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m-CPBA-mediated stereoselective synthesis of sulfonyl tetrahydropyrans

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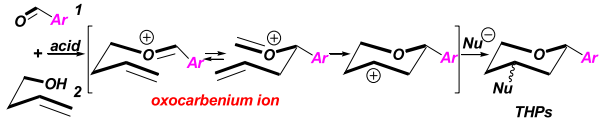
ABSTRACT

A stereoselective synthesis of sulfonyl tetrahydropyrans (THPs) **6** was performed with moderate to good yields by *m*-CPBA (*m*-chloroperoxybenzoic acid)-mediated ring-closure of β-hydroxy sulfones **5**. Skeleton **5** is prepared by cinnamylation of β-ketosulfones **3** in the presence of K_2CO_3 followed by $NaBH_4$-mediated reduction of the resulting skeleton **4** with a α-cinnamyl side arm in the co-solvent of THF and MeOH. The key structures of skeleton **6** were confirmed by X-ray crystallographic analysis. The reaction mechanism had been discussed.

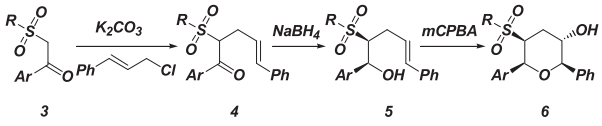
1. Introduction

Tetrahydropyran (THP) is an important component in numerous diversified molecules with biological activities,[1] synthetic intermediates,[2] and natural products.[3] A number of effective routes have been developed for functionalized THPs. Among the key transformations of poly-substituted THPs, Lewis acid-promoted Prins cyclization of an in situ generated oxocarbenium ion (from condensation of **1** and **2**) has been employed as a major route for synthesizing diversified THPs (Scheme 1).[4] Furthermore, a combination of the Prins reaction and Friedel–Crafts alkylation provided a facile access to the THP structures.[2c,d,3b]



Scheme 1. Synthesis of THPs via Prins reaction.

In an attempt to prepare new bioactive compounds with THP, we decided to prepare a series of new THPs having a sulfonyl substituent via $NaBH_4$-mediated stereoselective reduction, *m*-CPBA-mediated stereoselective epoxidation and sequential intramolecular ring-closure. In continuation of our investigation on the skeleton of β-ketosulfones **3**,[5] a three-step route of synthesizing sulfonyl THPs **6** with three stereocenters was investigated, including (i) α-cinnamylation of β-ketosulfones **3**, (ii) stereoselective reduction of the resulting **4**, and (iii) the epoxide ring-opening of the corresponding **5** with the hydroxyl group, as shown in Scheme 2.



Scheme 2. Three-step route of synthesizing sulfonyl THPs **6**.

2. Results and discussion

Initially, mono-C-cinnamylation of β-ketosulfones **3** (R=Me, Ph, 4-MeC_6H_4, 4-FC_6H_4, 4-$MeOC_6H_4$, 4-*t*-BuC_6H_4, 4-*n*-BuC_6H_4; Ar=Ph, 4-FC_6H_4, 4-$MeOC_6H_4$, 4-MeC_6H_4, 4-PhC_6H_4, 3-$NO_2C_6H_4$, 4-$CF_3C_6H_4$, 2-naphthalene) with K_2CO_3 in the presence of boiling acetone provided **4a**–**p** with good to excellent yields (85–95% via recrystallized from hexanes and EtOAc), as shown in Table 1.[5b] With the starting material **4** in hand, **4a** was chosen as the model substrate to examine the next step stereoselective reduction reaction. First, **4a** was treated with 3.0 equiv of $NaBH_4$ in the co-solvent of MeOH and THF (v/v=1:1) in the ice bath and resulted in major **5a** (88%) along with 7% yield of **5a′**. The structural framework of **5a** with a 3-sulfonyl 2,6-diphenyltetrahydropyran skeleton was determined by single-crystal X-ray crystallography (see Fig. 1).[6] The 2,6-diaryltetrahydropyran-4-one thiosemicarbazones had been synthesized and characterized for evaluation of potential antibacterial activity by Kabilan and co-workers.[1a] Based on the above results,

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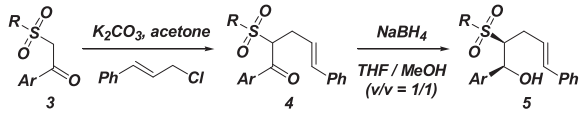
Table 1
Cinnamylation of **3** and reduction of **4**[a,b]



