Article

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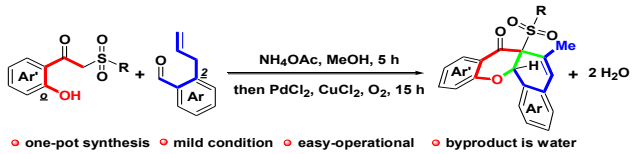
Construction of Sulfonyl Dihydrobenzo[*c*]xanthen-7-ones Core via $NH_4OAc/PdCl_2/CuCl_2$-Mediated Double Cyclocondensation of α-Sulfonyl *o*-Hydroxyacetophenones with 2-Allylbenzaldehydes

Nai-Chen Hsueh,[a] Min-Chen Tsai,[a] Meng-Yang Chang*[a,b] and Hsing-Yin Chen*[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; hychen@kmu.edu.tw



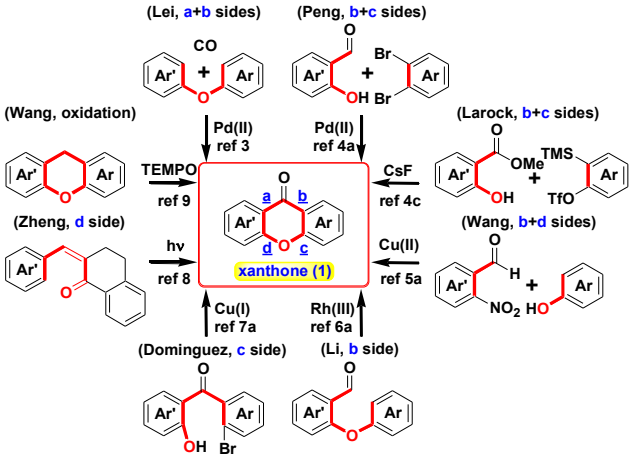
ABSTRACT: $NH_4OAc/PdCl_2/CuCl_2$ mediated domino double cyclocondensation of α-sulfonyl *o*-hydroxyacetophenones and 2-allylbenzaldehydes provides tetracyclic sulfonyl dihydrobenzo[*c*]xanthen-7-one core with good to excellent yields in MeOH. The intermediates contain a 3-sulfonyl flavanone motif. Only water is generated as a byproduct. The use of various catalysts and reaction conditions is studied for the facile-operational conversion.

Introduction

Recently, we explore a one-pot facile-operational route for the preparation of different benzofused carbo- or heterocyclic skeletons,[1] including nitrated or dioxa-benzobicycles,[1a-b] tetrahydrocyclobuta[*a*]naphthalenes,[1c] and benzofused azahomoisotwistanes[1d] by the concise functionalization of 2-allylbenzaldehydes (*o*-allyl benzaldehydes) under cascade annulation procedures. On the basis of these valuable results, we plan to construct the core skeleton of xanthone by the combination of 2-allylbenzaldehydes and *o*-hydroxyacetophenones under Knoevenagel/Wacker/aldol conditions *via* a one-step cascade conversion.

Xanthone is an important structural unit with a wide variety of natural products and bioactive molecules.[2] Accordingly, there exists a wide selection of methods for the synthesis of functionalized xanthones *via* different reagents and catalyst-promoted intermolecular or/and intramolecular cyclization. The bond formations for the core pyran-4-one of xanthone can be divided into two major synthetic types (Scheme 1)[3-9] including: (1) the intermolecular oxidative double carbonylation of diaryl ether with carbon monoxide (Pd^{II}; a+b bonds),[3] cycloannulation of salicylaldehydes with 1,2-dibromoarenes (Pd^{II}; b+c bonds),[4a] domino coupling-cyclization of salicylates with arynes (CsF; b+c bonds)[4c] or *ortho*-acylation of 2-nitrobenzaldehydes with phenols (Cu^{II}; b+d bonds),[5a] and (2) intramolecular cross dehydrogenative coupling (CDC) reaction of 2-aryloxybenzaldehydes (Rh^{III}; b bond),[6a] S_NAr *O*-arylation of 2-bromobenzophenones (Cu^{I}; c bond),[7a] or the photolytic oxa-6π electrocyclization of benzyliene-1-tetralones (hυ; d bond).[8] For the straightforward route, organocatalytic aerobic oxidation of benzylic sp^3 C-H bonds of xanthene (recyclable TEMPO) has been developed by the Wang group.[9]

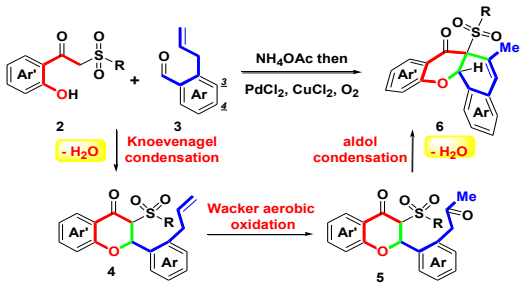
Scheme 1. Synthetic Routes of Functionalized Xanthones



However, development of a single-step cascade route for the simultaneous bond formation and ring-construction of xanthones from readily available starting materials still represents a continuing demand in the synthetic chemistry. The efficient cascade reaction can provide many advantages, especially in saving of reaction time and reagent cost, and combination of multiple steps.[10] Herein, we report on a one-pot novel synthesis of tetracyclic dihydrobenzo[*c*]xanthen-7-ones core (a xanthone derivative) by $NH_4OAc/PdCl_2/CuCl_2$-promoted dou-

ble cyclocondensation of *o*-hydroxyacetophenones with 2-allylbenzaldehydes *via* the domino Knoevenagel condensation/Wacker aerobic oxidation/aldol condensation procedure, as shown in Scheme 2.[11-13] In this reaction fashion, water (2 equiv) is released as the only byproduct.

Scheme 2. One-Pot Double Cyclocondensation of α-Sulfonyl *o*-Hydroxyacetophenones and 2-Allylbenzaldehydes

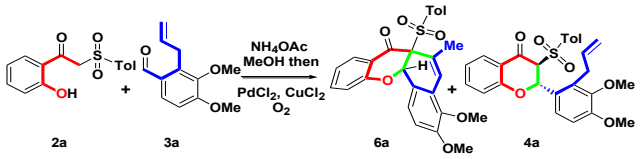


Results and Discussion

Required starting materials **2** were easily prepared from *o*-hydroxyacetophenones following a procedure in literature[14] that included α-bromination of *o*-hydroxyacetophenones followed by the nucleophilic substitution of the resulting α-bromo-*o*-hydroxyacetophenones with RSO_2Na. To examine the formation of the dihydrobenzo[*c*]xanthen-7-one core, our research began on the reaction of model compounds **2a** (R = Tol, Ar' = Ph, 0.5 mmol) and **3a** (Ar = 3,4-$(MeO)_2$Ph, 0.5 mmol) with the NH_4OAc (0.8 equiv) in MeOH (3 mL) at reflux for 5 h. 3-Sulfonyl flavanone **4a** was isolated as a sole isomer in a 92% yield under the Knoevenagel condensation conditions. In addition, by the determination of ^{1}H-NMR spectrum, two adjacent stereochemical centres of **4a** were in *trans*-configuration due to the steric hindrance between the allylaryl and the sulfonyl substituents. In the following step, the reaction of **4a** (0.5 mmol) with $PdCl_2$ (10 mol%) and $CuCl_2$ (1.5 equiv) provided **6a** (45%) in MeOH at 25 °C for 5 h in the presence of molecular oxygen under Wacker oxidation and intramolecular aldol condensation procedures. Because MeOH was the same solvent used for the two steps, a one-pot two-step synthetic route of the continous reaction was tried. As a first attempt, $PdCl_2$ and $CuCl_2$ were stepwise added to the resulting reaction mixture of Knoevenagel condensation at 25 °C. As a result, this one-pot reaction afforded **6a** at a better yield (60%) than a two-step route (41%) because NH_4OAc could promote the intramolecular ring-closure of *in-situ* formed **5a**. Then, by elongating the reaction time (5 → 15 and 20 h), the isolated yields of **6a** could be enchanced to 85% and 75% yields, respectively. However, by elevating the temperature (25 °C → reflux), **6a** was obtained in only a 40% yield. From the above results, it is seen that the combination of NH_4OAc, $PdCl_2$, and $CuCl_2$ in MeOH (standard conditions, Table 1, entry 1) gave the best results for the one-pot construction of a tetracyclic ring system.

Under these conditions, the variations for ammonium salts, palladium catalysts, copper(II) complexes, co-oxidants, and reaction solvents were examined, as shown in Table 1, entries 2-11. Initially, the effect of ammonium salts in the formation of tetracyclic skeleton was examined. However, after elongating the aliphatic chain (NH_4OAc → nBu$_4$NOAc), the yield of **6a** (75%) was not enhanced (entry 2). In particular, NH_4Cl could not trigger the Knoevenagel condensation so the desired **6a** could not be produced (entry 3). Among the isolated mixture, 7,8-dimethoxynaphthalen-2-ol (54%, by Wacker oxidation of **3a**)[11a] and the starting material **2a** (65%) were observed. Shaw *et al.* also reported similar observations.[15] We speculate that the basicity of the conjugated bases (acetate ion and chloride ion) could be a key factor affecting Knoevenagel condensation.[12a] When $PdCl_2$ was replaced by $Pd(OAc)_2$, **6a** was isolated at a 42% yield along with the formation of α-sulfonyl flavanone **4a** (45%) via an incomplete conversion (entry 4). By elongating the reaction time (15 → 30 h), the conversion from **4a** to **6a** could be increased to 1:2 (24% and 54%). The use of a $Pd(dba)_2$ catalyst decreased the yield of **6a** (8%) dramatically (entry 5). Next, $Cu(OAc)_2$ and CuF_2 were examined; however, both of them provided trace amounts of **6a** at low yields (entries 6-7). This meant that $CuCl_2$ was more appropriate than other copper(II) complexes in the Wacker oxidation of **4a**. As to oxidants, oxone® and $K_2S_2O_8$, were ineffective for the transformation and provided lower yields of **6a** (entries 8-9). In the comparison of THF and MeOH (entries 10-11), we found that MeOH was better than both THF and co-solvent of THF and MeOH (v/v = 1/1) in the generation of **6a** within 15 h. By elongating the reaction time (15 → 30 h), the conversion from **4a** to **6a** could be obviously increased. From these results, we concluded that the combination of $NH_4OAc/PdCl_2/CuCl_2$ provided optimal conditions (reflux, 5 h and 25 °C, 15 h) in the presence of an oxygen atmosphere for one-pot construction of a tetracyclic dihydrobenzo[*c*]xanthen-7-ones core skeleton.

