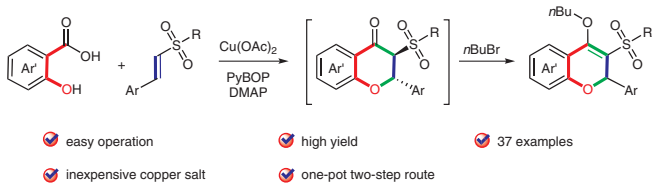
Synthesis M.-Y. Chang et al. Paper

Copper(II) Acetate Mediated Synthesis of 3-Sulfonyl-2-aryl-2*H*-chromenes

Meng-Yang Chang *[a,b]
Yu-Hsin Chen[a]
Han-Yu Chen[a]

[a] Department of Medicinal and Applied Chemistry, Kaohsiung Medical University, Kaohsiung 807, Taiwan, ROC
[b] Department of Medical Research, Kaohsiung Medical University Hospital, Kaohsiung 807, Taiwan, ROC
mychang@kmu.edu.tw



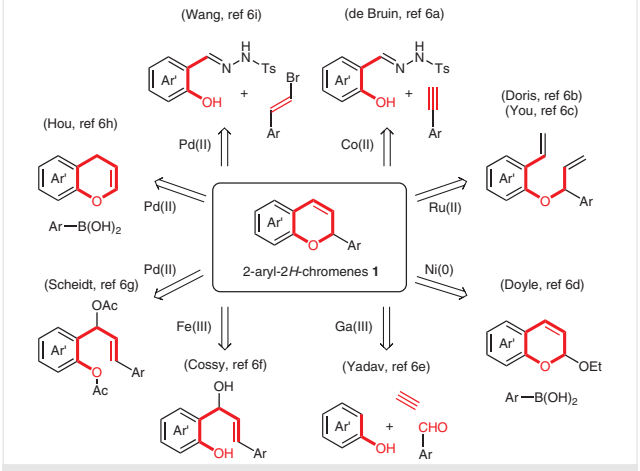
Received: 13.04.2019
Accepted after revision: 20.05.2019
Published online: 12.06.2019
DOI: 10.1055/s-0039-1689973; Art ID: ss-2019-h0221-op

Abstract This paper describes a concise, easy-operation, high-yielding method for the synthesis of 3-sulfonyl-2-aryl-2*H*-chromenes by a one-pot, straightforward two-step synthetic route, which includes (i) $Cu(OAc)_2$/PyBOP-mediated intermolecular [4+2] annulation of substituted salicylic acids with β-sulfonylstyrenes in the presence of DMAP in refluxing DMF, and (ii) sequential *O*-alkylation of the resulting sulfonylflavanones with *n*-butyl bromide. A plausible mechanism is proposed and discussed. This protocol provides a highly effective annulation via one carbon–oxygen (C–O) and one carbon–carbon (C–C) bond formations.

Key words copper(II) acetate, 2-aryl-2*H*-chromenes, salicylic acids, β-sulfonylstyrenes, intermolecular [4+2] annulation

2-Aryl-2*H*-chromene **1** is an important substructure[1] in a wide range of natural products[2a,b] (candenatenin E, hilgartene), bioactive molecules[2c] (acolbifene), and photochromic materials.[3] Due to the potential applications, the development of a one-pot synthetic route to access this motif has attracted significant attention and many attempts have been reported. The general approach toward 2-aryl-2*H*-chromenes **1** is based on a domino process by aldol condensation/oxa-Michael addition/reduction of substituted *o*-hydroxyacetophenones and benzaldehydes under basic conditions.[4] Typical organocatalyst-assisted formation of 2-aryl-2*H*-chromenes **1** has been investigated.[5] Recently, transition metals promoting the pioneering methods have been explored as the main strategies (Scheme 1).[6]

For example, de Bruin and co-workers reported that Co(II) complexes of porphyrins catalyze the metalloradical cyclization of salicyl *N*-tosylhydrazones with arylacetylenes.[6a] Both the Doris and You groups developed a Ru(II)-mediated ring-closing metathesis of *o*-*O*-allylstyrenes.[6b,c] Graham and Doyle demonstrated a Ni(0)-catalyzed cross-coupling of chromene acetals with arylboronic acids.[6d] Yadav and co-workers explored the Ga(III)-mediated multicomponent reaction of phenols, alkynes, and arylaldehydes.[6e] Cossy and co-workers described an Fe(III)-catalyzed intramolecular cyclization of *o*-(1-hydroxycinnamyl)phenols.[6f] The Scheidt group also reported a similar transformation with the Pd(II)-catalyzed facile annulation of *o*-(1-hydroxycinnamyl)phenol diacetates.[6g] Hou and co-workers examined the Pd(II)-catalyzed redox-relay Heck coupling of 4*H*-chromenes with arylboronic acids.[6h] Wang and co-workers studied the Pd(II)-catalyzed cross-coupling of salicyl *N*-tosylhydrazones with β-bromostyrenes.[6i] Environmentally benign synthetic methods have been developed by the Qu[7a] and Gois groups.[7b]



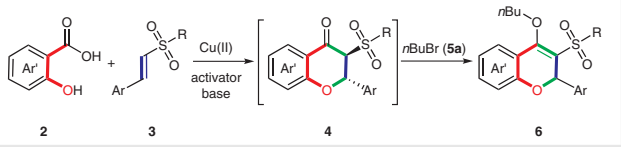
Scheme 1 Transition-metal-mediated synthetic routes to 2-aryl-2*H*-chromenes

Despite these advancements, some problems exist, such as multistep reactions, complicated catalytic systems, lack of broad substrate generality, and prefunctionalized frag-

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

ments. Therefore, further investigation of efficient synthetic methods toward 2-aryl-2*H*-chromenes **1** is still highly desired. Synthetic transformations from 2-aryl-2*H*-chromenes **1** to useful structural frameworks have been investigated, including dimerized chromenes, dihydrochalcones, flavones, and cyclopropylchromanes.[8]

Continuing our research on the synthetic applications of β-sulfonylstyrenes,[9a] we herein present a one-pot, copper(II) complex mediated synthesis of 3-sulfonyl-2-aryl-2*H*-chromenes **6** in the presence of an activator and a base via intermolecular [4+2] annulation of substituted salicylic acids **2** with β-sulfonylstyrenes **3**, followed by *O*-alkylation of the resulting sulfonylflavanones **4** with *n*-butyl bromide (**5a**), as shown in Scheme 2.

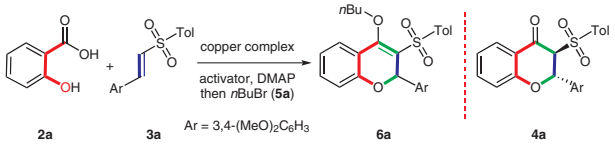


Scheme 2 Route to 3-sulfonyl-2-aryl-2*H*-chromenes **6**

In particular, so far there are no reports on the synthesis of 3-sulfonyl-2-aryl-2*H*-chromenes **6** with a pull–push nature.[10] In contrast to the literature on transition-metal-mediated reactions, we chose inexpensive copper complexes as the promoters to screen for the optimal reaction conditions. According to previous synthetic work,[9b] the initial study examining the formation of the 3-sulfonyl-2-aryl-2*H*-chromene skeleton commenced with the treatment of model substrates salicylic acid (**2a**, 0.3 mmol) and **3a** (Ar = 3,4-$(MeO)_2C_6H_3$, 0.33 mmol) using a combination of $Cu(OAc)_2$ (1.1 equiv), BOP (1.1 equiv), DMAP (1.1 equiv), and *n*BuBr (**5a**, 3.0 equiv) in $MeNO_2$ (3 mL). However, no reaction occurred at 25 °C for 5 or 25 hours (Table 1, entries 1, 2). In particular, when the reaction mixture was heated to reflux in $MeNO_2$ for 5 hours, two products, **4a** (78%) and **6a** (11%), were isolated (entry 3). With the aim of improving the yield of **6a**, the equivalents of **5a** were increased (3.0 → 10.0) during the process (entry 4). However, the ratio of **4a** and **6a** (1:7) was not enhanced. A reasonable hypothesis is that excess **5a** could be trapped by $MeNO_2$ (pK_a ~10) such that the transformation from **4a** to **6a** cannot be performed efficiently in the presence of DMAP.

When the reaction solvent was changed ($MeNO_2$ → DMF), the ratio of **4a** and **6a** was increased to 1:4 (16% and 65%) after 5 hours at 100 °C (entry 5). By elevating the reaction temperature to reflux, the ratio of **4a** and **6a** was enhanced to 1:15 (entry 6). However, an elongated time (10 h) did not alter the ratio (entry 7). Subsequently, another activator, PyBOP (a less toxic analogue of BOP), was examined (entry 8). An almost quantitative conversion from **4a** into **6a** was achieved. With DMAP and PyBOP controlled as base and activator, other copper(II) complexes were screened. For $Cu(OTf)_2$-mediated reaction conditions, the isolated

Table 1 Optimization of the Reaction Conditions[a]



Entry	Cu complex	Activator	Solvent	Temp	Time (h)	Yield (%) of **6a**[b]
1	$Cu(OAc)_2$	BOP	$MeNO_2$	25 °C	5	–[c]
2	$Cu(OAc)_2$	BOP	$MeNO_2$	25 °C	25	–[c]
3	$Cu(OAc)_2$	BOP	$MeNO_2$	reflux	5	11[d]
4[e]	$Cu(OAc)_2$	BOP	$MeNO_2$	reflux	5	72[d]
5	$Cu(OAc)_2$	BOP	DMF	100 °C	5	65[d]
6	$Cu(OAc)_2$	BOP	DMF	reflux	5	74[d]
7	$Cu(OAc)_2$	BOP	DMF	reflux	10	71[d]
8	$Cu(OAc)_2$	PyBOP	DMF	reflux	5	80
9	$Cu(OTf)_2$	PyBOP	DMF	reflux	5	70
10	CuF_2	PyBOP	DMF	reflux	5	32[f]
11	CuO	PyBOP	DMF	reflux	5	–[c]
12	$CuSO_4$	PyBOP	DMF	reflux	5	–[c]
13[g]	$Cu(OAc)_2$	PyBOP	DMF	reflux	5	–[c,d]
14[h]	$Cu(OAc)_2$	PyBOP	DMF	reflux	5	30
15[i]	$Cu(OAc)_2$	PyBOP	DMF	reflux	5	41

[a] Reaction conditions: **2a** (0.3 mmol), **3a** (1.1 equiv), Cu complex (1.1 equiv), activator (1.1 equiv), DMAP (40 mg, 0.33 mmol), *n*BuBr (**5a**, 140 mg, 1.0 mmol), solvent (3 mL).
[b] Isolated yields.
[c] Not detected.
[d] **4a** (entry 3, 78%; entry 4, 10%; entry 5, 16%; entries 6, 7, ~5%; entry 13, 89%).
[e] **5a** (10 equiv) used.
[f] **2a** and **3a** were recovered as major compounds.
[g] Without **5a**.
[h] $Cu(OAc)_2$ (0.3 equiv) used.
[i] $Cu(OAc)_2$ (0.5 equiv) used.

yield of **6a** (70%, entry 9) was slightly poorer than for $Cu(OAc)_2$. Using CuF_2, only 32% of **6a** was yielded along with the major recovery of starting materials **2a** and **3a** (entry 10). For CuO and $CuSO_4$, however, no desired **6a** (or **4a**) was detected (entries 11, 12). When **5a** was removed, only **4a** was isolated, in 89% yield (entry 13). Furthermore, catalytic amounts of $Cu(OAc)_2$ (0.3 and 0.5 equiv) were tested. However, **6a** was obtained in 30% and 41% yield, respectively (entries 14, 15).

From these observations, we concluded that the combination of $Cu(OAc)_2$ and PyBOP provided the optimal conditions (reflux, 5 h) in the presence of DMAP for a one-pot [4+2] annulation/*O*-*n*-butylation procedure. This expeditious synthetic route sets up a 3-sulfonyl-2-aryl-2*H*-chromene skeleton, including the formation of one C–O and one C–C bond via a formal [4+2] cycloaddition, under mild conditions.