Entry	**3**, R/Ar	**4**, (%)[c]	**5**, (%)[c]
1	**3a**, 4-MeC_6H_4/Ph	**4a**, 88	**5a**, 88
2	**3b**, 4-MeC_6H_4/4-FC_6H_4	**4b**, 90	**5b**, 84
3	**3c**, 4-MeC_6H_4/4-MeOC_6H_4	**4c**, 92	**5c**, 76
4	**3d**, 4-MeC_6H_4/4-MeC_6H_4	**4d**, 88	**5d**, 80
5	**3e**, 4-MeC_6H_4/4-PhC_6H_4	**4e**, 90	**5e**, 78
6	**3f**, 4-MeC_6H_4/3-$NO_2C_6H_4$	**4f**, 85	**5f**, 80
7	**3g**, 4-MeC_6H_4/4-$CF_3C_6H_4$	**4g**, 86	**5g**, 76
8	**3h**, 4-MeC_6H_4/2-naphthalene	**4h**, 85	**5h**, 82
9	**3i**, Ph/Ph	**4i**, 89	**5i**, 87
10	**3j**, Me/Ph	**4j**, 94	**5j**, 90
11	**3k**, Me/4-MeC_6H_4	**4k**, 95	**5k**, 92
12	**3l**, Ph/4-PhC_6H_4	**4l**, 90	**5l**, 90
13	**3m**, 4-FC_6H_4/Ph	**4m**, 86	**5m**, 86
14	**3n**, 4-MeOC_6H_4/Ph	**4n**, 85	**5n**, 85
15	**3o**, 4-*t*-BuC_6H_4/Ph	**4o**, 85	**5o**, 84
16	**3p**, 4-*n*-BuC_6H_4/Ph	**4p**, 86	**5p**, 80

[a] The reaction was run on a 1.0 mmol scale with **3**, K_2CO_3 (2.9 equiv), cinnamyl chloride (1.05 equiv), acetone (10 mL), reflux, 8 h.
[b] The reaction was run on a 1.0 mmol scale with **4**, $NaBH_4$ (3.0 equiv), MeOH (5 mL), THF (5 mL), ice bath, 3 h.
[c] The isolated yields.

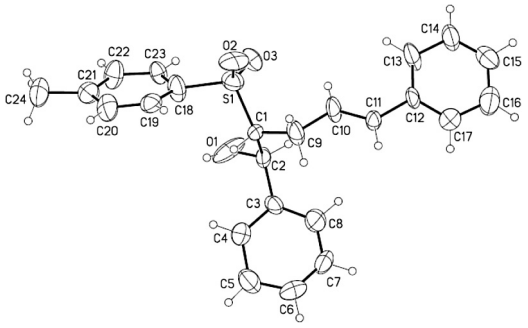
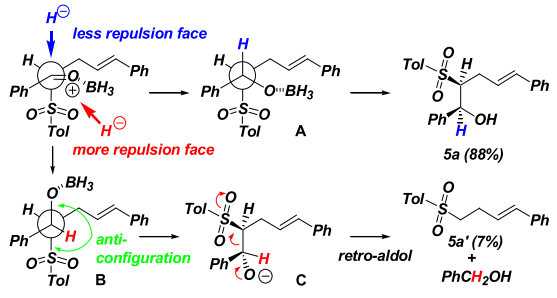


Fig. 1. X-ray structure of **5a**.

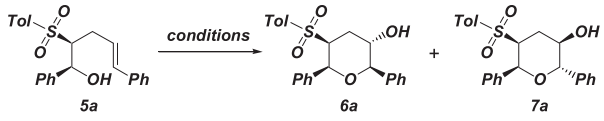
a reasonable explanation was shown in Scheme 3. According to the Felkin–Anh model,[7] the steric hindrance of sulfonyl substituent should inhibit the carbonyl addition of hydride such that the hydride should attack the carbonyl face with less-repulsion to generate the sole **5a** via intermediate **A**. In the minor pathway, after generating **B** and retro-aldol reaction of **C**, **5a**′ was formed.



Scheme 3. The possible mechanisms.

With the reduction conditions in hand (Table 1, entry 1, **4a**→**5a**), we further explored the conversion of other substrates. For the Ar and R groups of **4**, the aryl ring, with electron-withdrawing or electron-donating groups, was well tolerated, providing the desired **5** in moderate to good yields (76–92%). Then, substrate **5a** was treated with *m*-CPBA in the next stereoselective epoxidation. As shown in Table 2 and entry 1, **5a** was epoxidated with *m*-CPBA to provide **6a** (75%) and **7a** (12%) in the refluxing co-solvent of CH_2Cl_2 and DMF (v/v=1:1) for 3 h. By elongating the reaction time, entry 2 showed that **6a** and **7a** were isolated in 56% and 10% yields, respectively. However, a 20% yield of unknown products was observed. Entries 3–5 provided lower total yields of **6a** and **7a** along with a different ratio of epoxide mixture (20, 33, 48%). From the results, we believed that (i) the elongated reaction time easily caused the complex products, and (ii) a higher reaction temperature triggered the ring-opening of the corresponding epoxide (derived from epoxidation of **5a**) efficiently. For the one-pot epoxidative cyclization process, other epoxidation reagents were examined (see entries 6–8). To choose *t*-BuO_2H as the oxidant, no desired products were isolated and **5a** was recovered in 68% yield at rt for 3 h. Under refluxing CH_2Cl_2 condition, **5a** was converted into **6a** (18%), **7a** (20%), and epoxide mixture (35%) along with trace amounts of **5a** for 24 h. Furthermore, we found that the use of *t*-BuO_2H (2 equiv) and $TiCl_4$ (30 mol %) provides **6a** and **7a** in 36% and 45% yields in boiling CH_2Cl_2, respectively. By the addition of Lewis acid, no epoxide mixture was provided. Therefore, the optimized domino *m*-CPBA-mediated epoxidation/intramolecular S_N2 reaction process should be applied in the co-solvent CH_2Cl_2/DMF.

