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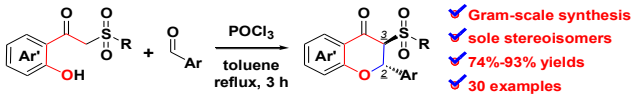
Gram-Scale Synthesis of 3-Sulfonyl Flavanones

Meng-Yang Chang,*[a,b] Yu-Lin Tsai[a] and Yu-Lun Chang[a]

[a]Department of Medicinal and Applied Chemistry, Kaohsiung Medical University, Kaohsiung 807, Taiwan [b]Department of Medical Research, Kaohsiung Medical University Hospital, Kaohsiung 807, Taiwan

*Email: mychang@kmu.edu.tw

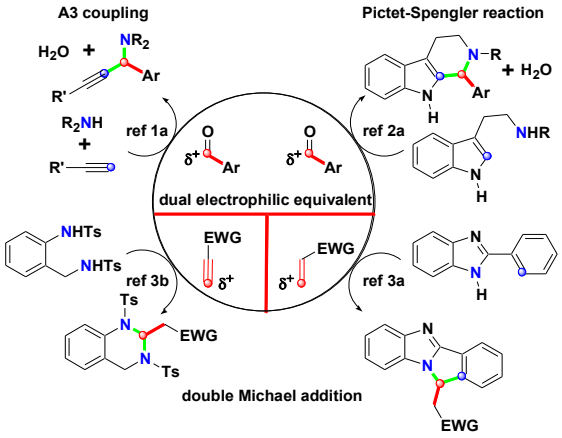


ABSTRACT: In this paper, an easy-operational, high-yielding method for the gram-scale synthesis of 3-sulfonyl flavanones is described by one-pot straightforward $POCl_3$ mediated intermolecular (5+1) annulation of β-ketosulfones with an *o*-hydroxyaryl group (dual nucleophile) and arylaldehydes (dual electrophile) in refluxing toluene for 3 h. 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.

Introduction

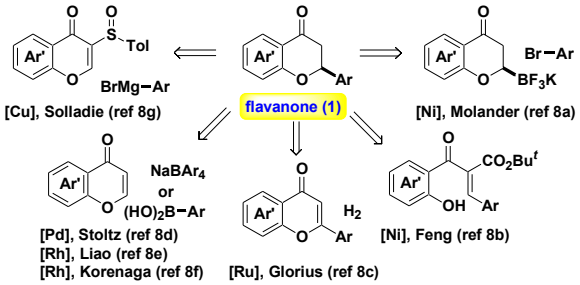
Traditionally, many synthetic routes, such as A3-type coupling[1], the Pictet-Spengler reaction,[2] and double Michael addition[3] exhibit a one-pot twice reaction of two nucleophile synthons and a dual electrophilic equivalent bearing a carbonyl unit or Michael acceptor (alkenyl or alkynyl), and these could construct diversified frameworks by a tandem intermolecular and/or intramolecular double-addition characteristic process (Scheme 1). In this reaction of two nucleophilic atoms attacking one-carbonyl or Michael acceptor carbon, water is released as the only by-product, or atom-economic pathways are exhibited. Moreover, these generated targets represent useful key intermediates, building blocks, bioactive compounds, natural products and functionalized materials based on transition-metal catalyzed cross-coupling, organocatalysis promoted annulation, Lewis acid-mediated cyclization and other diversified approaches.

Scheme 1. One-pot Route for Double Addition



According to our long-standing interest in synthetic applications of β-ketosulfones[4] and this duplicate addition protocol, β-(*o*-hydroxyaryl)ketosulfone (a β-arylketosulfone analog) was chosen as the starting material to develop the synthesis of 3-sulfonyl flavanones. Flavonoids (2-aryl dihydrobenzopyran-4-ones) are found in plant metabolites having biological activities such as anticancer antitumor, antioxidant, and antiproliferative properties.[5-6] Due to their potential applications, the development of a concise synthetic route has attracted significant attention, and many attempts have been reported. The general approach toward flavanone could be achieved from promoters mediating the ring-closure of 2'-hydroxychalcone.[7] The typical organocatalyst-promoted formation of flavanone is investigated.[8]

Scheme 2. Transition Metal Mediated Routes of Flavanones

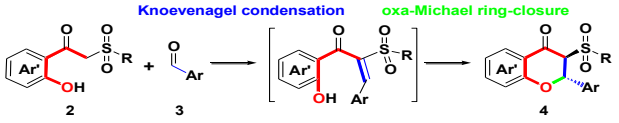


Results and Discussion

Recently, transition metals promoting the pioneering methods have been explored as main strategies (Scheme 2).[9] For example, Molander and co-worker reported that the photoredox Ni(II) complex mediated a direct α-arylation/heteroarylation of 2-BF_3K chromanones with bromoarenes.[9a] Feng *et al*. developed a Ni(II) complex mediated intramolecular oxa-Michael addition of *t*-butyl ester acti-

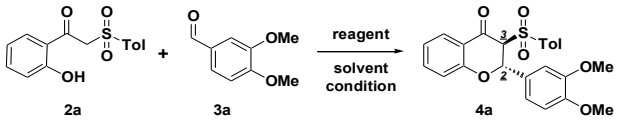
vated 2'-hydroxy-α,β-unsaturated ketones followed by decarboxylation.[9b] Glorius *et al.* demonstrated a Ru(II)-NHC catalyzed hydrogenation of flavones.[9c] Stoltz *et al.* explored the Pd(II) mediated conjugated addition of flavones with $ArB(OH)_2$.[9d] Both Liao and Korenaga groups described an Rh(I) catalyzed 1,4-addition of flavones with $NaBAr_4$ or $ArB(OH)_2$.[9e-f] The Solladie group also reported a similar transformation on a Cu(II) catalyzed Michael addition of flavones with ArMgBr.[9g] While flavanones have been successfully employed in many routes, to the best of our knowledge, no sulfonyl flavanones skeleton has been reported.[10] In spite of these advancements, some problems exist, such as expensive reagents, complicated catalytic systems, lack of broad generality, and prefunctionalized fragments. Therefore, further investigation into an efficient, easy-operational, high-yielding method for the gram-scale synthesis of 3-sulfonyl flavanones **4** is still highly desired. Herein, we present a one-pot intermolecular Knoevenagel condensation of β-ketosulfones **2** with an *o*-hydroxyaryl group and arylaldehydes **3**, followed by an intramolecular oxa-Michael ring-closure of the resulting sulfonyl (*E*)-chalcone via a (5+1) annulation mode (Scheme 3).

Scheme 3. Route of Sulfonyl Flavanones **4**



After searching related literature on Knoevenagel condensation,[11] we found that several metal chlorides have been chosen as promoters to trigger dehydration of active methylene with carbonyl compounds and also to play the key acidic source to initiate diversified reaction types.[12-27] The initial studies commenced with the treatment of model substrates **2a** (Ar' = Ph, R = Tol, 3.0 mmol) and **3a** (Ar = 3,4-$(MeO)_2C_6H_3$, 3.0 mmol) in the presence of a 0.3 equivalent of metal chlorides ($InCl_3$, $BiCl_3$, $CuCl_2$, $FeCl_3$, $ZnCl_2$, $MgCl_2$, $SnCl_2$, $PdCl_2$ and $AlCl_3$) in $MeNO_2$ (5 mL).[12-20] However, no reaction occurred at 25°C after 3 h. Especially when the reaction mixture was heated to reflux in $MeNO_2$ for 3 h, only $InCl_3$ and $BiCl_3$ produced better yields (31% and 20%) than the other eight metal chlorides in the formation of **4a**. After controlling $InCl_3$ and $BiCl_3$ as the promoters, the stoichiometric amount (1.0 equiv) provided slightly higher yields of **4a** (40% and 31%) under refluxing $MeNO_2$ conditions. Furthermore, after elongating the reaction time from 3 h to 30 h under the above-mentioned conditions (boiling $MeNO_2$, 1.0 equiv.), only trace amounts of **4a** were isolated, and a major complex mixture was observed. The results showed that metal chlorides would be inappropriate for the generation of **4a**. Under the consideration of economic issues, cheaper non-metal chlorides were used as the promoter to investigate the substrate's scope. With this idea in mind and changing the promoters from metal chlorides to metal-free promoters, $POCl_3$ was examined first and the reaction conditions were screened, as shown in Table 1. Initially, a 0.3 equivalent of $POCl_3$ only provided a 15% yield of **4a** in $MeNO_2$ at 25°C after 3 h (entry 1). However, an elongated time (30 h) did not enhance the yield of **4a** (entry 2). By using 1.0, 1.3, and 2.0 equivalents of $POCl_3$, similar yields (45%, 50%, 44%) of **4a** were shown in entries 3-5. Furthermore, controlling $POCl_3$ as the 1.3 equivalent, adding an elongated time (30 h), and using room temperature (25°C) still did not increase the yield (43%) of **4a** (entry 6). Then, to elevate the reaction temperature (25 → reflux), the yield of **4a** was enhanced to 76% (entry 7) in 3 h. But, an elongated time (30 h) at reflux temperature (102°C) decreased the yield (57%) of **4a** (entry 8). From the experiments, we found that a reflux temperature and a shorter time (3 h) were key factors affecting the $POCl_3$ (1.3 equiv) mediated reaction of **2a** and **3a**. To achieve better yields of **4a**, other solvents (toluene, benzene, DMF) were tested. When $MeNO_2$ was changed to toluene and benzene, higher yields (87% and 86%) were obtained (entries 9-10).