To study the substrate scope and limitations of this one-pot route, **2** and **3** were reacted with the combination of $Cu(OAc)_2$/PyBOP/DMAP and **5a** to afford diversified **6**, as shown in Table 2. With the optimal conditions established (Table 1, entry 8), we found that this route allowed a direct intermolecular Baylis–Hillman-type annulation of phenoxide donor **2** with Michael acceptors **3** under easy-operation and open-vessel conditions in moderate to good yields (73–88%). Among entries 1–30, the efficient formation of **6a–6ad** showed that these substituents (Ar′ for **2a–2e**; Ar, R for **3a–3z**) did not affect the yield. Regarding the electronic nature of the aryl substituents of **2** and **3**, not only electron-neutral groups but also the electron-withdrawing 4-fluorophenyl group and electron-donating oxygenated groups were suitable. For sulfonyl aliphatic substituents (R) of **3**, both the methyl and *n*-butyl group were well-tolerated. Compounds **6ac** and **6ad** with a β-alkoxysulfonyl motif (entries 29 and 30) are the analogues of two bioactive compounds with potent antiviral (BW683C)[11a] and anti-inflammatory activities (TNF-α inhibitor),[11b] as shown in Figure 1. Furthermore, the molecular structures of **6b**, **6q**, **6x–6z** and **6ab** were determined by single-crystal X-ray crystallography.[12]

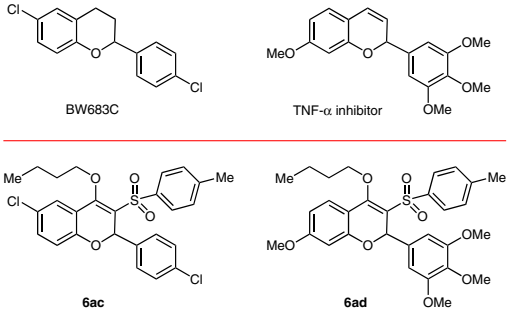
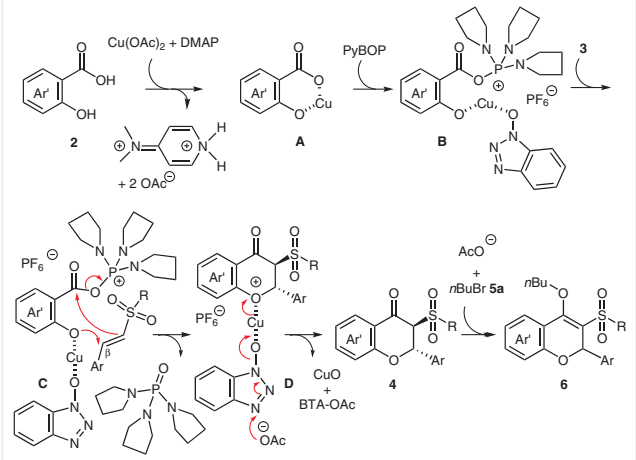


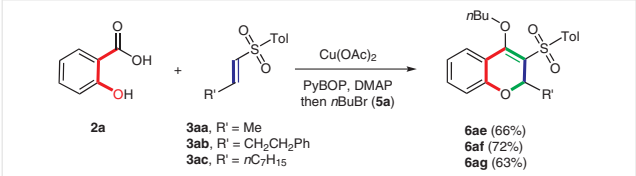
Figure 1 Structures of BW683C, a TNF-α inhibitor, **6ac**, and **6ad**

On the basis of the experimental results, a plausible mechanism for the formation of **6** is illustrated in Scheme 3. Initially, the DMAP-mediated complexation of $Cu(OAc)_2$ with the hydroxyl and carboxylic acid groups of **2** yields **A**.[13] By intermolecular cross-coupling of **A** with PyBOP, **B** should be afforded via O–P bond cleavage of PyBOP. Following the introduction of **3**, the oxy–copper arm of *in situ* generated **C** attacks the β-position of **3** via O–C bond formation. Subsequently, the corresponding formed α-anion promotes intramolecular C–C bond formation and the release of tripyrrolidinylphosphine oxide to produce **D**. Then, the construction of **4**, furnished via the acetate anion, mediates the removal of benzotriazoyl acetate (BTA-OAc) and copper oxide (CuO). Finally, the expeditious construction of **6** is furnished via another releasing acetate ion deprotonation of **4** followed by *O*-butylation of the resulting enolate of **4** with *n*BuBr (**5a**). After the reaction is complete (monitored by TLC), we find that there are a number of suspended brownish black particles generated in the product mixture. Furthermore, by the addition of 6 N $H_2SO_{4(aq)}$, the collected solids could be dissolved to form a blue solution. Therefore, we believe that CuO is produced. From the possible mechanism, we found that the stoichiometric amounts of $Cu(OAc)_2$, PyBOP, and DMAP required are at least 1 equivalent, such that a one-pot reaction provided a better yield of **6**.



Scheme 3 Plausible mechanism

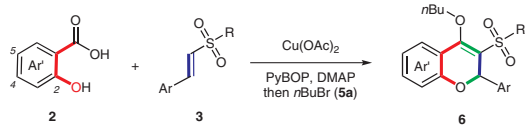
By replacing the aromatic (Ar) group with an aliphatic (R′) group as the β-substituent of **3**, the synthesis of sulfonylchromenes **6ae–6ag** was examined, as shown in Scheme 4. Under the optimal reactions conditions, the $Cu(OAc)_2$/PyBOP/DMAP-mediated cyclization of **2a** with **3aa–3ac** (R′ = Me, $(CH_2)_2Ph$, nC_7H_{15}) provided **6ae**, **6af**, and **6ag** in 66%, 72%, and 63% yield, respectively.



Scheme 4 Synthesis of **6ae–6ag**

Furthermore, when *n*-butyl bromide (**5a**) was changed to benzyl bromide (**5b**) (Scheme 5), the desired **6ah** was produced in 70% yield, along with the formation of **6ah-1** (11%), via one-pot annulation of **2a** with **3c**. For the generation of isomer **6ah-1**, we envision that the methyl group (for R) provides less steric hindrance to promotion of the occurrence of *C*-benzylation. Comparing the two alkyl bromides (butylation and benzylation), **5b** is more reactive than **5a** such that the opportunity for the selectivity of *C*-benzylation increases. Under similar conditions, however, treatment of **2a** with **3a** and **3e** provided the sole products **6ai** and **6aj** in 76% and 74% yield, respectively. Also, 1-naph-

Table 2 Synthesis of **6**[a]

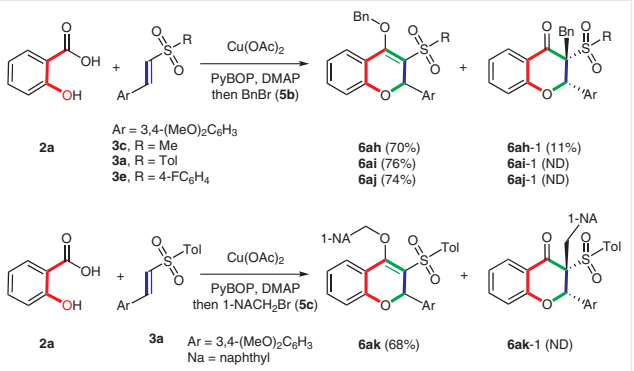


Entry	**2**, Ar′	**3**, Ar, R	Yield (%) of **6**[b]
1	**2a**, C_6H_4	**3a**, 3,4-$(MeO)_2C_6H_3$, Tol	**6a**, 80
2	**2a**, C_6H_4	**3b**, 3,4-$(MeO)_2C_6H_3$, Ph	**6b**, 84
3	**2a**, C_6H_4	**3c**, 3,4-$(MeO)_2C_6H_3$, Me	**6c**, 78
4	**2a**, C_6H_4	**3d**, 3,4-$(MeO)_2C_6H_3$, *n*Bu	**6d**, 78
5	**2a**, C_6H_4	**3e**, 3,4-$(MeO)_2C_6H_3$, 4-FC_6H_4	**6e**, 83
6	**2a**, C_6H_4	**3f**, 3,4-$(MeO)_2C_6H_3$, 4-$MeOC_6H_4$	**6f**, 86
7	**2a**, C_6H_4	**3g**, 3,4-$(MeO)_2C_6H_3$, 3-MeC_6H_4	**6g**, 80
8	**2a**, C_6H_4	**3h**, 3,4-$(MeO)_2C_6H_3$, 4-EtC_6H_4	**6h**, 81
9	**2a**, C_6H_4	**3i**, 3,4-$(MeO)_2C_6H_3$, 4-*i*PrC_6H_4	**6i**, 78
10	**2a**, C_6H_4	**3j**, 3,4-$(MeO)_2C_6H_3$, 4-*n*BuC_6H_4	**6j**, 76
11	**2a**, C_6H_4	**3k**, 3,4-$(MeO)_2C_6H_3$, 4-*t*BuC_6H_4	**6k**, 77
12	**2b**, 5-BrC_6H_3	**3a**, 3,4-$(MeO)_2C_6H_3$, Tol	**6l**, 73
13	**2c**, 5-ClC_6H_3	**3a**, 3,4-$(MeO)_2C_6H_3$, Tol	**6m**, 74
14	**2d**, $C_{10}H_6$ (2-naphthyl[c])	**3a**, 3,4-$(MeO)_2C_6H_3$, Tol	**6n**, 76
15	**2a**, C_6H_4	**3l**, Ph, Tol	**6o**, 84
16	**2a**, C_6H_4	**3m**, 4-$MeOC_6H_4$, Tol	**6p**, 86
17	**2a**, C_6H_4	**3n**, 3-$MeOC_6H_4$, Tol	**6q**, 88
18	**2a**, C_6H_4	**3o**, 4-FC_6H_4, Tol	**6r**, 76
19	**2a**, C_6H_4	**3p**, Tol, Tol	**6s**, 84
20	**2a**, C_6H_4	**3q**, 4-PhC_6H_4, Tol	**6t**, 73
21	**2a**, C_6H_4	**3r**, 2-naphthyl, Tol	**6u**, 78
22	**2a**, C_6H_4	**3s**, 3,4-$OCH_2OC_6H_3$, Tol	**6v**, 82
23	**2a**, C_6H_4	**3t**, 3,4-$Cl_2C_6H_3$, Tol	**6w**, 80
24	**2a**, C_6H_4	**3u**, 3,4,5-$(MeO)_3C_6H_2$, Tol	**6x**, 84
25	**2a**, C_6H_4	**3v**, 2-furyl, Tol	**6y**, 82
26	**2a**, C_6H_4	**3w**, 2-thienyl, Tol	**6z**, 83
27	**2a**, C_6H_4	**3x**, 3-pyridyl, Tol	**6aa**, 80
28	**2a**, C_6H_4	**3y**, 2-BrC_6H_4, Tol	**6ab**, 73
29	**2c**, 5-ClC_6H_3	**3z**, 4-ClC_6H_4, Tol	**6ac**, 79
30	**2e**, 4-$MeOC_6H_3$	**3u**, 3,4,5-$(MeO)_3C_6H_2$, Tol	**6ad**, 84

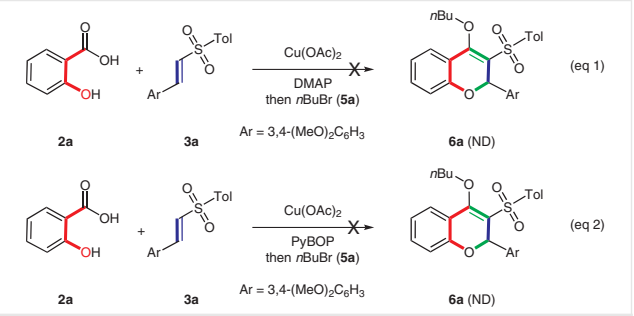
[a] Reaction conditions: **2a–2e** (0.3 mmol), **3a–3z** (1.1 equiv), $Cu(OAc)_2$ (60 mg, 0.33 mmol), PyBOP (172 mg, 0.33 mmol), DMAP (40 mg, 0.33 mmol), *n*BuBr (**5a**, 140 mg, 1.0 mmol), DMF (3 mL), 5 h, reflux.
[b] Isolated yields.
[c] **2d** = 1-hydroxy-2-naphthoic acid.

thylmethyl bromide (**5c**) afforded **6ak** in 68% yield (Scheme 5). The molecular structure of **6aj** was determined by single-crystal X-ray analysis.[12]

When the activator (PyBOP) was removed, no reaction was observed (Scheme 6, equation 1). On the other hand, the reaction could not be triggered in the absence of base (DMAP, equation 2). These two control experiments pointed out that PyBOP and DMAP are the key factors in effecting the tandem Michael addition–intramolecular cyclization.

