1.30−1.20 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.0, 160.4, 153.9, 143.1, 141.8, 135.3, 133.7, 131.9, 130.7, 129.8, 129.2, 128.1, 127.4, 126.8, 124.6, 120.7, 119.1, 116.7, 72.6, 31.6, 25.4, 23.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{24}H_{23}O_4^+$ 375.1591, found 375.1564.

*Phenyl (E)-3-(2-(2-Oxo-2H-chromen-3-yl)phenyl)acrylate (**3ae**).* The title compound **3ae** was synthesized following method A. The crude product was purified by using 2.0:8.0 ethyl acetate/hexane as an eluent: R_f = 0.7; white solid (38 mg, 45%); mp = 144−146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 15.9 Hz, 1H), 7.85−7.82 (m, 1H), 7.71 (s, 1H), 7.62−7.47 (m, 5H), 7.44−7.32 (m, 4H), 7.28 (s, 1H), 7.24 (t, J = 7.4 Hz, 1H), 7.14 (d, J = 7.9 Hz, 2H), 6.67 (d, J = 15.8 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.0, 160.4, 154.0, 150.7, 144.0, 143.1, 135.7, 133.5, 132.0, 130.9, 130.4, 129.4, 129.3, 128.1, 127.4, 127.0, 125.8, 124.7, 121.6, 119.2, 119.1, 116.8; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{24}H_{17}O_4^+$ 369.1121, found 369.1104.

*Methyl (E)-3-(5-Methyl-2-(2-oxo-2H-chromen-3-yl)phenyl)-acrylate (**3ba**).* The title compound **3ba** was synthesized following method A. The product was purified by using 1.5:8.5 ethyl acetate/hexane as an eluent: R_f = 0.7; white solid (51 mg, 69%); mp = 151−153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 15.8 Hz, 1H), 7.63 (s, 1H), 7.62−7.53 (m, 3H), 7.42 (d, J = 8.2 Hz, 1H), 7.36−7.28 (m, 3H), 6.45 (d, J = 15.8 Hz, 1H), 3.76 (s, 3H), 2.45 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.1, 160.5, 153.9, 142.8, 142.5, 139.1, 133.4, 132.6, 131.8, 130.9, 130.7, 128.0, 127.5, 127.4, 124.6, 119.5, 119.2, 116.7, 51.7, 21.3; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{20}H_{17}O_4^+$ 321.1121, found 321.1129.

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*Ethyl (E)-3-(5-Methyl-2-(2-oxo-2H-chromen-3-yl)phenyl)acrylate (**3bb**).* The title compound **3bb** was synthesized following method A. The crude product was purified by using 1.5:8.5 ethyl acetate/hexane as an eluent: R_f = 0.7; white solid (51 mg, 67%); mp = 130−132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 15.8 Hz, 1H), 7.63 (s, 1H), 7.61−7.53 (m, 3H), 7.42 (d, J = 8.3 Hz, 1H), 7.36−7.33 (m, 2H), 7.31−7.30 (m, 1H), 6.46 (d, J = 15.8 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 2.4 (s, 3H),1.29 (t, J = 7.1 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.7, 160.6, 153.9, 142.8, 142.3, 139.1, 133.5, 132.6, 131.8, 130.8, 130.7, 128.0, 127.4, 127.4, 124.6, 119.9, 119.2, 116.7, 60.5, 21.3, 14.3; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{21}H_{19}O_4^+$ 335.1278, found 335.1256.

*Cyclohexyl (E)-3-(5-Methyl-2-(2-oxo-2H-chromen-3-yl)phenyl)-acrylate (**3bd**).* The title compound **3bd** was synthesized following method A. The crude product was purified by using 2.0:8.0 ethyl acetate/hexane as an eluent: R_f = 0.6; white solid (49 mg, 55%); mp = 135−137 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 15.8 Hz, 1H), 7.63 (s, 1H), 7.61−7.53 (m, 3H), 7.42 (d, J = 8.3 Hz, 1H), 7.39−7.28 (m, 3H), 6.45 (d, J = 15.9 Hz, 1H), 4.89−4.82 (m, 1H), 2.44 (s, 3H), 1.88−1.83 (m, 2H), 1.74−1.45 (m, 2H), 1.51−1.22 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.1, 160.6, 153.9, 142.9, 141.9, 139.1, 133.5, 132.6, 131.8, 130.7, 130.6, 128.0, 127.4, 124.6, 120.4, 119.2, 116.7, 72.6, 31.6, 25.4, 23.6, 21.3; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{25}H_{25}O_4^+$ 389.1747, found 389.1730.

*Methyl (E)-3-(5-Methoxy-2-(2-oxo-2H-chromen-3-yl)phenyl)-acrylate (**3ca**).* The title compound **3ca** was synthesized following method A. The crude product was purified by using 2.5:7.5 ethyl acetate/hexane as an eluent: R_f = 0.6; white solid (54 mg, 70%); mp = 218−220 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (d, J = 16.2 Hz, 1H), 7.87 (d, J = 2.4 Hz, 1H), 7.82−7.80 (m, 2H), 7.59−7.53 (m, 2H), 7.40 (d, J = 8.6 Hz, 1H), 7.34 (td, J = 7.5, 1.1 Hz, 1H), 7.03 (d, J = 8.7 Hz, 1H), 6.63 (d, J = 16.2 Hz, 1H), 3.97 (s, 3H), 3.84 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.8, 160.6, 158.8, 153.4, 139.8, 138.9, 131.8, 131.3, 129.1, 127.8, 127.3, 127.2, 124.6, 123.5, 119.7, 119.1, 116.5, 111.2, 55.6, 51.7; HRMS (ESI)m/z [M + H]$^+$ calcd for $C_{20}H_{17}O_5^+$ 337.1071, found 337.1053.

*Cyclohexyl (E)-3-(5-Methoxy-2-(2-oxo-2H-chromen-3-yl)phenyl)-acrylate (**3cd**).* The title compound **3 cd** was synthesized following method A. The product was purified by using 2.0:8.0 ethyl acetate/hexane as an eluent: R_f = 0.5; white solid (44 mg, 48%); mp = 178−180 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, J = 15.6 Hz, 1H), 7.61 (s, 1H), 7.58−7.52 (m, 2H), 7.41 (d, J = 8.4 Hz, 1H), 7.32 (t, J = 7.6 Hz, 1H), 7.24 (d, J = 2.4 Hz, 1H), 7.03 (dd, J = 8.8, 2.8 Hz, 1H), 6.44 (d, J = 15.6 Hz, 1H), 4.89−4.82 (m, 1H), 3.90 (s, 3H), 1.87−1.82 (m, 2H), 1.73−1.65 (m, 3H), 1.54−1.32 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.0, 160.8, 160.0, 153.8, 142.8, 141.9, 135.0, 132.0, 131.7, 127.9, 127.0, 124.6, 120.8, 119.2, 116.7, 116.1, 111.4, 72.7, 55.5, 31.6, 25.4, 23.6; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{25}H_{25}O_5^+$ 405.1697, found 405.1692.

*Methyl (E)-3-(5-Chloro-2-(2-oxo-2H-chromen-3-yl)phenyl)-acrylate (**3da**).* The title compound **3da** was synthesized following method A. The crude product was purified by using 1.5:8.5 ethyl acetate/hexane as an eluent: R_f = 0.7; white solid (57 mg, 73%); mp = 185−187 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 2.1 Hz, 1H), 7.65−7.60 (m, 3H), 7.56 (dd, J = 7.8, 1.6 Hz, 1H), 7.46−7.40 (m, 3H), 7.38−7.33 (m, 1H), 6.45 (d, J = 15.8 Hz, 1H), 3.77 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.6, 160.2, 154.0, 143.3, 141.0, 135.4, 135.3, 133.6, 132.2, 132.1, 129.9, 128.2, 126.9, 126.4, 124.8, 121.0, 119.0, 116.8, 51.9; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{19}H_{14}ClO_4^+$ 341.0575, found 341.0545.

*Cyclohexyl (E)-3-(5-Chloro-2-(2-oxo-2H-chromen-3-yl)phenyl)-acrylate (**3dd**).* The title compound **3dd** was synthesized following method A. The crude product was purified by using 1.5:8.5 ethyl acetate/hexane as an eluent: R_f = 0.7; white solid (49 mg, 52%); mp = 177−179 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 2.0 Hz, 1H), 7.65−7.59 (m, 3H), 7.55 (dd, J = 7.8, 1.6 Hz, 1H), 7.46−7.40 (m, 3H), 7.35 (td, J = 7.5, 1.1 Hz, 1H), 6.46 (d, J = 15.8 Hz, 1H), 4.88−4.82 (m, 1H), 1.88−1.82 (m, 2H), 1.74−1.67 (m, 2H), 1.51−1.21 (m, 6H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.6, 160.2, 154.0, 143.3, 140.4, 135.5, 135.3, 133.6, 132.2, 132.1, 129.8, 128.1, 126.8, 126.3, 124.7, 122.0, 118.9, 116.8, 72.9, 31.5, 25.4, 23.6; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{24}H_{22}ClO_4^+$ 409.1201, found 409.1170.