Table 2
Epoxidation conditions of **5a**[a]

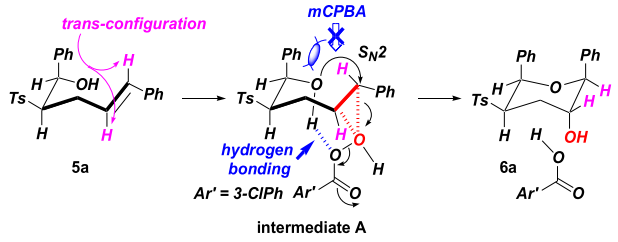


Entry	Oxidant, solvent (mL), temp (°C), time (h)	**6a**, (%)[b]	**7a**, (%)[b]
1	*m*-CPBA, CH_2Cl_2/DMF (5:5), reflux, 3	75	12
2[c]	*m*-CPBA, CH_2Cl_2/DMF (5:5), reflux, 8	56	10
3[d]	*m*-CPBA, CH_2Cl_2/DMF (5:5), 25, 24	14	10
4[d]	*m*-CPBA, $(CH_2Cl)_2$ (10), reflux, 3	32	21
5[d]	*m*-CPBA, CH_2Cl_2 (10), reflux, 3	18	10
6[e]	*t*-BuO_2H, CH_2Cl_2 (10), rt, 3	—	—
7[f]	*t*-BuO_2H, CH_2Cl_2 (10), reflux, 24	18	20
8[g]	*t*-BuO_2H, CH_2Cl_2 (10), reflux, 3	36	45

[a] The reaction was run on a 1.0 mmol scale with **5a**, oxidant (2.0 equiv).
[b] The isolated yields.
[c] The unknown products were obtained in 20% yield.
[d] The mixture of epoxide (for entry 3, 20%; entry 4, 33%; entry 5, 48%) was obtained.
[e] Compound **5a** was recovered in 68% yield.
[f] The mixture of epoxide was obtained in 35% yield.
[g] $TiCl_4$ (30 mol %) was added.

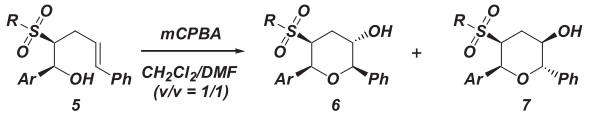
For a possible mechanism in the formation of major **6a**, the chair conformation of **5a** was first proposed, as shown in Scheme 4. Based on the reasonable prediction of the chelated intermediate **A** (conjugation of **4a** with *m*-CPBA), we believed that *m*-CPBA should epoxidize from the least repulsion since the phenyl group exhibited a stronger steric hindrance. With the direct hydrogen bonding of the hydroxyl group induction, the epoxidation of olefinic motif should be generated stereoselectively. When the orientation of the epoxide is formed in a *trans-configured* conformation in the opposite position of the hydroxyl group, the ring-opening of the epoxide should prefer to afford **6a** by an intramolecular S_N2 back-side attack under thermal conditions. Because olefinic motif was not epoxidized easily by *m*-CPBA from more repulsion face, **7a** was isolated in trace amounts.

With optimized conditions in hand (Table 2, entry 1), we further explored the substrate scope of the reaction, and the results are shown in Table 3. For the Ar and R groups of skeleton **5**, the phenyl ring, with both electron-withdrawing and electron-donating substituents, was well tolerated, providing the major products **6a**–**p** in



Scheme 4. Possible intermediate.

Table 3
Synthesis of **6** and **7**[a]



Entry	**5**, R/Ar	**6**, (%)[b]	**7**, (%)[b]
1	**5a**, 4-MeC_6H_4/Ph	**6a**, 75	**7a**, 12
2	**5b**, 4-MeC_6H_4/4-FC_6H_4	**6b**, 78	**7b**, 12
3	**5c**, 4-MeC_6H_4/4-MeOC_6H_4	**6c**, 85	**7c**, <5
4	**5d**, 4-MeC_6H_4/4-MeC_6H_4	**6d**, 80	**7d**, 10
5	**5e**, 4-MeC_6H_4/4-PhC_6H_4	**6e**, 75	**7e**, 11
6	**5f**, 4-MeC_6H_4/3-$NO_2C_6H_4$	**6f**, 7	**7f**, 15
7	**5g**, 4-MeC_6H_4/4-$CF_3C_6H_4$	**6g**, 66	**7g**, 16
8	**5h**, 4-MeC_6H_4/2-naphthalene	**6h**, 78	**7h**, 10
9	**5i**, Ph/Ph	**6i**, 80	**7i**, 10
10	**5j**, Me/Ph	**6j**, 74	**7j**, 10
11	**5k**, Me/4-MeC_6H_4	**6k**, 74	**7k**, 14
12	**5l**, Ph/4-PhC_6H_4	**6l**, 78	**7l**, 13
13	**5m**, 4-FC_6H_4/Ph	**6m**, 75	**7m**, 11
14	**5n**, 4-MeOC_6H_4/Ph	**6n**, 78	**7n**, 12
15	**5o**, 4-*t*-BuC_6H_4/Ph	**6o**, 80	**7o**, 12
16	**5p**, 4-*n*-BuC_6H_4/Ph	**6p**, 81	**7p**, 8