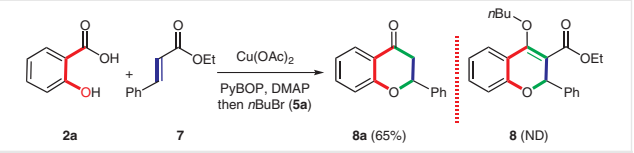


Scheme 5 Synthesis of **6ah–6ak** and **6ah-1** (ND = not detected)



Scheme 6 Control experiments (ND = not detected)

Under the optimal reaction conditions, this study examined replacement of the β-sulfonylstyrene with an α,β-unsaturated ethyl ester, as shown in Scheme 7. For the one-pot intermolecular [4+2] annulation of **2a** by treatment with **7**, however, the predicted *O*-*n*-butylated **8** could not be obtained. Interestingly, only **8a** was produced, in 65% yield, due to the reflux temperature triggering decarboxylation of the ethyl ester group. In the reaction process, there was no isolation of an *n*-butyl product. For the difference between β-sulfonylstyrene and α,β-unsaturated ethyl ester, we understand that the sulfonyl group could serve as a fastening substituent to stabilize *O*-butylation of the resulting sulfonylflavanones with *n*-butyl bromide under refluxing conditions. According to our results, the sulfonyl group plays a key electronic withdrawing role for constructing the framework of sulfonylchromenes.



Scheme 7 Reaction of **2a** and **7** (ND = not detected)

In summary, we have developed a $Cu(OAc)_2$/PyBOP/DMAP-mediated synthesis of sulfonylchromenes **6** in moderate to good yields via intermolecular [4+2] annulation of substituted salicylic acids **2** with β-sulfonylstyrenes **3**. The process provides a straightforward pathway for one carbon–oxygen and one carbon–carbon bond formations. The substrate scope and limitations were investigated for this facile and efficient transformation. Mechanistic investigations were undertaken and a plausible mechanism has been proposed. The molecular structures of key products were determined by X-ray crystal structure analysis. Further investigations regarding the synthetic application of β-sulfonylstyrenes are underway in our laboratory.

All reagents and solvents were commercial grade and were used without further purification. All reactions were routinely performed under a dry nitrogen atmosphere, with magnetic stirring. A heating mantle was used to provide a stable heat source. All products in organic solvents were dried with anhydrous $MgSO_4$ before concentration in vacuo. Melting points were obtained with an SMP3 melting point apparatus. ^1H (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on a Varian INOVA-400 spectrometer. Chemical shifts (δ) are reported in ppm and coupling constants (*J*) are given in hertz (Hz). High-resolution mass spectra were measured with a Bruker micrOTOF-Q double-focusing mass spectrometer by ESI using a hybrid ion trap. X-ray crystal structures were determined with a Bruker Enraf-Nonius single-crystal diffractometer (CAD4, Kappa CCD).

Skeleton 3; General Procedure[9a]

Ac_2O (510 mg, 5.0 mmol) was added to a stirred solution of arylacetaldehyde (5.0 mmol) at 25 °C. The mixture was stirred at 25 °C for 2 min. Polyphosphoric acid (490 mg, 5.0 mmol) was added slowly to the mixture at 25 °C for 3 min. The reaction mixture was stirred at 25 °C for 5 min. Then, sodium sulfonate (RSO_2Na, 10.0 mmol) was added to the mixture at 25 °C. The reaction mixture was stirred at 25 °C for 4 h. The residue was diluted with water (20 mL) and the mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with $NaHCO_3$ (3 × 10 mL) and brine, dried, filtered, and concentrated under reduced pressure to afford crude product. Purification on silica gel (hexanes/EtOAc, 8:1 to 4:1) afforded **3**. These materials are known compounds and their analytical data were consistent with the literature.[9a]

Skeleton 6 and Compound 4a; General Procedure

(Benzotriazol-1-yloxy)tripyrrolidinophosphonium hexafluorophosphate (PyBOP; 172 mg, 0.33 mmol) was added to a solution of salicylic acid **2** (0.3 mmol) and $Cu(OAc)_2$ (60 mg, 0.33 mmol) in DMF (2 mL) at 25 °C. The reaction mixture was stirred at 25 °C for 5 min. DMAP (40 mg, 0.33 mmol) was added and the reaction mixture was stirred at reflux for 2 h, then cooled to 25 °C. β-Sulfonylstyrene **3** (0.33 mmol) in DMF (1 mL) was added at 25 °C and the reaction mixture was stirred at reflux for an additional 1 h, then cooled to 25 °C. Then, bromide **5** (1.0 mmol) was added at 25 °C and the reaction mixture was stirred at reflux for an additional 2 h (monitored by TLC), then cooled to 25 °C and concentrated. The residue was diluted with water (10 mL) and the mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with brine, dried, filtered, and concentrated under reduced pressure to afford crude product. Purification on silica gel (hexanes/EtOAc, 8:1 to 4:1) afforded **6** and **4a**.

4-*n*-Butoxy-2-(3,4-dimethoxyphenyl)-3-(4-tolylsulfonyl)-2*H*-chromene (6a)

Yield: 119 mg (80%); colorless solid; mp 142–144 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59 (d, *J* = 8.4 Hz, 2 H), 7.28 (dd, *J* = 1.6, 7.6 Hz, 1 H), 7.21–7.17 (m, 3 H), 6.90 (dt, *J* = 0.8, 8.4 Hz, 1 H), 6.79–6.75 (m, 2 H), 6.72 (d, *J* = 2.0 Hz, 1 H), 6.63 (d, *J* = 8.4 Hz, 1 H), 6.45 (s, 1 H), 4.06–4.01 (m, 1 H), 3.92–3.86 (m, 1 H), 3.80 (s, 3 H), 3.62 (s, 3 H), 2.37 (s, 3 H), 1.93–1.85 (m, 2 H), 1.55–1.48 (m, 2 H), 1.02 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.0, 155.5, 149.4, 148.6, 143.9, 139.2, 132.8, 129.4, 129.0 (2 ×), 128.0 (2 ×), 124.0, 121.5, 120.82, 120.75, 118.1, 118.0, 111.0, 110.5, 76.1, 74.8, 55.7, 55.5, 32.0, 21.5, 19.0, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{28}H_{31}O_6S$: 495.1841; found: 495.1842.

2-(3,4-Dimethoxyphenyl)-3-(4-tolylsulfonyl)chroman-4-one (4a; For Table 1, Entry 5)

Yield: 21 mg (16%); colorless solid; mp 156–158 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72–7.68 (m, 3 H), 7.42 (dt, *J* = 1.6, 8.0 Hz, 1 H), 7.22 (d, *J* = 8.8 Hz, 2 H), 6.92 (dt, *J* = 0.8, 8.0 Hz, 1 H), 6.85 (dd, *J* = 0.8, 8.0 Hz, 1 H), 6.77 (s, 1 H), 6.68 (br s, 2 H), 6.49 (s, 1 H), 4.40 (d, *J* = 1.2 Hz, 1 H), 3.77 (s, 3 H), 3.75 (s, 3 H), 2.36 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 182.3, 158.8, 149.3, 145.6, 137.2, 134.2, 129.5 (2 ×), 129.4 (3 ×), 128.4, 126.8, 121.6, 120.8, 118.6, 118.2, 110.9, 109.6, 76.1, 72.7, 55.8, 55.8, 21.6.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{23}O_6S$: 439.1215; found: 439.1216.

Single-crystal X-ray analysis: crystals of **4a** were grown by slow diffusion of EtOAc into a solution of **4a** in CH_2Cl_2, which yielded colorless prisms. Compound **4a** crystallized in the monoclinic crystal system, space group $P2_1/c$, *a* = 21.002(3) Å, *b* = 11.9195(15) Å, *c* = 8.3067(11) Å, *V* = 2062.6(5) Å^3, *Z* = 4, d_{calcd} = 1.412 g/cm^3, *F*(000) = 920, 2θ range 0.977–26.475°, *R* indices (all data) R_1 = 0.0488, wR_2 = 0.1084.

4-*n*-Butoxy-2-(3,4-dimethoxyphenyl)-3-(phenylsulfonyl)-2*H*-chromene (6b)

Yield: 121 mg (84%); colorless solid; mp 101–103 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.73–7.70 (m, 2 H), 7.53–7.49 (m, 1 H), 7.40–7.36 (m, 2 H), 7.28 (dd, *J* = 1.6, 8.0 Hz, 1 H), 7.20 (ddt, *J* = 0.4, 1.6, 7.6 Hz, 1 H), 6.90 (dt, *J* = 0.4, 7.6 Hz, 1 H), 6.78–6.74 (m, 2 H), 6.72 (d, *J* = 2.0 Hz, 1 H), 6.61 (d, *J* = 8.4 Hz, 1 H), 6.46 (s, 1 H), 4.07–4.02 (m, 1 H), 3.91–3.85 (m, 1 H), 3.79 (s, 3 H), 3.61 (s, 3 H), 1.93–1.85 (m, 2 H), 1.57–1.46 (m, 2 H), 1.01 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.3, 155.6, 149.5, 148.6, 142.1, 133.0, 132.9, 129.3, 128.4 (2 ×), 127.9 (2 ×), 124.1, 121.5, 120.8, 120.4, 118.1 (2 ×), 111.0, 110.5, 76.1, 74.9, 55.7, 55.5, 31.9, 19.0, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{29}O_6S$: 481.1685; found: 481.1685.

Single-crystal X-ray analysis: crystals of **6b** were grown by slow diffusion of EtOAc into a solution of **6b** in CH_2Cl_2, which yielded colorless prisms. Compound **6b** crystallized in the monoclinic crystal system, space group $P2_1/c$, *a* = 12.1123(7) Å, *b* = 23.2762(17) Å, *c* = 8.6774(7) Å, *V* = 391.1(3) Å^3, *Z* = 4, d_{calcd} = 1.335 g/cm^3, *F*(000) = 1016, 2θ range 1.930–26.531°, *R* indices (all data) R_1 = 0.0489, wR_2 = 0.1181.

4-*n*-Butoxy-2-(3,4-dimethoxyphenyl)-3-(methylsulfonyl)-2*H*-chromene (6c)

Yield: 98 mg (78%); colorless gum.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39 (dd, *J* = 2.0, 8.0 Hz, 1 H), 7.26 (dt, *J* = 1.6, 8.0 Hz, 1 H), 6.98 (dt, *J* = 0.8, 7.6 Hz, 1 H), 6.93 (d, *J* = 1.6 Hz, 1 H), 6.89 (dd, *J* = 2.0, 8.4 Hz, 1 H), 6.81 (dd, *J* = 0.4, 8.4 Hz, 1 H), 6.72 (d, *J* = 8.4 Hz, 1 H), 6.29 (s, 1 H), 4.18–4.04 (m, 2 H), 3.81 (s, 3 H), 3.80 (s, 3 H), 3.06 (s, 3 H), 1.93–1.86 (m, 2 H), 1.60–1.52 (m, 2 H), 1.02 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.5, 155.7, 149.7, 149.1, 133.1, 129.9, 124.0, 121.6, 120.1, 119.7, 118.1, 117.9, 110.9, 110.7, 75.5, 75.2, 55.80, 55.76, 44.2, 32.0, 19.1, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{27}O_6S$: 419.1528; found: 419.1529.

4-*n*-Butoxy-3-(*n*-butylsulfonyl)-2-(3,4-dimethoxyphenyl)-2*H*-chromene (6d)

Yield: 108 mg (78%); colorless gum.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38 (dd, *J* = 1.6, 8.0 Hz, 1 H), 7.24 (dt, *J* = 1.6, 8.0 Hz, 1 H), 6.96 (dt, *J* = 1.2, 8.0 Hz, 1 H), 6.91–6.89 (m, 2 H), 6.80 (dd, *J* = 1.2, 8.4 Hz, 1 H), 6.71 (d, *J* = 8.8 Hz, 1 H), 6.26 (s, 1 H), 4.17–4.12 (m, 1 H), 4.07–4.01 (m, 1 H), 3.78 (s, 3 H), 3.76 (s, 3 H), 3.30–3.23 (m, 1 H), 3.07–2.99 (m, 1 H), 1.90–1.83 (m, 2 H), 1.68–1.60 (m, 2 H), 1.58–1.48 (m, 2 H), 1.40–1.30 (m, 2 H), 1.00 (t, *J* = 7.2 Hz, 3 H), 0.84 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.2, 155.6, 149.5, 148.8, 133.0, 130.1, 124.0, 121.5, 119.8, 119.4, 117.9 (2 ×), 110.7, 110.6, 75.6, 75.0, 55.73, 55.65, 55.62, 31.8, 23.4, 21.5, 18.9, 13.7, 13.4.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{33}O_6S$: 461.1998; found: 461.1999.