Table 1. Reaction Conditions[a]



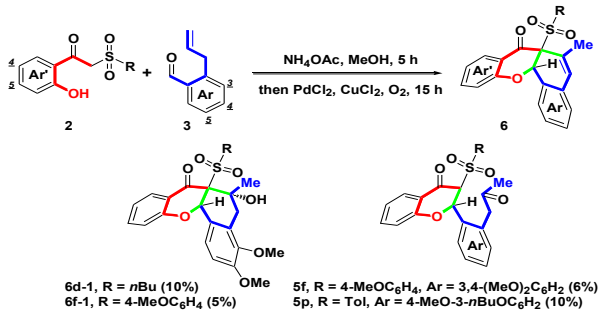
entry	variation from "standard conditions"	**6a** (%)[b]	**4a** (%)[b]
1	none	85	—[c]
2	nBu$_4$NOAc, instead of NH_4OAc	75	—[c]
3	NH_4Cl, instead of NH_4OAc	—[c]	—[c,d]
4	$Pd(OAc)_2$, instead of $PdCl_2$	42 (51)[e]	45 (24)[e]
5	$Pd(dba)_2$, instead of $PdCl_2$	8	66
6	$Cu(OAc)_2$ instead of $CuCl_2$	10	70
7	CuF_2, instead of $CuCl_2$	6	81
8	Oxone, instead of O_2	20	48
9	$K_2S_2O_8$, instead of O_2	5	66
10	THF, instead of MeOH	46 (72)[e]	40 (13)[e]
11	THF/MeOH (1/1), instead of MeOH	63 (80)[e]	20 (6)[e]

[a]The reactions were performed using a 0.5 mmol scale with **2a**, **3a** (1.0 equiv), ammonium salt (0.8 equiv), solvent (10 mL), at reflux for 5 h; then palladium catalyst (10 mol%), copper(II) complex (1.5 equiv), at 25 °C for 15 h. [b]Isolated yields. [c]No product was observed. [d]**2a** (65%) was recovered. [e]30 h.

To investigate the substrate scope and limitations of the route, **2** and **3** were treated with the combination of NH_4OAc, $PdCl_2$, and $CuCl_2$ to yield functionalized **6** under molecular oxygen atmosphere conditions (Table 2). By use of optimal conditions (Table 1, entry 1), we understood that this cascade route organized intramolecular double dehydrative annulation under facile and efficient conditions at good to excellent yields

(80%-95%). In entries 1-17, the one-pot formation of **6a-6q** exhibited that different Ar' and R (for **2a-2o**), and Ar substituents (for **3a-3c**) did not change the distribution of the isolated yields. For the electronic characteristics of Ar' substituent on **2**, electron-neutral, electron-withdrawing and electron-donating groups well-tolerated. For the R substituent of **2**, aliphatic (methyl and *n*-butyl) and aromatic sulfonyl groups were suitable. Different aryl oxygenated groups (Ar) on **3a-3c** were also appropriate to generate core structure **6**. Furthermore, the molecular structures of **6b**, **6e**, **6i** and **6q** were confirmed by single-crystal X-ray analysis.[16] For the reaction of **2d** and **3a**, the intermediate **6d-1** with a β-hydroxyketone was obtained at a 10% yield (entry 4). In addition, there were trace amounts (5% and 6%) generated in the formation **6f-1** and **5f** (entry 6). Similar results were observed for **5p** (10%, entry 16). The structures of **6d-1** and **5p** were confirmed by single-crystal X-ray crystallography.[16] Although the isolated yields of these intermediates were low, the generation of tertiary alcohols **6d-1**, **6f-1** and ketones **5f**, **5p** could properly explain the reaction pathway.

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

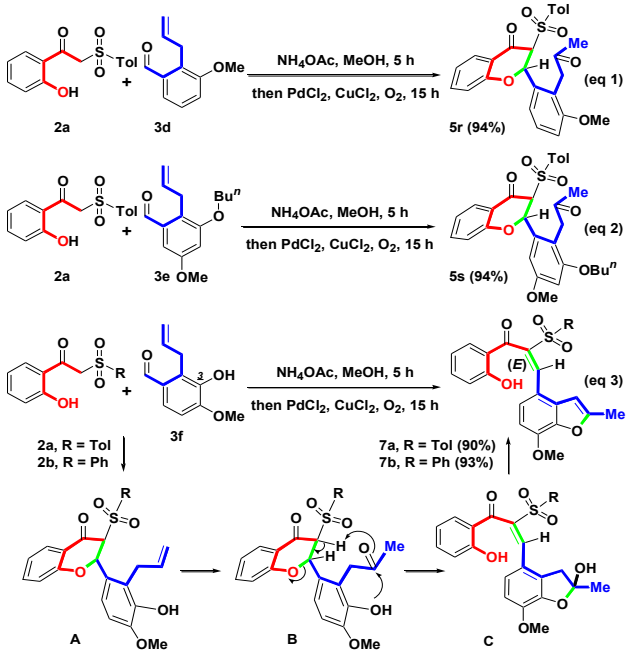


entry	**2**, Ar' =, R =	**3**, Ar =	**6**, (%)[b]
1	**2a**, Ph, Tol	**3a**, 3,4-$(MeO)_2C_6H_2$	**6a**, 85
2	**2b**, Ph, Ph	**3a**, 3,4-$(MeO)_2C_6H_2$	**6b**, 88
3	**2c**, Ph, Me	**3a**, 3,4-$(MeO)_2C_6H_2$	**6c**, 90
4	**2d**, Ph, *n*Bu	**3a**, 3,4-$(MeO)_2C_6H_2$	**6d**, 82[c]
5	**2e**, Ph, 4-FC_6H_4	**3a**, 3,4-$(MeO)_2C_6H_2$	**6e**, 84
6	**2f**, Ph, 4-$MeOC_6H_4$	**3a**, 3,4-$(MeO)_2C_6H_2$	**6f**, 80[d]
7	**2g**, Ph, 3-MeC_6H_4	**3a**, 3,4-$(MeO)_2C_6H_2$	**6g**, 84
8	**2h**, Ph, 4-EtC_6H_4	**3a**, 3,4-$(MeO)_2C_6H_2$	**6h**, 87
9	**2i**, Ph, 4-*i*PrC_6H_4	**3a**, 3,4-$(MeO)_2C_6H_2$	**6i**, 90
10	**2j**, Ph, 4-*n*BuC_6H_4	**3a**, 3,4-$(MeO)_2C_6H_2$	**6j**, 95
11	**2k**, Ph, 4-*t*BuC_6H_4	**3a**, 3,4-$(MeO)_2C_6H_2$	**6k**, 90
12	**2l**, 4-FC_6H_3, Tol	**3a**, 3,4-$(MeO)_2C_6H_2$	**6l**, 87
13	**2m**, 4-$MeOC_6H_3$, Tol	**3a**, 3,4-$(MeO)_2C_6H_2$	**6m**, 90
14	**2n**, 4-Br-2-naphthyl, Tol	**3a**, 3,4-$(MeO)_2C_6H_2$	**6n**, 87
15	**2a**, Ph, Tol	**3b**, 3-*i*PrO-4-$MeOC_6H_2$	**6o**, 86
16	**2a**, Ph, Tol	**3c**, 3-*n*BuO-4-$MeOC_6H_2$	**6p**, 83[e]
17	**2o**, 4-ClC_6H_3, Tol	**3a**, 3,4-$(MeO)_2C_6H_2$	**6q**, 88

[a]The reactions were performed using a 0.5 mmol scale with **2a-2o**, **3a-3h** (1.0 equiv), NH_4OAc (31 mg, 0.4 mmol) in MeOH (10 mL), at reflux for 5 h; then $PdCl_2$ (9 mg, 10 mol%), $CuCl_2$ (100 mg, 0.75 mmol), and $O_{2(g)}$ (1 atm), at 25 °C, 15 h. [b]Isolated yields. [c]**6d-1** (10%). [d]**6f-1** (5%) and **5f** (6%). [e]**5p** (10%).

By the use of $BF_3{\cdot}OEt_2/CH_2Cl_2$, the one-pot conversion from the intermediates to the desired dihydrobenzo[*c*]xanthen-7-one core could be achieved via a dehydration process. With these results, different 2-allylbenzaldehydes **3** were examined next. In particular, when the starting substrate was changed to **3d** (Ar = 3-$MeOC_6H_3$), only ketone **5r** was isolated as the product at a 94% yield, and the desired tetracyclic **6r** was not detected via the $NH_4OAc/PdCl_2/CuCl_2$-mediated cyclocondensation of **2a** with **3d** (Scheme 3, eq 1). On the other hand, by controlling **3e** (Ar = 3-*n*BuO-5-$MeOC_6H_2$) as the starting material, the uncyclized **5s** could be isolated at a 94% yield under similar conditions (eq 2). According to the resulting data, we found that a C4-oxygenated group on Ar of **3** could play an important role as a substituent in affecting the intramolecular ring-closure of **5r** or **5s**. For the relative stereochemistry, **5r** and **5s** were produced as the sole *trans*-configurated isomer by the determination of ^{1}H-NMR spectrum. The structural framework of **5s** was determined by single-crystal X-ray analysis.[16] Furthermore, after changing the methoxy to a hydroxyl group on the C3-position, treatment of **2a** with **3f** produced **7a** at a 90% yield (eq 3). For the formation of β-ketosulfone-conjugated benzofuran (for **7a**), **A** was formed by Knoevenagel condensation of **2a** with **3f** in the initial step. After the aerobic Wacker oxidation of the resulting **A** by $PdCl_2/CuCl_2$, the C3-hydroxyl group on the *in-situ* formed **B** could promote an intramolecular tandem reaction to afford the tertiary alcohol **C** via phenol-methyl ketone annulation, removal of the α-proton, and ring-opening of the flavanone sequence. Then, aromatization of **C** led to **7a**. Compared with the generation of **6** by intramolecular aldol condensation, the formation of a five-membered ring on **C** was favored to preceed. Similarly, the formation of **7b** was accomplished at a 93% yield by the reaction of **2b** with **3f**. The structure of **7a** was confirmed by single-crystal X-ray analysis.[16]

Scheme 3. Synthesis of **5r**, **5s** and **7a-7b**



Density functional theory (DFT) calculations were invoked to shed some light on the essential role of the C4-oxygenated group in the intramolecular ring-closure reaction. The ring-

closure of **5** was assumed to proceed through the elementary steps depicted at the bottom of Figure 1. The first step is the deprotonation of C-H connected to the sulfonyl group to form anionic intermediate **I**. Then **I** undergoes an intramolecular nucleophilic addition (**I** → **II**) followed by protonation to form tetracyclic intermediate **III**. Notice that this intermediate has been isolated in experiments (**6d-1** and **6f-1**). The following dehydration of **III** to form the final product **6** was supposed to be accomplished by the stepwise deprotonation (**III** → **IV**) and protonation (**IV** → **6**) processes. Firstly, the free energy changes of each step mentioned above were calculated for the **5a** (R_1 = R_2 = OMe) and **5r** (R_1 = OMe, R_2 = H) systems, and the results were compared to extract the effect of C4-substitution on the ring-closure reaction. However, it turned out that the calculated energies of each step for **5a** and **5r** were very similar (Table 3), which cannot account for different reaction behaviors observed in the two systems. The calculations showed that while the overall ring-closure reactions were slightly exergonic, the bottleneck in the reactions occurred at the second deprotonation step (**III** → **IV**); the reaction free energies of this step were 43.3 and 45.6 kcal/mol for **5a** and **5r**, respectively, which are thermodynamically inaccessible (Table 3). These results indicate that only the presence of C3,C4-oxygenated groups inhibit the promotion of the ring-closure reaction.