[a] The reaction was run on a 1.0 mmol scale with **5**, *m*-CPBA (2.0 equiv), CH_2Cl_2 (5 mL), DMF (5 mL), reflux, 3 h.
[b] The isolated yields.

66–85% yields and 5–16% yields of **7a**–**p** were isolated. The involvement of different substituents did not affect the procedure, and the distribution ratios (**6**/**7**) of the isolated yield were maintained in similar values. No obvious yield changes were exhibited for the generation of **6a**–**p** and **7a**–**p**. The structures of **6c**, **6n**, and **7o** were determined by single-crystal X-ray crystallography[6] (Figs. 2–4).

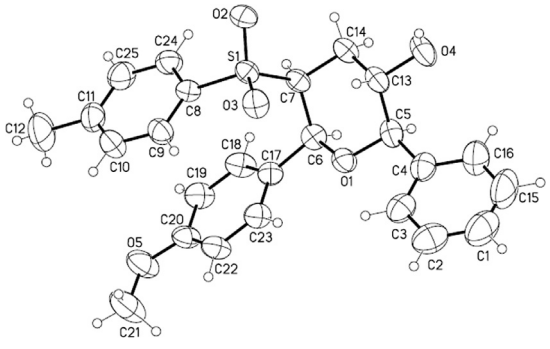


Fig. 2. X-ray structure of **6c**.

To explore the synthetic applications, the treatment of **6a** with Jones oxidation was further examined, as shown in Scheme 5. The Cr^{6+}-mediated reaction of **6a** should provide oxidation and migration routes for generating disubstituted tetrahydropyran-3-one **8** (46%) and furan **9** (25%). For a plausible mechanism, the

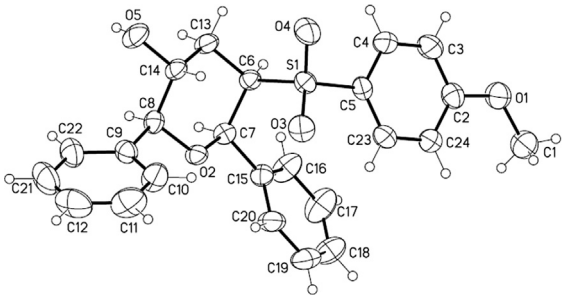


Fig. 3. X-ray structure of **6n**.

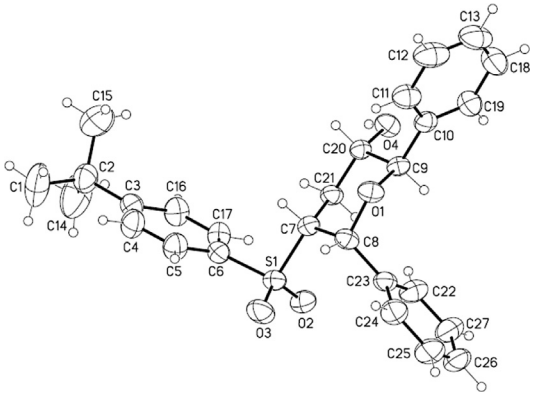
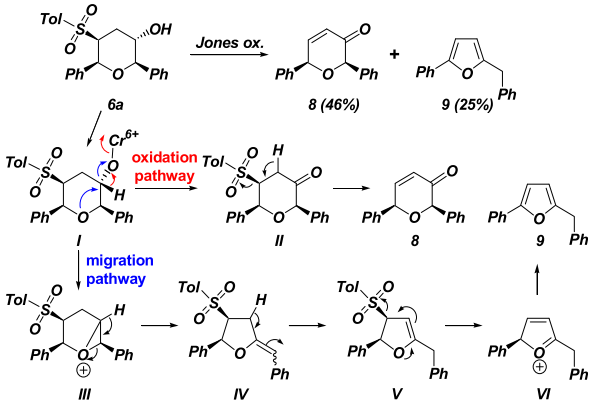


Fig. 4. X-ray structure of **7o**.



Scheme 5. Jones oxidation of **6a**.

conversion from **I** to **II** should be the main step. Subsequently, desulfonation of **II** afforded **8** under acidic conditions. In the minor pathway, after ring-contraction of **III**, olefin migration of **IV**, desulfonation of **V**, and sequential aromatization of **VI**, **9** was generated. For the reaction of **6a** with a Jones reagent, unexpected desulfonation was observed for two possible pathways.