4-*n*-Butoxy-2-(3,4-dimethoxyphenyl)-3-[(4-fluorophenyl)sulfonyl]-2*H*-chromene (6e)

Yield: 124 mg (83%); colorless solid; mp 137–139 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70–7.65 (m, 2 H), 7.29 (dd, *J* = 1.6, 7.6 Hz, 1 H), 7.20 (dt, *J* = 1.6, 8.0 Hz, 1 H), 7.08–7.00 (m, 2 H), 6.91 (dt, *J* = 0.8, 8.4 Hz, 1 H), 6.77–6.74 (m, 2 H), 6.68 (dd, *J* = 2.0, 8.0 Hz, 1 H), 6.59 (d, *J* = 8.4 Hz, 1 H), 6.42 (s, 1 H), 4.10–4.05 (m, 1 H), 4.00–3.91 (m, 1 H), 3.79 (s, 3 H), 3.65 (s, 3 H), 1.95–1.87 (m, 2 H), 1.58–1.48 (m, 2 H), 1.03 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.3 (d, *J* = 253.9 Hz), 157.4, 155.6, 149.6, 148.7, 138.1 (d, *J* = 3.1 Hz), 133.0, 130.7 (d, *J* = 9.1 Hz, 2 ×), 129.1, 124.0, 121.6, 120.7, 120.3, 118.1, 117.9, 115.5 (d, *J* = 21.9 Hz, 2 ×), 111.1, 110.4, 76.1, 75.1, 55.7, 55.6, 32.0, 19.0, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{28}FO_6S$: 499.1591; found: 499.1593.

4-*n*-Butoxy-2-(3,4-dimethoxyphenyl)-3-[(4-methoxyphenyl)sulfonyl]-2*H*-chromene (6f)

Yield: 132 mg (86%); colorless gum.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62 (d, *J* = 8.8 Hz, 2 H), 7.28 (dd, *J* = 1.6, 7.6 Hz, 1 H), 7.19 (dt, *J* = 1.6, 8.0 Hz, 1 H), 6.90 (dt, *J* = 0.8, 8.4 Hz, 1 H), 6.84 (d, *J* = 8.8 Hz, 2 H), 6.77–6.73 (m, 3 H), 6.62 (d, *J* = 9.2 Hz, 1 H), 6.43 (s, 1 H), 4.07–4.01 (m, 1 H), 3.97–3.90 (m, 1 H), 3.82 (s, 3 H), 3.80 (s, 3 H), 3.65 (s, 3 H), 1.95–1.87 (m, 2 H), 1.56–1.49 (m, 2 H), 1.03 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.2, 156.6, 155.5, 149.5, 148.6, 133.8, 132.7, 130.2 (2 ×), 129.4, 124.0, 121.5, 121.2, 120.8, 118.2, 118.0, 113.6 (2 ×), 111.1, 110.5, 76.2, 74.9, 55.8, 55.6 (2 ×), 32.0, 19.0, 14.0.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{28}H_{31}O_7S$: 511.1791; found: 511.1792.

4-*n*-Butoxy-2-(3,4-dimethoxyphenyl)-3-(3-tolylsulfonyl)-2*H*-chromene (6g)

Yield: 119 mg (80%); colorless solid; mp 121–123 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.57–7.54 (m, 1 H), 7.37 (br s, 1 H), 7.33–7.26 (m, 3 H), 7.20 (dt, *J* = 1.6, 8.0 Hz, 1 H), 6.91 (dt, *J* = 1.2, 7.6 Hz, 1 H), 6.78 (dd, *J* = 2.0, 8.0 Hz, 1 H), 6.77 (d, *J* = 8.8 Hz, 2 H), 6.74 (d, *J* = 8.4 Hz, 1 H), 6.45 (s, 1 H), 4.07–4.01 (m, 1 H), 3.95–3.86 (m, 1 H), 3.80 (s, 3 H), 3.62 (s, 3 H), 2.27 (s, 3 H), 1.93–1.85 (m, 2 H), 1.58–1.49 (m, 2 H), 1.02 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.1, 155.6, 149.5, 148.7, 141.9, 138.5, 133.7, 132.9, 129.4, 128.5, 128.3, 125.1, 124.0, 121.5, 120.9, 120.8, 118.09, 118.06, 111.1, 110.5, 76.2, 74.8, 55.8, 55.6, 32.0, 21.1, 19.0, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{28}H_{31}O_6S$: 495.1841; found: 495.1840.

4-*n*-Butoxy-2-(3,4-dimethoxyphenyl)-3-[(4-ethylphenyl)sulfonyl]-2*H*-chromene (6h)

Yield: 123 mg (81%); colorless solid; mp 114–116 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62 (d, *J* = 8.0 Hz, 2 H), 7.28 (dd, *J* = 1.6, 7.6 Hz, 1 H), 7.19 (d, *J* = 8.4 Hz, 2 H), 6.89 (dt, *J* = 0.8, 7.6 Hz, 1 H), 6.77 (dt, *J* = 2.0, 8.4 Hz, 1 H), 6.79–6.75 (m, 2 H), 6.71 (d, *J* = 2.0 Hz, 1 H), 6.62 (d, *J* = 8.4 Hz, 1 H), 6.45 (s, 1 H), 4.06–4.00 (m, 1 H), 3.92–3.84 (m, 1 H), 3.78 (s, 3 H), 3.59 (s, 3 H), 2.66 (q, *J* = 7.6 Hz, 2 H), 1.92–1.84 (m, 2 H), 1.56–1.46 (m, 2 H), 1.21 (t, *J* = 7.6 Hz, 3 H), 1.01 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.9, 155.5, 150.0, 149.4, 148.5, 139.4, 132.8, 129.3, 128.0 (2 ×), 127.8 (2 ×), 124.0, 121.4, 120.8, 120.7, 118.1, 118.0, 111.0, 110.5, 76.1, 74.8, 55.7, 55.5, 31.9, 28.7, 19.0, 15.1, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{29}H_{33}O_6S$: 509.1998; found: 509.1997.

4-*n*-Butoxy-2-(3,4-dimethoxyphenyl)-3-[(4-isopropylphenyl)sulfonyl]-2*H*-chromene (6i)

Yield: 122 mg (78%); colorless gum.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63 (d, *J* = 8.4 Hz, 2 H), 7.29 (dd, *J* = 1.6, 7.6 Hz, 1 H), 7.22 (d, *J* = 8.0 Hz, 2 H), 7.18 (dt, *J* = 0.8, 7.6 Hz, 1 H), 6.89 (dt, *J* = 1.2, 7.6 Hz, 1 H), 6.78–6.74 (m, 2 H), 6.69 (d, *J* = 2.0 Hz, 1 H), 6.61 (d, *J* = 8.0 Hz, 1 H), 6.45 (s, 1 H), 4.06–4.00 (m, 1 H), 3.92–3.83 (m, 1 H), 3.78 (s, 3 H), 3.58 (s, 3 H), 2.95–2.88 (m, 1 H), 1.92–1.84 (m, 2 H), 1.54–1.47 (m, 2 H), 1.21 (d, *J* = 6.8 Hz, 6 H), 1.01 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.9, 155.5, 154.5, 149.3, 148.5, 139.5, 132.7, 129.3, 128.1 (2 ×), 126.5 (2 ×), 124.0, 121.4, 120.8, 120.6, 118.1, 118.0, 110.9, 110.5, 76.1, 74.8, 55.7, 55.4, 34.1, 31.9, 23.6, 23.5, 18.9, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{30}H_{35}O_6S$: 523.2154; found: 523.2155.

4-*n*-Butoxy-3-[(4-*n*-butylphenyl)sulfonyl]-2-(3,4-dimethoxyphenyl)-2*H*-chromene (6j)

Yield: 122 mg (76%); colorless gum.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62 (d, *J* = 8.4 Hz, 2 H), 7.28 (dd, *J* = 1.6, 7.6 Hz, 1 H), 7.20 (dt, *J* = 0.8, 7.6 Hz, 1 H), 7.18 (d, *J* = 8.4 Hz, 2 H), 6.90 (t, *J* = 7.6 Hz, 1 H), 6.77–6.73 (m, 3 H), 6.61 (d, *J* = 8.0 Hz, 1 H), 6.45 (s, 1 H), 4.06–4.00 (m, 1 H), 3.88–3.83 (m, 1 H), 3.79 (s, 3 H), 3.61 (s, 3 H), 2.62 (t, *J* = 7.6 Hz, 2 H), 1.92–1.84 (m, 2 H), 1.60–1.46 (m, 4 H), 1.37–1.25 (m, 2 H), 1.01 (t, *J* = 7.6 Hz, 3 H), 0.91 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.0, 155.5, 149.4, 148.7, 148.6, 139.4, 132.8, 129.4, 128.4 (2 ×), 128.0 (2 ×), 124.0, 121.5, 120.8, 120.7, 118.2, 118.0, 111.0, 110.5, 76.1, 74.8, 55.7, 55.5, 35.5, 33.1, 32.0, 22.2, 19.0, 13.9, 13.8.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{31}H_{37}O_6S$: 537.2311; found: 537.2310.

4-*n*-Butoxy-3-[(4-*tert*-butylphenyl)sulfonyl]-2-(3,4-dimethoxyphenyl)-2*H*-chromene (6k)

Yield: 124 mg (77%); colorless gum.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 8.8 Hz, 2 H), 7.37 (d, *J* = 8.4 Hz, 2 H), 7.29 (dd, *J* = 1.6, 7.6 Hz, 1 H), 7.17 (dt, *J* = 1.6, 7.6 Hz, 1 H), 6.89 (dt, *J* = 1.2, 7.6 Hz, 1 H), 6.78–6.74 (m, 2 H), 6.69 (d, *J* = 2.0 Hz, 1 H), 6.60 (d, *J* = 8.4 Hz, 1 H), 6.45 (s, 1 H), 4.06–4.00 (m, 1 H), 3.89–3.82 (m, 1 H), 3.77 (s, 3 H), 3.57 (s, 3 H), 1.92–1.84 (m, 2 H), 1.54–1.47 (m, 2 H), 1.28 (s, 9 H), 1.01 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.9, 156.7, 155.4, 149.3, 148.5, 139.1, 132.7, 129.3, 127.7 (2 ×), 125.3 (2 ×), 124.0, 121.4, 120.8, 120.6, 118.1, 117.9, 110.9, 110.4, 76.1, 74.8, 55.6, 55.4, 35.0, 31.9, 30.9 (3 ×), 18.9, 13.8.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{31}H_{37}O_6S$: 537.2311; found: 537.2311.

6-Bromo-4-*n*-butoxy-2-(3,4-dimethoxyphenyl)-3-(4-tolylsulfonyl)-2*H*-chromene (6l)

Yield: 125 mg (73%); colorless gum.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55 (d, *J* = 8.4 Hz, 2 H), 7.38 (d, *J* = 2.0 Hz, 1 H), 7.26 (dd, *J* = 2.4, 8.8 Hz, 1 H), 7.17 (d, *J* = 7.6 Hz, 2 H), 6.70 (dt, *J* = 2.0, 8.0 Hz, 1 H), 6.69 (s, 1 H), 6.64 (d, *J* = 8.4 Hz, 1 H), 6.62 (d, *J* = 8.0 Hz, 1 H), 6.44 (s, 1 H), 4.05–3.94 (m, 2 H), 3.81 (s, 3 H), 3.64 (s, 3 H), 2.38 (s, 3 H), 1.95–1.86 (m, 2 H), 1.58–1.51 (m, 2 H), 1.04 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.5, 154.4, 149.6, 148.7, 144.1, 138.8, 135.3, 129.0 (2 ×), 128.7, 128.1 (2 ×), 126.5, 122.0, 120.8, 120.0, 119.8, 113.7, 111.1, 110.5, 76.4, 75.1, 55.8, 55.5, 31.9, 21.5, 18.9, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{28}H_{30}BrO_6S$: 573.0947; found: 573.0948.