Table 1. Synthesis of **4a**[a]



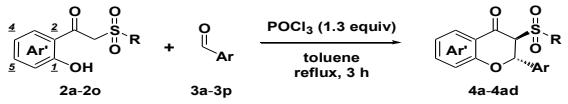
entry	reagent (equiv)	solvents	temp (°C)	time (h)	**4a**(%)[b-c]
1	$POCl_3$ (0.3)	$MeNO_2$	25	3	16
2	$POCl_3$ (0.3)	$MeNO_2$	25	30	15
3	$POCl_3$ (1.0)	$MeNO_2$	25	3	45
4	$POCl_3$ (1.3)	$MeNO_2$	25	3	50
5	$POCl_3$ (2.0)	$MeNO_2$	25	3	44
6	$POCl_3$ (1.3)	$MeNO_2$	25	30	43
7	$POCl_3$ (1.3)	$MeNO_2$	reflux	3	76
8	$POCl_3$ (1.3)	$MeNO_2$	reflux	30	57
9	$POCl_3$ (1.3)	toluene	reflux	3	87
10	$POCl_3$ (1.3)	benzene	reflux	3	85
11	$POCl_3$ (1.3)	DMF	reflux	3	16
12	$SOCl_2$ (1.3)	toluene	reflux	3	72
13	$(COCl)_2$ (1.3)	toluene	reflux	3	9
14	BCl_3 (1.3)	toluene	reflux	3	—[d]
15	TCCA (1.3)	toluene	reflux	3	—[e]

[a]The reactions were run on a 3.0 mmol scale with **2a**, **3a** (1.0 equiv), solvent (5 mL). [b]Isolated yields. [c]dr ratio >20:1. [d]Complex mixture. [e]No reaction.

However, after changing to DMF, only a 16% yield of **4a** was isolated (entry 11). On the other hand, adjusting $POCl_3$ to $SOCl_2$, $(COCl)_2$, BCl_3, and trichloroisocyanurate (TCCA), was studied. However, the conversion yields were not enhanced (entries 12-15). Entry 12 shows that $SOCl_2$ afforded a poorer yield (72%) than entry 9 (87%). In entry 13, $(COCl)_2$ provided trace amounts (9%) of **4a** along with a complex mixture. When BCl_3 was treated with the reaction conditions, only a complex mixture was produced (entry 14). In particular, no reaction was observed for the TCCA mediated annulation of **2a** and **3a** (entry 15). When $POCl_3$ served as a promoter, it would prefer to coordinate with the carbonyl group. We believed that *in-situ* formed HCl in the medium was responsible for the reaction which protonated the aldehydic carbonyl group of **3a**. On the other hand, $SOCl_2$ was giving decent yield (72%) due to the releasing HCl. However, $COCl_2$ having a bis electrophilic species might be reacting with the substrate as it had two nucleophilic sites giving some unidentified products thereby reducing the yield (9%). From our observations, we concluded that $POCl_3$ (1.3 equiv) refluxing toluene and 3 h would be optimal conditions for the one-pot cascade Knoevenagel condensation/oxa-Michael ring-closure proce-

dure. The expeditious synthetic route sets up sulfonyl flavanones, including the bond formation of the one C-O and the one C-C bonds via a formal (5+1) cycloaddition. The relative stereochemical structure of **4a** was determined by single-crystal X-ray crystallography.[28]

Table 2. Synthesis of **4a-4ad**[a]

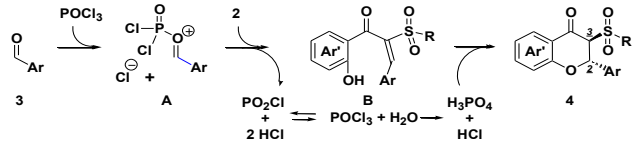


entry	**2a-2o**, Ar' =, R =	**3a-3p**, Ar =	**4a-4ad** (%)[b-c]
1	**2a**, Ph, Tol	**3a**, 3,4-$(MeO)_2C_6H_3$	**4a**, 87
2	**2b**, Ph, Ph	**3a**, 3,4-$(MeO)_2C_6H_3$	**4b**, 90
3	**2c**, Ph, Me	**3a**, 3,4-$(MeO)_2C_6H_3$	**4c**, 92
4	**2d**, Ph, *n*Bu	**3a**, 3,4-$(MeO)_2C_6H_3$	**4d**, 86
5	**2e**, Ph, 4-FC_6H_4	**3a**, 3,4-$(MeO)_2C_6H_3$	**4e**, 83
6	**2f**, Ph, 4-$MeOC_6H_4$	**3a**, 3,4-$(MeO)_2C_6H_3$	**4f**, 84
7	**2g**, Ph, 3-MeC_6H_4	**3a**, 3,4-$(MeO)_2C_6H_3$	**4g**, 87
8	**2h**, Ph, 4-EtC_6H_4	**3a**, 3,4-$(MeO)_2C_6H_3$	**4h**, 92
9	**2i**, Ph, 4-*i*PrC_6H_4	**3a**, 3,4-$(MeO)_2C_6H_3$	**4i**, 93
10	**2j**, Ph, 4-*n*BuC_6H_4	**3a**, 3,4-$(MeO)_2C_6H_3$	**4j**, 86
11	**2k**, Ph, 4-*t*BuC_6H_4	**3a**, 3,4-$(MeO)_2C_6H_3$	**4k**, 87
12	**2l**, 4-BrC_6H_3, Tol	**3a**, 3,4-$(MeO)_2C_6H_3$	**4l**, 84
13	**2m**, 4-ClC_6H_3, Tol	**3a**, 3,4-$(MeO)_2C_6H_3$	**4m**, 85
14	**2n**, naphthyl, Tol	**3a**, 3,4-$(MeO)_2C_6H_3$	**4n**, 82
15	**2a**, Ph, Tol	**3b**, Ph	**4o**, 88
16	**2a**, Ph, Tol	**3c**, 4-$MeOC_6H_4$	**4p**, 84
17	**2a**, Ph, Tol	**3d**, 3-$MeOC_6H_4$	**4q**, 82
18	**2a**, Ph, Tol	**3e**, 4-FC_6H_4	**4r**, 86
19	**2a**, Ph, Tol	**3f**, 4-MeC_6H_4	**4s**, 89
20	**2a**, Ph, Tol	**3g**, 4-PhC_6H_4	**4t**, 80
21	**2a**, Ph, Tol	**3h**, 2-naphthyl	**4u**, 78
22	**2a**, Ph, Tol	**3i**, 3,4-$CH_2O_2C_6H_3$	**4v**, 85
23	**2a**, Ph, Tol	**3j**, 3,4-$Cl_2C_6H_3$	**4w**, 80
24	**2a**, Ph, Tol	**3k**, 3,4,5-$(MeO)_3C_6H_2$	**4x**, 86
25	**2a**, Ph, Tol	**3l**, 2-furyl	**4y**, 92
26	**2a**, Ph, Tol	**3m**, 2-thienyl	**4z**, 88
27	**2a**, Ph, Tol	**3n**, 3-pyridyl	**4aa**, 90
28	**2a**, Ph, Tol	**3o**, 2-BrC_6H_4	**4ab**, 74
29	**2m**, 4-ClC_6H_3, Tol	**3p**, 4-ClC_6H_4	**4ac**, 80
30	**2o**, 5-$MeOC_6H_3$, Tol	**3k**, 3,4,5-$(MeO)_3C_6H_2$	**4ad**, 86

[a]The reactions were run on a 3.0 mmol scale with **2a-2o**, **3a-3p** (1.0 equiv), $POCl_3$ (1.3 equiv), toluene (5 mL), reflux, 3 h. [b]Isolated yields. [c]dr ratio >20:1.

To study the scope and limitations of this one-pot approach, **2a-2o** and **3a-3p** were reacted with $POCl_3$ to afford diversified **4a4ad**, as shown in Table 2. With optimal conditions established (Table 1, entry 9), we found that this route allowed a direct (5+1) annulation under easy-operational conditions with moderate to good yields (74%-93%). Among entries 1-30, the efficient formation of **4a-4ad** showed that these substituents (for **2a-2o**, Ar' and R; for **3a-3p**, Ar) did not affect the yields. For the electronic nature of aryl substituents (Ar') of **2a-2o**, not only the electron-neutral phenyl group but also the electron-withdrawing 4-halophenyl group and electron-donating 5-methoxyphenyl group were suitable. After a naphthyl (Ar', for **2n**) group was applied to the reaction conditions, **4n** was isolated in an 82% yield (entry 14). For sulfonyl substituents (R) of **2a-2o**, both the aliphatic (Me, *n*Bu) groups and aromatic (Tol, Ph, 4-FC_6H_4, 4-$MeOC_6H_4$, 3-MeC_6H_4, 4-EtC_6H_4, 4-*i*PrC_6H_4, 4-*n*BuC_6H_4, 4-*t*BuC_6H_4) groups were well-tolerated. Different aryl groups (Ar) on **3a-3p** were also suitable to form **4a-4ad**. However, entry 29 shows that lower yields (74%) of **4ab** were observed due to the steric hindrance of the *ortho*-bromo group on the aryl (Ar') ring. Furthermore, the relative stereochemical structures of **4a**, **4e**, and **4ab** were determined by Single-crystal X-ray crystallography.[28]

Scheme 4. Plausible Mechanism

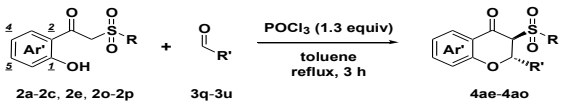


On the basis of the experimental results, a plausible mechanism for the formation of **4** is illustrated in Scheme 4. Initially, an oxygen atom of the carbonyl group on **3** attacked $POCl_3$ to yield **A** and released a chloride anion via an O-P bond formation. By the involvement of **2**, the chloride anion should deprotonate the α-proton of **2** to generate an enolate ion. Following the intermolecular Knoevenagel condensation of **A** with the resulting enolate ion of **2**, **B** could be generated along with the *in-situ* formed PO_2Cl and 2.0 equivalents of HCl. After the reaction equilibrium was achieved, we found that the reaction equation "PO_2Cl + 2 HCl ⇆ $POCl_3$ + H_2O" occurred easily.[29] Furthermore, the mixture of $POCl_3$ and H_2O converted into Brønsted acids, H_3PO_4, and HCl. According to the previous experiment, **B** possessed an (*E*)-configurated orientation due to the effect of steric hindrance between the aryl (Ar) and sulfonyl (SO_2R) groups.[30] Finally, the *ortho*-hydroxy on aryl substituent (Ar') promoted a subsequent intramolecular oxa-Michael ring-closure of **B** to provide **4** via a C-O bond formation under acidic conditions. On the basis of **B** with an (*E*)-form regioisomer, two stereochemical centers (C2 and C3) on **4** were orientated as a *trans*-conformation. The ratio of the diastereomers **4** was >20:1 by the determination of ^{1}H-NMR spectra. Products **4** were obtained as racemates.