3. Conclusion

We have developed a stereoselective synthesis of 3-sulfonyl tetrahydropyrans **6** performed with moderate to good yields by the *m*-CPBA-mediated ring-closure of **5**. Skeleton **5** is easily prepared by the cinnamylation of **3** in the presence of K_2CO_3 followed by $NaBH_4$-mediated reduction of the resulting **4** with an α-cinnamyl side arm in the co-solvent of THF and MeOH. The structures of the key products were confirmed by X-ray crystallography. Further investigation regarding synthetic applications of β-ketosulfones will be conducted and published in due course.

4. Experimental section

4.1. General

THF was distilled prior to use. All other reagents and solvents were obtained from commercial sources and used without further purification. Reactions were routinely carried out under an atmosphere of dry nitrogen with magnetic stirring. Products in organic solvents were dried with anhydrous magnesium sulfate before concentration in vacuo. Melting points were determined with an 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 (Hz). 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).

4.2. Representative procedure of skeleton 4

A representative procedure of skeleton **4** is as follows: K_2CO_3 (400 mg, 2.9 mmol) was added to a solution of **3** (1.0 mmol) in acetone (10 mL) at rt. The reaction mixture was stirred at rt for 10 min. Cinnamyl chloride (1.05 mmol) was added to the reaction mixture at rt. The reaction mixture was stirred at reflux for 8 h. The reaction mixture was cooled to rt, concentrated, and extracted with CH_2Cl_2 (3×20 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=6:1 to 1:1) afforded **4**.

*4.2.1. Compound (**4a**).*[5b] Yield=88% (343 mg); colorless solid; mp=112–113 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{24}H_{23}O_3S$ 391.1368, found 391.1374; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96–7.94 (m, 2H), 7.68 (d, J=8.0 Hz, 2H), 7.59–7.56 (m, 1H), 7.46–7.42 (m, 2H), 7.31 (d, J=8.4 Hz, 2H), 7.24–7.15 (m, 5H), 6.41 (d, J=15.6 Hz, 1H), 5.93 (dt, J=7.2, 15.6 Hz, 1H), 5.21 (dd, J=4.0, 10.4 Hz, 1H), 3.06–2.92 (m, 2H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.00, 145.46, 137.01, 137.01, 136.45, 134.03, 133.90, 129.74 (2×), 129.54 (2×), 128.98 (2×), 128.66 (2×), 128.40 (2×), 127.55, 126.11 (2×), 123.07, 69.50, 31.69, 21.61.

*4.2.2. Compound (**4b**).* Yield=90% (367 mg); colorless solid; mp=119–123 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{24}H_{22}FO_3S$ 409.1274, found 409.1281; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (d, J=8.8 Hz, 2H), 7.66 (d, J=8.4 Hz, 2H), 7.44–7.41 (m, 2H), 7.33 (d, J=8.0 Hz, 2H), 7.25–7.16 (m, 5H), 6.39 (d, J=16.0 Hz, 1H), 5.90 (dt, J=7.2, 16.0 Hz, 1H), 5.13 (dd, J=4.0, 10.8 Hz, 1H), 3.03–2.88 (m, 2H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.88, 145.71, 140.72, 136.39, 135.35, 134.26, 133.04, 130.47 (2×), 129.78 (2×), 129.65 (2×), 129.06 (2×), 128.47 (2×), 127.68, 126.14 (2×), 122.85, 69.70, 31.65, 21.69.

*4.2.3. Compound (**4c**).* Yield=92% (386 mg); colorless gum; HRMS (ESI, M^++1) calcd for $C_{25}H_{25}O_4S$ 421.1474, found 421.1481; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J=9.2 Hz, 2H), 7.68 (d, J=8.0 Hz, 2H), 7.31 (d, J=8.0 Hz, 2H), 7.23–7.14 (m, 5H), 6.91 (d, J=8.8 Hz, 2H), 6.42 (d, J=16.0 Hz, 1H), 5.93 (dt, J=7.2, 16.0 Hz, 1H), 5.15 (dd, J=4.0, 10.4 Hz, 1H), 3.84 (s, 3H), 3.03–2.94 (m, 2H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.86, 164.25, 145.31, 136.51, 133.79, 133.29, 131.53 (2×), 130.06, 129.71 (2×), 129.46 (2×), 128.35 (2×), 127.46, 126.08 (2×), 123.32, 113.89 (2×), 69.20, 55.48, 31.63, 21.59.

*4.2.4. Compound (**4d**).* Yield=88% (356 mg); colorless solid; mp=94–96 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{25}H_{25}O_3S$ 405.1524, found 405.1530; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 (d, J=8.4 Hz, 2H), 7.69 (d, J=8.4 Hz, 2H), 7.31 (d, J=8.0 Hz, 2H), 7.26–7.15 (m, 7H), 6.42 (d, J=15.6 Hz, 1H), 5.93 (dt, J=7.2, 15.6 Hz, 1H), 5.19 (dd, J=4.0, 10.4 Hz, 1H), 3.06–2.92 (m, 2H), 2.43 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.34, 145.34, 145.07, 136.48, 134.57, 133.88, 133.30, 129.71 (2×), 129.47 (2×), 129.35 (2×), 129.15 (2×), 128.34 (2×), 127.46, 126.08 (2×), 123.20, 69.34, 31.65, 21.59 (2×).