4-*n*-Butoxy-6-chloro-2-(3,4-dimethoxyphenyl)-3-(4-tolylsulfonyl)-2*H*-chromene (6m)

Yield: 117 mg (74%); colorless gum.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.53 (d, *J* = 8.0 Hz, 2 H), 7.23 (d, *J* = 2.4 Hz, 1 H), 7.17 (d, *J* = 8.0 Hz, 2 H), 7.12 (dd, *J* = 2.8, 8.8 Hz, 1 H), 6.72–6.68 (m, 3 H), 6.62 (d, *J* = 8.4 Hz, 1 H), 6.43 (s, 1 H), 4.06–3.93 (m, 2 H), 3.80 (s, 3 H), 3.63 (s, 3 H), 2.37 (s, 3 H), 1.95–1.86 (m, 2 H), 1.58–1.50 (m, 2 H), 1.03 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.7, 153.9, 149.7, 148.7, 144.1, 138.8, 132.4, 129.0 (2 ×), 128.8, 128.1 (2 ×), 126.6, 123.6, 122.1, 120.9, 119.6, 119.4, 111.1, 110.5, 76.4, 75.1, 55.8, 55.5, 31.9, 21.5, 18.9, 13.8.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{28}H_{30}ClO_6S$: 529.1452; found: 529.1451.

4-*n*-Butoxy-2-(3,4-dimethoxyphenyl)-3-(4-tolylsulfonyl)-2*H*-benzo[*h*]chromene (6n)

Yield: 124 mg (76%); colorless solid; mp 156–158 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17 (dd, *J* = 1.2, 7.6 Hz, 1 H), 7.73 (d, *J* = 8.4 Hz, 2 H), 7.69 (dd, *J* = 1.2, 7.2 Hz, 1 H), 7.50–7.41 (m, 2 H), 7.35 (d, *J* = 8.8 Hz, 1 H), 7.31 (d, *J* = 8.4 Hz, 1 H), 7.23 (d, *J* = 8.0 Hz, 2 H), 6.89 (dd, *J* = 2.0, 8.0 Hz, 1 H), 6.85 (d, *J* = 2.0 Hz, 1 H), 6.73 (s, 1 H), 6.59 (d, *J* = 8.0 Hz, 1 H), 4.09–4.03 (m, 1 H), 3.85–3.80 (m, 1 H), 3.74 (s, 3 H), 3.60 (s, 3 H), 2.40 (s, 3 H), 1.94–1.86 (m, 2 H), 1.59–1.43 (m, 2 H), 1.02 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.1, 152.9, 149.4, 148.5, 143.8, 139.6, 135.7, 129.7, 129.1 (2 ×), 128.3, 128.0 (2 ×), 127.6, 126.2, 125.1, 122.6, 121.0, 120.5, 120.0, 118.0, 112.6, 110.7, 110.5, 76.5, 74.8, 55.7, 55.4, 32.0, 21.5, 19.0, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{32}H_{33}O_6S$: 545.1998; found: 545.1996.

4-*n*-Butoxy-2-phenyl-3-(4-tolylsulfonyl)-2*H*-chromene (6o)

Yield: 109 mg (84%); colorless solid; mp 119–121 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55 (d, *J* = 8.4 Hz, 2 H), 7.30–7.15 (m, 9 H), 6.90 (dt, *J* = 1.2, 7.6 Hz, 1 H), 6.77 (dd, *J* = 1.2, 8.4 Hz, 1 H), 6.51 (s, 1 H), 4.08–4.03 (m, 1 H), 3.93–3.88 (m, 1 H), 2.38 (s, 3 H), 1.94–1.85 (m, 2 H), 1.56–1.49 (m, 2 H), 1.03 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.0, 155.6, 143.9, 139.1, 137.1, 132.8, 129.0 (2 ×), 128.9, 128.3 (2 ×), 128.02 (2 ×), 127.99 (2 ×), 124.2, 121.5, 120.7, 118.0, 117.9, 76.3, 74.7, 32.0, 21.5, 19.0, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{27}O_4S$: 435.1630; found: 435.1632.

4-*n*-Butoxy-2-(4-methoxyphenyl)-3-(4-tolylsulfonyl)-2*H*-chromene (6p)

Yield: 120 mg (86%); colorless solid; mp 118–120 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55 (d, *J* = 8.0 Hz, 2 H), 7.28 (dd, *J* = 1.2, 8.0 Hz, 1 H), 7.21–7.15 (m, 5 H), 6.90 (dt, *J* = 1.2, 8.4 Hz, 1 H), 6.75 (dt, *J* = 0.8, 8.4 Hz, 1 H), 6.69 (d, *J* = 8.8 Hz, 2 H), 6.46 (s, 1 H), 4.07–4.01 (m, 1 H), 3.93–3.88 (m, 1 H), 3.73 (s, 3 H), 2.38 (s, 3 H), 1.93–1.85 (m, 2 H), 1.56–1.49 (m, 2 H), 1.03 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 160.0, 156.8, 155.5, 143.8, 139.1, 132.7, 129.5 (2 ×), 129.2, 129.0 (2 ×), 128.0 (2 ×), 124.1, 121.4, 120.8, 118.01, 117.96, 113.6 (2 ×), 75.8, 74.7, 55.1, 31.9, 21.5, 19.0, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{29}O_5S$: 465.1736; found: 465.1734.

4-*n*-Butoxy-2-(3-methoxyphenyl)-3-(4-tolylsulfonyl)-2*H*-chromene (6q)

Yield: 122 mg (88%); colorless solid; mp 133–135 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59 (d, *J* = 8.4 Hz, 2 H), 7.28 (dd, *J* = 1.2, 8.4 Hz, 1 H), 7.21–7.16 (m, 3 H), 7.08 (dt, *J* = 1.2, 7.6 Hz, 1 H), 6.90 (dt, *J* = 1.2, 8.4 Hz, 1 H), 6.84 (d, *J* = 7.6 Hz, 1 H), 6.79–6.77 (m, 3 H), 6.49 (s, 1 H), 4.08–4.02 (m, 1 H), 3.92–3.86 (m, 1 H), 3.63 (s, 3 H), 2.37 (s, 3 H), 1.93–1.85 (m, 2 H), 1.57–1.46 (m, 2 H), 1.02 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.4, 157.1, 155.6, 143.9, 139.1, 138.4, 132.8, 130.2, 129.3, 129.0 (2 ×), 128.9, 128.0 (2 ×), 124.2, 121.5, 120.3, 117.9, 114.7, 113.3, 76.1, 74.8, 54.9, 31.9, 21.5, 19.0, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{29}O_5S$: 465.1736; found: 465.1735.

Single-crystal X-ray analysis: crystals of **6q** were grown by slow diffusion of EtOAc into a solution of **6q** in CH_2Cl_2, which yielded colorless prisms. Compound **6q** crystallized in the monoclinic crystal system, space group $P2_1/n$, *a* = 6.727(3) Å, *b* = 12.012(5) Å, *c* = 28.621(14) Å, *V* = 2312.6(19) Å^3, *Z* = 4, d_{calcd} = 1.334 g/cm^3, *F*(000) = 984, 2θ range 1.423–27.009°, *R* indices (all data) R_1 = 0.1112, wR_2 = 0.1804.

4-*n*-Butoxy-2-(4-fluorophenyl)-3-(4-tolylsulfonyl)-2*H*-chromene (6r)

Yield: 103 mg (76%); colorless solid; mp 153–155 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58 (d, *J* = 8.4 Hz, 2 H), 7.28 (dd, *J* = 1.6, 8.0 Hz, 1 H), 7.25–7.18 (m, 5 H), 6.92 (dt, *J* = 1.2, 8.4 Hz, 1 H), 6.90–6.84 (m, 2 H), 6.77 (dt, *J* = 0.8, 8.4 Hz, 1 H), 6.48 (s, 1 H), 4.07–4.01 (m, 1 H), 3.90–3.84 (m, 1 H), 2.39 (s, 3 H), 1.92–1.84 (m, 2 H), 1.55–1.46 (m, 2 H), 1.02 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.0 (d, *J* = 246.4 Hz), 157.1, 155.4, 144.1, 139.1, 133.1 (d, *J* = 3.1 Hz), 133.0, 130.0 (d, *J* = 8.4 Hz, 2 ×), 129.1 (2 ×), 128.0 (2 ×), 124.3, 121.6, 120.6, 118.02, 117.99, 115.3 (d, *J* = 22.0 Hz, 2 ×), 75.5, 74.8, 32.0, 21.5, 19.0, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{26}FO_4S$: 453.1536; found: 453.1536.

4-*n*-Butoxy-2-(4-tolyl)-3-(4-tolylsulfonyl)-2*H*-chromene (6s)

Yield: 113 mg (84%); colorless gum.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56 (d, *J* = 8.4 Hz, 2 H), 7.27 (dd, *J* = 1.6, 8.0 Hz, 1 H), 7.21–7.12 (m, 5 H), 6.98 (d, *J* = 7.6 Hz, 2 H), 6.89 (dt, *J* = 1.2, 7.6 Hz, 1 H), 6.76 (dt, *J* = 0.8, 8.4 Hz, 1 H), 6.47 (s, 1 H), 4.07–4.01 (m, 1 H), 3.92–3.86 (m, 1 H), 2.39 (s, 3 H), 2.27 (s, 3 H), 1.92–1.84 (m, 2 H), 1.57–1.49 (m, 2 H), 1.02 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.0, 155.7, 143.8, 139.2, 138.8, 134.1, 132.8, 129.0 (4 ×), 128.1 (2 ×), 128.0 (2 ×), 124.2, 121.4, 120.8, 118.2, 118.0, 76.1, 74.7, 32.0, 21.6, 21.1, 19.0, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{29}O_4S$: 449.1787; found: 449.1785.

2-(1,1′-Biphenyl-4-yl)-4-*n*-butoxy-3-(4-tolylsulfonyl)-2*H*-chromene (6t)

Yield: 112 mg (73%); colorless solid; mp 145–147 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, *J* = 8.4 Hz, 2 H), 7.53–7.50 (m, 2 H), 7.44–7.40 (m, 4 H), 7.36–7.31 (m, 4 H), 7.25–7.11 (m, 3 H), 6.93 (dt, *J* = 1.2, 8.0 Hz, 1 H), 6.82 (dd, *J* = 0.8, 8.4 Hz, 1 H), 6.57 (s, 1 H), 4.11–4.05 (m, 1 H), 3.95–3.90 (m, 1 H), 2.38 (s, 3 H), 1.95–1.87 (m, 2 H), 1.60–1.49 (m, 2 H), 1.04 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.0, 155.6, 143.9, 141.8, 140.4, 139.2, 136.1, 132.9, 129.0 (2 ×), 128.7 (2 ×), 128.5 (2 ×), 128.0 (2 ×), 127.5, 127.04 (2 ×), 126.99 (2 ×), 124.3, 121.5, 120.7, 118.1, 118.0, 76.1, 74.8, 32.0, 21.5, 19.0, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{32}H_{31}O_4S$: 511.1943; found: 511.1943.

4-*n*-Butoxy-2-(naphthalen-2-yl)-3-(4-tolylsulfonyl)-2*H*-chromene (6u)

Yield: 113 mg (78%); colorless solid; mp 157–159 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 7.6 Hz, 1 H), 7.70 (d, *J* = 8.4 Hz, 1 H), 7.63 (d, *J* = 8.0 Hz, 2 H), 7.54–7.38 (m, 5 H), 7.32 (dd, *J* = 1.6, 8.0 Hz, 1 H), 7.17 (dt, *J* = 1.6, 8.8 Hz, 1 H), 7.11 (d, *J* = 8.0 Hz, 2 H), 6.89 (dt, *J* = 0.8, 7.6 Hz, 1 H), 6.78 (dd, *J* = 0.8, 8.0 Hz, 1 H), 6.69 (s, 1 H), 4.11–4.06 (m, 1 H), 3.99–3.93 (m, 1 H), 2.36 (s, 3 H), 1.98–1.90 (m, 2 H), 1.63–1.53 (m, 2 H), 1.05 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.5, 155.6, 144.0, 139.1, 134.2, 133.4, 132.9, 132.6, 129.1 (2 ×), 128.30, 128.26, 128.1 (2 ×), 127.6, 127.4, 126.4, 126.0, 125.7, 124.3, 121.6, 120.4, 118.2, 118.0, 76.2, 74.9, 32.0, 21.5, 19.0, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{30}H_{29}O_4S$: 485.1787; found: 485.1788.