To explore this $POCl_3$ mediated annulation route, a one-pot synthesis of 3-sulfonyl chromanones was undertaken, as shown in Table 3. By changing the aryl (Ar) group to an aliphatic (R' = CF_3, fluoral) group on aldehyde skeleton **3**, we found that this one-pot route still allowed a direct (5+1) annulation mode and provided 3-sulfonyl chromanones **4ae-4aj** with a 2-trifluoromethyl group in moderate yields (55%-69%, entries 1-6) under easy-operational reaction conditions under the above-mentioned conditions. **4ah** and **4aj** with tetrafluoro atoms were also prepared (entries 4 and 6). For the polyfluoro chromanone skeleton, potential bioactive properties were reported.[31] In entries 7-11, Et, Me, $(CH_2)_2Ph$, and *n*C_7H_{15} (R') groups showed lower yields (22%-38%) than the Ar group in the generation of **4ak-4ao**. A possible reason could be that $POCl_3$ could make the enolization of **3r-3u** easier such that the Knoevenagel reaction of **2** could be initiated with some difficulty. Furthermore, the relative stereochemical structures of

4af and **4aj** were determined by Single-crystal X-ray crystallography.[28] By the determination of ^{1}H-NMR spectra on **4ae-4ao**, only the diastereomeric ratio (dr) of **4am** was 9:1, and others were >20:1. In Scheme 5, 3-sulfonyl flindersiachromanone **4an** could be synthesized by one-pot route. Flindersiachromanone was isolated from extracts of the bark of *Flindersia laevicarpa*, and it was synthesized by different routes.[8a,9c,32]

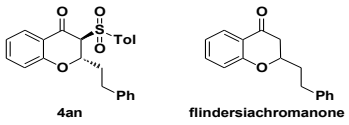
Table 3. Synthesis of **4ae-4ao**[a]



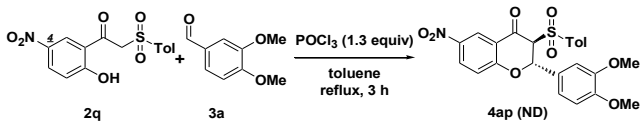
entry	**2a-2c**, **2e**, **2o-2p**, Ar' =, R =	**3q-3u**, R' =	**4ae-4ao**, (%)[b-c]
1	**2c**, Ph, Me	**3q**, CF_3	**4ae**, 62
2	**2b**, Ph, Ph	**3q**, CF_3	**4af**, 55
3	**2a**, Ph, Tol	**3q**, CF_3	**4ag**, 68
4	**2p**, 4-FC_6H_3, Tol	**3q**, CF_3	**4ah**, 69
5	**2o**, 5-$MeOC_6H_3$, Tol	**3q**, CF_3	**4ai**, 56
6	**2e**, Ph, 4-FC_6H_4	**3q**, CF_3	**4aj**, 65
7	**2a**, Ph, Tol	**3r**, Et	**4ak**, 30
8	**2e**, Ph, 4-FC_6H_4	**3s**, Me	**4al**, 22
9	**2a**, Ph, Tol	**3s**, Me	**4am**, 31[d]
10	**2a**, Ph, Tol	**3t**, $(CH_2)_2Ph$	**4an**, 35
11	**2a**, Ph, Tol	**3u**, nC_7H_{15}	**4ao**, 38

[a]The reactions were run on a 3.0 mmol scale with **2a-2c** and **2o-2p**, **3q-3u** (1.0 equiv), $POCl_3$ (1.3 equiv), toluene (5 mL), reflux, 3 h. [b]Isolated yields. [c]dr ratio >20:1. [d]dr ratio = 9:1.

Scheme 5. Structures of **4an** and Flindersiachromanone



Scheme 6. Reaction of **2q** with **3a**



By adjusting the Ar' as the electron-withdrawing 4-nitrophenyl group, **2q** was involved in the above condition (Scheme 6). When **2q** was reacted with **3a**, however, no desired **4ap** was detected. And, only starting material **2q** was recovered (82%) along with 65% of **3a**. One possible reason could be that C4-nitro group of **2q** could not promote the electron density efficiently to the *para*-hydroxy position such that $POCl_3$-mediated Knoevenagel condensation occurred more difficultly. Although substrate **2** was inappropriate to the electron-withdrawing group, the present route still provided novel and efficient synthesis of the sulfonyl flavanones.

In summary, we have developed an easy-operational, high-yielding method for gram-scale synthesis of 3-sulfonyl flavanones via $POCl_3$ mediated with β-(*o*-hydroxyaryl)ketosulfones and arylaldehydes in refluxing toluene for 3 h in moderate to good yields. The synthesis of 3-sulfonyl chromanones was accomplished by the one-pot protocol. The formal (5+1) annulation process provides a straightforward pathway for one carbon-oxygen and one carbon-carbon bond formations. The substrate scope and limitations are investigated for facile and efficient transformation. Related plausible mechanisms have been proposed. The structures of the key products were confirmed by X-ray crystallography. Further investigations regarding the synthetic application of β-ketosulfones will be conducted and published in due course.

Experimental Section

General. All reagents and solvents were obtained from commercial sources and used without further purification. Reactions were routinely carried out under an atmosphere of dry air with magnetic stirring. The heating mantle is used to provide a stable heat source. Products in organic solvents were dried with anhydrous magnesium sulfate before concentration in vacuo. Melting points were determined with a SMP3 melting apparatus. ^{1}H and ^{13}C NMR spectra were recorded on a Varian INOVA-400 spectrometer operating at 400 and at 100 MHz, respectively. Chemical shifts (δ) are reported in parts per million (ppm) and the coupling constants (*J*) are given in Hertz. High resolution mass spectra (HRMS) were measured with a mass spectrometer Finnigan/Thermo Quest MAT 95XL. X-ray crystal structures were obtained with an Enraf-Nonius FR-590 diffractometer (CAD4, Kappa CCD).

For the starting compounds **2a-2p**, the general synthetic procedure has been described in our previous reports.[4a] For the starting compounds **3a-3u**, these reagents were obtained from commercial sources and used without further purification.

*General synthetic procedure of skeleton **4** is as follows:* phosphorus oxychloride ($POCl_3$, 600 mg, 3.9 mmol) was added to a solution of **3** (3.0 mmol) in dry toluene (3 mL) at 25 °C. The reaction mixture was stirred for 10 min at reflux. Then, **2** (3.0 mmol) in dry toluene (2 mL) was added to the reaction mixture. The reaction mixture was stirred at reflux for 3 h, cooled to 25 °C and the solvent was concentrated. The residue was diluted with water (10 mL) and the mixture was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product under reduced pressure. Purification on silica gel (hexanes/EtOAc = 10/1~4/1) afforded **4** as racemates.

(2S,3S*)-2-(3,4-Dimethoxyphenyl)-3-(toluene-4-sulfonyl)chroman-4-one (**4a**)*. **4a** was synthesized according to general synthetic procedure from **2a** (870 mg, 3.0 mmol) and **3a** (500 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 87% (1.14 g); Colorless solid; mp = 156-158 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{24}H_{23}O_6S$ 439.1215, found 439.1216; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72-7.68 (m, 3H), 7.42 (dt, *J* = 1.6, 8.0 Hz, 1H), 7.22 (d, *J* = 8.8 Hz, 2H), 6.92 (dt, *J* = 0.8, 8.0 Hz, 1H), 6.85 (d, *J* = 0.8, 8.0 Hz, 1H), 6.77 (s, 1H), 6.68 (br s, 2H), 6.49 (s, 1H), 4.40 (d, *J* = 1.2 Hz, 1H), 3.77 (s, 3H), 3.75 (s, 3H), 2.36 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 182.3, 158.8, 149.3, 145.6, 137.2, 134.2, 129.5 (2x), 129.4 (3x), 128.4, 126.8, 121.6, 120.8, 118.6, 118.2, 110.9, 109.6, 76.1, 72.7, 55.78, 55.77, 21.6. Single-crystal X-Ray diagram: crystal of compound **4a** was grown by slow diffusion of EtOAc into a solution of compound **4a** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group P 21/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 to 26.475°, R indices (all data) R1 = 0.0488, wR2 = 0.1084.

(2S,3S*)-3-Benzenesulfonyl-2-(3,4-dimethoxyphenyl)chroman-4-one (**4b**)*. **4b** was synthesized according to general synthetic procedure from **2b** (828 mg, 3.0 mmol) and **3a** (500 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 90% (1.14 g); Colorless solid; mp = 157-159 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{23}H_{21}O_6S$ 425.1059, found 425.1060; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84-7.82 (m, 2H), 7.71 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.58-7.54 (m, 1H), 7.44 (d, *J* = 8.0 Hz, 2H), 7.42-7.38 (m, 1H), 6.91 (dt, *J* = 0.8, 8.0 Hz, 1H), 6.84 (d, *J* = 0.8, 8.0 Hz, 1H), 6.77 (s, 1H), 6.69 (br s, 2H), 6.50 (s, 1H), 4.43 (d, *J* = 1.2 Hz, 1H), 3.78 (s, 3H), 3.75 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 182.1, 158.7, 149.3 (2x), 137.4, 137.2, 134.4, 129.4 (2x), 128.9 (2x), 128.3, 126.8, 121.7, 120.8, 118.7, 118.2, 111.0, 109.7, 76.2, 72.8, 55.8 (2x).