*Phenyl (E)-3-(5-Chloro-2-(2-oxo-2H-chromen-3-yl)phenyl)-acrylate (**3de**).* The title compound **3de** was synthesized following method A. The crude product was purified by using 2.0:8.0 ethyl acetate/hexane as an eluent: R_f = 0.6; white solid (41 mg, 44%); mp = 192−194 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82−7.78 (m, 2H), 7.69 (s, 1H), 7.64−7.55 (m, 2H), 7.50 (dd, J = 8.3, 2.1 Hz, 1H), 7.45−7.33 (m, 5H), 7.27−7.23 (m, 1H), 7.16−7.12 (m, 2H), 6.67 (d, J = 15.8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.6, 160.2, 154.0, 150.6, 143.4, 142.7, 135.4, 135.2, 133.9, 132.3, 132.2, 130.3, 129.4, 128.2, 127.0, 126.3, 125.9, 124.8, 121.5, 120.5, 118.9, 116.9; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{24}H_{16}ClO_4^+$ 403.0732, found 403.0699.

*Methyl (E)-3-(5-Fluoro-2-(2-oxo-2H-chromen-3-yl)phenyl)-acrylate (**3ea**).* The title compound **3ea** was synthesized following method A. The crude product was purified by using 1.5:8.5 ethyl acetate/hexane as an eluent: R_f = 0.5; white solid (67 mg, 90%); mp = 143−145 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66−7.60 (m, 3H), 7.56 (dd, J = 7.6, 1.6 Hz, 1H), 7.46−7.41 (m, 3H), 7.36 (td, J = 7.6, 1.2 Hz, 1H), 7.19 (td, J = 8.0, 2.4 Hz, 1H), 6.45 (d, J = 16.0 Hz, 1H), 3.77 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.8 (d, J = 250 Hz), 162.7, 154.0, 143.3, 141.2 (d, J = 2.5 Hz), 135.9 (d, J = 7.9 Hz), 132.7 (d, J = 8.4 Hz), 132.1, 131.4 (d, J = 3.2 Hz), 128.1, 126.5, 124.8, 120.9, 119.0, 117.1 (d, J = 21.7 Hz), 116.8, 113.4 (d, J = 22.5 Hz), 51.8; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{19}H_{14}FO_4^+$ 325.0871, found 325.0852.

*Cyclohexyl (E)-3-(5-Fluoro-2-(2-oxo-2H-chromen-3-yl)phenyl)-acrylate (**3ed**).* The title compound **3ed** was synthesized following method A. The crude product was purified by using 2.0:8.0 ethyl acetate/hexane as an eluent: R_f = 0.4; white solid (54 mg, 60%); mp = 167−169 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83−7.72 (m, 1H), 7.66−7.65 (m, 1H), 7.63−7.58 (m, 1H), 7.58−7.54 (m, 1H), 7.48−7.42 (m, 3H), 7.37−7.33 (m, 1H), 7.21−7.14 (m, 1H), 6.44 (d, J = 16.0 Hz, 1H), 4.89−4.83 (m, 1H), 1.88−1.83 (m, 2H), 1.72−1.68 (m, 2H), 1.53−1.43 (m, 2H), 1.44−1.32 (m, 3H), 1.30−1.27 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.7, 162.7 (d, J = 230.0 Hz), 154.0, 143.3, 140.7 (d, J = 2.4 Hz), 136.0 (d, J = 8.3 Hz), 132.7 (d, J = 8.6 Hz), 132.1, 131.5, 131.3, 128.1, 126.4, 124.7, 121.9, 119.0, 117.0 (d, J = 22.0 Hz), 116.8, 116.6, 116.5, 113.4 (d, J = 22.4 Hz), 72.9, 31.5, 25.4, 23.6; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{24}H_{22}FO_4^+$ 393.1497, found 393.1496.

*Methyl (E)-3-(2-(6-Methyl-2-oxo-2H-chromen-3-yl)phenyl)-acrylate (**3fa**).* The title compound **3fa** was synthesized following method A. The crude product was purified by using 1.5:8.5 ethyl acetate/hexane as an eluent: R_f = 0.7; white solid (59.5 mg, 81%); mp = 164−166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75−7.73 (m, 1H), 7.71 (d, J = 15.9 Hz, 1H), 7.60 (s, 1H), 7.50−7.39 (m, 4H), 7.33−7.31 (m, 2H), 6.46 (d, J = 15.8 Hz, 1H), 3.76 (s, 3H), 2.45 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.0, 160.6, 152.1, 143.1, 142.4, 135.6, 134.4, 133.7, 133.0, 130.8, 129.9, 129.1, 127.9, 127.3, 126.9, 119.7, 118.9, 116.5, 51.7, 20.8; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{20}H_{17}O_4^+$ 321.1121, found 321.1092.

*Cyclohexyl (E)-3-(2-(6-Methyl-2-oxo-2H-chromen-3-yl)phenyl)-acrylate (**3fd**).* The title compound **3fd** was synthesized following method A. The crude product was purified by using 2.0:8.0 ethyl acetate/hexane as an eluent: R_f = 0.7; white solid (53.5 mg, 60%); mp = 146−148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77−7.75 (m, 1H), 7.71 (d, J = 15.8 Hz, 1H), 7.60 (s, 1H), 7.48−7.43 (m, 3H), 7.40 (dd, J = 8.8, 2.1 Hz, 1H), 7.33−7.31 (m, 2H), 6.45 (d, J = 15.8 Hz, 1H), 4.89−4.83 (m, 1H), 2.45 (s, 3H), 1.88−1.82 (m, 2H), 1.73−1.66 (m, 2H), 1.56−1.43 (m, 3H), 1.42−1.32 (m, 2H), 1.30−1.20 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 166.1, 160.7, 152.1, 143.1, 141.9, 135.5, 134.3, 133.7, 133.0, 130.8, 129.8, 129.1, 127.8, 127.1, 126.8, 120.6, 118.8, 116.4, 72.6, 31.6, 25.4, 23.6, 20.8; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{25}H_{25}O_4^+$ 389.1747, found 389.1715.

*Methyl (E)-3-(2-(6-Methoxy-2-oxo-2H-chromen-3-yl)phenyl)-acrylate (**3ga**).* The title compound **3ga** was synthesized following method A. The crude product was purified by using 2.5:7.5 ethyl acetate/hexane as an eluent: R_f = 0.3; white solid (59 mg, 76%); mp = 142−144 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76−7.73 (m, 1H), 7.70 (d, J = 15.6 Hz, 1H), 7.61 (s, 1H), 7.50−7.42 (m, 3H), 7.35 (d, J = 8.8

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Hz, 1H), 7.18 (dd, J = 8.8, 2.8 Hz, 1H), 6.97 (d, J = 2.8 Hz, 1H), 6.46 (d, J = 16.0 Hz, 1H), 3.88 (s, 3H), 3.76 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.0, 160.5, 156.3, 148.4, 142.9, 142.4, 135.5, 133.6, 130.8, 130.0, 129.2, 127.8, 126.9, 119.8, 119.7, 119.4, 117.8, 110.1, 55.9, 51.7; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{20}H_{17}O_5^+$ 337.1071, found 337.1065.

*Cyclohexyl (E)-3-(2-(6-Methoxy-2-oxo-2H-chromen-3-yl)phenyl)-acrylate (**3gd**).* The title compound **3gd** was synthesized following method A. The crude product was purified by using 2.5:7.5 ethyl acetate/hexane as an eluent: R_f = 0.3; white solid (59.5 mg, 64%); mp = 143−145 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.78−7.75 (m, 1H), 7.71 (d, J = 15.6 Hz, 1H), 7.61 (s, 1H), 7.50−7.42 (m, 3H), 7.36 (d, J = 8.8 Hz, 1H), 7.18 (dd, J = 9.2, 2.8 Hz, 1H), 6.97 (d, J = 3.2 Hz, 1H), 6.46 (d, J = 16.0 Hz, 1H), 4.89−4.83 (m, 1H), 3.88 (s, 3H), 1.88−1.83 (m, 2H), 1.73−1.68 (m, 2H), 1.56−1.44 (m, 3H), 1.42−1.43 (m, 1H), 1.31−1.23 (m, 1H), 0.92−0.86 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.1, 160.6, 156.2, 148.4, 142.9, 141.8, 135.4, 133.7, 130.7, 129.8, 129.1, 127.7, 126.8, 120.7, 119.7, 119.4, 117.8, 110.0, 72.6, 55.9, 31.6, 25.4, 23.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{25}H_{25}O_5^+$ 405.1697, found 405.1692.

*Methyl (E)-3-(2-(6-Chloro-2-oxo-2H-chromen-3-yl)phenyl)-acrylate (**3ha**).* The title compound **3ha** was synthesized following method A. The crude product was purified by using 1.5:8.5 ethyl acetate/hexane as an eluent: R_f = 0.7; white solid (39 mg, 50%); mp = 209−211 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.76−7.73 (m, 1H), 7.67 (d, J = 15.9 Hz, 1H), 7.58 (s, 1H), 7.57−7.53 (m, 2H), 7.52−7.47 (m, 2H), 7.45−7.41 (m, 1H), 7.38 (d, J = 8.6 Hz, 1H), 6.47 (d, J = 15.8 Hz, 1H), 3.78 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 167.0, 159.8, 152.3, 142.1, 141.7, 134.8, 133.7, 131.9, 130.7, 130.0, 130.0, 129.5, 128.7, 127.3, 127.0, 120.1, 120.0, 118.2, 51.8; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{19}H_{14}ClO_4^+$ 341.0575, found 341.0543.