*4.2.5. Compound (**4e**).* Yield=90% (419 mg); colorless solid; mp=125–127 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{30}H_{27}O_3S$ 467.1681, found 467.1688; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (d, J=8.4 Hz, 2H), 7.68–7.55 (m, 6H), 7.49–7.35 (m, 3H), 7.30 (d, J=8.4 Hz, 2H), 7.24–7.11 (m, 5H), 6.39 (d, J=15.6 Hz, 1H), 5.91 (dt, J=7.2, 15.6 Hz, 1H), 5.19 (dd, J=4.0, 10.4 Hz, 1H), 3.03–2.89 (m, 2H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.43, 146.73, 145.54, 139.53, 136.52, 135.72, 134.11, 133.24 (2×), 129.85 (2×), 129.72 (2×), 129.60 (2×), 128.98 (2×), 128.46 (2×), 127.61, 127.36 (2×), 127.29 (2×), 126.17 (2×), 123.17, 69.64, 31.75, 21.70.

*4.2.6. Compound (**4f**).* Yield=85% (370 mg); colorless solid; mp=150–152 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{24}H_{22}NO_5S$ 436.1219, found 436.1218; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.73 (t, J=2.0 Hz, 1H), 8.42 (dd, J=1.2, 8.4 Hz, 1H), 8.32 (d, J=7.6 Hz, 2H), 7.70–7.66 (m, 3H), 7.35 (d, J=8.0 Hz, 2H), 7.21–7.15 (m, 4H), 6.42 (d, J=15.6 Hz, 1H), 5.91 (dt, J=7.2, 15.6 Hz, 1H), 5.19 (dd, J=4.0, 10.4 Hz, 1H), 3.06–2.92 (m, 2H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.21, 148.36, 146.01, 138.11, 136.20, 134.68, 134.53, 132.85, 130.31, 129.82 (2×), 129.73 (2×), 128.94 (2×), 128.01, 127.80, 126.14 (2×), 123.82, 122.41, 69.99, 31.47, 21.69.

*4.2.7. Compound (**4g**).* Yield=86% (394 mg); colorless solid; mp=79–81 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{25}H_{22}F_3O_3S$ 459.1242, found 459.1243; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, J=8.0 Hz, 2H), 7.71 (d, J=8.4 Hz, 2H), 7.66 (d, J=8.4 Hz, 2H), 7.33 (d, J=8.0 Hz, 2H), 7.25–7.16 (m, 5H), 6.40 (d, J=15.6 Hz, 1H), 5.90 (dt, J=7.2, 15.6 Hz, 1H), 5.17 (dd, J=4.0, 10.4 Hz, 1H), 3.06–2.90 (m, 2H), 2.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.43, 145.86, 139.62, 136.30, 134.50, 132.99, 130.32, 129.78 (2×), 129.72 (2×), 129.37 (2×), 128.91, 128.50 (2×), 127.77 (2×), 126.15 (2×), 125.78 (q, J=3.8 Hz), 122.63, 70.07, 31.59, 21.66.

*4.2.8. Compound (**4h**).* Yield=85% (374 mg); colorless solid; mp=126–127 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{28}H_{25}O_3S$ 441.1524, found 441.1530; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.44 (s, 1H), 7.99–7.94 (m, 2H), 7.87–7.85 (m, 2H), 7.69 (d, J=8.4 Hz, 2H), 7.62 (dt, J=1.2, 6.8 Hz, 1H), 7.56 (dt, J=1.2, 6.8 Hz, 1H), 7.28 (d, J=8.4 Hz, 2H), 7.21–7.12 (m, 5H), 6.45 (d, J=15.6 Hz, 1H), 5.97 (dt, J=7.2, 15.6 Hz, 1H), 5.34 (dd, J=4.0, 10.4 Hz, 1H), 3.12–2.98 (m, 2H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.79, 145.54, 136.50, 135.85, 134.38, 134.13, 133.29, 132.25, 131.62, 129.95, 129.83 (2×), 129.59 (2×), 129.16, 128.68, 128.43 (2×), 127.71, 127.58, 126.99, 126.16 (2×), 123.98, 123.23, 69.76, 31.72, 21.61.

*4.2.9. Compound (**4i**).* Yield=89% (335 mg); colorless solid; mp=114–115 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{23}H_{21}O_3S$ 377.1212, found 377.1212; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94–7.92 (m, 2H), 7.82–7.80 (m, 2H), 7.68–7.64 (m, 1H), 7.60–7.51 (m, 3H), 7.48–7.43 (m, 2H), 7.24–7.15 (m, 5H), 6.41 (d, J=16.0 Hz, 1H), 5.93 (dt, J=6.8, 16.0 Hz, 1H), 5.21 (dd, J=4.0, 10.0 Hz, 1H), 3.07–2.93 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.90, 136.98, 136.45, 136.32, 134.33, 134.20, 134.04, 129.78 (2×), 128.99 (2×), 128.93 (2×), 128.75 (2×), 128.49 (2×), 127.63, 126.17 (2×), 122.98, 69.52, 31.68.