(2S,3S*)-2-(3,4-Dimethoxyphenyl)-3-methanesulfonylchroman-4-one (**4c**)*. **4c** was synthesized according to general synthetic procedure from **2c** (642 mg, 3.0 mmol) and **3a** (500 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 92% (1.00 g); Colorless solid; mp = 144-146 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{18}H_{19}O_6S$ 363.0902, found 363.0903; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.55 (dt, *J* = 2.0, 8.4 Hz, 1H), 7.06 (dd, *J* = 0.8, 8.4 Hz, 1H), 7.01 (dt, *J* = 0.8, 8.0 Hz, 1H), 6.82 (s, 1H), 6.73 (br s, 2H), 6.45 (d, *J* = 0.8 Hz, 1H), 4.32 (d, *J* = 0.8 Hz, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.12 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 183.1, 159.3, 149.39, 149.36, 138.0, 128.4, 127.2, 122.1, 120.5, 118.72, 118.65, 111.0, 109.8, 74.7, 70.6, 55.83, 55.81, 41.3.

(2S,3S*)-3-(n-Butane-1-sulfonyl)-2-(3,4-dimethoxyphenyl)chroman-4-one (**4d**)*. **4d** was synthesized according to general synthetic procedure from **2d** (768 mg, 3.0 mmol) and **3a** (500 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 86% (1.04 g); Colorless oil; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{21}H_{25}O_6S$ 405.1372, found 405.1374; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.85 (dd, *J* = 1.6, 8.4 Hz, 1H), 7.53 (dt, *J* = 1.6, 8.4 Hz, 1H), 7.04 (dd, *J* = 0.4, 8.4 Hz, 1H), 7.00 (dt, *J* = 0.8, 8.0 Hz, 1H), 6.81 (s, 1H), 6.72 (br s, 2H), 6.44 (d, *J* = 1.2 Hz, 1H), 4.29 (d, *J* = 1.6 Hz, 1H), 3.79 (s, 3H), 3.77 (s, 3H), 3.27-3.22 (m, 2H), 1.91-1.83 (m, 2H), 1.52-1.44 (m, 2H), 0.94 (t, *J* = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 183.4, 159.3, 149.32, 149.28, 137.8, 128.6, 127.0, 121.9, 120.6, 118.7, 118.6, 110.9, 109.8, 74.6, 68.6, 55.8, 53.1, 23.3 (2x), 21.5, 13.4.

(2S,3S*)-2-(3,4-Dimethoxyphenyl)-3-(4-fluorobenzenesulfonyl)chroman-4-one (**4e**)*. **4e** was synthesized according to general synthetic procedure from **2e** (882 mg, 3.0 mmol) and **3a** (500 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 83% (1.10 g); Colorless solid; mp = 159-161 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{23}H_{20}FO_6S$ 443.0965, found 443.0964; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86-7.81 (m, 2H), 7.70 (dt, *J* = 1.6, 8.0 Hz, 1H), 7.43 (dt, *J* = 1.6, 8.8 Hz, 1H), 7.11-7.05 (m, 2H), 6.93 (dt, *J* = 0.8, 8.0 Hz, 1H), 6.84 (dd, *J* = 0.4, 8.4 Hz, 1H), 6.77 (d, *J* = 0.8 Hz, 1H), 6.71-6.66 (m, 2H), 6.49 (s, 1H), 4.43 (d, *J* = 1.2 Hz, 1H), 3.78 (s, 3H), 3.77 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 182.0, 166.2 (d, *J* = 257.0 Hz), 158.6, 149.4, 149.3, 137.5, 133.2 (d, *J* = 3.1 Hz), 132.4 (d, *J* = 9.9 Hz, 2x), 128.1, 126.8, 121.9, 120.7, 118.7, 118.2, 116.1 (d, *J* = 22.7 Hz, 2x), 111.0, 109.7, 76.3, 72.9, 55.81, 55.79. Single-crystal X-Ray diagram: crystal of compound **4e** was grown by slow diffusion of EtOAc into a solution of compound **4e** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group P 21/c, a = 20.5754(16) Å, b = 11.9457(8) Å, c = 8.2774(6) Å, V = 2031.3(3) Å^3, Z = 4, d_{calcd} = 1.447 g/cm^3, F(000) = 920, 2θ range 0.991 to 26.478°, R indices (all data) R1 = 0.0489, wR2 = 0.0997.

(2S,3S*)-2-(3,4-Dimethoxyphenyl)-3-(4-methoxybenzenesulfonyl)chroman-4-one (**4f**)*. **4f** was synthesized according to general synthetic procedure from **2f** (918 mg, 3.0 mmol) and **3a** (500 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 84% (1.14 g); Colorless solid; mp = 152-154 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{24}H_{23}O_7S$ 455.1165, found 455.1168; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 9.2 Hz, 2H), 7.69 (dt, *J* = 1.6, 8.0 Hz, 1H), 7.37 (dt, *J* = 1.6, 8.8 Hz, 1H), 6.87 (dt, *J* = 1.2, 8.0 Hz, 1H), 6.84-6.82 (m, 1H), 6.82 (d, *J* = 8.8 Hz, 2H), 6.75 (d, *J* = 1.2 Hz, 1H), 6.66-6.63 (m, 2H), 6.44 (s, 1H), 4.41 (d, *J* = 1.2 Hz, 1H), 3.75 (s, 3H), 3.72 (s, 3H), 3.71 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 182.2, 164.1, 158.6, 149.08, 149.05, 137.1, 131.5 (2x), 128.3, 128.2, 126.6, 121.5, 120.7, 118.5, 118.0, 113.9 (2x), 110.8, 109.5, 76.2, 72.7, 55.62, 55.59, 55.5.

(2S,3S*)-2-(3,4-Dimethoxyphenyl)-3-(toluene-3-sulfonyl)chroman-4-one (**4g**)*. **4g** was synthesized according to general synthetic procedure from **2g** (870 mg, 3.0 mmol) and **3a** (500 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 87% (1.14 g); Colorless solid; mp = 176-178 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{24}H_{23}O_6S$ 439.1215, found 439.1216; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.64-7.61 (m, 2H), 7.40 (dt, *J* = 1.6, 8.8 Hz, 1H), 7.35-7.29 (m, 2H), 6.91 (dt, *J* = 1.2, 8.0 Hz, 1H), 6.84 (dd, *J* = 0.8, 8.4 Hz, 1H), 6.77 (s, 1H), 6.69-6.68 (m, 2H), 6.48 (s, 1H), 4.42 (d, *J* = 0.8 Hz, 1H), 3.78 (s, 3H), 3.75 (s, 3H), 2.33 (s, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 182.1, 158.7, 149.3 (2x), 139.2, 137.3, 136.9, 135.2, 129.6, 128.7, 128.3, 126.8, 126.6, 121.7, 120.8, 118.7, 118.1, 111.0, 109.6, 76.2, 72.8, 55.79, 55.78, 21.1.

(2S,3S*)-2-(3,4-Dimethoxyphenyl)-3-(4-ethylbenzenesulfonyl)chroman-4-one (**4h**)*. **4h** was synthesized according to general synthetic procedure from **2h** (912 mg, 3.0 mmol) and **3a** (500 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 92% (1.25 g); Colorless oil; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{25}H_{25}O_6S$ 453.1372, found 453.1375; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.4 Hz, 2H), 7.71 (dt, *J* = 1.6, 8.0 Hz, 1H), 7.39 (dt, *J* = 1.6, 8.8 Hz, 1H), 7.23 (d, *J* = 8.4 Hz, 2H), 6.91 (dt, *J* = 0.8, 8.0 Hz, 1H), 6.82 (dd, *J* = 0.8, 8.0 Hz, 1H), 6.77 (s, 1H), 6.69 (br s, 2H), 6.49 (s, 1H), 4.41 (d, *J* = 1.2 Hz, 1H), 3.78 (s, 3H), 3.76 (s, 3H), 2.65 (q, *J* = 7.6 Hz, 2H), 1.19 (t, *J* = 7.6 Hz, 3H); ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 182.3, 158.7, 151.7, 149.32, 149.30, 137.3, 134.3, 129.6 (2x), 128.4, 128.3 (2x),

126.9, 121.7, 120.8, 118.7, 118.2, 111.0, 109.7, 76.3, 72.9, 55.8 (2x), 28.9, 15.0.

(2S,3S*)-2-(3,4-Dimethoxyphenyl)-3-(4-isopropylbenzenesulfonyl)chroman-4-one (**4i**)*. **4i** was synthesized according to general synthetic procedure from **2i** (954 mg, 3.0 mmol) and **3a** (500 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 93% (1.30 g); Colorless solid; mp = 153-155 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{26}H_{27}O_6S$ 467.1528, found 467.1530; ^1H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.4 Hz, 2H), 7.69 (dt, *J* = 1.6, 8.0 Hz, 1H), 7.37 (dt, *J* = 1.6, 8.4 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.89 (dt, *J* = 0.8, 8.0 Hz, 1H), 6.79 (dd, *J* = 0.8, 8.4 Hz, 1H), 6.77 (s, 1H), 6.69 (br s, 2H), 6.49 (s, 1H), 4.42 (d, *J* = 0.8 Hz, 1H), 3.78 (s, 3H), 3.76 (s, 3H), 2.93-2.86 (m, 1H), 1.19 (d, *J* = 6.8 Hz, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 182.2, 158.7, 156.2, 149.3, 137.2, 134.3, 129.7 (2x), 128.4, 126.9 (2x), 126.8 (2x), 121.6, 120.8, 118.7, 118.1, 111.0, 109.6, 76.5, 73.0, 55.8 (2x), 34.2, 23.5, 23.4.

(2S,3S*)-3-(4-n-Butylbenzenesulfonyl)-2-(3,4-dimethoxyphenyl)chroman-4-one (**4j**)*. **4j** was synthesized according to general synthetic procedure from **2j** (996 mg, 3.0 mmol) and **3a** (500 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 80% (1.15 g); Colorless solid; mp = 123-125 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{27}H_{29}O_6S$ 481.1685, found 481.1687; ^1H NMR (400 MHz, $CDCl_3$): δ 7.72-7.68 (m, 3H), 7.37 (dt, *J* = 2.0, 8.4 Hz, 1H), 7.19 (d, *J* = 8.4 Hz, 2H), 6.89 (dt, *J* = 0.8, 8.0 Hz, 1H), 6.80 (dd, *J* = 0.8, 8.4 Hz, 1H), 6.77 (s, 1H), 6.68 (br d, *J* = 0.8 Hz, 2H), 6.48 (s, 1H), 4.42 (d, *J* = 1.2 Hz, 1H), 3.77 (s, 3H), 3.75 (s, 3H), 2.59 (t, *J* = 7.6 Hz, Hz, 2H), 1.55-1.48 (m, 2H), 1.33-1.24 (m, 2H), 0.91 (d, *J* = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 182.2, 158.7, 150.4, 149.3, 149.2, 137.2, 134.3, 129.4 (2x), 128.8 (2x), 128.4, 126.8, 121.6, 120.8, 118.6, 118.1, 110.9, 109.6, 76.4, 72.9, 55.77, 55.75, 35.5, 32.9, 22.1, 13.8.