We next considered the possible influences of chelation on the ring-closure reaction as the two methoxy groups in *ortho* positions of **5a** provide a suitable structural motif to bind with metal ions. Two metal reagents, $PdCl_2$ and $CuCl_2$, were used in the one-pot synthesis. To determine which metal reagent had a higher binding affinity with **5a**, the reaction of **5a** + $MCl_2(MeOH)_2$ → **5a**-MCl_2 + 2MeOH, where M = Pd or Cu and MeOH is a coordinated solvent molecule, was calculated. The results showed that the binding of **5a** with $CuCl_2$ was more favorable than with $PdCl_2$; the former was slightly exergonic (ΔG = –1.0 kcal/mol) whereas the latter was slightly endergonic (ΔG = 1.2 kcal/mol). Accordingly, the effect of binding with $CuCl_2$ was explored. The free energy changes of each step involved in the ring-closure reaction were computed for the **5a**-$CuCl_2$ system and compared with **5a** (Table 3 and Figure 1). It can be clearly seen that the presence of $CuCl_2$ displays a relatively minor effect on the energy of the steps until the formation of **III**, but significantly lowers the energy cost for the second deprotonation step (**III** → **IV**), rendering the ring-closure reaction feasible. Mulliken population analysis revealed that except for the intermediate **IV**, chelation induces non-negligible charge polarization from **5a** to $CuCl_2$, but the oxidation state of Cu remains at +2; the negative charge and spin density on $CuCl_2$ were in the range of –|0.296~0.400| and 0.919~0.936 a.u., respectively (Table 4). On the contrary, for **IV** the negative charge and spin density on $CuCl_2$ dramatically increased to –1.036 a.u. and diminished to zero, respectively, implying that a redox reaction between **5a** and $CuCl_2$ occurred in **IV**. The electron transfer from **5a** to $CuCl_2$ can also be clearly seen by the spin density plots of **III** and **IV** (see Supporting Information, Figure S1). This rationalizes why the $CuCl_2$ chelation provides abnormally large stabilization for the deprotonated intermediate **IV**. Since the copper was reduced to Cu(I) in **IV**, the coordination interaction between the two methoxy groups and $CuCl_2^-$ was weakend in **IV**, which can be evidenced by the longer coordination distance compared to other intermediates (see Supporting Information, Table S1).

To make sure that the above-mentioned results are not functional dependent, the ring-closure reactions for **5a** and **5a**-$CuCl_2$ were recalculated by using two other popular DFT methods (see Supporting Information, Figures S2 and S3). All the three DFT calculations consistently pointed out that the main effect of $CuCl_2$ chelation is lowering the deprotonation energy of **III** → **IV**. In addition, we also calculated the reaction of **5a**-$PdCl_2$, although the $PdCl_2$ was shown to be less capable of coordinateing with **5a** than $CuCl_2$. The results showed that the $PdCl_2$ can also facilitate the ring-closure reaction by decreasing the energy cost of the second deprotonation step but is less efficient than the $CuCl_2$ (see Supporting Information, Table S2).

On the basis of the present DFT results, we conclude that the requirement of a simultaneous presence of two alkoxy groups at C3 and C4 positions for the ring-closure reaction is not ascribed to a simple substitution effect, but because the two alkoxy groups in *ortho* positions provide a rigid framework to chelate the $CuCl_2$ reagent, which is beneficial for stabilizing the deprotonated intermediate in the ring-closure reaction.

Figure 1. B3LYP-D3/LANL2DZ(Cu)/6-31+G*(H,C,O,S,Cl) Free Energy Profiles (kcal/mol) of the Ring-Closure Reaction for **5a** (black) and **5a**-$CuCl_2$ (red).

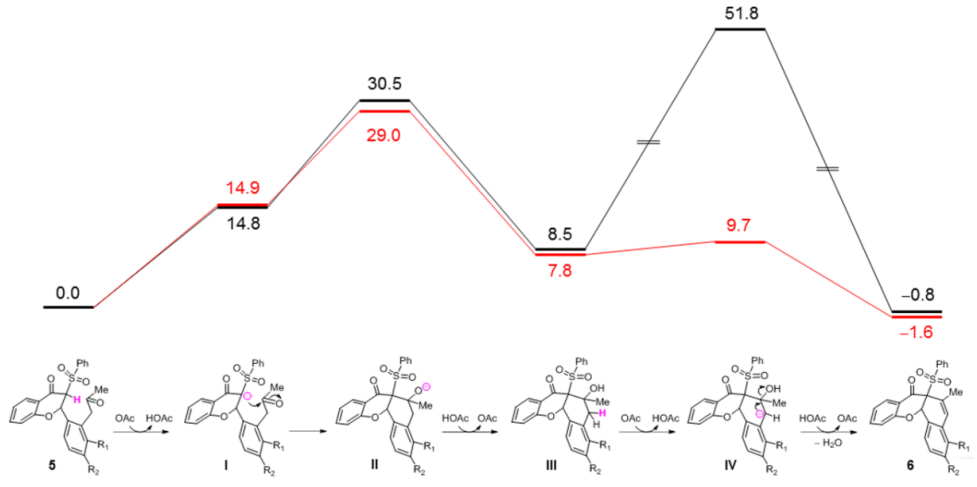


Table 3. B3LYP-D3/LANL2DZ(Cu)/6-31+G*(H,C,O,S,Cl) free energy changes (kcal/mol) of the elementary steps involved in the ring-closure reaction.

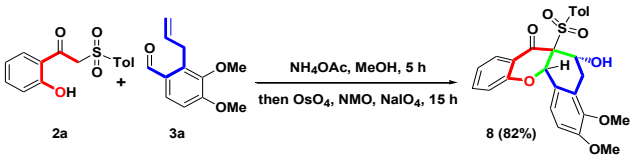
	5r[a]	**5a**[b]	**5a**-$CuCl_2$
5 → I	14.0	14.8	14.9
I → II	16.9	15.7	14.1
II → III	–23.6	–22.0	–21.2
III → IV	45.6	43.3	1.9
IV → 6	–53.6	–52.6	–11.3
Overall energy	–0.7	–0.8	–1.6

[a]R_1 = OMe, R_2 = H. [b]R_1 = R_2 = OMe.

Table 4. Mulliken charge and spin density on $CuCl_2$ for the ring-closure reaction of **5a**-$CuCl_2$.

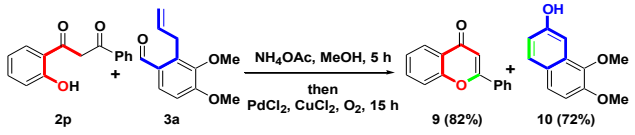
	charge	spin density
5	–0.296	0.936
I	–0.330	0.932
II	–0.400	0.919
III	–0.340	0.933
IV	–1.036	0.000
6	–0.362	0.931

Scheme 4. Synthesis of **8**



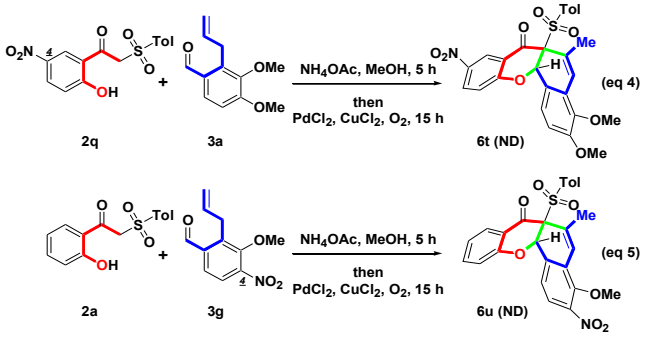
In contrast to the formation of **6a**, one-carbon diminishing on the terminal olefin of **3a** was examined next. By OsO_4/NMO-mediated double bond-cleavage of the *in-situ* generated **4a** (derived from Knoevenagel condensation of **2a** and **3a**), **8** was isolated at an 82% yield (Scheme 4). Based on the resulting aldehyde group, only β-hydroxyketone moiety was formed via the intramolecular aldol procedure. Under the reaction conditions, no expected dehydrated product was detected since the secondary alcohol (for **8**) was not easier to eliminate than the tertiary alcohol (for **6a**).

Scheme 5. Synthesis of **9-10**



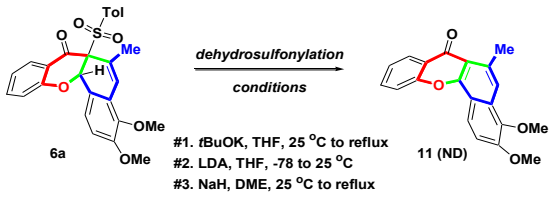
With optimal reaction conditions, this study examined replacing β-ketosulfone with β-diketone, as shown in Scheme 5. When a one-pot reaction of **2p** was treated with **3a** in the presence of NH_4OAc, however, the predicted tetracyclic skeleton could not be obtained, and only **9** and **10** were produced at 82% and 72% yields, respectively. One possible reason could be that intramolecular cyclocondensation (Baker-Venkataraman condensation) of **2p** itself[17] was easier to initiate than intermolecular cyclodehydration of **2p** with **3a** (Knoevenagel condensation) such that **3a** could be directly oxidized with $PdCl_2$/$CuCl_2$ to produce **10** at a 72% yield via intramolecular aldol condensation.[11a] For the major difference between β-ketosulfone with β-diketone, we understood that the sulfonyl group could serve as a fastening substituent to construct the sulfonyl flavanone intermediate such that the tetracyclic core could be established under the aerobic Wacker oxidation. According to the results, the sulfonyl group played a key role in constructing the framework of sulfonyl dihydrobenzo[*c*]xanthen-7-one core.