*Cyclohexyl (E)-3-(2-(6-Chloro-2-oxo-2H-chromen-3-yl)phenyl)-acrylate (**3hd**).* The title compound **3hd** was synthesized following method A. The crude product was purified by using 1.5:8.5 ethyl acetate/hexane as an eluent: R_f = 0.7; white solid (41 mg, 44%); mp = 182−184 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.78−7.72 (m, 1H), 7.67 (d, J = 15.8 Hz, 1H), 7.58 (s, 1H), 7.56−7.53 (m, 2H), 7.51−7.43 (m, 3H), 7.38−7.43 (m, 1H), 6.46 (d, J = 15.8 Hz, 1H), 4.89−4.83 (m, 1H), 1.90−1.84 (m, 2H), 1.74−1.68 (m, 2H), 1.57−1.46 (m, 3H), 1.44−1.34 (m, 2H), 1.31−1.21 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.0, 159.8, 152.3, 141.7, 141.5, 134.8, 133.7, 131.8, 130.6, 129.9, 129.9, 129.4, 128.6, 127.2, 126.9, 120.9, 120.1, 118.2, 72.7, 31.6, 25.4, 23.6; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{24}H_{22}ClO_4^+$ 409.1201, found 409.1197.

*Methyl (E)-3-(2-(3-Oxo-3H-benzo[f]chromen-2-yl)phenyl)-acrylate (**3ia**).* The title compound **3ia** was synthesized following method A. The crude product was purified by using 1.5:8.5 ethyl acetate/hexane as an eluent: R_f = 0.7; white solid (64 mg, 78%); mp = 232−234 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.46 (s, 1H), 8.22 (d, J = 8.4 Hz, 1H), 8.07 (d, J = 9.0 Hz, 1H), 7.97 (dd, J = 8.1, 1.3 Hz, 1H), 7.80−7.68 (m, 3H), 7.63−7.50 (m, 5H), 6.50 (d, J = 15.8 Hz, 1H), 3.73 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 168.0, 160.4, 153.8, 142.5, 139.0, 135.8, 133.8, 133.4, 130.9, 130.4, 130.1, 129.3, 129.2, 129.1, 128.4, 127.0, 126.4, 126.2, 121.4, 119.9, 116.9, 113.3, 51.7; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{23}H_{17}O_4^+$ 357.1121, found 357.1090.

*Cyclohexyl (E)-3-(2-(3-Oxo-3H-benzo[f]chromen-2-yl)phenyl)-acrylate (**3id**).* The title compound **3id** was synthesized following method A. The crude product was purified by using 2.0:8.0 ethyl acetate/hexane as an eluent: R_f = 0.7; white solid (61.5 mg, 63%); mp = 198−200 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 1H), 8.21 (d, J = 8.4 Hz, 1H), 8.06 (d, J = 9.0 Hz, 1H), 7.97 (d, J = 8.1 Hz, 1H), 7.81−7.76 (m, 2H), 7.69 (ddd, J = 8.4, 6.9, 1.4 Hz, 1H), 7.62−7.48 (m, 5H), 6.49 (d, J = 15.8 Hz, 1H), 4.85−4.79 (m, 1H), 1.82−1.75 (m, 2H), 1.65−1.57 (m, 2H), 1.50−1.36 (m, 3H), 1.34−1.24 (m, 2H), 1.20−1.11 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.0, 160.5, 153.8, 141.9, 139.1, 135.7, 133.9, 133.3, 130.8, 130.4, 129.9, 129.2, 129.2, 129.1, 128.4, 126.9, 126.2, 126.1, 121.4, 120.8, 116.8, 113.3, 72.6, 31.5, 25.3, 23.5; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{28}H_{25}O_4^+$ 425.1747, found 425.1713.

Representative Procedure for *ortho*-Halogenation (Method B). An oven-dried 10 mL round-bottom flask was charged with 3-phenyl-2*H*-chromen-2-one **1a** (0.23 mmol, 51 mg), NBS **4a** (0.25 mmol, 45 mg), $Pd(OAc)_2$ (10 mol %, 5.15 mg), $K_2S_2O_8$ (2 equiv, 124 mg), TfOH (2 equiv, 41 μL), and 1,2-dichloroethane (2 mL). The reaction mixture was heated with stirring in an oil bath at 80 °C for 24 h. After completion of the reaction, the reaction mixture was cooled to an ambient temperature, basified with aqueous $NaHCO_3$ solution, and then extracted with ethyl acetate (3 × 5 mL). The combined organic layer was washed with water (2 × 5 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The resulting residue was purified by column chromatography over silica gel 60 (100−200 mesh size) using *n*-hexane/ethyl acetate as an eluting system to give **5aa** (50 mg, 73%).

*3-(2-Bromophenyl)-2H-chromen-2-one (**5aa**).*[25] The title compound **5aa** was synthesized following method B: R_f = 0.3; white solid (50 mg, 73%); mp = 181−183 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.71 (d, J = 8.0 Hz, 1H), 7.62−7.56 (m, 2H), 7.44−7.42 (m, 3H), 7.35 (t, J = 8.0 Hz, 1H), 7.32−7.30 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.8, 154.0, 142.5, 135.8, 133.1, 131.9, 131.3, 130.2, 128.8, 128.1, 127.5, 124.6, 123.6, 119.0, 116.8; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{15}H_{10}BrO_2^+$ 300.9859, found 300.9843.

*3-(2-Bromo-4-methylphenyl)-2H-chromen-2-one (**5ba**).* The title compound **5ba** was synthesized following method B. The crude product was purified by using 1.5:8.5 ethyl acetate/hexane as an eluent: R_f = 0.5; white solid (48 mg, 67%); mp = 156−158 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.61−7.53 (m, 3H), 7.41 (d, J = 8.4 Hz, 1H), 7.35−7.28 (m, 2H), 7.23−7.20 (m, 1H), 2.40 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.9, 153.9, 142.4, 140.6, 133.6, 132.8, 131.7, 131.0, 128.7, 128.3, 128.1, 124.5, 123.3, 119.1, 116.7, 20.9; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{16}H_{12}BrO_2^+$ 315.0015, found 315.0012.

*3-(2-Bromo-4-methoxyphenyl)-2H-chromen-2-one (**5ca**).* The title compound **5ca** was synthesized following method B. The crude product was purified by using 2.5:7.5 ethyl acetate/hexane as an eluent: R_f = 0.4; white solid (44 mg, 58%); mp = 148−150 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, J = 2.0 Hz, 1H), 7.81 (s, 1H), 7.75 (dd, J = 8.8, 2.4 Hz, 1H), 7.56 (t, J = 7.6 Hz, 2H), 7.39 (d, J = 8.4 Hz, 1H), 7.33 (td, J = 7.6, 1.2 Hz, 1H), 7.00 (d, J = 8.0 Hz, 1H), 3.97 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.4, 156.4, 153.4, 139.1, 133.2, 131.4, 129.0, 128.4, 127.9, 126.5, 124.6, 119.6, 116.5, 111.7, 111.6, 56.4; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{16}H_{12}BrO_3^+$ 330.9964, found 330.9932.

*3-(2-Bromo-4-chlorophenyl)-2H-chromen-2-one (**5da**).* The title compound **5da** was synthesized following method B. The crude product was purified by using 1.5:8.5 ethyl acetate/hexane as an eluent: R_f = 0.6; white solid (48.5 mg, 63%); mp = 167−169 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.72 (d, J = 2.0 Hz, 1H), 7.63−7.61 (m, 1H), 7.58−7.56 (m, 1H), 7.43−7.41 (m, 1H), 7.40−7.37 (m, 2H), 7.36−7.33 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.6, 154.0, 142.9, 135.4, 134.3, 132.8, 132.1, 132.1, 129.8, 128.2, 127.8, 124.7, 124.1, 118.8, 116.8; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{15}H_9BrClO_2^+$ 334.9469, found 334.9439.

*3-(2-Bromo-4-fluorophenyl)-2H-chromen-2-one (**5ea**).* The title compound **5ea** was synthesized following method B. The crude product was purified by using 2.0:8.0 ethyl acetate/hexane as an eluent: R_f = 0.4; white solid (52 mg, 71%); mp = 157−159 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.63−7.56 (m, 2H), 7.47−7.39 (m, 3H), 7.35 (td, J = 7.6, 1.2 Hz, 1H), 7.14 (td, J = 8.4, 2.8 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.38 (d, J = 251.3 Hz), 159.8, 154.0, 142.9, 132.4 (d, J = 8.7 Hz), 132.0, 131.9 (d, J = 3.7 Hz), 128.1, 127.8, 124.7, 124.0 (d, J = 9.7 Hz), 120.5 (d, J = 24.4 Hz), 118.9, 116.8, 114.8 (d, J = 21.2 Hz); HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{15}H_9BrFO_2^+$ 318.9764, found 318.9749.