(2S,3S*)-3-(4-t-Butylbenzenesulfonyl)-2-(3,4-dimethoxyphenyl)chroman-4-one (**4k**)*. **4k** was synthesized according to general synthetic procedure from **2k** (996 mg, 3.0 mmol) and **3a** (500 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 87% (1.25 g); Colorless solid; mp = 181-183 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{27}H_{29}O_6S$ 481.1685, found 481.1684; ^1H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 8.8 Hz, 2H), 7.70 (dt, *J* = 1.6, 8.0 Hz, 1H), 7.38 (d, *J* = 8.8 Hz, 2H), 7.35 (dt, *J* = 1.6, 8.8 Hz, 1H), 6.88 (dt, *J* = 0.8, 8.0 Hz, 1H), 6.78 (dt, *J* = 0.8, 8.0 Hz, 1H), 6.78 (s, 1H), 6.68 (br s, 2H), 6.48 (s, 1H), 4.43 (d, *J* = 1.2 Hz, 1H), 3.77 (s, 3H), 3.75 (s, 3H), 1.25 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 182.2, 158.6, 158.4, 149.3, 149.2, 137.2, 133.9, 129.4 (2x), 128.3, 126.8, 125.7 (2x), 121.6, 120.8, 118.6, 118.0, 110.9, 109.6, 76.5, 72.9, 55.78, 55.76, 35.2, 30.8 (3x).

(2S,3S*)-6-Bromo-2-(3,4-dimethoxyphenyl)-3-(toluene-4-sulfonyl)chroman-4-one (**4l**)*. **4l** was synthesized according to general synthetic procedure from **2l** (1.1 g, 3.0 mmol) and **3a** (500 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 84% (1.30 g); Colorless solid; mp = 155-157 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{24}H_{22}BrO_6S$ 517.0321, found 517.0320; ^1H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, *J* = 2.8 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 2H), 7.50 (dd, *J* = 2.0, 8.8 Hz, 1H), 7.27 (d, *J* = 8.0 Hz, 2H), 6.80 (d, *J* = 8.8 Hz, 1H), 6.75 (d, *J* = 2.0 Hz, 1H), 6.69 (d, *J* = 8.4 Hz, 1H), 6.64 (dd, *J* = 2.0, 8.4 Hz, 1H), 6.50 (s, 1H), 4.40 (d, *J* = 0.8 Hz, 1H), 3.78 (s, 3H), 3.77 (s, 3H), 2.40 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 181.4, 157.7, 149.5, 149.4, 145.9, 139.7, 134.1, 129.6 (2x), 129.3 (2x), 129.1, 127.8, 121.9, 120.3, 118.7, 114.3, 110.9, 109.7, 76.2, 72.1, 55.84, 55.78, 21.6.

(2S,3S*)-6-Chloro-2-(3,4-dimethoxyphenyl)-3-(toluene-4-sulfonyl)chroman-4-one (**4m**)*. **4m** was synthesized according to general synthetic procedure from **2m** (972 mg, 3.0 mmol) and **3a** (500 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 85% (1.20 g); Colorless solid; mp = 154-156 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{24}H_{22}ClO_6S$ 473.0826, found 473.0827; ^1H NMR (400 MHz, $CDCl_3$): δ 7.70-7.67 (m, 3H), 7.37 (dd, *J* = 2.8, 8.8 Hz, 1H), 7.27 (d, *J* = 8.4 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 1H), 6.76 (d, *J* = 2.0 Hz, 1H), 6.69 (d, *J* = 8.4 Hz, 1H), 6.64 (dd, *J* = 2.0, 8.4 Hz, 1H), 6.50 (s, 1H), 4.40 (d, *J* = 0.8 Hz, 1H), 3.78 (s, 3H), 3.77 (s, 3H), 2.40 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 181.6, 157.2, 149.5, 149.4, 145.9, 137.0, 134.2, 129.7 (2x), 129.3 (2x), 127.8, 127.2, 126.1, 121.4, 120.0, 118.7, 110.9, 109.7, 76.2, 72.1, 55.85, 55.78, 21.6.

(2S,3S*)-2-(3,4-Dimethoxyphenyl)-3-(toluene-4-sulfonyl)-2,3-dihydrobenzo[h]chromen-4-one (**4n**)*. **4n** was synthesized according to general synthetic procedure from **2n** (1.02 g, 3.0 mmol) and **3a** (500 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 82% (1.20 g); Colorless solid; mp = 175-177 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{28}H_{25}O_6S$ 489.1372, found 489.1372; ^1H NMR (400 MHz, $CDCl_3$): δ 8.25 (dd, *J* = 0.8, 8.4 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.65 (d, *J* = 8.8 Hz, 1H), 7.60 (dt, *J* = 1.6, 8.4 Hz, 1H), 7.51 (dt, *J* = 1.2, 8.4 Hz, 2H), 7.30 (d, *J* = 8.8 Hz, 1H), 7.04 (d, *J* = 8.4 Hz, 2H), 6.82 (d, *J* = 2.0 Hz, 1H), 6.73 (dd, *J* = 2.4, 8.0 Hz, 1H), 6.66 (d, *J* = 8.8 Hz, 1H), 4.48 (d, *J* = 0.8 Hz, 1H), 3.75 (s, 3H), 3.69 (s, 3H), 2.12 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 181.5, 157.0, 149.4, 149.3, 145.6, 137.9, 133.9, 130.1, 129.3 (4x), 128.2, 127.8, 126.4, 124.4, 123.5, 121.5, 121.0, 118.4, 115.6, 111.0, 109.3, 77.0, 72.8, 55.78, 55.76, 21.3.

(2S,3S*)-2-Phenyl-3-(toluene-4-sulfonyl)chroman-4-one (**4o**)*. **4o** was synthesized according to general synthetic procedure from **2a** (870 mg, 3.0 mmol) and **3b** (318 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 88% (1.00 g); Colorless solid; mp = 131-133 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{22}H_{19}O_4S$ 379.1004, found 379.1006; ^1H NMR (400 MHz, $CDCl_3$): δ 7.72-7.70 (m, 3H), 7.46 (dt, *J* = 1.6, 8.4 Hz, 1H), 7.27-7.19 (m, 7H), 6.95 (dd, *J* = 0.8, 7.6 Hz, 1H), 6.91 (dd, *J* = 0.8, 8.4 Hz, 1H), 6.57 (s, 1H), 4.39 (d, *J* = 1.6 Hz, 1H), 2.38 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 182.0, 159.0, 145.7, 137.4, 136.2, 134.2, 129.6 (2x), 129.4 (2x), 129.0 (2x), 128.7, 126.9, 126.1 (2x), 121.7, 120.8, 118.2, 76.2, 73.0, 21.6.

(2S,3S*)-2-(4-Methoxyphenyl)-3-(toluene-4-sulfonyl)chroman-4-one (**4p**)*. **4p** was synthesized according to general synthetic procedure from **2a** (870 mg, 3.0 mmol) and **3c** (408 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr

was >20:1; Yield = 84% (1.03 g); Colorless solid; mp = 121-123 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{23}H_{21}O_5S$ 409.1110, found 409.1112; ^1H NMR (400 MHz, $CDCl_3$): δ 7.72-7.68 (m, 3H), 7.42 (dt, *J* = 1.6, 8.4 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 8.4 Hz, 2H), 6.92 (dt, *J* = 0.8, 8.0 Hz, 1H), 6.85 (dd, *J* = 0.8, 8.4 Hz, 1H), 6.77 (d, *J* = 8.8 Hz, 2H), 6.50 (s, 1H), 4.38 (d, *J* = 0.8 Hz, 1H), 3.71 (s, 3H), 2.37 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 182.3, 159.7, 158.8, 145.6, 137.2, 134.3, 129.5 (2x), 129.3 (2x), 128.0, 127.6 (2x), 126.8, 121.6, 120.7, 118.3, 114.3 (2x), 76.0, 72.8, 55.2, 21.6.

(2S,3S*)-2-(3-Methoxyphenyl)-3-(toluene-4-sulfonyl)chroman-4-one (**4q**)*. **4q** was synthesized according to general synthetic procedure from **2a** (870 mg, 3.0 mmol) and **3d** (408 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 82% (1.00 g); Colorless solid; mp = 148-150 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{23}H_{21}O_5S$ 409.1110, found 409.1108; ^1H NMR (400 MHz, $CDCl_3$): δ 7.72-7.69 (m, 3H), 7.45 (dt, *J* = 1.6, 8.4 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.16 (t, *J* = 8.4 Hz, 1H), 6.93 (dt, *J* = 0.8, 8.0 Hz, 1H), 6.91 (dd, *J* = 0.8, 8.4 Hz, 1H), 6.77-6.74 (m, 3H), 6.53 (s, 1H), 4.38 (d, *J* = 1.2 Hz, 1H), 3.69 (s, 3H), 2.37 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 181.9, 159.9, 159.0, 145.7, 137.7, 137.3, 134.2, 130.0, 129.5 (2x), 129.3 (2x), 126.9, 121.7, 120.7, 118.1, 118.0, 113.8, 112.1, 76.1, 73.0, 55.1, 21.6.