Scheme 6. Reactions of **2q** with **3a**, and **2a** with **3g**



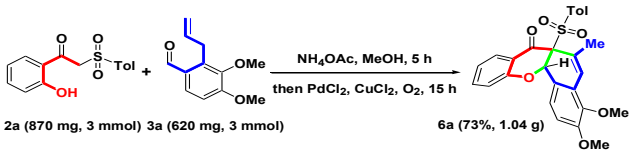
By adjusting the Ar' as the electron-withdrawing nitro group, **2q** was involved in the above conditions (Scheme 6, eq 4). When **2q** was reacted with **3a**, however, no desired **6t** was detected. And, only strating material **2q** was recovered (82%) along with 65% of **10**. One possible reason could be that C4-nitro group of **2q** could not promote the electron density efficiently to the *para*-hydroxy position such that Knoevenagel condensation occurred more difficultly. On the other way, exchanging the C4-nitro group from *o*-hydroxyacetophenone **2q** to 2-allylbenzaldehyde **3g** was examined next (eq 5). Under the above conditions, the desired **6u** was still not provided by the treatment of **2a** with **3g**, and only complex mirture was observed. Although substrates **2** and **3** was inappropriate to the electron-withdrawing group, the present route still provided novel and efficient synthesis of the tetracyclic sulfonyl dihydrobenzo[*c*]xanthen-7-one core skeleton.

Scheme 7. Dehydrosulfonylation of **6a**



After producing the sulfonyl dihydrobenzo[*c*]xanthen-7-one, construction of oxygenated naphthochromone skeleton[18] by the dehydrosulfonylation of skeleton **6** was studied (Scheme 7). But, when mode compound **6a** was reacted with *t*BuOK in THF at 25 °C for 10 h, no reaction was detected. Even after elongating the time to 30 h and elevating the temperature to reflux, no reactions were observed. Next, by choosing LDA as the base to remove the $TolSO_2H$, no desired products were provided (from -78 to 25 °C, in THF, 10-30 h), and only the starting material **6a** was recovered. Next, changing the base to NaH and the solvent to glyme (DME), it was found that there was no reaction in the temperature range of 25-85 °C (rt → reflux). The results showed that the benzylic proton on **6a** possessed a great steric hindrance such that the deprotontion was not preferred to trigger.

Scheme 8. Gram-Scale Synthesis of **6a**



2a (870 mg, 3 mmol) 3a (620 mg, 3 mmol) 6a (73%, 1.04 g)

Because of the potential application of this protocol in synthesis of tetracyclic sulfonyl dihydrobenzo[*c*]xanthen-7-ones core, attempts to scale up the transformation would improve the significance of the results. Thus, the development of a gram-scale synthetic method was highly in demand. When the scale for the $NH_4OAc/PdCl_2/CuCl_2$-promoted double cyclocondensation of **2a** and **3a** increased to 3.0 mmol (870 mg) and 3.0 mmol (620 mg), **6a** was isolated in a 73% (1.04 g) yield, as shown in Scheme 8.

In conclusion, we have explored a $NH_4OAc/PdCl_2/CuCl_2$-promoted one-pot efficient synthesis of tetracyclic sulfonyl dihydrobenzo[*c*]xanthen-7-one core system by a domino double cyclocondensation of α-sulfonyl *o*-hydroxyacetophenone and 2-allylbenzaldehydes in MeOH at good to excellent yields. Sulfonyl flavanone was the key intermediate. The one-pot synthetic route produces diversified **4** via a cascade pathway of one carbon-oxygen and two carbon-carbon bond formations. The molecular structures of the important products were determined by single-crystal X-ray crystallography. DFT calculations have been included to shed light on the essential role of the two alkoxy groups in *ortho* positions played in the ring-closure reaction of **5**. Further investigations regarding the synthetic application of α-sulfonyl *o*-hydroxyacetophenones **2** and 2-allylbenzaldehydes **3** are underway in our laboratory.

Experimental Section

General. Commercially available reagents and solvents were used without further purification. All reactions were carried by standard procedures under an air atmosphere (an open-vessel condition). All products in EtOAc were dried with anhydrous magnesium sulfate before concentration in vacuo under reduced pressure. Melting points (mp) were recorded with a SMP3 melting apparatus. ^1H (400 MHz) and $^{13}C\{^1H\}$ NMR (100 MHz) spectroscopic data were measured on a Varian INOVA-400 spectrometer, respectively. Chemical shift values (δ) are reported in ppm relative to $CDCl_3$ as the internal standards, and coupling contants (*J* values) are reported in Hertz (Hz). High-resolution mass spectroscopic data (HRMS) were measured with a double focusing mass spectrometer by ESI using a hybrid ion-trap. X-ray single crystal structures were determined with a diffractometer (CAD4, Kappa CCD).

For the starting substrates **2** and **3**, these compounds were known and their related analytical data (e.g., HRMS, ^1H NMR and $^{13}C\{^1H\}$ NMR) were identical with those in the references 19-20.

*A representative synthetic procedure of **4a**, **5**, **6** and **7** is as follows*: NH_4OAc (31 mg, 0.4 mmol) was added to a solution of **2** (0.5 mmol) and **3** (0.5 mmol) in MeOH (10 mL) at 25 °C. Then, the reaction mixture was refluxed for 5 h. The reaction was traced by TLC until the starting materials were consumed. The reaction mixture was cooled to 25 °C. Furthermore, $PdCl_2$ (9 mg, 10 mol%) and $CuCl_2$ (100 mg, 0.75 mmol) were added to the reaction mixture. Then, molecular oxygen was bubbled into the mixture for 2 h, and stirring occurred at 25 °C for 15 h. The reaction mixture was concentrated and extracted with EtOAc (3 x 60 mL). The combined organic layers were washed with brine (2 x 10 mL), dried ($MgSO_4$), filtered and evaporated to afford crude product mixture under reduced pressure. The remaining mixture was separated by column chromatography (silica gel, hexanes/EtOAc = 30/1~10/1 as eluent) affording **4a**, **5**, **6** and **7**.

(2S,3S*)-2-(2-Allyl-3,4-dimethoxyphenyl)-3-tosylchroman-4-one (**4a**)*. In Table 1, entry 7. Yield = 81% (194 mg); Colorless solid; mp = 145-147 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{27}H_{27}O_6S$ 479.1528, found 479.1523; ^1H NMR (400 MHz, $CDCl_3$): δ 7.76 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.43 (dt, *J* = 2.0, 7.6 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 6.94 (dt, *J* = 0.8, 8.0 Hz, 1H), 6.81 (dt, *J* = 0.4, 8.0 Hz, 1H), 6.68 (s, 1H), 6.67 (d, *J* = 8.8 Hz, 1H), 6.56 (d, *J* = 8.8 Hz, 1H), 6.09-6.00 (m, 1H), 5.12 (dq, *J* = 1.6, 10.0 Hz, 1H), 5.03 (dq, *J* = 1.6, 16.8 Hz, 1H), 4.30 (d, *J* = 0.8 Hz, 1H), 3.79 (s, 3H), 3.75 (s, 3H), 3.74-3.68 (m, 1H), 3.63-3.57 (m, 1H), 2.38 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 182.7, 159.3, 153.2, 147.9, 145.6, 137.3, 136.3, 134.2, 132.0, 129.5 (2x), 129.3 (2x), 127.5, 126.7, 121.7, 121.4, 120.3, 118.2, 115.8, 109.9, 73.5, 72.6, 60.8, 55.5, 29.9, 21.6.

(6aS,12aS*)-3,4-Dimethoxy-6-methyl-6a-tosyl-6a,12a-dihydro-7H-benzo[c]xanthen-7-one (**6a**)*. Yield = 85% (202 mg); Colorless solid; mp = 129-131 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{27}H_{25}O_6S$ 477.1372, found 477.1380; ^1H NMR (400 MHz, $CDCl_3$): δ 7.97 (dd, *J* = 2.0, 8.0 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 2H), 7.46 (dt, *J* = 1.6, 8.4 Hz, 1H), 7.16 (d, *J* = 8.4 Hz, 2H), 7.08 (q, *J* = 1.2 Hz, 1H), 7.06 (d, *J* = 8.0 Hz, 1H), 7.04 (dd, *J* = 1.2, 8.4 Hz, 1H), 6.89 (dd, *J* = 0.4, 8.4 Hz, 1H), 6.79 (d, *J* = 8.0 Hz, 1H), 5.90 (s, 1H), 3.87 (s, 3H), 3.83 (s, 3H), 2.36 (s, 3H), 1.78 (d, *J* = 1.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 185.5, 161.3, 153.8, 145.0, 144.6, 136.6, 135.0, 131.0 (2x), 128.8 (2x), 128.0, 126.3, 126.2, 124.8, 124.6, 123.2, 122.2, 120.9, 117.8, 111.3, 77.83, 77.52, 61.3, 55.7, 21.56, 21.50.

(6aS,12aS*)-3,4-Dimethoxy-6-methyl-6a-(phenylsulfonyl)-6a,12a-dihydro-7H-benzo[c]xanthen-7-one (**6b**)*. Yield = 88% (203 mg); Colorless solid; mp = 158-160 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{26}H_{23}O_6S$ 463.1215, found 463.1220; ^1H NMR (400 MHz, $CDCl_3$): δ 7.97 (dd, *J* = 1.6, 7.6 Hz, 1H), 7.84-7.81 (m, 2H), 7.53-7.45 (m, 2H), 7.39-7.35 (m, 2H), 7.10-7.04 (m, 3H), 6.90 (d, *J* = 8.4 Hz, 1H), 6.80 (d, *J* = 8.4 Hz, 1H), 5.93 (s, 1H), 3.87 (s, 3H), 3.83 (s, 3H), 1.78 (d, *J* = 1.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 185.5, 161.3, 153.8, 144.6, 137.9, 136.7, 133.8, 131.0 (2x), 128.1 (2x), 128.0, 126.4, 126.3, 124.7, 124.6, 123.0, 122.3, 120.9, 117.8, 111.4, 77.8, 77.6, 61.4, 55.8, 21.4; X-Ray data: compound **6b** crystallizes in the triclinic crystal system, space group P -1, *a* = 8.9974(4) Å, *b* = 11.1134(5) Å, *c* = 12.3498(6) Å, *V* = 1095.29(9) Å^3, *Z* = 2, d_{calcd} = 1.402 g/cm^3, *F*(000) = 484, 2θ range 1.791~26.439°, R indices (all data) R1 = 0.0451, wR2 = 0.1058.