2-(Benzo[1,3]dioxol-5-yl)-4-*n*-butoxy-3-(4-tolylsulfonyl)-2*H*-chromene (6v)

Yield: 118 mg (82%); colorless solid; mp 159–161 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, *J* = 8.4 Hz, 2 H), 7.28 (dd, *J* = 1.6, 7.6 Hz, 1 H), 7.22–7.18 (m, 3 H), 6.90 (dt, *J* = 0.8, 7.6 Hz, 1 H), 6.77 (dt, *J* = 0.8, 8.0 Hz, 1 H), 6.72 (dd, *J* = 2.0, 8.0 Hz, 1 H), 6.71 (s, 1 H), 6.59 (d, *J* = 8.0 Hz, 1 H), 6.41 (s, 1 H), 5.87 (d, *J* = 1.2 Hz, 1 H), 5.86 (d, *J* = 1.6 Hz, 1 H), 4.06–4.01 (m, 1 H), 3.90–3.85 (m, 1 H), 2.38 (s, 3 H), 1.92–1.84 (m, 2 H), 1.55–1.48 (m, 2 H), 1.02 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.9, 155.4, 148.1, 147.6, 143.9, 139.1, 132.8, 131.0, 129.0 (3 ×), 128.0 (2 ×), 124.2, 122.1, 121.5, 120.6, 117.9, 108.4, 107.8, 101.1, 76.0, 74.7, 31.9, 21.5, 19.0, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{27}O_6S$: 479.1528; found: 479.1530.

4-*n*-Butoxy-2-(3,4-dichlorophenyl)-3-(4-tolylsulfonyl)-2*H*-chromene (6w)

Yield: 120 mg (80%); colorless solid; mp 118–120 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66 (d, *J* = 8.4 Hz, 2 H), 7.30 (dd, *J* = 1.6, 7.6 Hz, 1 H), 7.29–7.20 (m, 5 H), 7.13 (dd, *J* = 2.0, 8.4 Hz, 1 H), 6.94 (dt, *J* = 0.8, 8.4 Hz, 1 H), 6.79 (d, *J* = 8.0 Hz, 1 H), 6.45 (s, 1 H), 4.07–4.01 (m, 1 H), 3.88–3.83 (m, 1 H), 2.41 (s, 3 H), 1.92–1.84 (m, 2 H), 1.55–1.48 (m, 2 H), 1.02 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.6, 155.1, 144.4, 138.8, 137.3, 133.2, 133.0, 132.5, 130.4, 130.0, 129.3 (2 ×), 127.9 (2 ×), 127.4, 124.5, 122.0, 119.7, 118.0, 117.8, 75.1, 74.8, 31.9, 21.6, 19.0, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{25}Cl_2O_4S$: 503.0851; found: 503.0852.

4-*n*-Butoxy-3-(4-tolylsulfonyl)-2-(3,4,5-trimethoxyphenyl)-2*H*-chromene (6x)

Yield: 132 mg (84%); colorless solid; mp 125–127 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62 (d, *J* = 8.4 Hz, 2 H), 7.29 (dd, *J* = 1.6, 7.6 Hz, 1 H), 7.24–7.20 (m, 1 H), 7.19 (d, *J* = 8.4 Hz, 2 H), 6.91 (dt, *J* = 1.2, 8.0 Hz, 1 H), 6.80 (dd, *J* = 0.8, 8.4 Hz, 1 H), 6.43 (d, *J* = 0.4 Hz, 1 H), 6.42 (s, 2 H), 4.06–4.01 (m, 1 H), 3.89–3.82 (m, 1 H), 3.77 (s, 3 H), 3.57 (s, 6 H), 2.37 (s, 3 H), 1.92–1.85 (m, 2 H), 1.54–1.47 (m, 2 H), 1.01 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.2, 155.5, 152.9 (2 ×), 144.0, 139.2, 138.2, 132.9, 132.3 (2 ×), 129.0 (2 ×), 128.0 (2 ×), 124.0, 121.6, 120.5, 118.0, 105.1 (2 ×), 76.3, 75.0, 60.7, 55.7 (2 ×), 31.9, 21.5, 19.0, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{29}H_{33}O_7S$: 525.1947; found: 525.1948.

Single-crystal X-ray analysis: crystals of **6x** were grown by slow diffusion of EtOAc into a solution of **6x** in CH_2Cl_2, which yielded colorless prisms. Compound **6x** crystallized in the monoclinic crystal system, space group $P2_1/c$, *a* = 8.5862(10) Å, *b* = 11.7120(13) Å, *c* = 26.193(3) Å, *V* = 2631.5(5) Å^3, *Z* = 4, d_{calcd} = 1.324 g/cm^3, *F*(000) = 1112, 2θ range 1.905–26.501°, *R* indices (all data) R_1 = 0.0458, wR_2 = 0.1176.

4-*n*-Butoxy-2-(furan-2-yl)-3-(4-tolylsulfonyl)-2*H*-chromene (6y)

Yield: 104 mg (82%); colorless solid; mp 155–157 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 8.0 Hz, 2 H), 7.30 (dd, *J* = 1.6, 7.6 Hz, 1 H), 7.25–7.21 (m, 4 H), 6.93 (dt, *J* = 1.2, 8.0 Hz, 1 H), 6.84 (dd, *J* = 0.8, 8.4 Hz, 1 H), 6.51 (s, 1 H), 6.15 (dd, *J* =1.6, 3.2 Hz, 1 H), 6.07 (d, *J* = 3.2 Hz, 1 H), 4.06–4.02 (m, 1 H), 3.94–3.89 (m, 1 H), 2.40 (s, 3 H), 1.91–1.84 (m, 2 H), 1.55–1.48 (m, 2 H), 1.02 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.5, 155.6, 150.6, 144.0, 143.5, 139.1, 132.8, 129.1 (2 ×), 127.9 (2 ×), 124.3, 121.7, 118.9, 117.9, 117.8, 111.1, 110.1, 74.9, 69.1, 31.9, 21.5, 19.0, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{25}O_5S$: 425.1423; found: 425.1423.

Single-crystal X-ray analysis: crystals of **6y** were grown by slow diffusion of EtOAc into a solution of **6y** in CH_2Cl_2, which yielded colorless prisms. Compound **6y** crystallized in the monoclinic crystal system, space group *C*2/*c*, *a* = 26.290(2) Å, *b* = 8.3391(7) Å, *c* = 19.8288(16) Å, *V* = 4128.0(6) Å^3, *Z* = 8, d_{calcd} = 1.366 g/cm^3, *F*(000) = 1792, 2θ range 1.631–26.445°, *R* indices (all data) R_1 = 0.1300, wR_2 = 0.2920.

4-*n*-Butoxy-2-(thiophen-2-yl)-3-(4-tolylsulfonyl)-2*H*-chromene (6z)

Yield: 110 mg (83%); colorless solid; mp 156–158 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, *J* = 8.4 Hz, 2 H), 7.32 (dd, *J* = 1.6, 7.6 Hz, 1 H), 7.25 (dt, *J* = 1.6, 7.6 Hz, 1 H), 7.19 (d, *J* = 8.0 Hz, 2 H), 7.13 (dd, *J* = 1.2, 8.8 Hz, 1 H), 6.96 (dd, *J* = 1.2, 7.6 Hz, 1 H), 6.96–6.92 (m, 1 H), 6.85 (dd, *J* = 0.8, 8.0 Hz, 1 H), 6.79 (dd, *J* = 3.6, 5.2 Hz, 1 H), 6.72 (d, *J* = 0.4 Hz, 1 H), 4.08–4.02 (m, 1 H), 3.94–3.89 (m, 1 H), 2.38 (s, 3 H), 1.93–1.85 (m, 2 H), 1.57–1.46 (m, 2 H), 1.02 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.7, 155.2, 143.9, 140.6, 139.1, 132.9, 129.0 (2 ×), 128.0, 127.9 (2 ×), 126.8, 126.2, 124.3, 121.8, 121.4, 118.3, 118.1, 74.9, 71.5, 31.9, 21.5, 19.0, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{25}O_4S_2$: 441.1194; found: 441.1196.

Single-crystal X-ray analysis: crystals of **6z** were grown by slow diffusion of EtOAc into a solution of **6z** in CH_2Cl_2, which yielded colorless prisms. Compound **6z** crystallized in the monoclinic crystal system, space group $P2_1/n$, *a* = 12.2582(7) Å, *b* = 8.5061(4) Å, *c* = 21.0937(11) Å, *V* = 2185.5(2) Å^3, *Z* = 4, d_{calcd} = 1.339 g/cm^3, *F*(000) = 928, 2θ range 1.837–26.519°, *R* indices (all data) R_1 = 0.0517, wR_2 = 0.1010.

3-[4-*n*-Butoxy-3-(4-tolylsulfonyl)-2*H*-chromen-2-yl]pyridine (6aa)

Yield: 104 mg (80%); colorless gum.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.52 (d, *J* = 2.4 Hz, 1 H), 8.47 (dd, *J* = 1.6, 8.8 Hz, 1 H), 7.60 (d, *J* = 8.4 Hz, 2 H), 7.52 (dt, *J* = 2.0, 8.0 Hz, 1 H), 7.29 (dd, *J* = 1.6, 8.0 Hz, 1 H), 7.21 (dt, *J* = 2.0, 8.0 Hz, 1 H), 7.19 (d, *J* = 8.0 Hz, 2 H), 7.10 (dd, *J* = 0.4, 8.0 Hz, 1 H), 6.92 (dt, *J* = 1.2, 7.6 Hz, 1 H), 6.78 (dd, *J* = 0.8, 8.0 Hz, 1 H), 6.54 (s, 1 H), 4.07–4.02 (m, 1 H), 3.88–3.82 (m, 1 H), 2.38 (s, 3 H), 1.91–1.82 (m, 2 H), 1.55–1.45 (m, 2 H), 1.00 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.5, 155.1, 150.1, 149.4, 144.3, 138.9, 135.4, 133.2, 132.7, 129.3 (2 ×), 127.8 (2 ×), 124.4, 123.2, 122.0, 119.6, 118.0, 117.9, 75.0, 74.1, 31.9, 21.5, 19.0, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{26}NO_4S$: 436.1583; found: 436.1584.

2-(2-Bromophenyl)-4-*n*-butoxy-3-(4-tolylsulfonyl)-2*H*-chromene (6ab)

Yield: 112 mg (73%); colorless solid; mp 162–164 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62–7.58 (m, 3 H), 7.30 (dd, *J* = 1.6, 7.6 Hz, 1 H), 7.20–7.16 (m, 3 H), 7.12–7.07 (m, 1 H), 6.94 (s, 1 H), 6.93–6.88 (m, 3 H), 6.76 (dd, *J* = 0.4, 8.0 Hz, 1 H), 4.09–4.04 (m, 1 H), 3.95–3.89 (m, 1 H), 2.39 (s, 3 H), 1.95–1.86 (m, 2 H), 1.59–1.48 (m, 2 H), 1.03 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.8, 155.2, 144.1, 138.8, 134.9, 133.6, 132.9, 130.6, 129.6, 129.1 (2 ×), 128.1 (2 ×), 126.9, 124.8, 124.1, 121.7, 119.8, 118.1, 118.0, 74.9, 74.7, 32.0, 21.5, 19.0, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{26}BrO_4S$: 513.0735; found: 513.0733.

Single-crystal X-ray analysis: crystals of **6ab** were grown by slow diffusion of EtOAc into a solution of **6ab** in CH_2Cl_2, which yielded colorless prisms. Compound **6ab** crystallized in the monoclinic crystal system, space group $P2_1/n$, *a* = 12.2442(6) Å, *b* = 8.7485(4) Å, *c* = 21.6094(11) Å, *V* = 2288.57(19) Å^3, *Z* = 4, d_{calcd} = 1.490 g/cm^3, *F*(000) = 1056, 2θ range 1.805–26.405°, *R* indices (all data) R_1 = 0.0299, wR_2 = 0.0634.