(2S,3S*)-2-(4-Fluorophenyl)-3-(toluene-4-sulfonyl)chroman-4-one (**4r**)*. **4r** was synthesized according to general synthetic procedure from **2a** (870 mg, 3.0 mmol) and **3e** (372 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 86% (1.02 g); Colorless solid; mp = 156-158 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{22}H_{18}FO_4S$ 397.0910, found 397.0912; ^1H NMR (400 MHz, $CDCl_3$): δ 7.72-7.68 (m, 3H), 7.45 (dt, *J* = 1.6, 8.4 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.22-7.18 (m, 2H), 6.97-6.93 (m, 3H), 6.89 (dd, *J* = 0.8, 8.4 Hz, 1H), 6.53 (s, 1H), 4.37 (d, *J* = 0.8 Hz, 1H), 2.37 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 181.9, 162.6 (d, *J* = 247.1 Hz), 158.7, 145.8, 137.4, 134.1, 132.0 (d, *J* = 3.5 Hz), 129.5 (2x), 129.3 (2x), 128.06 (d, *J* = 8.4 Hz, 2x), 126.9, 121.8, 120.7, 118.2, 116.0 (d, *J* = 21.2 Hz, 2x), 75.7, 72.8, 21.6.

(2S,3S*)-3-(Toluene-4-sulfonyl)-2-p-tolylchroman-4-one (**4s**)*. **4s** was synthesized according to general synthetic procedure from **2a** (870 mg, 3.0 mmol) and **3f** (360 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 89% (1.05 g); Colorless solid; mp = 157-159 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{23}H_{21}O_4S$ 393.1161, found 393.1162; ^1H NMR (400 MHz, $CDCl_3$): δ 7.72-7.70 (m, 3H), 7.43 (dt, *J* = 1.6, 8.4 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.4 Hz, 2H), 7.05 (d, *J* = 8.0 Hz, 2H), 6.92 (dt, *J* = 0.8, 8.0 Hz, 1H), 6.88 (dd, *J* = 0.8, 8.8 Hz, 1H), 6.53 (s, 1H), 4.40 (d, *J* = 1.2 Hz, 1H), 2.37 (s, 3H), 2.24 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 182.1, 158.9, 145.6, 138.5, 137.2, 134.2, 133.0, 129.6 (2x), 129.5 (2x), 129.3 (2x), 126.8, 126.0 (2x), 121.6, 120.7, 118.2, 76.1, 72.8, 21.5, 20.9.

(2S,3S*)-2-Biphenyl-4-yl-3-(toluene-4-sulfonyl)chroman-4-one (**4t**)*. **4t** was synthesized according to general synthetic procedure from **2a** (870 mg, 3.0 mmol) and **3g** (546 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 80% (1.09 g); Colorless solid; mp = 123-125 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{28}H_{23}O_4S$ 455.1317, found 455.1318; ^1H NMR (400 MHz, $CDCl_3$): δ 7.41-7.38 (m, 3H), 7.15-7.11 (m, 5H), 7.08-7.04 (m, 2H), 7.01-6.99 (m, 1H), 6.97-6.90 (m, 4H), 6.64-6.59 (m, 2H), 6.28 (s, 1H), 4.10 (d, *J* = 1.2 Hz, 1H), 2.05 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 182.1, 159.0, 145.7, 141.6, 139.9, 137.4, 135.1, 134.2, 129.6 (2x), 129.4 (2x), 128.8 (2x), 127.6 (2x), 127.0 (3x), 126.9 (2x), 126.6 (2x), 121.7, 118.3, 76.1, 72.9, 21.6.

(2S,3S*)-2-Naphthalen-2-yl-3-(toluene-4-sulfonyl)chroman-4-one (**4u**)*. **4u** was synthesized according to general synthetic procedure from **2a** (870 mg, 3.0 mmol) and **3h** (468 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 78% (1.00 g); Colorless solid; mp = 141-143 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{26}H_{21}O_4S$ 429.1161, found 429.1160; ^1H NMR (400 MHz, $CDCl_3$): δ 7.79-7.68 (m, 6H), 7.58 (br s, 1H), 7.48-7.39 (m, 4H), 7.26 (d, *J* = 8.8 Hz, 2H), 6.96-6.91 (m, 2H), 6.73 (s, 1H), 4.57 (d, *J* = 1.2 Hz, 1H), 2.39 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 182.1, 158.9, 145.7, 137.4, 134.3, 133.4, 132.9, 132.7, 129.6 (2x), 129.4 (2x), 129.2, 128.1, 127.5, 126.9, 126.8, 126.7, 125.5, 123.6, 121.8, 120.8, 118.3, 76.2, 72.6, 21.6.

(2S,3S*)-2-Benzo[1,3]dioxol-5-yl-3-(toluene-4-sulfonyl)chroman-4-one (**4v**)*. **4v** was synthesized according to general synthetic procedure from **2a** (870 mg, 3.0 mmol) and **3i** (450 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 85% (1.08 g); Colorless solid; mp = 198-200 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{23}H_{19}O_6S$ 423.0902, found 423.0902; ^1H NMR (400 MHz, $CDCl_3$): δ 7.72 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 2H), 7.44 (dt, *J* = 2.0, 8.4 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.94 (dd, *J* = 1.2, 8.0 Hz, 1H), 6.87 (dd, *J* = 0.8, 8.4 Hz, 1H), 6.71 (d, *J* = 1.6 Hz, 1H), 6.66 (d, *J* = 8.0 Hz, 1H), 6.63 (dd, *J* = 1.6, 8.0 Hz, 1H), 6.45 (s, 1H), 5.90 (d, *J* = 1.2 Hz, 1H), 5.89 (d, *J* = 1.2 Hz, 1H), 4.33 (d, *J* = 1.2 Hz, 1H), 2.38 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 182.1, 158.7, 148.3, 147.9, 145.7, 137.3, 134.2, 129.9, 129.5 (2x), 129.4 (2x), 126.9, 121.7, 120.7, 119.9, 118.3, 108.4, 106.8, 101.4, 76.0, 72.8, 21.6.

(2S,3S*)-2-(3,4-Dichlorophenyl)-3-(toluene-4-sulfonyl)chroman-4-one (**4w**)*. **4w** was synthesized according to general synthetic procedure from **2a** (870 mg, 3.0 mmol) and **3j** (522 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 80% (1.07 g); Colorless solid; mp = 159-161 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{22}H_{17}Cl_2O_4S$ 447.0225, found 447.0224; ^1H NMR (400 MHz, $CDCl_3$): δ 7.71 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 2H), 7.49 (dt, *J* = 2.0, 8.4 Hz, 1H), 7.34 (d, *J* = 8.4 Hz, 1H), 7.32 (d, *J* = 2.4 Hz, 1H), 7.25 (d, *J* = 8.4 Hz, 2H), 7.05 (dd, *J* = 2.0, 8.4 Hz, 1H), 6.98 (dd, *J* = 0.8, 8.0 Hz, 1H), 6.93 (d, *J* = 8.4 Hz, 1H), 6.51 (s, 1H), 4.33 (d, *J* = 1.2 Hz, 1H), 2.39 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 181.5, 158.4, 146.0, 137.7, 136.4, 134.0, 133.4, 131.0, 129.7 (2x), 129.43, 129.37 (2x), 128.3, 127.1, 125.3, 122.2, 120.6, 118.2, 75.1, 72.4, 21.7.

(2S,3S*)-3-(Toluene-4-sulfonyl)-2-(3,4,5-trimethoxyphenyl)chroman-4-one (**4x**)*. **4x** was synthesized according to general synthetic procedure from **2a** (870 mg, 3.0

mmol) and **3k** (588 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 86% (1.21 g); Colorless solid; mp = 190-192 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{25}H_{25}O_7S$ 469.1321, found 469.1322; ^1H NMR (400 MHz, $CDCl_3$): δ 7.70 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.43 (dt, *J* = 2.0, 8.4 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 2H), 6.93 (dt, *J* = 0.8, 8.4 Hz, 1H), 6.87 (dd, *J* = 0.8, 8.4 Hz, 1H), 6.47 (d, *J* = 0.4 Hz, 1H), 6.38 (d, *J* = 0.8 Hz, 2H), 4.39 (d, *J* = 1.2 Hz, 1H), 3.73 (s, 3H), 3.68 (s, 6H), 2.34 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 182.0, 158.8, 153.4 (2x), 145.7, 138.0, 137.3, 134.0, 131.5, 129.4 (2x), 129.3 (2x), 126.8, 121.7, 120.7, 117.9, 103.4 (2x), 76.3, 72.9, 60.6, 55.9 (2x), 21.5.

(2S,3S*)-2-Furan-2-yl-3-(toluene-4-sulfonyl)chroman-4-one (**4y**)*. **4y** was synthesized according to general synthetic procedure from **2a** (870 mg, 3.0 mmol) and **3l** (288 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 92% (1.02 g); Colorless solid; mp = 151-153 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{20}H_{17}O_5S$ 369.0797, found 369.0798; ^1H NMR (400 MHz, $CDCl_3$): δ 7.76 (dd, *J* = 2.0, 8.0 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 2H), 7.41 (dt, *J* = 2.0, 8.4 Hz, 1H), 7.28 (t, *J* = 1.2 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.95 (dt, *J* = 0.8, 8.4 Hz, 1H), 6.81 (dd, *J* = 0.8, 8.4 Hz, 1H), 6.48 (d, *J* = 1.2 Hz, 1H), 6.24 (br s, 1H), 6.23 (br s, 1H), 4.33 (d, *J* = 1.2 Hz, 1H), 2.36 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 181.9, 158.3, 149.0, 145.7, 143.6, 137.0, 134.1, 129.5 (2x), 129.3 (2x), 126.8, 121.9, 120.4, 118.3, 110.5, 110.1, 70.9, 70.8, 21.6.

(2R,3S*)-2-Thiophen-2-yl-3-(toluene-4-sulfonyl)chroman-4-one (**4z**)*. **4z** was synthesized according to general synthetic procedure from **2a** (870 mg, 3.0 mmol) and **3m** (336 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 88% (1.01 g); Colorless solid; mp = 139-141 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{20}H_{17}O_4S_2$ 385.0568, found 385.0566; ^1H NMR (400 MHz, $CDCl_3$): δ 7.75 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.71 (d, *J* = 8.8 Hz, 2H), 7.43 (dt, *J* = 1.6, 8.8 Hz, 1H), 7.23 (d, *J* = 8.4 Hz, 2H), 7.20 (dd, *J* = 1.2, 8.0 Hz, 1H), 6.95 (dt, *J* = 0.8, 8.4 Hz, 1H), 6.90 (dt, *J* = 1.2, 8.4 Hz, 1H), 6.46-6.84 (m, 2H), 6.70 (br d, *J* = 1.2 Hz, 1H), 4.39 (d, *J* = 1.2 Hz, 1H), 2.37 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 181.9, 158.1, 145.8, 139.0, 137.2, 134.1, 129.5 (2x), 129.4 (2x), 127.1, 126.9 (2x), 126.8, 122.1, 120.6, 118.7, 73.4, 72.7, 21.6.