(6aS,12aS*)-3,4-Dimethoxy-6-methyl-6a-(methylsulfonyl)-6a,12a-dihydro-7H-benzo[c]xanthen-7-one (**6c**)*. Yield = 90% (180 mg); Colorless solid; mp = 159-161 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{21}H_{21}O_6S$ 401.1059, found 401.1063; ^1H NMR (400

MHz, $CDCl_3$): δ 8.00 (dd, *J* = 2.0, 8.0 Hz, 1H), 7.51 (dt, *J* = 2.0, 8.8 Hz, 1H), 7.24 (br s, 1H), 7.17 (d, *J* = 8.4 Hz, 1H), 7.09 (dt, *J* = 0.8, 8.0 Hz, 1H), 6.95 (dd, *J* = 0.4, 8.4 Hz, 1H), 6.89 (d, *J* = 8.4 Hz, 1H), 5.90 (s, 1H), 3.90 (s, 3H), 3.88 (s, 3H), 3.10 (s, 3H), 2.02 (d, *J* = 1.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 186.4, 161.5, 154.2, 145.0, 137.1, 128.0, 127.3, 126.4, 124.4, 123.0, 122.9, 122.4, 120.3, 117.9, 111.6, 76.7, 76.3, 61.5, 55.7, 42.3, 21.3.

(6aS,12aS*)-6a-(n-Butylsulfonyl)-3,4-dimethoxy-6-methyl-6a,12a-dihydro-7H-benzo[c]xanthen-7-one* ***(6d)***. Yield = 82% (181 mg); Colorless solid; mp = 68-70 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{24}H_{27}O_6S$ 443.1528, found 443.1536; ^1H NMR (400 MHz, $CDCl_3$): δ 7.99 (dd, *J* = 2.0, 8.0 Hz, 1H), 7.51 (dt, *J* = 1.6, 8.8 Hz, 1H), 7.22 (d, *J* = 1.2 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 1H), 7.09 (dt, *J* = 0.8, 8.0 Hz, 1H), 6.95 (dd, *J* = 0.8, 8.4 Hz, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 5.92 (s, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 3.75-3.67 (m, 1H), 3.13-3.06 (m, 1H), 2.01 (d, *J* = 1.2 Hz, 3H), 1.86-1.74 (m, 2H), 1.48-1.39 (m, 2H), 0.91 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 186.9, 161.6, 154.0, 144.9, 137.1, 128.0, 127.3, 126.3, 124.3, 123.3, 122.8, 122.3, 120.5, 118.0, 111.5, 76.8, 76.7, 61.5, 55.7, 53.7, 22.3, 21.9, 21.6, 13.6.

(6R,6aR*,12aS*)-6a-(n-Butylsulfonyl)-6-hydroxy-3,4-dimethoxy-6-methyl-5,6,6a,12a-tetrahydro-7H-benzo[c]xanthen-7-one* ***(6d-1)***. Yield = 10% (23 mg); Colorless solid; mp = 190-192 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{24}H_{29}O_7S$ 461.1634, found 461.1630; ^1H NMR (400 MHz, $CDCl_3$): δ 7.80 (dd, *J* = 2.0, 8.0 Hz, 1H), 7.48 (dt, *J* = 1.6, 8.4 Hz, 1H), 7.33 (dd, *J* = 0.8, 8.8 Hz, 1H), 7.00 (dd, *J* = 0.8, 8.4 Hz, 1H), 6.94 (dt, *J* = 1.2, 8.0 Hz, 1H), 6.80 (d, *J* = 8.8 Hz, 1H), 6.45 (s, 1H), 5.00 (br s, 1H), 3.79 (s, 3H), 3.73 (s, 3H), 3.64-3.56 (m, 1H), 3.49-3.41 (m, 1H), 3.14 (d, *J* = 17.6 Hz, 1H), 2.86 (d, *J* = 17.6 Hz, 1H), 1.95-1.85 (m, 2H), 1.52-1.43 (m, 2H), 1.46 (d, *J* = 0.8 Hz, 3H), 0.95 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 191.2, 159.3, 152.3, 145.3, 137.9, 129.5 (2x), 127.0, 124.1, 123.0, 122.0, 119.2, 111.7, 75.9, 75.8, 74.2, 60.1, 56.8, 55.6, 39.8, 22.65, 22.57, 21.9, 13.6; X-Ray data: compound **6d-1** crystallizes in the orthorhombic crystal system, space group P n a 21, *a* = 17.864(4) Å, *b* = 15.417(4) Å, *c* = 7.9315(18) Å, *V* = 2184.5(9) Å^3, *Z* = 4, d_{calcd} = 1.400 g/cm^3, *F*(000) = 976, 2*θ* range 1.745~26.357°, R indices (all data) R1 = 0.0500, wR2 = 0.0925.

(6aS,12aS*)-6a-((4-Fluorophenyl)sulfonyl)-3,4-dimethoxy-6-methyl-6a,12a-dihydro-7H-benzo[c]xanthen-7-one* ***(6e)***. Yield = 84% (202 mg); Colorless solid; mp = 152-154 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{26}H_{22}FO_6S$ 481.1121, found 481.1129; ^1H NMR (400 MHz, $CDCl_3$): δ 7.97 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.85-7.81 (m, 2H), 7.48 (dt, *J* = 2.0, 9.2 Hz, 1H), 7.09-7.01 (m, 5H), 6.90 (dd, *J* = 0.4, 8.4 Hz, 1H), 6.81 (d, *J* = 8.4 Hz, 1H), 5.91 (s, 1H), 3.87 (s, 3H), 3.84 (s, 3H), 1.77 (d, *J* = 1.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 185.4, 165.9 (d, *J* = 256.2 Hz), 161.3, 153.9 (2x), 144.7, 136.8, 133.8 (d, *J* = 9.9 Hz, 2x), 128.0, 126.4, 126.1, 124.59, 124.57, 123.3, 122.3, 120.8, 117.8, 115.3 (d, *J* = 21.9 Hz, 2x), 111.6, 77.7, 77.6, 61.3, 55.8, 21.4; X-Ray data: compound **6e** crystallizes in the monoclinic crystal system, space group P 21/c, *a* = 10.8679(10) Å, *b* = 22.598(2) Å, *c* = 9.3473(8) Å, *V* = 2174.9(4) Å^3, *Z* = 4, d_{calcd} = 1.467 g/cm^3, *F*(000) = 848, 2*θ* range 1.802~26.492°, R indices (all data) R1 = 0.0534, wR2 = 0.1142.

(6aS,12aS*)-3,4-Dimethoxy-6a-((4-methoxyphenyl)sulfonyl)-6-methyl-6a,12a-dihydro-7H-benzo[c]xanthen-7-one* ***(6f)***. Yield = 80% (197 mg); Colorless liquid; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{27}H_{25}O_7S$ 493.1321, found 493.1326; ^1H NMR (400 MHz, $CDCl_3$): δ 7.97 (dd, *J* = 2.0, 8.0 Hz, 1H), 7.74 (d, *J* = 9.2 Hz, 2H), 7.46 (dt, *J* = 1.6, 8.8 Hz, 1H), 7.06 (d, *J* = 8.0 Hz, 2H), 7.04 (dd, *J* = 0.4, 8.0 Hz, 1H), 6.89 (dd, *J* = 0.4, 8.4 Hz, 1H), 6.82 (d, *J* = 8.8 Hz, 2H), 6.80 (dd, *J* = 0.4, 8.4 Hz, 1H), 5.90 (s, 1H), 3.87 (s, 3H), 3.84 (s, 3H), 3.83 (s, 3H), 1.78 (d, *J* = 1.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 185.6, 163.9, 161.3, 153.7, 144.6, 136.6, 133.2 (2x), 129.2, 128.0, 126.2, 126.1, 125.0, 124.6, 123.3, 122.2, 120.9, 117.8, 113.3 (2x), 111.4, 77.9, 77.4, 61.3, 55.7, 55.6, 21.5.

(6R,6aR*,12aS*)-6-Hydroxy-3,4-dimethoxy-6a-((4-methoxyphenyl)sulfonyl)-6-methyl-5,6,6a,12a-tetrahydro-7H-benzo[c]xanthen-7-one* ***(6f-1)***. Yield = 5% (13 mg); Colorless solid; mp = 164-166 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{27}H_{27}O_8S$ 511.1427, found 511.1435; ^1H NMR (400 MHz, $CDCl_3$): δ 7.72 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.55 (d, *J* = 7.6 Hz, 2H), 7.20 (dt, *J* = 1.6, 8.4 Hz, 1H), 7.10 (d, *J* = 8.8 Hz, 1H), 6.85 (d, *J* = 7.6 Hz, 1H), 6.71-6.66 (m, 3H), 6.41 (s, 1H), 6.31 (d, *J* = 8.0 Hz, 1H), 4.50 (br s, 1H), 3.80 (s, 3H), 3.74 (s, 6H), 3.10 (d, *J* = 18.0 Hz, 1H), 2.97 (d, *J* = 18.4 Hz, 1H), 2.26 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 183.8, 164.2, 157.9, 152.2, 145.8, 136.5, 132.1 (2x), 131.5, 130.7, 130.0, 127.0, 124.8, 122.0, 121.72, 121.69, 117.9, 114.1, 113.2, 111.0, 76.2, 75.7, 60.0, 55.7, 55.5, 37.2, 29.2.

(2S,3S*)-2-(3,4-Dimethoxy-2-(2-oxopropyl)phenyl)-3-((4-methoxyphenyl)sulfonyl)chroman-4-one* ***(5f)***. Yield = 6% (15 mg); Colorless solid; mp = 179-181 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{27}H_{27}O_8S$ 511.1427, found 511.1430; ^1H NMR (400 MHz, $CDCl_3$): δ 7.76 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.71 (d, *J* = 8.8 Hz, 2H), 7.42 (dt, *J* = 2.0, 8.4 Hz, 1H), 6.94 (dt, *J* = 1.2, 8.0 Hz, 1H), 6.91 (d, *J* = 9.2 Hz, 2H), 6.72 (dd, *J* = 0.4, 8.4 Hz, 1H), 6.68 (d, *J* = 8.4 Hz, 1H), 6.61 (d, *J* = 8.4 Hz, 1H), 6.51 (s, 1H), 4.37 (d, *J* = 0.8 Hz, 1H), 4.09 (s, 2H), 3.84 (s, 3H), 3.76 (s, 3H), 3.75 (s, 3H), 2.40 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 205.7, 182.8, 164.3, 158.7, 153.1, 148.1, 142.0, 137.4, 131.6 (2x), 128.5, 127.6, 126.7, 121.8, 121.7, 120.3, 118.4, 114.2 (2x), 110.6, 73.7, 72.0, 60.5, 55.7, 55.5, 41.3, 30.1.