*3-(2-Bromophenyl)-6-methyl-2H-chromen-2-one (**5fa**).*[26] The title compound **5fa** was synthesized following method B. The crude product was purified by using 1.5:8.5 ethyl acetate/hexane as an eluent: R_f = 0.5; white solid (53.5 mg, 74%); mp = 137−139 °C (lit.[26] mp 141−142 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 6.8 Hz, 2H), 7.42−7.38 (m, 3H), 7.35−7.31 (m, 2H), 7.29−7.27 (m, 1H), 2.45 (s,

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3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.0, 152.1, 142.6, 135.9, 134.3, 133.1, 132.9, 131.4, 130.1, 128.6, 127.9, 127.4, 123.6, 118.8, 116.4, 20.8; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{16}H_{12}BrO_2^+$ 315.0015, found 315.0012.

*3-(2-Bromophenyl)-6-chloro-2H-chromen-2-one (**5ha**).* The title compound **5ha** was synthesized following method B. The crude product was purified by using 1.5:8.5 ethyl acetate/hexane as an eluent: R_f = 0.5; white solid (51 mg, 66%); mp = 165−167 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 8.0 Hz, 1H), 7.68 (s, 1H), 7.55−7.53 (m, 2H), 7.47−7.36 (m, 3H), 7.34−7.30 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.2, 152.3, 141.2, 135.3, 133.2, 131.8, 131.2, 130.5, 130.0, 129.9, 127.5, 127.3, 123.4, 120.0, 118.2; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{15}H_9BrClO_2^+$ 334.9469, found 334.9449.

*2-(2-Bromophenyl)-3H-benzo[f]chromen-3-one (**5ia**).*[25] The title compound **5ia** was synthesized following method B. The crude product was purified by using 1.5:8.5 ethyl acetate/hexane as an eluent: R_f = 0.6; white solid (56 mg, 70%); mp = 162−164 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.56 (s, 1H), 8.26 (d, J = 8.0 Hz, 1H), 8.05 (d, J = 9.2 Hz, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.75 (dd, J = 8.0, 1.2 Hz, 1H), 7.73−7.69 (m, 1H), 7.63−7.59 (m, 1H), 7.55 (d, J = 8.8 Hz, 1H), 7.52 (dd, J = 7.6, 1.6 Hz, 1H), 7.46 (td, J = 7.2, 1.2 Hz, 1H), 7.33 (td, J = 8.0, 2.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.8, 153.8, 138.6, 136.1, 133.2, 131.5, 130.4, 130.2, 129.2, 129.1, 128.4, 127.6, 127.6, 126.1, 123.7, 121.5, 116.9, 113.2; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{19}H_{12}BrO_2^+$ 351.0015, found 350.9994.

*3-(2-Chlorophenyl)-2H-chromen-2-one (**5ab**).*[27] The title compound **5ab** was synthesized following method B. The crude product was purified by using 2.0:8.0 ethyl acetate/hexane as an eluent: R_f = 0.4; white solid (43.5 mg, 74%); mp = 135−137 °C (lit.[27] mp 138 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.62−7.55 (m, 2H), 7.53−7.51 (m, 1H), 7.45−7.40 (m, 2H), 7.39−7.32 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.8, 154.0, 142.7, 133.78, 133.7, 131.9, 131.4, 130.1, 129.9, 128.1, 127.1, 126.8, 124.6, 119.1, 116.7; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{15}H_{10}ClO_2^+$ 257.0364, found 257.0341.

*3-(2-Chloro-4-methylphenyl)-2H-chromen-2-one (**5bb**).* The title compound **5bb** was synthesized following method B. The crude product was purified by using 2.0:8.0 ethyl acetate/hexane as an eluent: R_f = 0.5; white solid (42 mg, 68%); mp = 138−140 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.60−7.54 (m, 2H), 7.41 (d, J = 8.0 Hz, 1H), 7.35−7.33 (m, 2H), 7.31 (s, 1H), 7.18−7.16 (m, 1H), 2.40 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.0, 153.9, 142.5, 140.5, 133.2, 131.7, 131.1, 130.7, 130.4, 128.0, 127.7, 127.1, 124.5, 119.1, 116.7, 21.0; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{16}H_{12}ClO_2^+$ 271.0520, found 271.0530.

*3-(2-Chloro-4-methoxyphenyl)-2H-chromen-2-one (**5cb**).* The title compound **5cb** was synthesized following method B. The crude product was purified by using 2.5:7.5 ethyl acetate/hexane as an eluent: R_f = 0.4; white solid (37 mg, 56%); mp = 155−157 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.77 (d, J = 2.4 Hz, 1H), 7.70 (dd, J = 8.6, 2.2 Hz, 1H), 7.58−7.54 (m, 2H), 7.41−7.39 (m, 1H), 7.35−7.31 (m, 1H), 7.03 (d, J = 8.4 Hz, 1H), 3.98 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 155.5, 139.1, 131.4, 130.2, 130.2, 128.2, 127.9, 127.8, 126.7, 124.6, 122.7, 119.6, 116.5, 115.1, 111.8, 56.3; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{16}H_{12}ClO_3^+$ 287.0469, found 287.0469.

*3-(2,4-Dichlorophenyl)-2H-chromen-2-one (**5db**).*[28] The title compound **5db** was synthesized following method B. The crude product was purified by using 2.0:8.0 ethyl acetate/hexane as an eluent: R_f = 0.4; white solid (51 mg, 77%); mp = 181−183 °C (lit.[28] mp 187−189 °C); ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.63−7.58 (m, 1H), 7.58−7.53 (m, 2H), 7.42 (d, J = 8.4 Hz, 1H), 7.40−7.33 (m, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.7, 154.0, 143.0, 135.4, 134.5, 132.3, 132.2, 132.2, 129.8, 128.2, 127.2, 126.0, 124.7, 118.9, 116.8; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{15}H_9Cl_2O_2^+$ 290.9974, found 290.9985.

*3-(2-Chloro-4-fluorophenyl)-2H-chromen-2-one (**5eb**).* The title compound **5eb** was synthesized following method B. The crude product was purified by using 1.5:7.5 ethyl acetate/hexane as an eluent: R_f = 0.7; white solid (44 mg, 70%); mp = 182−184 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.55−7.52 (m, 3H), 7.44−7.36 (m, 4H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 162.58 (d, J = 260.2 Hz), 159.8, 154.0, 143.0, 134.7 (d, J = 10.4 Hz), 132.5 (d, J = 8.9 Hz), 132.1, 129.9 (d, J = 3.7 Hz), 128.1, 126.1, 124.6, 118.9, 117.4 (d, J = 24.7 Hz), 116.8, 114.3 (d, J = 21.3 Hz); HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{15}H_9ClFO_2^+$ 275.0270, found 275.0249.

*3-(2-Chlorophenyl)-6-methyl-2H-chromen-2-one (**5fb**).* The title compound **5fb** was synthesized following method B. The crude product was purified by using 2.0:8.0 ethyl acetate/hexane as an eluent: R_f = 0.5; white solid (50.5 mg, 81%); mp = 149−151 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.53−7.50 (m, 1H), 7.45−7.42 (m, 1H), 7.41−7.34 (m, 4H), 7.32 (d, J = 8.4 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.1, 152.1, 142.7, 134.3, 133.9, 133.7, 132.9, 131.4, 130.0, 129.9, 127.9, 126.9, 126.8, 118.8, 116.4, 20.8; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{16}H_{12}ClO_2^+$ 271.0520, found 271.0530.

*3-(2-Chlorophenyl)-6-methoxy-2H-chromen-2-one (**5gb**).* The title compound **5gb** was synthesized following method B. The crude product was purified by using 2.5:7.5 ethyl acetate/hexane as an eluent: R_f = 0.3; white solid (49.5 mg, 75%); mp = 169−171 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.53−7.50 (m, 1H), 7.45−7.42 (m, 1H), 7.38−7.34 (m, 3H), 7.17 (dd, J = 8.8, 2.8 Hz, 1H), 6.99 (d, J = 2.8 Hz, 1H), 3.88 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.0, 156.2, 148.4, 142.5, 133.8, 133.6, 131.4, 130.0, 129.9, 127.4, 126.8, 119.7, 119.4, 117.7, 110.1, 55.9; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{16}H_{12}ClO_3^+$ 287.0469, found 287.0443.

*6-Chloro-3-(2-chlorophenyl)-2H-chromen-2-one (**5hb**).* The title compound **5hb** was synthesized following method B. The crude product was purified by using 1.5:8.5 ethyl acetate/hexane as an eluent: R_f = 0.6; white solid (38 mg, 57%); mp = 182−184 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (s, 1H), 7.63−7.56 (m, 2H), 7.45−7.42 (m, 2H), 7.35 (td, J = 7.6, 1.2 Hz, 1H), 7.29−7.26 (m, 1H), 7.12−7.07 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.2, 152.3, 141.4, 133.6, 133.3, 131.8, 131.3, 130.3, 130.0, 129.9, 128.3, 127.3, 126.9, 120.1, 118.2; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{15}H_9Cl_2O_2^+$ 290.9974, found 290.9964.