4-*n*-Butoxy-6-chloro-2-(4-chlorophenyl)-3-(4-tolylsulfonyl)-2*H*-chromene (6ac)

Yield: 119 mg (79%); colorless gum.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56 (d, *J* = 8.4 Hz, 2 H), 7.23 (d, *J* = 2.0 Hz, 1 H), 7.20 (d, *J* = 8.4 Hz, 2 H), 7.17–7.12 (m, 5 H), 6.71 (d, *J* = 8.4 Hz, 1 H), 6.46 (s, 1 H), 4.06–4.00 (m, 1 H), 3.95–3.89 (m, 1 H), 2.40 (s, 3 H), 1.94–1.85 (m, 2 H), 1.56–1.48 (m, 2 H), 1.04 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.0, 153.8, 144.4, 138.7, 135.2, 135.1, 132.7, 129.5 (2 ×), 129.2 (2 ×), 128.7 (2 ×), 128.0 (2 ×), 127.0, 124.0, 121.8, 119.5, 119.4, 75.8, 75.2, 32.0, 21.6, 19.0, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{26}H_{25}Cl_2O_4S$: 503.0851; found: 503.0853.

4-*n*-Butoxy-7-methoxy-3-(4-tolylsulfonyl)-2-(3,4,5-trimethoxyphenyl)-2*H*-chromene (6ad)

Yield: 140 mg (84%); colorless solid; mp 146–148 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, *J* = 8.0 Hz, 2 H), 7.21–7.17 (m, 3 H), 6.46 (dd, *J* = 2.4, 8.8 Hz, 1 H), 6.43 (s, 2 H), 6.41 (s, 1 H), 6.33 (d, *J* = 2.4 Hz, 1 H), 4.06–4.00 (m, 1 H), 3.92–3.86 (m, 1 H), 3.78 (s, 3 H), 3.73 (s, 3 H), 3.58 (s, 6 H), 2.37 (s, 3 H), 1.91–1.84 (m, 2 H), 1.55–1.47 (m, 2 H), 1.01 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.7, 157.8, 157.5, 152.9 (2 ×), 143.7, 139.6, 132.6, 129.0 (2 ×), 127.93, 127.87 (2 ×), 125.4, 117.2, 111.0, 108.6, 105.1 (2 ×), 102.9, 76.9, 75.1, 60.7, 55.7 (2 ×), 55.4, 32.0, 21.5, 19.0, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{30}H_{35}O_8S$: 555.2053; found: 555.2053.

4-*n*-Butoxy-2-methyl-3-(4-tolylsulfonyl)-2*H*-chromene (6ae)

Yield: 74 mg (66%); colorless solid; mp 75–77 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (d, *J* = 8.4 Hz, 2 H), 7.30 (dd, *J* = 0.8, 8.8 Hz, 2 H), 7.29–7.24 (m, 2 H), 6.93 (dt, *J* = 1.2, 7.6 Hz, 1 H), 6.88 (dd, *J* = 1.2, 8.8 Hz, 1 H), 5.59 (q, *J* = 6.4 Hz, 1 H), 3.97–3.91 (m, 1 H), 3.73–3.67 (m, 1 H), 2.40 (s, 3 H), 1.83–1.74 (m, 3 H), 1.47–1.40 (m, 1 H), 1.36 (d, *J* = 6.4 Hz, 3 H), 0.96 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.6, 155.2, 143.9, 139.8, 132.6, 129.3 (2 ×), 127.5 (2 ×), 124.3, 122.6, 121.3, 117.8, 117.5, 74.3, 71.4, 31.8, 21.4, 19.6, 18.8, 13.8.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{25}O_4S$: 373.1474; found: 373.1474.

4-*n*-Butoxy-2-phenethyl-3-(4-tolylsulfonyl)-2*H*-chromene (6af)

Yield: 100 mg (72%); colorless gum.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, *J* = 8.0 Hz, 2 H), 7.35–7.13 (m, 9 H), 6.99 (dt, *J* = 1.2, 8.0 Hz, 1 H), 6.94 (d, *J* = 8.0 Hz, 1 H), 5.49 (dd, *J* = 3.2, 10.4 Hz, 1 H), 4.02–3.96 (m, 1 H), 3.72–3.63 (m, 1 H), 2.88–2.73 (m, 2 H), 2.43 (s, 3 H), 2.18–2.08 (m, 1 H), 2.01–1.92 (m, 1 H), 1.85–1.77 (m, 2 H), 1.52–1.39 (m, 2 H), 1.00 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.9, 155.1, 143.9, 140.8, 139.7, 132.7, 129.3 (2 ×), 128.24 (2 ×), 128.22 (2 ×), 127.6 (2 ×), 125.8, 124.4, 121.7, 121.5, 118.0, 117.7, 74.44, 74.39, 34.9, 31.8, 31.6, 21.4, 18.8, 13.8.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{28}H_{31}O_4S$: 463.1943; found: 463.1942.

4-*n*-Butoxy-2-heptyl-3-(4-tolylsulfonyl)-2*H*-chromene (6ag)

Yield: 86 mg (63%); colorless solid; mp 77–79 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (d, *J* = 8.4 Hz, 2 H), 7.32 (dd, *J* = 0.8, 8.8 Hz, 2 H), 7.26 (dt, *J* = 1.6, 8.0 Hz, 2 H), 6.94 (dt, *J* = 1.2, 7.6 Hz, 1 H), 6.91 (dd, *J* = 1.2, 8.8 Hz, 1 H), 5.41 (dd, *J* = 3.2, 10.0 Hz, 1 H), 3.97–3.91 (m, 1 H), 3.67–3.61 (m, 1 H), 2.43 (s, 3 H), 1.82–1.73 (m, 3 H), 1.59–1.51 (m, 1 H), 1.47–1.38 (m, 4 H), 1.28–1.22 (m, 8 H), 0.97 (t, *J* = 7.2 Hz, 3 H), 0.86 (t, *J* = 6.8 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.8, 155.5, 144.0, 140.0, 132.7, 129.4 (2 ×), 127.8 (2 ×), 124.4, 122.3, 121.4, 118.2, 117.9, 75.2, 74.4, 33.5, 31.9, 31.7, 29.1, 28.9, 25.4, 22.6, 21.6, 19.0, 14.1, 13.9.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{27}H_{37}O_4S$: 457.2413; found: 457.2412.

4-Benzyloxy-2-(3,4-dimethoxyphenyl)-3-(methylsulfonyl)-2*H*-chromene (6ah)

Yield: 95 mg (70%); colorless solid; mp 154–156 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60–7.58 (m, 2 H), 7.50–7.39 (m, 4 H), 7.29 (dt, *J* = 1.6, 8.0 Hz, 1 H), 7.00 (dt, *J* = 0.8, 8.0 Hz, 1 H), 6.96 (d, *J* = 2.0 Hz, 1 H), 6.93 (dd, *J* = 2.0, 8.0 Hz, 1 H), 6.85 (dd, *J* = 0.8, 8.0 Hz, 1 H), 6.73 (d, *J* = 8.0 Hz, 1 H), 6.35 (s, 1 H), 5.17 (d, *J* = 10.4 Hz, 1 H), 5.08 (d, *J* = 10.0 Hz, 1 H), 3.80 (s, 3 H), 3.79 (s, 3 H), 3.03 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.8, 155.6, 149.7, 149.0, 135.6, 133.2, 129.7, 128.7 (3 ×), 128.5 (2 ×), 123.9, 121.7, 120.9, 119.7, 118.1, 117.5, 110.8, 110.7, 76.6, 75.5, 55.7, 55.6, 44.1.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{25}O_6S$: 453.1372; found: 453.1372.

3-Benzyl-2-(3,4-dimethoxyphenyl)-3-(methylsulfonyl)chroman-4-one (6ah-1)

Yield: 15 mg (11%); colorless solid; mp 205–207 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (dd, *J* = 1.6, 8.0 Hz, 1 H), 7.59 (dt, *J* = 2.0, 8.4 Hz, 1 H), 7.35–7.27 (m, 5 H), 7.13 (dt, *J* = 0.8, 8.0 Hz, 1 H), 7.05 (dd, *J* = 0.8, 8.0 Hz, 1 H), 6.92 (d, *J* = 2.4 Hz, 1 H), 6.88 (dd, *J* = 2.4, 8.4 Hz, 1 H), 6.73 (d, *J* = 8.4 Hz, 1 H), 5.68 (s, 1 H), 3.85 (s, 3 H), 3.85 (d, *J* = 14.8 Hz, 1 H), 3.72 (s, 3 H), 3.60 (d, *J* = 14.4 Hz, 1 H), 2.52 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 188.5, 160.7, 150.0, 148.4, 137.5, 133.1, 131.2 (2 ×), 128.4 (2 ×), 127.7, 127.6, 126.6, 122.2, 121.8, 120.4, 118.4, 113.0, 110.5, 82.1, 75.9, 55.82, 55.78, 41.1, 36.6.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{25}O_6S$: 453.1372; found: 453.1374.

4-Benzyloxy-2-(3,4-dimethoxyphenyl)-3-(4-tolylsulfonyl)-2*H*-chromene (6ai)

Yield: 120 mg (76%); colorless solid; mp 143–145 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60–7.58 (m, 2 H), 7.50–7.43 (m, 5 H), 7.34 (dd, *J* = 1.2, 8.0 Hz, 1 H), 7.24–7.20 (m, 1 H), 7.06 (d, *J* = 8.0 Hz, 2 H), 6.91 (dd, *J* = 1.2, 8.0 Hz, 1 H), 6.81–6.77 (m, 2 H), 6.73 (d, *J* = 2.0 Hz, 1 H), 6.63 (d, *J* = 8.0 Hz, 1 H), 6.50 (s, 1 H), 5.09 (d, *J* = 10.4 Hz, 1 H), 5.04 (d, *J* = 10.8 Hz, 1 H), 3.81 (s, 3 H), 3.60 (s, 3 H), 2.33 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.4, 155.6, 149.5, 148.6, 143.9, 138.9, 136.0, 133.0, 130.6, 130.4, 129.3, 129.0 (2 ×), 128.7 (2 ×), 128.5, 128.2 (2 ×), 128.1 (2 ×), 124.0, 121.6, 120.9, 118.1, 111.0, 110.5, 76.3, 76.2, 55.8, 55.5, 21.5.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{31}H_{29}O_6S$: 529.1685; found: 529.1688.

4-Benzyloxy-2-(3,4-dimethoxyphenyl)-3-[(4-fluorophenyl)sulfonyl]-2*H*-chromene (6aj)

Yield: 118 mg (74%); colorless solid; mp 160–162 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61–7.55 (m, 4 H), 7.52–7.45 (m, 3 H), 7.37 (dd, *J* = 1.6, 8.0 Hz, 1 H), 7.26–7.22 (m, 1 H), 6.95–6.89 (m, 3 H), 6.80 (dd, *J* = 0.8, 8.0 Hz, 1 H), 6.77 (d, *J* = 2.0 Hz, 1 H), 6.70 (dd, *J* = 2.0, 8.4 Hz, 1 H), 6.61 (d, *J* = 8.4 Hz, 1 H), 6.48 (s, 1 H), 5.13 (d, *J* = 10.4 Hz, 1 H), 5.08 (d, *J* = 10.4 Hz, 1 H), 3.81 (s, 3 H), 3.66 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.3 (d, *J* = 253.9 Hz), 156.8, 155.6, 149.7, 148.8, 137.8 (d, *J* = 3.1 Hz), 135.8, 133.3, 130.9 (d, *J* = 9.1 Hz, 2 ×), 129.1, 128.74 (2 ×), 128.68, 128.3 (2 ×), 124.0, 121.7, 121.4, 120.7, 118.2, 117.6, 115.5 (d, *J* = 21.9 Hz, 2 ×), 111.1, 110.5, 76.5, 76.2, 55.8, 55.6.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{30}H_{26}FO_6S$: 533.1434; found: 533.1432.

Single-crystal X-ray analysis: crystals of **6aj** were grown by slow diffusion of EtOAc into a solution of **6aj** in CH_2Cl_2, which yielded colorless prisms. Compound **6aj** crystallized in the monoclinic crystal system, space group $P2_1/c$, *a* = 12.1195(4) Å, *b* = 16.7902(5) Å, *c* = 13.7432(5) Å, *V* = 2567.39(15) Å^3, *Z* = 4, d_{calcd} = 1.378 g/cm^3, *F*(000) = 1112, 2θ range 1.830–26.396°, *R* indices (all data) R_1 = 0.0773, wR_2 = 0.1101.