(6aS,12aS*)-3,4-Dimethoxy-6-methyl-6a-(m-tolylsulfonyl)-6a,12a-dihydro-7H-benzo[c]xanthen-7-one* ***(6g)***. Yield = 84% (200 mg); Colorless liquid; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{27}H_{25}O_6S$ 477.1372, found 477.1378; ^1H NMR (400 MHz, $CDCl_3$): δ 7.98 (dd, *J* = 2.0, 8.0 Hz, 1H), 7.60 (d, *J* = 7.6 Hz, 1H), 7.57 (s, 1H), 7.47 (dt, *J* = 2.0, 8.4 Hz, 1H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.23 (t, *J* = 7.6 Hz, 1H), 7.08-7.04 (m, 3H), 6.89 (dd, *J* = 0.4, 8.4 Hz, 1H), 6.79 (d, *J* = 8.4 Hz, 1H), 5.91 (s, 1H), 3.86 (s, 3H), 3.81 (s, 3H), 2.33 (s, 3H), 1.86 (d, *J* = 1.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 185.3, 161.2, 153.7, 144.6, 138.2, 137.5, 136.6, 134.6, 131.2, 128.2, 128.1, 127.9, 126.3, 126.2, 124.9, 124.6, 123.0, 122.2, 121.0, 117.7, 111.3, 77.9, 77.6, 61.3, 55.8, 21.5, 21.3.

(6aS,12aS*)-6a-((4-Ethylphenyl)sulfonyl)-3,4-dimethoxy-6-methyl-6a,12a-dihydro-7H-benzo[c]xanthen-7-one* ***(6h)***. Yield = 87% (213 mg); Colorless solid; mp = 146-148 °C (re-crystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{28}H_{27}O_6S$ 491.1528, found 491.1532; ^1H NMR (400 MHz, $CDCl_3$): δ 7.98 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.46 (dt, *J* = 2.0, 9.2 Hz, 1H), 7.17 (d, *J* = 8.4 Hz, 2H), 7.08-7.03 (m, 3H), 6.89 (dd, *J* = 0.8, 8.4 Hz, 1H), 6.77 (d, *J* = 8.4 Hz, 1H), 5.91 (s, 1H), 3.85 (s, 3H), 3.82 (s, 3H), 2.64 (q, *J* = 7.6 Hz, 2H), 1.81 (d, *J* = 1.6 Hz, 3H), 1.21 (t, *J* = 7.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 185.4, 161.3, 153.7, 151.0, 144.5, 136.6, 135.1, 131.0 (2x), 128.0, 127.6 (2x), 126.3, 126.1, 124.9, 124.6, 123.1, 122.2, 120.9, 117.8, 111.2, 77.9, 77.5, 61.2, 55.6, 28.8, 21.5, 14.9.

(6aS,12aS*)-6a-((4-Isopropylphenyl)sulfonyl)-3,4-dimethoxy-6-methyl-6a,12a-dihydro-7H-benzo[c]xanthen-7-one* ***(6i)***. Yield = 90% (227 mg); Colorless solid; mp = 164-166 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{29}H_{29}O_6S$ 505.1685, found 505.1693; ^1H NMR (400 MHz, $CDCl_3$): δ 7.99 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 2H), 7.46 (dt, *J* = 1.6, 8.4 Hz, 1H), 7.17 (d, *J* = 8.4 Hz, 2H), 7.08-7.02 (m, 3H), 6.88 (d, *J* = 8.0 Hz, 1H), 6.75 (d, *J* = 8.4 Hz, 1H), 5.92 (s, 1H), 3.84 (s, 3H), 3.81 (s, 3H), 2.92-2.85 (m, 1H), 1.85 (d, *J* = 1.6 Hz, 3H), 1.205 (d, *J* = 6.8 Hz, 3H), 1.203 (d, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 185.3, 161.3, 155.5, 153.7, 144.4, 136.6, 135.1, 131.1 (2x), 128.1, 126.3, 126.2 (2x), 126.0, 125.1, 124.6, 123.0, 122.2, 121.0, 117.8, 111.2, 77.9, 77.5, 61.2, 55.6, 34.2, 23.5, 23.4, 21.5; X-Ray data: compound **6i** crystallizes in the monoclinic crystal system, space group P 21/c, *a* = 10.1806(11) Å, *b* = 22.707(2) Å, *c* = 11.1057(13) Å, *V* = 2446.3(5) $Å^3$, *Z* = 4, d_{calcd} = 1.370 g/cm^3, *F*(000) = 1064, 2*θ* range 2.099~26.458°, R indices (all data) R1 = 0.0414, wR2 = 0.0909.

(6aS,12aS*)-6a-((4-n-Butylphenyl)sulfonyl)-3,4-dimethoxy-6-methyl-6a,12a-dihydro-7H-benzo[c]xanthen-7-one* ***(6j)***. Yield = 95% (246 mg); Colorless solid; mp = 103-105 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{30}H_{31}O_6S$ 519.1841, found 519.1849; ^1H NMR (400 MHz, $CDCl_3$): δ 7.97 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.46 (dt, *J* = 2.0, 9.2 Hz, 1H), 7.16 (d, *J* = 8.4 Hz, 2H), 7.09-7.03 (m, 3H), 6.89 (d, *J* = 8.0 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 5.92 (s, 1H), 3.86 (s, 3H), 3.83 (s, 3H), 2.60 (t, *J* = 7.6 Hz, 2H), 1.79 (d, *J* = 1.2 Hz, 3H), 1.57-1.51 (m, 2H), 1.36-1.25 (m, 2H), 0.93 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 185.5, 161.3, 153.7, 149.9, 144.5, 136.6, 135.1, 131.0 (2x), 128.1 (2x), 128.0, 126.3, 126.1, 124.9, 124.6, 123.1, 122.2, 120.9, 117.8, 111.2, 77.8, 77.5, 60.3, 55.7, 35.6, 33.0, 22.3, 21.5, 13.9.

(6aS,12aS*)-6a-((4-(tert-Butyl)phenyl)sulfonyl)-3,4-dimethoxy-6-methyl-6a,12a-dihydro-7H-benzo[c]xanthen-7-one* ***(6k)***. Yield = 90% (233 mg); Colorless solid; mp = 165-167 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{30}H_{31}O_6S$ 519.1841, found 519.1847; ^1H NMR (400 MHz, $CDCl_3$): δ 7.99 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.70 (d, *J* = 8.8 Hz, 2H), 7.46 (dt, *J* = 2.0, 9.2 Hz, 1H), 7.33 (d, *J* = 8.4 Hz, 2H), 7.07-7.06 (m, 2H), 7.03 (d, *J* = 8.0 Hz, 1H), 6.88 (dd, *J* = 0.4, 8.0 Hz, 1H), 6.74 (d, *J* = 8.4 Hz, 1H), 5.93 (s, 1H), 3.83 (s, 3H), 3.81 (s, 3H), 1.86 (d, *J* = 1.6 Hz, 3H), 1.27 (s, 9H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 185.3, 161.3, 157.8, 153.6, 144.4, 136.6, 134.7, 130.8 (2x), 128.1, 126.3, 126.0, 125.2, 125.1 (2x), 124.7, 123.0, 122.2, 121.1, 117.7, 111.1, 78.0, 77.5, 61.2, 55.5, 35.2, 30.9 (3x), 21.5.

(6aS,12aS*)-9-Fluoro-3,4-dimethoxy-6-methyl-6a-tosyl-6a,12a-dihydro-7H-benzo[c]xanthen-7-one* ***(6l)***. Yield = 87% (215 mg); Colorless solid; mp = 130-132 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{27}H_{24}FO_6S$ 495.1278, found 495.1283; ^1H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 8.4 Hz, 2H), 7.61 (dd, *J* = 3.2, 8.4 Hz, 1H), 7.19 (dt, *J* = 3.2, 7.6 Hz, 1H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.09 (q, *J* = 1.2 Hz, 1H), 7.05 (d, *J* = 8.0 Hz, 1H), 6.89 (dd, *J* = 4.4, 9.2 Hz, 1H), 6.80 (d, *J* = 8.4 Hz, 1H), 5.88 (s, 1H), 3.87 (s, 3H), 3.83 (s, 3H), 2.36 (s, 3H), 1.77 (d, *J* = 1.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 185.0, 157.7, 157.5 (d, *J* = 241.8 Hz), 153.9, 145.2, 144.6, 134.7, 131.0 (2x), 128.8 (2x), 126.3, 126.2, 124.6, 124.5, 124.2, 122.9, 119.7, 119.6, 112.9, 112.7, 111.3, 78.2, 61.3, 55.7, 21.6, 21.5.

(6aS,12aS*)-3,4,10-Trimethoxy-6-methyl-6a-tosyl-6a,12a-dihydro-7H-benzo[c]xanthen-7-one* ***(6m)***. Yield = 90% (228 mg); Colorless solid; mp = 116-118 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{28}H_{27}O_7S$ 507.1478, found 507.1485; ^1H NMR (400 MHz, $CDCl_3$): δ 7.90 (d, *J* = 9.2 Hz, 1H), 7.72 (d, *J* = 8.4 Hz, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.07 (s, 1H), 7.06 (d, *J* = 8.0 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.61 (dd, *J* = 2.0, 8.4 Hz, 1H), 6.33 (d, *J* = 2.4 Hz, 1H), 5.89 (s, 1H), 3.87 (s, 3H), 3.84 (s, 3H), 3.78 (s, 3H), 2.36 (s, 3H), 1.75 (d, *J* = 1.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 183.8, 166.5, 163.3, 153.8, 144.9, 144.6, 135.2, 131.0 (2x), 129.8, 129.0, 128.8 (2x), 126.4, 125.9, 125.2, 124.4, 123.3, 111.4, 111.2, 100.2, 78.0, 77.5, 61.3, 55.74, 55.70, 21.6, 21.5.

(6aS,14aS*)-9-Bromo-3,4-dimethoxy-6-methyl-6a-tosyl-6a,14a-dihydro-7H-dibenzo[c,h]xanthen-7-one* ***(6n)***. Yield = 87% (263 mg); Colorless liquid; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{31}H_{26}BrO_6S$ 605.0634, found 605.0640; ^1H NMR (400 MHz, $CDCl_3$): δ 8.20 (s, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 8.12 (dd, *J* = 0.8, 8.4 Hz, 1H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.71 (dd, *J* = 0.8, 8.0 Hz, 1H), 7.51 (dt, *J* = 0.8, 8.0 Hz, 1H), 7.18 (d,, *J* = 8.0 Hz, 2H), 7.14 (d, *J* = 8.4 Hz, 1H), 7.11 (br q, *J* = 0.8 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 6.06 (s, 1H), 3.91 (s, 3H), 3.86 (s, 3H), 2.36 (s, 3H), 1.79 (d, *J* = 1.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 183.9, 159.6, 154.0, 145.2, 144.6, 135.5, 134.8, 131.4, 131.0 (2x), 128.9 (2x), 127.5, 127.2, 126.6, 126.3, 125.4, 125.3, 124.8, 124.6, 124.2, 122.8, 116.1, 115.6, 111.3, 78.9, 77.3, 61.3, 55.8, 21.6, 21.5.