*4.2.10. Compound (**4j**).*[5b] Yield=94% (295 mg); colorless solid; mp=114–116 °C (recrystallized from hexanes and EtOAc); HRMS

(ESI, M^++1) calcd for $C_{18}H_{19}O_3S$ 315.1055, found 315.1057; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03–8.01 (m, 2H), 7.64–7.60 (m, 1H), 7.52–7.47 (m, 2H), 7.27–7.18 (m, 5H), 6.51 (d, *J*=16.0 Hz, 1H), 6.00 (dt, *J*=6.8, 16.0 Hz, 1H), 5.03 (dd, *J*=4.0, 10.0 Hz, 1H), 3.20–3.11 (m, 2H), 3.01 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.47, 136.57, 136.21, 134.44, 134.41, 129.11 (2×), 128.91 (2×), 128.48 (2×), 127.77, 126.19 (2×), 122.51, 68.50, 37.64, 32.41.

*4.2.11. Compound (**4k**).* Yield=95% (312 mg); colorless solid; mp=162–164 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{19}H_{21}O_3S$ 329.1212, found 329.1215; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92 (d, *J*=8.4 Hz, 2H), 7.30–7.15 (m, 7H), 6.50 (d, *J*=15.6 Hz, 1H), 6.00 (dt, *J*=6.8, 15.6 Hz, 1H), 4.99 (dd, *J*=4.0, 10.0 Hz, 1H), 3.22–3.09 (m, 2H), 2.99 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.82, 145.75, 136.29, 134.31, 134.14, 129.65 (2×), 129.31 (2×), 128.47 (2×), 127.73, 126.21 (2×), 122.69, 68.40, 37.65, 32.35, 21.70.

*4.2.12. Compound (**4l**).* Yield=90% (407 mg); colorless solid; mp=133–135 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{29}H_{25}O_3S$ 453.1524, found 453.1533; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04–8.01 (m, 2H), 7.85–7.82 (m, 2H), 7.72–7.39 (m, 10H), 7.25–7.15 (m, 5H), 6.44 (d, *J*=15.6 Hz, 1H), 5.95 (dt, *J*=7.2, 15.6 Hz, 1H), 5.25 (dd, *J*=4.4, 10.4 Hz, 1H), 3.09–2.95 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.31, 146.76, 139.48, 136.48, 136.32, 135.64, 134.33, 134.21, 129.82 (2×), 129.67 (2×), 128.98 (2×), 128.95 (2×), 128.49, 128.46 (2×), 127.64, 127.38 (2×), 127.29 (2×), 126.18 (2×), 123.05, 69.59, 31.69.

*4.2.13. Compound (**4m**).* Yield=86% (339 mg); colorless solid; mp=116–118 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{23}H_{20}FO_3S$ 395.1117, found 395.1120; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95–7.93 (m, 2H), 7.84–7.79 (m, 2H), 7.62–7.58 (m, 1H), 7.48–7.44 (m, 2H), 7.25–7.15 (m, 7H), 6.42 (d, *J*=15.6 Hz, 1H), 5.92 (dt, *J*=7.2, 15.6 Hz, 1H), 5.22 (dd, *J*=3.6, 10.8 Hz, 1H), 3.07–2.89 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.03, 166.25 (d, *J*=256.2 Hz), 136.87, 136.36, 134.34, 134.19, 132.78 (d, *J*=9.9 Hz, 2×), 132.18, 129.00 (2×), 128.83 (2×), 128.47 (2×), 127.70, 126.17 (2×), 122.71, 116.29 (d, *J*=22.7 Hz, 2×), 69.53, 31.84.

*4.2.14. Compound (**4n**).* Yield=85% (345 mg); colorless solid; mp=128–130 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{24}H_{23}O_4S$ 407.1317, found 407.1320; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, *J*=7.6 Hz, 2H), 7.73 (d, *J*=8.8 Hz, 2H), 7.59–7.55 (m, 1H), 7.46–7.41 (m, 2H), 7.30–7.15 (m, 5H), 6.97 (d, *J*=8.8 Hz, 2H), 6.42 (d, *J*=15.6 Hz, 1H), 5.94 (dt, *J*=6.8, 15.6 Hz, 1H), 5.22 (dd, *J*=4.0, 10.0 Hz, 1H), 3.85 (s, 3H), 3.06–2.92 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.15, 164.18, 137.01, 136.43, 133.95, 133.87, 131.90 (2×), 128.93 (2×), 128.64 (2×), 128.37 (2×), 127.62, 127.50, 126.07 (2×), 123.11, 114.08 (2×), 69.50, 55.58, 31.72.