2-(3,4-Dimethoxyphenyl)-4-(naphthalen-1-ylmethoxy)-3-(4-tolylsulfonyl)-2*H*-chromene (6ak)

Yield: 118 mg (68%); colorless solid; mp 150–152 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.26–8.24 (m, 1 H), 7.96–7.93 (m, 2 H), 7.76 (d, *J* = 6.8 Hz, 1 H), 7.62–7.55 (m, 3 H), 7.53 (d, *J* = 8.8 Hz, 2 H), 7.32 (dd, *J* = 1.2, 7.6 Hz, 1 H), 7.23 (dt, *J* = 1.6, 7.6 Hz, 1 H), 6.99 (d, *J* = 8.4 Hz, 2 H), 6.86 (dt, *J* = 0.8, 8.4 Hz, 1 H), 6.83 (dt, *J* = 0.8, 8.4 Hz, 1 H), 6.80 (dd, *J* = 2.0, 8.4 Hz, 1 H), 6.74 (d, *J* = 2.4 Hz, 1 H), 6.63 (d, *J* = 8.0 Hz, 1 H), 6.54 (s, 1 H), 5.63 (d, *J* = 11.6 Hz, 1 H), 5.40 (d, *J* = 11.6 Hz, 1 H), 3.81 (s, 3 H), 3.60 (s, 3 H), 2.27 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.9, 155.7, 149.6, 148.7, 143.9, 138.9, 133.6, 133.1, 132.2, 131.1, 129.3, 129.1, 129.0 (2 ×), 128.7, 128.1 (3 ×), 126.6, 126.1, 126.0, 125.4, 124.3, 123.8, 121.8, 121.6, 120.9, 118.1, 111.1, 110.6, 76.3, 74.3, 55.8, 55.5, 21.4.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{35}H_{31}O_6S$: 579.1841; found: 579.1842.

2-Phenylchroman-4-one (8a)[14]

PyBOP (172 mg, 0.33 mmol) was added to a solution of **2a** (41 mg, 0.3 mmol) and $Cu(OAc)_2$ (60 mg, 0.33 mmol) in DMF (2 mL) at 25 °C. The reaction mixture was stirred at 25 °C for 5 min. DMAP (40 mg, 0.33 mmol) was added and the reaction mixture was stirred at reflux for 2 h, then cooled to 25 °C. Ethyl ester **7** (58 mg, 0.33 mmol) in DMF (1 mL) was added at 25 °C and the reaction mixture was stirred at reflux for an additional 1 h, then cooled to 25 °C. Then, **5a** (138 mg, 1.0 mmol) was added at 25 °C and the reaction mixture was stirred at reflux for an additional 2 h (monitored by TLC), then cooled to 25 °C and concentrated. The residue was diluted with water (10 mL) and the mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with brine, dried, filtered, and concentrated under reduced pressure to afford crude product. Purification on silica gel (hexanes/EtOAc, 8:1 to 4:1) afforded **8a**.

Yield: 44 mg (65%); colorless solid; mp 77–79 °C (recrystallized from hexanes/EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94 (dd, *J* = 1.6, 8.0 Hz, 1 H), 7.54–7.39 (m, 6 H), 7.08–7.04 (m, 2 H), 5.49 (dd, *J* = 2.8, 13.2 Hz, 1 H), 3.10 (dd, *J* = 13.2, 16.8 Hz, 1 H), 2.90 (dd, *J* = 2.8, 16.8 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.0, 161.5, 138.7, 136.2, 128.84 (2 ×), 128.76, 127.0, 126.1 (2 ×), 121.6, 120.9, 118.1, 79.6, 44.6.

HRMS (ESI-TOF): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{13}O_2$: 225.0916; found: 225.0918.

Funding Information

The authors would like to thank the Ministry of Science and Technology of the People's Republic of China for financial support (MOST 106-2628-M-037-001-MY3).

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0039-1689973.

References

(1) For reviews on the synthesis of chromenes, see: (a) Majumdar, N.; Paul, N. D.; Mandal, S.; de Bruin, B.; Wulff, W. D. *ACS Catal.* **2015**, *5*, 2329. (b) Shi, Y.-L.; Shi, M. *Org. Biomol. Chem.* **2007**, *5*, 1499. (c) Ferreira, S. B.; da Silva, F. de. C.; Pinto, A. C.; Gonzaga, D. T. G.; Ferreira, V. F. *J. Heterocycl. Chem.* **2009**, *46*, 1080. (d) Ellis, G. P.; Lockhart, I. M. In *The Chemistry of Heterocyclic Compounds: Chromenes, Chromanones, and Chromones, Vol. 31*; Ellis, G. P., Ed.; Wiley-VCH: New York, **2009**, 1–196.

(2) Biological activities of 2-aryl-2*H*-chromenes. For candenatenin E, see: (a) Cheenpracha, S.; Karalai, C.; Ponglimanont, C.; Kanjana-Opas, A. *J. Nat. Prod.* **2009**, *72*, 1395. For hilgartene, see: (b) Gómez-Garibay, F.; Calderón, J. S.; De La O Arciniega, M.; Céspedes, C. L.; Téllez-Valdés, O.; Taboada, J. *Phytochemistry* **1999**, *52*, 1159. For acolbifene, see: (c) Gauthier, S.; Caron, B.; Cloutier, J.; Dory, Y. L.; Farve, A.; Larouche, D.; Mailhot, J.; Ouellet, C.; Schwerdtfeger, A.; Leblanc, G.; Martel, C.; Simard, J.; Mérand, Y.; Bélanger, A.; Labrie, C.; Labrie, F. *J. Med. Chem.* **1997**, *40*, 2117.

(3) For photochromism of 2,2-diaryl-2*H*-chromenes, see: (a) Queiroz, M.-J. R. P.; Abreu, A. S.; Ferreira, P. M. T.; Oliveira, M. M.; Dubest, R.; Aubard, J.; Samat, A. *Org. Lett.* **2005**, *7*, 4811. (b) Moorthy, J. N.; Venkatakrishnan, P.; Samanta, S.; Kumar, D. K. *Org. Lett.* **2007**, *9*, 919. (c) Berdnikova, D. V.; Paululat, T.; Jonusauskas, G.; Peregudova, S. M.; Fedorova, O. A. *Org. Lett.* **2017**, *19*, 5633; and references cited therein.

(4) For general syntheses of 2-aryl-2*H*-chromenes, see: (a) Clark-Lewis, J. W.; Jemison, R. W. *Aust. J. Chem.* **1968**, *21*, 2247. (b) Cushman, M.; Nagarathnam, D. *J. Med. Chem.* **1991**, *34*, 798.

(5) Organocatalyst-mediated syntheses of 2-aryl-2*H*-chromenes. For THT, see: (a) Ye, L.-W.; Sun, X.-L.; Zhu, C.-Y.; Tang, Y. *Org. Lett.* **2006**, *8*, 3853. For amines, see: (b) Wang, Q.; Finn, M. G. *Org. Lett.* **2000**, *2*, 4063. For Brønsted acids, see: (c) Moquist, P. N.; Kodama, T.; Schaus, S. E. *Angew. Chem. Int. Ed.* **2010**, *49*, 7096. For $BF_3{\cdot}OEt_2$, see: (d) Doodeman, R.; Rutjes, F. P. J. T.; Hiemstra, H. *Tetrahedron Lett.* **2000**, *41*, 5979. (e) Gil-Negrete, J. M.; Sestelo, J. P.; Sarandeses, L. A. *Org. Lett.* **2016**, *18*, 4316.

(6) Transition-metal-mediated syntheses of 2-aryl-2*H*-chromenes. For Co(II), see: (a) Paul, N. D.; Mandal, S.; Otte, M.; Cui, X.; Zhang, X. P.; de Bruin, B. *J. Am. Chem. Soc.* **2014**, *136*, 1090. For Ru(II), see: (b) Hardouin, C.; Burgaud, L.; Valleix, A.; Doris, E. *Tetrahedron Lett.* **2003**, *44*, 435. (c) He, H.; Ye, K.-Y.; Wu, Q.-F.; Dai, L.-X.; You, S.-L. *Adv. Synth. Catal.* **2012**, *354*, 1084. For Ni(0), see: (d) Graham, T. J. A.; Doyle, A. G. *Org. Lett.* **2012**, *14*, 1616. For Ga(III), see: (e) Yadav, J. S.; Reddy, B. V. S.; Biswas, S. K.; Sengupta, S. *Tetrahedron Lett.* **2009**, *50*, 5798. For Fe(III), see: (f) Calmus, L.; Corbu, A.; Cossy, J. *Adv. Synth. Catal.* **2015**, *357*, 1381. For Pd(II), see: (g) Zeng, B.-S.; Yu, X.; Siu, P. W.; Scheidt, K. A. *Chem. Sci.* **2014**, *5*, 2277. (h) Jiang, Z.-Z.; Gao, A.; Li, H.; Chen, D.; Ding, C.-H.; Xu, B.; Hou, X.-L. *Chem. Asian J.* **2017**, *12*, 3119. (i) Xia, Y.; Xia, Y.; Zhang, Y.; Wang, J. *Org. Biomol. Chem.* **2014**, *12*, 9333.

(7) For water-mediated syntheses of 2-aryl-2*H*-chromenes, see: (a) Zhang, F.-Z.; Tian, Y.; Li, G.-X.; Qu, J. *J. Org. Chem.* **2015**, *80*, 1107. (b) Candeias, N. R.; Veiros, L. F.; Afonso, C. A. M.; Gois, P. M. P. *Eur. J. Org. Chem.* **2009**, 1859.

(8) Synthetic applications of 2-aryl-2*H*-chromenes. For dimerization, see: (a) Luan, Y.; Sun, H.; Schaus, S. E. *Org. Lett.* **2011**, *13*, 6480. (b) Devakaram, R.; StC. Black, D.; Kumar, N. *Tetrahedron Lett.* **2010**, *51*, 3636. For flavones, see: (c) Banerjee, D.; Kayal, U.; Maiti, G. *Tetrahedron Lett.* **2016**, *57*, 1667. For dihydrochalcones, see: (d) Maiti, G.; Kayal, U.; Karmakar, R.; Bhattacharya, R. N. *Tetrahedron Lett.* **2012**, *53*, 6321. For cyclopropanations, see: (e) Stokes, S.; Mustain, R.; Pickle, L.; Mead, K. T. *Tetrahedron Lett.* **2012**, *53*, 3890.

(9) (a) Chang, M.-Y.; Wu, Y.-S.; Hsiao, Y.-T. *Synthesis* **2018**, *50*, 4651. (b) Chang, M.-Y.; Chen, Y.-H.; Wang, H.-S. *J. Org. Chem.* **2018**, *83*, 2361.

(10) Domino oxa-Michael/aldol condensation. For a 3-formyl group, see: (a) Climent, M. J.; Iborra, S.; Sabater, M. J.; Vidal, J. D. *Appl. Catal., A* **2014**, *481*, 27. (b) Shen, H.; Yang, K.-F.; Shi, Z.-H.; Jiang, J.-X.; Lai, G.-Q.; Xu, L.-W. *Eur. J. Org. Chem.* **2011**, 5031. For a 3-nitro group, see: (c) Liu, S.-X.; Jia, C.-M.; Yao, B.-Y.; Chen, X.-L.; Zhang, Q. *Synthesis* **2016**, *48*, 407.

(11) (a) Bauer, D. J.; Selway, J. W. T.; Batchelor, J. F.; Tisdale, M.; Caldwell, I. C.; Young, D. A. B. *Nature* **1981**, *292*, 369. (b) Cheng, J.-F.; Ishikawa, A.; Ono, Y.; Arrhenius, T.; Zadzan, A. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 3647.

(12) CCDC 1811124 (**4a**), CCDC 1835628 (**6b**), CCDC 1835629 (**6q**), CCDC 1835630 (**6x**), CCDC 1835631 (**6y**), CCDC 1835632 (**6z**), CCDC 1835633 (**6ab**), and CCDC 1842006 (**6aj**) contain the supplementary crystallographic data for this paper. The data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/getstructures.

(13) For the complexation of Cu(II) with salicylic acids, see: (a) Chen, H.-J.; Lin, Z.-Y.; Li, M.-Y.; Lian, R.-J.; Xue, Q.-W.; Chung, J.-L.; Chen, S.-C.; Chen, Y.-J. *Tetrahedron* **2010**, *66*, 7755. (b) Lin, C. J.; Zheng, Y. Q.; Zhang, D. Y.; Xu, W. *Russ. J. Coord. Chem.* **2014**, *40*, 932.

(14) (a) Shaikh, M.; Atyam, K. K.; Sahu, M.; Ranganath, K. V. S. *Chem. Commun.* **2017**, *53*, 6029. (b) Ren, X.; Han, C.; Feng, X.; Du, H. *Synlett* **2017**, *28*, 2421.