(6aS,12aS*)-4-Isopropoxy-3-methoxy-6-methyl-6a-tosyl-6a,12a-dihydro-7H-benzo[c]xanthen-7-one* ***(6o)***. Yield = 86% (217 mg); Colorless liquid; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{29}H_{29}O_6S$ 505.1685, found 505.1690; ^1H NMR (400 MHz, $CDCl_3$): δ 7.94 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 2H), 7.46 (dt, *J* = 1.6, 8.4 Hz, 1H), 7.22 (d, *J* = 8.4 Hz, 2H), 7.15 (br t, *J* = 0.8 Hz, 1H), 7.08 (d, *J* = 8.4 Hz, 1H), 7.04 (dt, *J* = 0.8, 8.0 Hz, 1H), 6.90 (d, *J* = 8.0 Hz, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 5.90 (s, 1H), 4.47-4.41 (m, 1H), 3.86 (s, 3H), 2.39 (s, 3H), 1.67 (d, *J* = 1.2 Hz, 3H), 1.36 (d, *J* = 6.0 Hz, 3H), 1.32 (d, *J* = 6.4 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 185.9, 161.4, 154.0, 145.0, 142.8, 136.6, 135.5, 131.0 (2x), 128.8 (2x), 127.9, 127.5, 127.4, 123.9, 123.6, 123.3, 122.1, 120.8, 117.8, 111.2, 77.8, 77.6, 75.6, 55.7, 22.6, 22.5, 21.6, 21.5.

(6aS,12aS*)-4-n-Butoxy-3-methoxy-6-methyl-6a-tosyl-6a,12a-dihydro-7H-benzo[c]xanthen-7-one (**6p**)*. Yield = 83% (215 mg); Colorless liquid; HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{30}H_{31}O_6S$ 519.1841, found 519.1848; ^1H NMR (400 MHz, $CDCl_3$): δ 7.96 (dd, *J* = 2.0, 8.0 Hz, 1H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.46 (dt, *J* = 1.6, 8.4 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 1.6 Hz, 1H), 7.07-7.03 (m, 2H), 6.89 (dd, *J* = 0.4, 8.4 Hz, 1H), 6.79 (d, *J* = 8.0 Hz, 1H), 5.90 (s, 1H), 3.95 (t, *J* = 6.8 Hz, 2H), 3.85 (s, 3H), 2.37 (s, 3H), 1.80-1.74 (m, 2H), 1.74 (d, *J* = 1.2 Hz, 3H), 1.57-1.48 (m, 2H), 1.00 (t, *J* = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 185.7, 161.3, 153.9, 145.0, 144.0, 136.6, 135.1, 131.0 (2x), 128.8 (2x), 128.0, 126.7, 126.5, 124.3, 124.2, 123.2, 122.2, 120.9, 117.8, 111.3, 77.8, 77.6, 73.6, 55.7, 32.2, 21.59, 21.56, 19.2, 13.9.

(2S,3S*)-2-(3-n-Butoxy-4-methoxy-2-(2-oxopropyl)phenyl)-3-tosylchroman-4-onee (**5p**)*. Yield = 10% (27 mg); Colorless solid; mp = 179-181 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{30}H_{33}O_7S$ 537.1947, found 537.1942; ^1H NMR (400 MHz, $CDCl_3$): δ 7.76 (dd, *J* = 1.6, 8.0 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.41 (dt, *J* = 1.6, 8.4 Hz, 1H), 7.26 (d, *J* = 8.0 Hz, 2H), 6.93 (dt, *J* = 1.2, 8.0 Hz, 1H), 6.72 (dd, *J* = 0.8, 8.4 Hz, 1H), 6.66 (d, *J* = 8.8 Hz, 1H), 6.59 (d, *J* = 8.4 Hz, 1H), 6.51 (s, 1H), 4.38 (d, *J* = 0.8 Hz, 1H), 4.11 (s, 2H), 3.88 (dt, *J* = 2.4, 8.0 Hz, 2H), 3.73 (s, 3H), 2.39 (s, 3H), 2.37 (s, 3H), 1.70-1.63 (m, 2H), 1.48-1.39 (m, 2H), 0.95 (t, *J* = 7.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 205.6, 182.6, 158.8, 153.1, 147.5, 145.6, 137.4, 134.2, 129.6 (2x), 129.3 (2x), 128.3, 127.6, 126.6, 121.6, 121.4, 120.3, 118.3, 110.5, 73.5, 72.7, 71.8, 55.5, 41.5, 32.3, 30.0, 21.6, 19.1, 13.8; X-Ray data: compound **5p** crystallizes in the monoclinic crystal system, space group P 21/c, *a* = 16.7195(5) Å, *b* = 15.7342(5) Å, *c* = 10.2217(3) Å, *V* = 2688.96(14) $Å^3$, *Z* = 4, d_{calcd} = 1.326 g/cm^3, *F*(000) = 1136, 2*θ* range 1.218~26.497°, R indices (all data) R1 = 0.0420, wR2 = 0.0854.

(6aS,12aS*)-9-Chloro-3,4-dimethoxy-6-methyl-6a-tosyl-6a,12a-dihydro-7H-benzo[c]xanthen-7-one (**6q**)*. Yield = 88% (224 mg); Colorless solid; mp = 155-157 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{27}H_{24}ClO_6S$ 511.0982, found 511.0986; ^1H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, *J* = 2.8 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.39 (dd, *J* = 2.4, 8.8 Hz, 1H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.08 (q, *J* = 1.6 Hz, 1H), 7.04 (d, *J* = 8.4 Hz, 1H), 6.85 (d, *J* = 8.8 Hz, 1H), 6.79 (d, *J* = 8.4 Hz, 1H), 5.87 (s, 1H), 3.87 (s, 3H), 3.83 (s, 3H), 2.36 (s, 3H), 1.78 (d, *J* = 1.2 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 184.7, 159.7, 153.9, 145.2, 144.5, 136.5, 134.6, 130.9 (2x), 128.8 (2x), 127.7, 127.1, 126.3, 126.2, 124.6, 124.4, 122.6, 121.5, 119.6, 111.3, 78.1, 77.3, 61.2, 55.7, 21.5, 21.4; X-Ray data: compound **6q** crystallizes in the triclinic crystal system, space group P -1, *a* = 12.9789(10) Å, *b* = 12.9834(10) Å, *c* = 15.1869(12) Å, *V* = 2300.4(3) $Å^3$, *Z* = 2, d_{calcd} = 1.475 g/cm^3, *F*(000) = 1064, 2*θ* range 1.463~26.436°, R indices (all data) R1 = 0.0427, wR2 = 0.0858.

(2S,3S*)-2-(3-Methoxy-2-(2-oxopropyl)phenyl)-3-tosylchroman-4-one (**5r**)*. Yield = 94% (218 mg); Colorless solid; mp = 146-148 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{26}H_{25}O_6S$ 465.1372, found 465.1780; ^1H NMR (400 MHz, $CDCl_3$): δ 7.72-7.68 (m, 3H), 7.44 (dt, *J* = 1.6, 8.8 Hz, 1H), 7.23 (d, *J* = 8.0 Hz, 2H), 6.98 (d, *J* = 7.6 Hz, 1H), 6.93 (dt, *J* = 0.8, 8.0 Hz, 1H), 6.89 (d, *J* = 8.4 Hz, 1H), 6.73 (s, 1H), 6.70 (d, *J* = 8.0 Hz, 1H), 6.52 (s, 1H), 4.39 (d, *J* = 1.2 Hz, 1H), 3.67 (s, 3H), 3.57 (d, *J* = 0.4 Hz, 2H), 2.37 (s, 3H), 2.09 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 206.1, 182.0, 158.9, 157.7, 145.7, 137.3, 136.6, 134.1, 131.5, 129.5 (2x), 129.4 (2x), 126.9, 124.3, 121.7, 120.8, 118.12, 118.09, 108.4, 76.2, 72.9, 55.3, 44.8, 29.4, 21.6.

(2S,3S*)-2-(3-n-Butoxy-5-methoxy-2-(2-oxopropyl)phenyl)-3-tosylchroman-4-one (**5s**)*. Yield = 94% (252 mg); Colorless solid; mp = 141-143 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{30}H_{33}O_7S$ 537.1947, found 537.1943; ^1H NMR (400 MHz, $CDCl_3$): δ 7.72-7.69 (m, 3H), 7.41 (dt, *J* = 1.6, 8.4 Hz, 1H), 7.22 (d, *J* = 8.4 Hz, 2H), 6.93 (dt, *J* = 1.2, 8.0 Hz, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 6.49 (s, 1H), 6.34 (s, 2H), 4.39 (d, *J* = 0.8 Hz, 1H), 3.81-3.69 (m, 2H), 3.62 (s, 3H), 3.59 (s, 2H), 2.36 (s, 3H), 2.05 (s, 3H), 1.64-1.57 (m, 2H), 1.42-1.33 (m, 2H), 0.89 (t, *J* = 7.6 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 206.7, 182.0, 159.0, 158.4, 157.8, 145.7, 137.3, 136.4, 134.1, 129.5 (2x), 129.4 (2x), 126.9, 121.7, 120.8, 118.0, 112.7, 102.5, 101.4, 76.5, 73.0, 68.0, 55.6, 38.2, 31.0, 29.2, 21.6, 19.1, 13.7; X-Ray data: compound **5s** crystallizes in the triclinic crystal system, space group P -1, *a* = 12.6557(11) Å, *b* = 14.4552(12) Å, *c* = 16.5189(15) Å, *V* = 2781.4(4) $Å^3$, *Z* = 2, d_{calcd} = 1.281 g/cm^3, *F*(000) = 1136, 2*θ* range 1.530~26.487°, R indices (all data) R1 = 0.0996, wR2 = 0.1882.