*2-(2-Chlorophenyl)-3H-benzo[f]chromen-3-one (**5ib**).* The title compound **5ib** was synthesized following method B. The crude product was purified by using 2.0:8.0 ethyl acetate/hexane as an eluent: R_f = 0.5; white solid (62 mg, 88%); mp = 160−162 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 8.27 (d, J = 8.4 Hz, 1H), 8.06 (d, J = 8.8 Hz, 1H), 7.97 (d, J = 8.4 Hz, 1H), 7.71 (t, J = 7.2 Hz, 1H), 7.61 (t, J = 7.6 Hz, 1H), 7.58−7.52 (m, 3H), 7.44−7.39 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.9, 153.8, 138.7, 134.1, 133.8, 133.2, 131.5, 130.4, 130.1, 130.0, 129.2, 129.1, 128.3, 126.9, 126.1, 126.0, 121.5, 116.9, 113.2; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{19}H_{12}ClO_2^+$ 307.0520, found 307.0492.

Representative Procedure for *ortho*-Trifluoroethoxylation (Method C). An oven-dried 10 mL round-bottom flask was charged with 3-phenyl-2*H*-chromen-2-one **1a** (0.23 mmol, 51 mg), $Pd(OAc)_2$ (10 mol %, 5.15 mg), $K_2S_2O_8$ (2 equiv, 124 mg), and TFA (0.45 mmol, 35 μL) and TFE (2 mL). The reaction mixture was heated with stirring in an oil bath at 80 °C for 24 h and then cooled to room temperature. The reaction mixture was basified with aqueous $NaHCO_3$ solution and then extracted with ethyl acetate (3 × 5 mL). The organic layer was washed with water (2 × 5 mL) and dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure. The resulting residue was purified by column chromatography over silica gel 60 (100−200 mesh size) using *n*-hexane/ethyl acetate as the eluent to give **7a** in 69% (51 mg) yield.

*3-(2-(2,2,2-Trifluoroethoxy)phenyl)-2H-chromen-2-one (**7a**).* The title compound **7a** was synthesized following method C: R_f = 0.5; white solid (51 mg, 69%); mp = 181−183 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.59−7.53 (m, 2H), 7.49−7.45 (m, 1H), 7.43−7.40 (m, 2H), 7.33 (t, J = 7.6 Hz, 1H), 7.18 (t, J = 7.6 Hz, 1H), 7.03 (d, J = 8.4 Hz, 1H), 4.44 (q, J = 8.0 Hz, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.3, 155.2, 153.8, 142.2, 131.4 (d, J = 12.6 Hz), 130.4, 127.9, 125.4 (d, J = 5.3 Hz), 124.4, 123.3 (q, J = 260.0 Hz), 122.9, 119.4, 116.6, 113.8, 67.0 (q, J = 35.2 Hz); HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{17}H_{12}F_3O_3^+$ 321.0733, found 321.0704.

*3-(4-Methyl-2-(2,2,2-trifluoroethoxy)phenyl)-2H-chromen-2-one (**7b**).* The title compound **7b** was synthesized following method C. The crude product was purified by using 1.5:8.5 ethyl acetate/hexane as an

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eluent: R_f = 0.6; white solid (42 mg, 54%); mp = 175−179 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (s, 1H), 7.58−7.55 (m, 1H), 7.54−7.51 (m, 1H), 7.40 (d, J = 8.4 Hz, 1H), 7.37 (d, J = 7.6 Hz, 1H), 7.34−7.30 (m, 1H), 7.00−6.98 (m, 1H), 6.84 (s, 1H), 4.42 (q, J = 8.2 Hz, 2H), 2.43 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.5, 155.1, 153.7, 141.9, 140.8, 131.3, 131.1, 127.8, 125.3, 124.4, 123.6, 123.5 (q, J = 217.1 Hz), 122.3, 119.5, 116.6, 114.7, 66.8 (q, J = 35.5 Hz), 21.6; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{18}H_{14}F_3O_3^+$ 335.0890, found 335.0861.

*6-Methyl-3-(2-(2,2,2-trifluoroethoxy)phenyl)-2H-chromen-2-one (**7f**).* The title compound **7f** was synthesized following method C. The crude product was purified by using 2.0:8.0 ethyl acetate/hexane as an eluent: R_f = 0.5; white solid (48 mg, 63%); mp = 161−163 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.47 (d, J = 7.7 Hz, 1H), 7.42 (td, J = 7.9, 1.8 Hz, 1H), 7.37 (d, J = 8.3 Hz, 1H), 7.29 (d, J = 8.6 Hz, 2H), 7.18 (t, J = 7.5 Hz, 1H), 7.03 (d, J = 8.3 Hz, 1H), 4.43 (q, J = 8.2 Hz, 2H), 2.45 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.5, 155.3, 151.9, 142.2, 134.1, 132.5, 131.4, 130.2, 127.7, 125.6, 125.2, 123.4 (q, J = 256.3 Hz), 122.9, 119.1, 116.3, 113.9, 67.1 (q, J = 35.0 Hz), 20.8; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{18}H_{14}F_3O_3^+$ 335.0890, found 335.0861.

*6-Methoxy-3-(2-(2,2,2-trifluoroethoxy)phenyl)-2H-chromen-2-one (**7g**).* The title compound **7g** was synthesized following method C. The crude product was purified by using 2.5:7.5 ethyl acetate/hexane as an eluent: R_f = 0.3; white solid (46 mg, 57%); mp = 153−155 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.49−7.41 (m, 2H), 7.34 (d, J = 9.2 Hz, 1H), 7.20−7.13 (m, 2H), 7.03 (dd, J = 8.4, 1.2 Hz, 1H), 6.96 (d, J = 2.8 Hz, 1H), 4.44 (q, J = 8.4 Hz, 2H), 3.89 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.5, 156.1, 155.3, 148.2, 142.0, 131.4, 130.3, 125.7, 125.4, 123.3 (q, J = 263.3 Hz), 122.9, 119.7, 119.2, 117.6, 113.9, 110.0, 67.3 (q, J = 35.5 Hz), 55.9; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{18}H_{14}F_3O_4^+$ 351.0839, found 351.0807.

*6-Chloro-3-(2-(2,2,2-trifluoroethoxy)phenyl)-2H-chromen-2-one (**7h**).* The title compound **7h** was synthesized following method C. The crude product was purified by using 1.5:8.5 ethyl acetate/hexane as an eluent: R_f = 0.4; white solid (49.5 mg, 61%); mp = 147−149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (s, 1H), 7.54−7.50 (m, 2H), 7.48−7.42 (m, 2H), 7.36−7.34 (m, 1H), 7.19 (t, J = 7.6 Hz, 1H), 7.03 (d, J = 8.4 Hz, 1H), 4.44 (q, J = 8.1 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.7, 155.2, 152.1, 140.8, 131.4, 131.3, 130.6, 129.7, 127.1, 126.6, 124.8, 123.3 (q, J = 270.0 Hz), 122.9, 120.4, 118.0, 113.7, 66.9 (q, J = 35.7 Hz); HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{17}H_{11}ClF_3O_3^+$ 355.0343, found 355.0310.

*2-(2-(2,2,2-Trifluoroethoxy)phenyl)-3H-benzo[f]-chromen-3-one (**7i**).* The title compound **7i** was synthesized following method C. The crude product was purified by using 2.0:8.0 ethyl acetate/hexane as an eluent: R_f = 0.4; white solid (53 mg, 62%); mp = 182−184 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.66 (s, 1H), 8.27 (d, J = 8.4 Hz, 1H), 8.03 (d, J = 9.2 Hz, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.70 (t, J = 7.6 Hz, 1H), 7.60 (t, J = 7.4 Hz, 2H), 7.55 (d, J = 8.8 Hz, 1H), 7.46 (t, J = 7.6 Hz, 1H), 7.23 (t, J = 7.6 Hz, 1H), 7.07 (d, J = 8.4 Hz, 1H), 4.48 (q, J = 8.2 Hz, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.5, 155.2, 153.4, 138.3, 132.8, 131.6, 130.4, 130.3, 129.2, 129.0, 128.2, 126.0, 125.5, 124.7, 123.3 (q, J = 276.6 Hz), 122.9, 121.4, 116.9, 113.7, 113.5, 66.9 (q, J = 35.6 Hz); HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{21}H_{14}F_3O_3^+$ 371.0890, found 371.0859.

Representative Procedure for *ortho*-Hydroxylation (Method D). An oven-dried 10 mL round-bottom flask was charged with 3-phenyl-2*H*-chromen-2-one **1a** (0.23 mmol, 51 mg), $Pd(OAc)_2$ (10 mol %, 5.15 mg), and $K_2S_2O_8$ (2 equiv, 124 mg). Subsequently, TFA (2 mL) was added to the flask and refluxed in an oil bath at 90 °C for 1 h. After completion of the reaction, the reaction mixture was cooled to an ambient temperature, basified with aqueous $NaHCO_3$ solution, and extracted with ethyl acetate (3 × 5 mL). The combined organic layer was washed with water (2 × 5 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The resulting residue was purified by column chromatography over silica gel 60 (100−200 mesh size) using *n*-hexane/ethyl acetate as the eluent to give **8a** in 93% (51 mg) yield.