(2S,3S*)-3-Pyridin-2-yl-3-(toluene-4-sulfonyl)chroman-4-one (**4aa**)*. **4aa** was synthesized according to general synthetic procedure from **2a** (870 mg, 3.0 mmol) and **3n** (321 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 90% (1.02 g); Colorless solid; mp = 136-138 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{21}H_{18}NO_4S$ 380.0957, found 380.0957; ^1H NMR (400 MHz, $CDCl_3$): δ 8.54 (d, *J* = 2.4 Hz, 1H), 8.51 (dd, *J* = 1.2, 4.8 Hz, 1H), 7.71 (dt, *J* = 1.6, 8.8 Hz, 1H), 7.68 (d, *J* = 8.8 Hz, 2H), 7.54-7.51 (m, 1H), 7.47 (dt, *J* = 2.0, 8.4 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.20 (dd, *J* = 3.2, 8.0 Hz, 1H), 6.97 (dt, *J* = 1.2, 8.4 Hz, 1H), 6.92 (dd, *J* = 0.8, 8.4 Hz, 1H), 6.61 (s, 1H), 4.36 (d, *J* = 1.2 Hz, 1H), 2.38 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 181.5, 158.5, 150.0, 147.8, 145.9, 137.7, 134.1, 133.8, 132.1, 129.6 (2x), 129.4 (2x), 127.0, 123.6, 122.2, 120.7, 118.3, 74.6, 72.4, 21.6.

(2S,3S*)-2-(2-Bromophenyl)-3-(toluene-4-sulfonyl)chroman-4-one (**4ab**)*. **4ab** was synthesized according to general synthetic procedure from **2a** (870 mg, 3.0 mmol) and **3o** (552 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 74% (1.01 g); Colorless solid; mp = 158-160 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{22}H_{18}BrO_4S$ 457.0109, found 457.0110; ^1H NMR (400 MHz, $CDCl_3$): δ 7.70 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 2H), 7.57 (dt, *J* = 2.0, 8.4 Hz, 1H), 7.56 (dd, *J* = 2.0, 8.0 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.15-7.08 (m, 2H), 7.08-7.00 (m, 3H), 6.80 (s, 1H), 4.47 (d, *J* = 1.2 Hz, 1H), 2.40 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 181.8, 159.9, 145.7, 137.7, 134.9, 134.5, 134.0, 130.2, 129.7 (2x), 129.3 (2x), 127.7, 127.1, 127.0, 121.9, 121.5, 120.6, 117.7, 76.1, 71.3, 21.7. Single-crystal X-Ray diagram: crystal of compound **4ab** was grown by slow diffusion of EtOAc into a solution of compound **4ab** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the orthorhombic crystal system, space group P 21 21 21, *a* = 8.6975(7) Å, *b* = 11.1079(9) Å, *c* = 19.6779(17) Å, *V* = 1901.1(3) Å^3, *Z* = 4, d_{calcd} = 1.598 g/cm^3, *F*(000) = 928, 2*θ* range 2.070 to 26.508°, R indices (all data) R1 = 0.0342, wR2 = 0.0561.

(2S,3S*)-6-Chloro-2-(4-chlorophenyl)-3-(toluene-4-sulfonyl)chroman-4-one (**4ac**)*. **4ac** was synthesized according to general synthetic procedure from **2m** (972 mg, 3.0 mmol) and **3p** (420 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 80% (1.07 g); Colorless solid; mp = 172-174 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{22}H_{17}Cl_2O_4S$ 447.0225, found 447.0225; ^1H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 8.4 Hz, 2H), 7.64 (dd, *J* = 2.8, 8.8 Hz, 1H), 7.38 (dd, *J* = 2.8, 8.8 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.09 (d, *J* = 8.0 Hz, 2H), 6.88 (d, *J* = 9.2 Hz, 1H), 6.51 (s, 1H), 4.31 (d, *J* = 1.2 Hz, 1H), 2.38 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 181.1, 157.1, 146.1, 137.3, 135.0, 134.1, 134.0, 129.8 (2x), 129.33 (2x), 129.30 (2x), 127.6, 127.5 (2x), 126.2, 121.3, 120.0, 75.8, 72.1, 21.7.

(2S,3S*)-7-Methoxy-3-(toluene-4-sulfonyl)-2-(3,4,5-trimethoxyphenyl)chroman-4-one (**4ad**)*. **4ad** was synthesized according to general synthetic procedure from **2o** (960 mg, 3.0 mmol) and **3k** (588 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 86% (1.28 g); Colorless solid; mp = 195-197 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{26}H_{27}O_8S$ 499.1427, found 499.1428; ^1H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 8.0 Hz, 2H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.24 (d, *J* = 8.4 Hz, 2H), 6.51 (dd, *J* = 2.4, 8.8 Hz, 1H), 6.43 (s, 1H), 6.40 (s, 2H), 6.32 (d, *J* = 2.4 Hz, 1H), 4.30 (d, *J* = 0.8 Hz, 1H), 3.79 (s, 3H), 3.75 (s, 3H), 3.70 (s, 6H), 2.38 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 180.3, 167.3, 161.0, 153.4 (2x), 145.6, 138.1, 134.2, 131.8, 129.5 (2x), 129.3 (2x), 128.7, 114.7, 110.5, 103.5 (2x), 100.8, 76.5, 72.6, 60.7, 56.0 (2x), 55.7, 21.6.

(2S,3S*)-3-Methanesulfonyl-2-trifluoromethylchroman-4-one (**4ae**)*. **4ae** was synthesized according to general synthetic procedure from **2c** (642 mg, 3.0 mmol) and **3q** (294 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 62% (547 mg); Colorless solid; mp = 138-140 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{11}H_{10}F_3O_4S$ 295.0252, found 295.0253; ^1H NMR (400 MHz, $CDCl_3$): δ 7.93 (dd, *J* = 2.0,

8.0 Hz, 1H), 7.63 (t, *J* = 5.6 Hz, 1H), 7.15 (t, *J* = 8.0 Hz, 1H), 7.10 (d, *J* = 8.4 Hz, 1H), 5.70 (q, *J* = 8.0 Hz, 1H), 4.11 (s, 1H), 3.19 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 180.6, 158.2, 138.4, 127.1, 123.23, 123.18 (q, *J* = 283.5 Hz), 118.1 (2x), 71.2 (q, *J* = 33.4 Hz), 64.6, 41.2.

(2S,3S*)-3-Benzenesulfonyl-2-trifluoromethylchroman-4-one (**4af**).* **4af** was synthesized according to general synthetic procedure from **2b** (828 mg, 3.0 mmol) and **3q** (294 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 55% (587 mg); Colorless solid; mp = 123-125 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{12}F_3O_4S$ 357.0408, found 357.0409; ^1H NMR (400 MHz, $CDCl_3$): δ 7.81-7.79 (m, 2H), 7.77 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.64-7.60 (m, 1H), 7.53-7.46 (m, 3H), 7.07-7.03 (m, 1H), 6.93 (d, *J* = 8.4 Hz, 1H), 5.77 (q, *J* = 8.4 Hz, 1H), 4.22 (d, *J* = 0.8 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 179.5, 157.7, 137.7, 136.2, 135.0, 129.4 (2x), 129.2 (2x), 126.8, 123.7 (d, *J* = 284.3 Hz), 122.9, 119.7, 117.7, 73.0 (q, *J* = 32.6 Hz), 66.9. Single-crystal X-Ray diagram: crystal of compound **4af** was grown by slow diffusion of EtOAc into a solution of compound **4af** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the orthorhombic crystal system, space group P n a 21, a = 24.1977(12) Å, b = 9.9696(5) Å, c = 12.6028(6) Å, V = 3040.3(3) $Å^3$, Z = 4, d_{calcd} = 1.557 g/cm^3, *F*(000) = 1456, 2*θ* range 1.683~26.419°, R indices (all data) R1 = 0.0574, wR2 = 0.1359.

(2S,3S*)-3-(Toluene-4-sulfonyl)-2-trifluoromethylchroman-4-one (**4ag**).* **4ag** was synthesized according to general synthetic procedure from **2a** (870 mg, 3.0 mmol) and **3q** (294 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 68% (755 mg); Colorless solid; mp = 139-141 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{14}F_3O_4S$ 371.0565, found 371.0566; ^1H NMR (400 MHz, $CDCl_3$): δ 7.76 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.53-7.49 (m, 1H), 7.27 (d, *J* = 8.8 Hz, 2H), 7.07-7.03 (m, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 5.76 (q, *J* = 7.6 Hz, 1H), 4.18 (s, 1H), 2.39 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 179.7, 157.8, 146.4 (2x), 137.6, 133.2, 129.8 (2x), 129.4 (2x), 126.8, 123.1 (q, *J* = 284.8 Hz), 122.8, 117.7, 73.0 (q, *J* = 33.3 Hz), 66.9, 21.7.

(2S,3S*)-6-Fluoro-3-(toluene-4-sulfonyl)-2-trifluoromethylchroman-4-one (**4ah**).* **4ah** was synthesized according to general synthetic procedure from **2p** (924 mg, 3.0 mmol) and **3q** (294 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 69% (803 mg); Colorless solid; mp = 122-124 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{17}H_{13}F_4O_4S$ 389.0471, found 389.0472; ^1H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, *J* = 8.4 Hz, 2H), 7.43 (dd, *J* = 3.2, 8.0 Hz, 1H), 7.31 (d, *J* = 8.8 Hz, 1H), 7.28-7.23 (m, 2H), 6.97 (dd, *J* = 4.0, 9.2 Hz, 1H), 5.76 (q, *J* = 6.4 Hz, 1H), 4.17 (s, 1H), 2.43 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 179.2, 159.0, 156.6, 154.0 (d, *J* = 2.3 Hz), 146.7, 133.2, 130.0 (2x), 129.5 (2x), 125.1 (d, *J* = 24.2 Hz), 123.1 (d, *J* = 284.3 Hz), 119.6 (d, *J* = 6.9 Hz), 112.0 (d, *J* = 24.2 Hz), 73.1 (q, *J* = 33.3 Hz), 66.5, 21.7.