*(E)-1-(2-Hydroxyphenyl)-3-(7-methoxy-2-methylbenzofuran-4-yl)-2-tosylprop-2-en-1-one (**7a**)*. Yield = 90% (208 mg); Colorless solid; mp = 154-156 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{26}H_{23}O_6S$ 463.1215, found 463.1224; ^1H NMR (400 MHz, $CDCl_3$): δ 7.73-7.71 (m, 3H), 7.39 (dt, *J* = 1.6, 8.8 Hz, 1H), 7.24 (d, *J* = 7.6 Hz, 2H), 6.91 (dt, *J* = 0.8, 8.0 Hz, 1H), 6.83 (dd, *J* = 0.4, 8.4 Hz, 1H), 6.76 (s, 1H), 6.69 (dd, *J* = 0.4, 8.4 Hz, 1H), 6.64 (d, *J* = 1.2 Hz, 1H), 6.46 (d, *J* = 8.0 Hz, 1H), 4.46 (d, *J* = 1.2 Hz, 1H), 3.88 (s, 3H), 2.50 (d, *J* = 1.2 Hz, 3H), 2.38 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 182.4, 158.9, 156.6, 145.6, 145.3, 143.9, 137.2, 134.3, 129.5 (2x), 129.3 (2x), 128.8, 126.8, 121.6, 120.5, 120.4, 119.8, 118.1, 104.6, 101.6, 74.7, 71.9, 55.9, 21.6, 14.1; X-Ray data: compound **7a** crystallizes in the monoclinic crystal system, space group P 21/c, *a* = 10.8962(7) Å, *b* = 16.0021(8) Å, *c* = 14.7675(9) Å, *V* = 2500.4(3) $Å^3$, *Z* = 4, d_{calcd} = 1.229 g/cm^3, *F*(000) = 968, 2*θ* range 1.907~26.425°, R indices (all data) R1 = 0.0609, wR2 = 0.1106.

*(E)-1-(2-Hydroxyphenyl)-3-(7-methoxy-2-methylbenzofuran-4-yl)-2-(phenylsulfonyl)prop-2-en-1-one (**7b**)*. Yield = 93% (208 mg); Colorless solid; mp = 125-127 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{25}H_{21}O_6S$ 449.1059, found 449.1063; ^1H NMR (400 MHz, $CDCl_3$): δ 7.86-7.84 (m, 2H), 7.72 (dd, *J* = 2.0, 8.0 Hz, 1H), 7.60-7.56 (m, 1H), 7.48-7.44 (m, 2H), 7.38 (dt, *J* = 1.6, 8.8 Hz, 1H), 6.91 (dt, *J* = 0.8, 8.0 Hz, 1H), 6.82 (dd, *J* = 0.4, 8.4 Hz, 1H), 6.77 (s, 1H), 6.69 (d, *J* = 8.4 Hz, 1H), 6.64 (d, *J* = 0.8 Hz, 1H), 6.47 (d, *J* = 8.4 Hz, 1H), 4.50 (d, *J* = 1.2 Hz, 1H), 3.89 (s, 3H), 2.51 (d, *J* = 0.8 Hz, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 182.2, 158.9, 156.7, 145.3, 143.9, 137.4, 137.2, 134.5, 129.4 (3x), 128.91 (2x), 128.85, 126.8, 121.7, 120.4, 119.7, 118.1, 104.6, 101.6, 74.7, 72.0, 55.9, 14.1.

(6R,6aS*,12aS*)-6-Hydroxy-3,4-dimethoxy-6a-tosyl-5,6,6a,12a-tetrahydro-7H-benzo[c]xanthen-7-one* ***(8)***. NH_4OAc (31 mg, 0.4 mmol) was added to a solution of **2a** (145 mg, 0.5 mmol) and **3a** (103 mg, 0.5 mmol) in MeOH (10 mL) at 25 °C. Then, the reaction mixture was refluxed for 5 h. The reaction was traced by TLC until the starting materials were consumed. The reaction mixture was cooled to 25 °C. Furthermore, freshly prepared OsO_4 (1.0 M in THF, 3 mL) and NMO (50% in H_2O, 350 mg, 1.5 mmol) was added to the reaction mixture at 25 °C. And, the reaction mixture was stirred at 25 °C for 15 h. The reaction mixture was concentrated and extracted with EtOAc (3 x 60 mL). The combined organic layers were washed with brine (2 x 10 mL), dried ($MgSO_4$), filtered and evaporated to afford crude product mixture under reduced pressure. The remaining mixture was separated by column chromatography (silica gel, hexanes/EtOAc = 30/1~10/1 as eluent) affording **8**. Yield = 82% (197 mg); Colorless solid; mp > 250 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{26}H_{25}O_7S$ 481.1321, found 481.1332; ^1H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 8.4 Hz, 2H), 7.53 (dd, *J* = 1.6, 7.6 Hz, 1H), 7.33 (dt, *J* = 1.6, 8.4 Hz, 1H), 7.26 (dd, *J* = 0.8, 8.8 Hz, 1H), 7.14 (d, *J* = 8.4 Hz, 2H), 6.81 (dd, *J* = 0.8, 8.4 Hz, 1H), 6.79 (dt, *J* = 0.8, 8.0 Hz, 1H), 6.74 (d, *J* = 8.8 Hz, 1H), 6.56 (s, 1H), 5.24 (dd, *J* = 2.4, 3.6 Hz, 1H), 3.75 (s, 3H), 3.72 (s, 3H), 3.08 (dd, *J* = 2.4, 18.4 Hz, 1H), 2.91 (dd, *J* = 3.6, 18.4 Hz, 1H), 2.32 (s, 3H), 1.80 (br s, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 184.6, 158.4, 152.2, 146.3, 145.8, 136.8, 132.9, 130.5 (2x), 129.1, 129.0 (2x), 126.8, 124.9, 122.1, 121.6, 121.3, 118.8, 111.4, 74.6, 74.3, 67.5, 60.0, 55.6, 29.4, 21.5.

*2-Phenylchromen-4-one (**9**)*[17] *and 7,8-dimethoxynaphthalen-2-ol (**10**)*.[11a] NH_4OAc (31 mg, 0.4 mmol) was added to a solution of **2p** (120 mg, 0.5 mmol) and **3a** (103 mg, 0.5 mmol) in MeOH (10 mL) at 25 °C. Then, the reaction mixture was refluxed for 5 h. The reaction was traced by TLC until the starting materials were consumed. The reaction mixture was cooled to 25 °C. Furthermore, $PdCl_2$ (9 mg, 10 mol%) and $CuCl_2$ (100 mg, 1.5 mmol) was added to the reaction mixture. Then, molecular oxygen was bubbled into the mixture for 2 h, and stirring occurred at 25 °C for 15 h. The reaction mixture was concentrated and extracted with EtOAc (3 x 60 mL). The combined organic layers were washed with brine (2 x 10 mL), dried ($MgSO_4$), filtered and evaporated to afford crude product mixture under reduced pressure. The remaining mixture was separated by column chromatography (silica gel, hexanes/EtOAc = 30/1~10/1 as eluent) affording **9** and **10**.

For **9**: Yield = 82% (91 mg); Colorless solid; mp = 94-95 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{15}H_{11}O_2$ 223.0759, found 223.0765; ^1H NMR (400 MHz, $CDCl_3$): δ 8.24 (dd, *J* = 1.6, 8.0 Hz, 1H), 8.02-7.86 (m, 2H), 7.72 (dt, J = 1.6, 8.4 Hz, 1H), 7.60 (dd, *J* = 1.6, 8.4 Hz, 1H), 7.56-7.48 (m, 3H), 7.45 (dt, *J* = 1.2, 8.0 Hz, 1H), 7.06 (d, *J* = 1.2 Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 178.7, 164.5, 156.2, 134.4, 132.0, 131.2, 129.1 (2x), 126.4, 125.7 (2x), 125.6, 123.0, 118.1, 106.9. **9** is known compound and the analytical data are consistent with those in the reference 17. For **10**: Yield = 72% (73 mg); Colorless solid; mp = 125-126 °C (recrystallized from hexanes and EtOAc); HRMS (ESI-TOF) *m/z*: $[M + H]^+$ calcd for $C_{12}H_{13}O_3$ 205.0865, found 205.0872; ^1H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 8.4 Hz, 1H), 7.52 (d, *J* = 8.8 Hz, 1H), 7.45 (d, *J* = 2.4 Hz, 1H), 7.11 (d, *J* = 8.8 Hz, 1H), 7.02 (dd, *J* = 2.4, 8.8 Hz, 1H), 6.76 (s, 1H), 3.97 (s, 3H), 3.91 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 154.5, 148.9, 141.1, 130.2, 129.8, 125.2, 124.4, 116.7, 112.1, 102.8, 60.8, 56.6. **10** is known compound and the analytical data are consistent with those in the reference 11a.

*Gram-Scale Synthesis of Compound **6a***. NH_4OAc (185 mg, 2.4 mmol) was added to a solution of **2a** (870 mg, 3.0 mmol) and **3a** (620 mg, 3.0 mmol) in MeOH (60 mL) at 25 °C. Then, the reaction mixture was refluxed for 5 h. The reaction was traced by TLC until the starting materials were consumed. The reaction mixture was cooled to 25 °C. Furthermore, $PdCl_2$ (54 mg, 10 mol%) and $CuCl_2$ (600 mg, 4.5 mmol) were added to the reaction mixture. Then, molecular oxygen was bubbled into the mixture for 2 h, and stirring occurred at 25 °C for 15 h. The reaction mixture was concentrated and extracted with EtOAc (4 x 80 mL). The combined organic layers were washed with brine (2 x 10 mL), dried ($MgSO_4$), filtered and evaporated to afford crude product mixture under reduced pressure. The remaining mixture was separated by column chromatography (silica gel, hexanes/EtOAc = 30/1~10/1 as eluent) affording **6a** (1.04 g, 73%).

DFT calculation. The B3LYP-D3 method was employed for the present DFT calculations. The transition metals Cu and Pd were described by LANL2DZ basis sets with effective core potentials, whereas the remaining elements were described by 6-31+G* basis sets. Geometry optimizations and vibrational frequency calculations were carried under solution phase described by the SMD solvation model (solvent = methanol). The thermal correction to Gibbs free energy with zero-point vibrational energies was made at standard conditions of 1 atm and 298.15 K. The setting of ultrafine grids was adopted for numerical integrations. All the calculations were achieved by using the Gaussian 09 program.[21]

ASSOCIATED CONTENT

Supporting Information

Scanned photocopies of NMR spectral data for all compounds, DFT results and optimized coordinates, and X-ray analysis data of **6b**, **6d-1**, **6e**, **6i**, **5p**, **6q**, **5s** and **7a**. This information is available free of charge via the Internet at http: //pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

*Email: mychang@kmu.edu.tw

*Email: hychen@kmu.edu.tw

ORCID

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

Hsing-Yin Chen: 0000-0003-3948-8915

Notes

The authors declare no competing financial interest.

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