*3-(2-Hydroxyphenyl)-2H-chromen-2-one (**8a**)..*[18,29] The title compound **8a** was synthesized following method D: R_f = 0.2; white solid (51 mg, 93%); mp = 214−216 °C (lit.[29] mp 212−213 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.64 (td, J = 7.6, 1.6 Hz, 2H), 7.50−7.48 (m, 1H), 7.43−7.33 (m, 3H), 7.10 (dd, J = 8.0, 1.2 Hz, 1H), 7.06 (td, J = 7.6, 1.2 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.2, 155.0, 153.1, 143.8, 132.2, 131.1, 130.7, 128.2, 127.4, 125.2, 123.2, 121.4, 119.6, 119.5, 116.7; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{15}H_{11}O_3^+$ 239.0703, found 239.0685.

*3-(2-Hydroxy-4-methylphenyl)-2H-chromen-2-one (**8b**).* The title compound **8b** was synthesized following method D. The crude product was purified by using 2.5:7.5 ethyl acetate/hexane as an eluent: R_f = 0.2; white solid (51.5 mg, 89%); mp = 201−203 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (s, 1H), 7.69 (s, 1H), 7.64−7.60 (m, 2H), 7.47 (d, J = 8.4 Hz, 1H), 7.40 (t, J = 7.6 Hz, 1H), 7.22 (d, J = 7.6 Hz, 1H), 6.91 (s, 1H), 6.87 (d, J = 8.0 Hz, 1H), 2.38 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.4, 154.8, 153.0, 143.1, 141.6, 131.9, 130.5, 128.1, 127.4, 125.2, 122.3, 120.2, 120.1, 119.6, 116.6, 21.1; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{16}H_{13}O_3^+$ 253.0859, found 253.0835.

*3-(2-Hydroxy-4-methoxyphenyl)-2H-chromen-2-one (**8c**).*[30] The title compound **8c** was synthesized following method D. The crude product was purified by using 2.5:7.5 ethyl acetate/hexane as an eluent: R_f = 0.3; white solid (37 mg, 60%); mp = 173−175 °C (lit.[30] mp 171−172 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.57−7.51 (m, 2H), 7.38 (d, J = 8.0 Hz, 1H), 7.35−7.32 (m, 1H), 7.31 (t, J = 1.8 Hz, 1H), 7.29 (d, J = 1.2 Hz, 1H), 6.95 (d, J = 8.4 Hz, 1H), 3.97 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.6, 153.3, 147.2, 145.5, 138.8, 131.1, 128.0, 127.7, 124.4, 120.9, 119.8, 116.4, 114.7, 110.5, 100.0, 56.1; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{16}H_{13}O_4^+$ 269.0808, found 269.0804.

*3-(4-Chloro-2-hydroxyphenyl)-2H-chromen-2-one (**8d**).* The title compound **8d** was synthesized following method D. The crude product was purified by using 2.0:8.0 ethyl acetate/hexane as an eluent: R_f = 0.4; white solid (41 mg, 66%); mp = 215−217 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (s, 1H), 7.68−7.64 (m, 2H), 7.49 (d, J = 8.8 Hz, 1H), 7.45−7.41 (m, 1H), 7.28 (d, J = 2.8 Hz, 1H), 7.11 (d, J = 2.0 Hz, 1H), 7.04 (dd, J = 8.4, 2.0 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.3, 155.8, 153.1, 143.9, 136.6, 132.4, 131.4, 128.3, 126.5, 125.4, 121.8, 121.6, 119.9, 119.4, 116.7; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{15}H_{10}ClO_3^+$ 273.0313, found 273.0320.

*3-(4-Fluoro-2-hydroxyphenyl)-2H-chromen-2-one (**8e**).* The title compound **8e** was synthesized following method D. The crude product was purified by using 2.5:7.5 ethyl acetate/hexane as an eluent: R_f = 0.5; white solid (45 mg, 77%); mp = 166−168 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.94 (s, 1H), 7.67−7.63 (m, 2H), 7.49 (d, J = 8.8 Hz, 1H), 7.42 (t, J = 7.6 Hz, 1H), 7.32−7.30 (m, 1H), 6.83−6.75 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.7 (d, J = 247.6 Hz), 156.8 (d, J = 12.2 Hz), 153.0, 143.6, 132.4, 132.3, 131.8 (d, J = 10.3 Hz), 128.2, 126.6, 125.4, 119.4, 119.4, 116.7, 108.6 (d, J = 21.6 Hz), 106.8 (d, J = 23.4 Hz); HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{15}H_{10}FO_3^+$ 257.0608, found 257.0607.

*3-(2-Hydroxyphenyl)-6-methyl-2H-chromen-2-one (**8f**).*[31] The title compound **8f** was synthesized following method D. The crude product was purified by using 2.5:7.5 ethyl acetate/hexane as an eluent: R_f = 0.2; white solid (42 mg, 72%); mp = 163−165 °C (lit.[31] mp 167−168 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.76 (bs, 1H), 7.45−7.40 (m, 2H), 7.38−7.35 (m, 2H), 7.32 (dd, J = 7.6, 1.6 Hz, 1H), 7.09 (dd, J = 8.0, 1.2 Hz, 1H), 7.05 (td, J = 7.6, 1.2 Hz, 1H), 2.48 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.5, 155.0, 151.3, 143.8, 135.1, 133.3, 131.0, 130.7, 127.9, 127.2, 123.3, 121.3, 119.6, 119.3, 116.3, 20.8; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{16}H_{13}O_3^+$ 253.0859, found 253.0835.

*3-(2-Hydroxyphenyl)-6-methoxy-2H-chromen-2-one (**8g**).*[32] The title compound **8g** was synthesized following method D. The crude product was purified by using 3.0:7.0 ethyl acetate/hexane as an eluent: R_f = 0.2; white solid (50 mg, 81%); mp = 146−148 °C (lit.[32] mp 144−145 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.80 (s, 1H), 7.42−7.37 (m, 2H), 7.33 (d, J = 7.6 Hz, 1H), 7.22 (d, J = 8.4 Hz, 1H), 7.11−7.05 (m, 2H), 3.91 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.4, 156.7, 155.1, 147.7, 143.6, 131.1, 130.7, 127.8, 123.3, 121.4, 120.3, 119.9, 119.6, 117.7, 109.8, 55.9: HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{16}H_{13}O_4^+$ 269.0808, found 269.0804.

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*6-Chloro-3-(2-hydroxyphenyl)-2H-chromen-2-one (**8h**).*[29] The title compound **8h** was synthesized following method D. The crude product was purified by using 2.0:8.0 ethyl acetate/hexane as an eluent: R_f = 0.3; white solid (36 mg, 58%); mp = 226−228 °C (lit.[29] mp 230−231 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H), 7.62 (d, J = 2.4 Hz, 1H), 7.58 (dd, J = 8.8, 2.4 Hz, 1H), 7.44−7.38 (m, 2H), 7.32 (dd, J = 7.6, 1.6 Hz, 1H), 7.11−7.05 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 162.5, 154.9, 151.5, 142.2, 132.0, 131.4, 130.7, 130.6, 128.7, 127.3, 122.8, 121.5, 120.5, 119.5, 118.1; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{15}H_{10}ClO_3^+$: 273.0313, found 273.0320.

*2-(2-Hydroxyphenyl)-3H-benzo[f]chromen-3-one (**8i**).*[33] The title compound **8i** was synthesized following method D. The crude product was purified by using 2.0:8.0 ethyl acetate/hexane as an eluent: R_f = 0.4; white solid (63.5 mg, 96%); mp = 213-215 °C (lit.[33] mp 216−217 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (s, 1H), 8.37 (d, J = 8.4 Hz, 1H), 8.09 (d, J = 8.8 Hz, 1H), 7.99 (d, J = 8.0 Hz, 1H), 7.86 (s, 1H), 7.84−7.74 (m, 1H), 7.68−7.64 (m, 1H), 7.60 (d, J = 9.2 Hz, 1H), 7.46−7.41 (m, 2H), 7.15−7.09 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 163.3, 155.3, 153.0, 139.7, 133.7, 131.1, 130.8, 130.6, 129.2, 129.0, 128.6, 126.6, 126.4, 123.6, 121.6, 121.5, 119.7, 116.5, 114.0; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{19}H_{13}O_3^+$ 289.0859, found 289.0844.

Representative Procedure for the Synthesis of Coumestan (Method E). An oven-dried 10 mL round-bottom flask was charged with 3-(2-hydroxyphenyl)-2*H*-chromen-2-one **8a** (0.21 mmol, 50 mg), DDQ (0.42 mmol, 95 mg), and toluene (2 mL). The reaction mixture was refluxed in an oil bath at 120 °C for 24 h. After completion of the reaction, the reaction mixture was cooled to an ambient temperature and diluted with water (15 mL). The mixture was extracted with ethyl acetate (3 × 5 mL). The combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by column chromatography over silica gel 60 (100−200 mesh size) using *n*-hexane/ethyl acetate as the eluent to afford **9a** in 78% (38.5 mg) yield.