(2S,3S*)-7-Methoxy-3-(toluene-4-sulfonyl)-2-trifluoromethyl-chroman-4-one (**4ai**).* **4ai** was synthesized according to general synthetic procedure from **2o** (960 mg, 3.0 mmol) and **3q** (294 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 56% (672 mg); Colorless solid; mp = 123-125 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{18}H_{16}F_3O_5S$ 401.0671, found 401.0670; ^1H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, *J* = 8.8 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 6.61 (dd, *J* = 2.4, 8.8 Hz, 1H), 6.40 (d, *J* = 2.4 Hz, 1H), 5.74 (q, *J* = 8.0 Hz, 1H), 4.12 (d, *J* = 0.8 Hz, 1H), 3.84 (s, 3H), 2.41 (s, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 177.8, 167.4, 159.9, 146.3, 133.4, 129.8 (2x), 129.4 (2x), 128.7, 123.1 (d, *J* = 284.3 Hz), 113.6, 111.5, 100.7, 73.1 (q, *J* = 32.6 Hz), 66.6, 55.9, 21.7.

(2S,3S*)-3-(4-Fluoro-benzenesulfonyl)-2-trifluoromethyl-chroman-4-one (**4aj**).* **4aj** was synthesized according to general synthetic procedure from **2e** (882 mg, 3.0 mmol) and **3q** (294 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 65% (729 mg); Colorless solid; mp = 151-153 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{11}F_4O_4S$ 375.0314, found 375.0315; ^1H NMR (400 MHz, $CDCl_3$): δ 7.83-7.80 (m, 2H), 7.77 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.56-7.52 (m, 1H), 7.18-7.13 (m, 2H), 7.09-7.05 (m, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 5.77 (q, *J* = 7.6 Hz, 1H), 4.20 (s, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 179.5, 166.6 (d, *J* = 257.7 Hz), 157.7, 137.9, 132.6 (d, *J* = 9.9 Hz, 2x), 132.2 (d, *J* = 3.0 Hz), 126.8, 123.08, 123.06 (d, *J* = 284.3 Hz), 121.6, 117.8, 116.6 (d, *J* = 22.7 Hz, 2x), 73.0 (q, *J* = 33.4 Hz), 67.0. Single-crystal X-Ray diagram: crystal of compound **4aj** was grown by slow diffusion of EtOAc into a solution of compound **4aj** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the triclinic crystal system, space group P-1, a = 8.3801(12) Å, b = 9.4312(12) Å, c = 11.0839(15) Å, V = 745.01(18) $Å^3$, Z = 2, d_{calcd} = 1.669 g/cm^3, *F*(000) = 380, 2*θ* range 1.976~26.815°, R indices (all data) R1 = 0.0489, wR2 = 0.1165.

(2S,3S*)-2-Ethyl-3-(toluene-4-sulfonyl)chroman-4-one (**4ak**).* **4ak** was synthesized according to general synthetic procedure from **2a** (870 mg, 3.0 mmol) and **3r** (174 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 30% (298 mg); Colorless solid; mp = 131-133 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{18}H_{19}O_4S$ 331.1004, found 331.1003; ^1H NMR (400 MHz, $CDCl_3$): δ 7.75 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.64 (d, *J* = 8.4 Hz, 2H), 7.43 (dt, *J* = 1.6, 8.4 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 2H), 6.95 (dt, *J* = 1.2, 8.0 Hz, 1H), 6.80 (dd, *J* = 1.4, 8.4 Hz, 1H), 5.31 (ddd, *J* = 0.8, 5.2, 10.0 Hz, 1H), 3.85 (d, *J* = 1.2 Hz, 1H), 2.36 (s, 3H), 1.91-1.83 (m, 1H), 1.60-1.49 (m, 1H), 1.01 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 182.6, 158.2, 145.5, 137.1, 134.4, 129.4 (2x), 129.3 (2x), 126.9, 121.5, 120.2, 118.5, 77.0, 72.7, 25.3, 21.6, 10.0.

(2S,3S*)-3-(4-Fluorobenzenesulfonyl)-2-methylchroman-4-one (**4al**).* **4al** was synthesized according to general synthetic procedure from **2e** (882 mg, 3.0 mmol) and **3s** (132 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 22% (210 mg); Colorless solid; mp = 130-132 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{16}H_{14}FO_4S$ 321.0597, found 321.0598; ^1H NMR (400 MHz, $CDCl_3$): δ 7.80-7.74 (m, 3H), 7.46-7.42 (m, 1H), 7.09-7.03 (m, 2H), 6.96 (dt, *J* = 0.2, 8.4 Hz, 1H), 6.77 (dd, *J* = 0.4, 8.4 Hz, 1H), 5.62 (dq, *J* = 0.8, 6.8 Hz, 1H), 3.85 (d, *J* = 0.8 Hz, 1H), 1.45 (d, *J* = 6.8 Hz, 3H); $^{13}C\{^{1}H\}$

NMR (100 MHz, $CDCl_3$): δ 182.3, 166.2 (d, J = 256.2 Hz), 158.1, 137.5, 132.38, 132.33 (d, J = 9.9 Hz, 2x), 126.9, 121.7, 119.7, 118. 6, 116.1 (d, J = 22.7 Hz, 2x), 73.7, 72.1, 18.4.

(2S,3S*)-2-Methyl-3-(toluene-4-sulfonyl)chroman-4-one (**4am**)*. **4am** was synthesized according to general synthetic procedure from **2a** (870 mg, 3.0 mmol) and **3s** (132 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >9:1; Yield = 31% (294 mg); Colorless solid; mp = 59-61 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{17}O_4S$ 317.0848, found 317.0846; Two isomers, ratio > 10:1; For major isomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (ddd, J = 0.4, 1.6, 8.0 Hz, 1H), 7.63 (d, J = 8.4 Hz, 2H), 7.43 (ddd, J = 1.6, 7.2, 8.8 Hz, 1H), 7.19 (d, J = 8.0 Hz, 2H), 6.94 (dt, J = 1.2, 8.4 Hz, 1H), 6.79 (dd, J = 0.4, 8.4 Hz, 1H), 5.61 (dq, J = 1.2, 6.8 Hz, 1H), 3.82 (d, J = 1.6 Hz, 1H), 2.35 (s, 3H), 1.44 (d, J = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 182.6, 158.2, 145.5, 137.2, 134.3, 129.4 (2x), 129.2 (2x), 126.8, 121.5, 119.8, 118.5, 73.6, 71.9, 21.6, 18.4.

(2S,3S*)-2-Phenethyl-3-(toluene-4-sulfonyl)chroman-4-one (**4an**)*. **4an** was synthesized according to general synthetic procedure from **2a** (870 mg, 3.0 mmol) and **3t** (402 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 35% (426 mg); Colorless gum; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{24}H_{23}O_4S$ 407.1317, found 407.1318; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (dd, J = 1.6, 8.0 Hz, 1H), 7.63 (d, J = 8.4 Hz, 2H), 7.46 (ddd, J = 1.6, 7.2, 8.8 Hz, 1H), 7.29-7.17 (m, 5H), 7.13-7.11 (m, 2H), 6.98 (dt, J = 1.2, 8.4 Hz, 1H), 6.85 (dd, J = 0.4, 8.4 Hz, 1H), 5.44-5.40 (m, 1H), 3.84 (d, J = 1.2 Hz, 1H), 2.78-2.74 (m, 2H), 2.36 (s, 3H), 2.23-2.14 (m, 1H), 1.83-1.74 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 182.5, 158.0, 145.5, 139.7, 137.2, 134.3, 129.4 (2x), 129.2 (2x), 128.6 (2x), 128.3 (2x), 126.9, 126.3, 121.6, 120.2, 118.5, 74.8, 72.7, 33.4, 31.5, 21.6.

(2S,3S*)-2-n-Heptyl-3-(toluene-4-sulfonyl)chroman-4-one (**4ao**)*. **4ao** was synthesized according to general synthetic procedure from **2a** (870 mg, 3.0 mmol) and **3u** (384 mg, 3.0 mmol) in dry toluene (5 mL). The ratio of dr was >20:1; Yield = 38% (456 mg); Colorless gum; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{23}H_{29}O_4S$ 401.1787, found 401.1788; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (dd, J = 1.6, 8.0 Hz, 1H), 7.63 (d, J = 8.4 Hz, 2H), 7.43 (dt, J = 2.0, 8.8 Hz, 1H), 7.19 (d, J = 8.0 Hz, 2H), 6.94 (dt, J = 1.2, 8.4 Hz, 1H), 6.79 (dd, J = 0.8, 8.4 Hz, 1H), 5.41-5.38 (m, 1H), 3.83 (d, J = 1.2 Hz, 1H), 2.35 (s, 3H), 1.89-1.80 (m, 1H), 1.51-1.40 (m, 3H), 1.35-1.21 (m, 8H), 0.85 (t, J = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 182.6, 158.2, 145.4, 137.1, 134.4, 129.4 (2x), 129.3 (2x), 126.8, 121.4, 120.1, 118.5, 75.6, 72.8, 31.8, 31.5, 28.9, 28.7, 25.3, 22.5, 21.6, 14.0.

ASSOCIATED CONTENT

Supporting Information

Scanned photocopies of NMR spectral data for all compounds and X-ray analysis data of **4a**, **4e**, **4ab**, **4af** and **4aj**. This information is available free of charge via the Internet at http: //pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

*Email: mychang@kmu.edu.tw

ORCID

Meng-Yang Chang: 0000-0002-1983-8570

Notes

The authors declare no competing financial interest.

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