*6H-Benzofuro[3,2-c]chromen-6-one (**9a**).*[34] The title compound **9a** was synthesized following method E: R_f = 0.6; white solid (38.5 mg, 78%); mp = 184−186 °C (lit.[34] mp 187−188 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19−8.15 (m, 1H), 8.07 (dd, J = 7.6, 1.6 Hz, 1H), 7.72−7.69 (m, 1H), 7.66−7.62 (m, 1H), 7.55−7.49 (m, 3H), 7.47−7.42 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.0, 158.1, 155.6, 153.7, 131.9, 126.8, 125.2, 124.7, 123.5, 121.9, 121.9, 117.5, 112.7, 111.8, 105.9; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{15}H_9O_3^+$ 237.0546, found 237.0542.

*9-Methyl-6H-benzofuro[3,2-c]chromen-6-one (**9b**).*[35] The title compound **9b** was synthesized following method E. The crude product was purified by using 1.0:8.0 ethyl acetate/hexane as an eluent: R_f = 0.7; white solid (32 mg, 61%); mp = 196−198 °C (lit.[35] mp 199−200 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18−8.13 (m, 1H), 7.83 (s, 1H), 7.69−7.65 (m, 1H), 7.52−7.45 (m, 2H), 7.42−7.41 (m, 2H), 2.51 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.0, 158.3, 155.5, 151.9, 134.6, 133.0, 126.6, 125.2, 123.6, 121.8, 121.5, 117.2, 112.3, 111.7, 105.8, 21.0; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{16}H_{11}O_3^+$ 251.0703, found 251.0682.

*9-Chloro-6H-benzofuro[3,2-c]chromen-6-one (**9d**).*[36] The title compound **9d** was synthesized following method E. The crude product was purified by using 1.5:8.5 ethyl acetate/hexane as an eluent: R_f = 0.7; white solid (49 mg, 86%); mp = 230−232 °C (lit.[36] mp 239 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.4 Hz, 1H), 8.05 (dd, J = 8.0, 1.6 Hz, 1H), 7.71 (d, J = 1.6 Hz, 1H), 7.68−7.64 (m, 1H), 7.54 (dd, J = 8.4, 0.8 Hz, 1H), 7.49−7.44 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.5, 157.7, 155.5, 153.8, 132.7, 132.3, 126.1, 124.8, 122.4, 122.2, 121.9, 117.6, 112.5, 112.4, 105.7; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{15}H_8ClO_3^+$ 271.0156, found 271.0138.

*9-Fluoro-6H-benzofuro[3,2-c]chromen-6-one (**9e**).*[37] The title compound **9e** was synthesized following method E. The crude product was purified by using 1.0:9.0 ethyl acetate/hexane as an eluent: R_f = 0.8; white solid (37 mg, 69%); mp = 233−235 °C (lit.[37] mp 240−241 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (dd, J = 8.6, 5.5 Hz, 1H), 8.05 (dd, J = 7.6, 1.6 Hz, 1H), 7.67−7.63 (m, 1H), 7.54 (dd, J = 8.8, 1.2 Hz, 1H), 7.48−7.42 (m, 2H), 7.28−7.23 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.9 (d, J = 254.2 Hz), 160.7, 160.6, 157.9, 153.6, 132.0, 124.8, 122.5 (d, J = 10.0 Hz), 121.8, 119.8 (d, J = 1.8 Hz), 117.6, 113.6 (d, J = 23.6 Hz), 112.5, 105.7, 100.1 (d, J = 27.3 Hz); HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{15}H_8FO_3^+$ 255.0452, found 255.0459.

*2-Methyl-6H-benzofuro[3,2-c]chromen-6-one (**9f**).*[38] The title compound **9f** was synthesized following method E. The crude product was purified by using 1.0:9.0 ethyl acetate/hexane as an eluent: R_f = 0.8; white solid (35 mg, 67%); mp = 158−160 °C (lit.[38] mp 166−168 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04−8.00 (m, 2H), 7.64−7.59 (m, 1H), 7.53−7.48 (m, 2H), 7.44−7.40 (m, 1H), 7.31−7.29 (m, 1H), 2.56 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.6, 158.2, 156.0, 153.5, 137.5, 131.6, 126.6, 124.6, 121.7, 121.3, 120.8, 117.4, 112.8, 112.0, 105.9, 21.9; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{16}H_{11}O_3^+$ 251.0703, found 251.0681.

*2-Methoxy-6H-benzofuro[3,2-c]chromen-6-one (**9g**).*[39] The title compound **9g** was synthesized following method E. The crude product was purified by using 1.5:8.5 ethyl acetate/hexane as an eluent: R_f = 0.6; white solid (38.5 mg, 69%); mp = 154−156 °C (lit.[39] mp 155−157 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17−8.15 (m, 1H), 7.69−7.67 (m, 1H), 7.52−7.42 (m, 4H), 7.18 (dd, J = 9.2, 2.8 Hz, 1H), 3.95 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.9, 158.2, 156.4, 155.5, 148.2, 126.8, 125.2, 123.6, 121.9, 120.3, 118.7, 112.8, 111.7, 106.0, 103.4, 56.0; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{16}H_{11}O_4^+$ 267.0652, found 267.0628.

*2-Chloro-6H-benzofuro[3,2-c]chromen-6-one (**9h**).*[40] The title compound **9h** was synthesized following method E. The crude product was purified by using 1.5:8.5 ethyl acetate/hexane as an eluent: R_f = 0.7; white solid (45 mg, 80%); mp = 231−233 °C (lit.[40] mp 236−238 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19−8.17 (m, 1H), 8.05 (d, J = 2.4 Hz, 1H), 7.72−7.70 (m, 1H), 7.60−7.55 (m, 2H), 7.53−7.51 (m, 1H), 7.48 (d, J = 8.8 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 158.7, 157.5, 155.7, 152.0, 131.9, 130.3, 127.3, 125.5, 123.2, 122.0, 121.4, 119.0, 113.8, 111.9, 106.6; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{15}H_8ClO_3^+$ 271.0156, found 271.0183.

*8H-Benzo[f]benzofuro[3,2-c]chromen-8-one (**9i**).*[40] The title compound **9i** was synthesized following method E. The crude product was purified by using 1.0:9.0 ethyl acetate/hexane as an eluent: R_f = 0.7; white solid (45 mg, 75%); mp = 206−208 °C (lit.[40] mp 210−212 °C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.20 (d, J = 8.4 Hz, 1H), 8.23−8.20 (m, 1H), 8.02 (d, J = 9.2 Hz, 1H), 7.93 (d, J = 8.4 Hz, 1H), 7.81−7.77 (m, 2H), 7.64−7.59 (m, 2H), 7.57−7.49 (m, 2H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 161.4, 158.1, 155.5, 153.9, 133.1, 130.4, 128.8, 128.8, 127.5, 126.8, 126.4, 125.5, 125.4, 122.9, 121.9, 117.4, 111.7, 107.1, 106.1. HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{19}H_{11}O_3^+$ 287.0703, found 287.0681.

Synthesis of 2-(2-Oxo-2*H*-chromen-3-yl)phenyl Trifluoromethanesulfonate (10). To a solution of compound **8a** (0.21 mmol, 50 mg) in dry dichloromethane was added Et_3N (0.32 mmol, 45 μL) at 0 °C, and the mixture was stirred for 15 min. Triflic anhydride (0.42 mmol, 2 equiv) was added with stirring, the reaction flask was brought to room temperature, and the mixture continued stirring for 4 h. The reaction was quenched with saturated aqueous $NaHCO_3$ solution and extracted with dichloromethane (2 × 5 mL). The combined layer was dried over anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure to get the crude product. The obtained compound was triturated by diethyl ether (1 mL) to get compound **10**: R_f = 0.5; white solid (61 mg, 79%); mp = 164−166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.64−7.56 (m, 3H), 7.48−7.55 (m, 2H), 7.45−7.42 (m, 2H), 7.38−7.34 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.5, 154.0, 147.1, 143.7, 132.4, 132.2, 130.7, 128.8, 128.5, 128.3, 124.8, 123.6, 122.0, 118.7, 118.4 (q, J = 320 Hz), 116.8; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{16}H_{10}F_3O_5S^+$ 371.0196, found 371.0163.

Synthesis of 3-(2-((4-Propylphenyl)ethynyl)phenyl)-2*H*-chromen-2-one (12). Compound **10** (0.13 mmol, 48 mg), 1-ethynyl-4-propylbenzene **11** (0.20 mmol, 1.5 equiv), $Pd(OAc)_2$ (10 mol %, 3.0 mg), PPh_3 (20 mol %, 68 mg), and K_3PO_4 (0.20 mmol, 42 mg) were taken in a reaction pressure tube, and 2 mL of DMSO was added under a N_2 atmosphere. The reaction mixture was stirred for 24 h at 80 C in an oil bath. After completion of the reaction, the reaction mixture was diluted by water (10 mL) and extracted with ethyl acetate (3 × 5 mL). The combined organic layer was dried over anhydrous

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Na_2SO_4 and concentrated under reduced pressure to get crude product. The obtained crude was purified by column using ethyl acetate/*n*-hexane (1.5:8.5 v/v) as an eluent: R_f = 0.5; off white solid (40 mg, 84%); mp = 110−112 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.69−7.67 (m, 1H), 7.62−7.56 (m, 3H), 7.44−7.41 (m, 2H), 7.35−7.31 (m, 1H), 7.27−7.24 (m, 2H), 7.09 (d, J = 8.4 Hz, 2H), 2.57 (t, J = 7.6 Hz, 2H), 1.65−1.59 (m, 2H), 0.93 (t, J = 7.3 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.4, 153.9, 143.4, 142.5, 136.4, 132.8, 131.6, 131.3, 129.9, 128.5, 128.5, 128.1, 127.9, 127.4, 124.5, 122.8, 120.1, 119.3, 116.6, 93.9, 87.5, 37.9, 24.3, 13.7; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{26}H_{21}O_2^+$ 365.1536, found 365.1506.

Synthesis of (*E*)-3-(2-(2-Oxo-2*H*-chromen-3-yl)phenyl)acrylic Acid (13). Compound **3ab** (0.16 mmol, 51 mg) was added to a solution of KOH in MeOH (2 mL, 20% w/v), and the reaction mixture was stirred overnight at room temperature. After complete consumption of the starting material, methanol was removed in a vacuum, and the obtained crude product was purified by column using methanol/DCM (1:9, v/v) as an eluent: R_f = 0.1; white solid (36.5 mg, 78%); mp = 220−222 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.09 (s, 1H), 7.93−7.91 (m, 1H), 7.80 (dd, J = 8.0, 1.6 Hz, 1H), 7.71−7.67 (m, 1H), 7.54−7.40 (m, 6H), 6.52 (d, J = 16.0 Hz, 1H); ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 168.0, 160.1, 153.8, 143.9, 141.6, 136.0, 133.6, 132.6, 131.4, 130.4, 129.5, 129.2, 127.3, 127.0, 125.3, 121.2, 119.5, 116.6; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{18}H_{13}O_4^+$ 293.0808, found 293.0784.

Synthesis of Ethyl 2,3-Dibromo-3-(2-(2-oxo-2*H*-chromen-3-yl)phenyl)propanoate (14). Compound **3ab** (0.16 mmol, 51 mg) was dissolved in $CHCl_3$ (2 mL) and cooled to 0 °C for 10 min, and then 1 M bromine in DCM solution (32 μL) was added dropwise. The reaction mixture was brought to room temperature and stirred for 12 h, and a sodium thiosulfate solution was added . The organic layer was separated, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to get the crude product. The crude product was triturated by diethyl ether (0.5 mL) to obtain compound **14** (71 mg, 93%) as a white solid: mp = 110−112 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1H), 7.65−7.52 (m, 4H), 7.48−7.44 (m, 2H), 7.38−7.34 (m, 2H), 5.43 (s, 1H), 4.89 (s, 1H), 4.31 (q, J = 7.2, 2H), 1.32 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 167.7, 160.3, 154.0, 134.7, 132.1, 130.9, 130.8, 130.7, 129.9, 129.8, 129.8, 129.2, 128.2, 124.7, 119.0, 116.8, 62.7, 49.6, 42.0, 13.8; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{20}H_{17}Br_2O_4^+$ 478.9488, found 478.9508.

Synthesis of 2-(2-Oxo-2*H*-chromen-3-yl)benzonitrile (15). To an oven-dried pressure tube (10 mL) were added **5aa** (0.17 mmol, 51 mg), CuCN (0.20 mmol, 18 mg), and DMF (2 mL). The vial was capped, and the reaction mixture was heated at 155 °C for 16 h in an oil bath. After complete consumption of the starting material, the reaction mixture was dissolved in ethyl acetate and washed with chilled water (2 × 5 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to get the crude product. The crude product was purified by a column using ethyl acetate/*n*-hexane (2.0:8.0 v/v) as an eluent: R_f = 0.3; white solid (32 mg, 76%); mp = 190−192 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1H), 7.84−7.81 (m, 1H), 7.74−7.69 (m, 2H), 7.66−7.61 (m, 2H), 7.57−7.53 (m, 1H), 7.44 (d, J = 8.8 Hz, 1H), 7.39−7.35 (m, 1H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 159.9, 154.1, 143.3, 138.2, 133.5, 132.6, 132.6, 130.9, 129.1, 128.5, 125.3, 124.8, 118.8, 117.8, 116.8, 112.4; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{16}H_{10}NO_2^+$ 248.0706, found 248.0684.

Synthesis of 3-(2-(Pyridin-4-yl)phenyl)-2*H*-chromen-2-one (17). To an oven-dried pressure tube (10 mL) were added compound **5aa** (0.17 mmol, 51 mg), pyridin-4-ylboronic acid (0.25 mmol, 30 mg), K_2CO_3 (0.34 mmol, 47 mg), and toluene/water/2-propanol (2 mL, 9:0.5:0.5 v/v). The mixture was purged with nitrogen for 10 min at room temperature, and thereafter, Pd(dppf)Cl_2 (10 mol %, 12.5 mg) was added. The mixture was again purged with nitrogen for 10 min. The vial was capped and heated at 85 °C for 16 h in an oil bath. After completion of the reaction, the solvent was removed in a vacuum, and the obtained crude product was purified by column using ethyl acetate/*n*-hexane (7:3 v/v) as an eluent: R_f = 0.2; white solid (46 mg, 90%); mp = 222−224 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.54 (d, J = 5.2 Hz, 2H), 7.57−7.50 (m, 5H), 7.48−7.40 (m, 2H), 7.35−7.30 (m, 1H), 7.28−7.25 (m, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 160.1, 153.7, 149.8, 149.1, 142.5, 139.1, 133.4, 131.7, 130.8, 130.0, 129.3, 128.7, 128.7, 127.9, 124.6, 123.8, 119.0, 116.7; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{20}H_{14}NO_2^+$ 300.1019, found 300.0995.

Procedure for the Competition Experiment. An oven-dried 10 mL round-bottom flask was charged with a magnetic stir bar, 3-(4-methoxyphenyl)-2*H*-chromen-2-one **1c** (0.23 mmol, 58 mg), 3-(4-fluorophenyl)-2*H*-chromen-2-one **1e** (0.23 mmol, 55 mg), **2a** (0.9 mmol, 81 μL), Pd$(OAc)_2$ (10 mol %, 5.15 mg), $K_2S_2O_8$ (2 equiv, 124 mg), and TFA/TFAA (2 mL, 9:1 v/v). The reaction mixture was refluxed with stirring in an oil bath at 90 °C for 3 h. After completion of reaction, the reaction mixture was cooled to an ambient temperature, basified with aqueous $NaHCO_3$ solution, and extracted with ethyl acetate (3 × 5 mL). The organic layer was washed with water (2 × 5 mL), and the combined organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel (100−200 mesh size) using *n*-hexane/ethyl acetate as the eluent, and a mixture of **3ca** and **3ea** was analyzed by ^{1}H NMR. The ratio of two **3ca** and **3ea** was found to be 1:2.7.

A similar procedure was followed for the competition experiment between **1g** and **1h** by taking 6-methoxy-3-phenyl-2*H*-chromen-2-one **1g** (0.23 mmol, 58 mg) and 6-chloro-3-phenyl-2*H*-chromen-2-one **1h** (0.23 mmol, 59 mg). The mixture of **3ga** and **3ha** obtained was analyzed by the ^{1}H NMR. The ratio of two **3ga** and **3ha** was found to be 2:1.

Procedure for Radical Scavenging Experiment. An oven-dried 10 mL round-bottom flask was charged with 3-phenyl-2*H*-chromen-2-one **1a** (0.23 mmol, 51 mg), methyl acrylate **2a** (0.9 mmol, 81 μL), Pd$(OAc)_2$ (10 mol %, 5.15 mg), $K_2S_2O_8$ (2 equiv, 124 mg), TEMPO or BHT (2 equiv) and TFA/TFAA (2 mL, 9:1 v/v), and TEMPO or BHT (2 equiv). The reaction mixture was refluxed with stirring in an oil bath at 90 °C for 3 h. The reaction mixture was cooled to an ambient temperature, basified with aqueous $NaHCO_3$ solution (5 mL), and then extracted with ethyl acetate (3 × 5 mL). The combined organic layer was washed with water (2 × 5 mL) and dried over anhydrous Na_2SO_4, and the solvent was evaporated under reduced pressure. The resulting residue was purified by column chromatography over silica gel 60 (100−200 mesh size) using *n*-hexane/ethyl acetate as an eluting system to give **3aa** in 77% (using TEMPO) and 76% (using BHT).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.joc.1c01097.

Copies of ^{1}H, ^{13}C{^{1}H} NMR, and single-crystal X-ray analysis of **3aa**, **5ab**, and **8a** (PDF)

Accession Codes

CCDC 1989999, 2071530, and 2071538 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Author Contributions

The manuscript was written through contributions of all authors. V.N.S. conducted all of the experimental work and collected spectral data. R.K. recorded and analyzed single-crystal X-ray data. V.N.S., D.K., and A.K. analyzed the spectral data. A.K. proposed and supervised the research work. All authors discussed the results, corrected the manuscript, and have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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