*4.2.15. Compound (**4o**).* Yield=85% (367 mg); colorless gum; HRMS (ESI, M^++1) calcd for $C_{27}H_{29}O_3S$ 433.1837, found 433.1842; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91–7.89 (m, 2H), 7.71 (d, *J*=8.8 Hz, 2H), 7.57–7.53 (m, 1H), 7.50 (d, *J*=8.8 Hz, 2H), 7.44–7.40 (m, 2H), 7.24–7.15 (m, 5H), 6.43 (d, *J*=16.0 Hz, 1H), 5.94 (dt, *J*=7.2, 16.0 Hz, 1H), 5.20 (dd, *J*=4.8, 12.0 Hz, 1H), 3.06–3.00 (m, 2H), 1.32 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.99, 158.27, 137.05, 136.50, 134.05, 133.87, 133.48, 129.59 (2×), 128.92 (2×), 128.65 (2×), 128.43 (2×), 127.57, 126.14 (2×), 125.95 (2×), 123.20, 69.47, 35.25, 31.43, 30.96 (3×).

*4.2.16. Compound (**4p**).* Yield=86% (372 mg); colorless solid; mp=83–85 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{27}H_{29}O_3S$ 433.1837, found 433.1841; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94–7.92 (m, 2H), 7.71 (d, *J*=8.8 Hz, 2H), 7.57–7.54 (m, 1H), 7.44–7.40 (m, 2H), 7.30 (d, *J*=8.0 Hz, 2H), 7.24–7.15 (m, 5H), 6.43 (d, *J*=15.6 Hz, 1H), 5.95 (dt, *J*=7.2, 15.6 Hz, 1H), 5.23 (dd, *J*=4.8, 12.0 Hz, 1H), 3.06–3.01 (m, 2H), 2.69–2.65 (m, 2H), 1.63–1.56 (m, 2H), 1.39–1.30 (m, 2H), 0.95 (t, *J*=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.94, 150.21, 136.98, 136.44, 133.99, 133.83, 133.62, 129.68 (2×), 128.88 (4×), 128.61 (2×), 128.37 (2×), 127.51, 126.08 (2×), 123.13, 69.41, 35.52, 32.93, 31.50, 22.16, 13.78.

4.3. Representative procedure of skeleton 5

A representative procedure of skeleton **5** is as follows: $NaBH_4$ (100 mg, 3.0 mmol) was added to a solution of **4** (1.0 mmol) in a co-solvent of THF (5 mL) and MeOH (5 mL) at ice bath. The reaction mixture was stirred for 3 h at ice bath and the solvent was concentrated. The residue was diluted with water (10 mL) and the mixture was extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with brine, dried, filtered, and evaporated to afford crude product. Purification on silica gel (hexanes/EtOAc=8:1 to 3:1) afforded **5**.

*4.3.1. Compound (**5a**).* Yield=88% (345 mg); colorless solid; mp=140–141 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{24}H_{25}O_3S$ 393.1524, found 393.1533; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, *J*=8.4 Hz, 2H), 7.36–7.17 (m, 10H), 7.01 (d, *J*=8.0 Hz, 2H), 5.84 (d, *J*=16.0 Hz, 1H), 5.42 (dt, *J*=7.6, 16.0 Hz, 1H), 5.15 (d, *J*=8.8 Hz, 1H), 3.55–3.49 (m, 1H), 2.57–2.43 (m, 1H), 2.41 (s, 3H), 2.26–2.19 (m, 1H), 2.02 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.08, 139.38, 136.58, 135.30, 132.45, 129.79 (2×), 128.76 (2×), 128.58, 128.52 (2×), 128.25 (2×), 127.34 (2×), 127.23, 125.91 (2×), 124.53, 73.07, 70.67, 30.46, 21.51. Single-crystal X-ray diagram: crystal of compound **5a** was grown by slow diffusion of EtOAc into a solution of compound **5a** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the orthorhombic crystal system, space group $P2_12_12_1$, a=6.9943(4) Å, b=12.0306(9) Å, c=23.6891(18) Å, V=1993.3(2) Å^3, Z=4, d_{calcd}=1.308 g/cm^3, $F(000)$=832, 2θ range 1.719–26.388°, R indices (all data) $R1$=0.2676, $wR2$=0.4649.

*4.3.2. Compound (**5b**).* Yield=84% (344 mg); colorless gum; HRMS (ESI, M^++1) calcd for $C_{24}H_{24}FO_3S$ 411.1430, found 411.1431; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, *J*=8.4 Hz, 2H), 7.34–7.29 (m, 4H), 7.25–7.15 (m, 3H), 7.03–6.97 (m, 4H), 5.83 (d, *J*=15.6 Hz, 1H), 5.45 (dt, *J*=7.6, 15.6 Hz, 1H), 5.14 (d, *J*=8.4 Hz, 1H), 4.51 (br s, 1H), 3.49–3.44 (m, 1H), 2.48–2.43 (m, 1H), 2.42 (s, 3H), 2.26–2.16 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.73 (d, *J*=245.6 Hz), 145.31, 136.50, 135.31 (d, *J*=3.8 Hz), 135.18, 132.71, 129.93 (2×), 129.11 (d, *J*=8.3 Hz, 2×), 128.82 (2×), 128.40 (2×), 127.43, 125.95 (2×), 124.25, 115.48 (d, *J*=21.2 Hz, 2×), 72.42, 70.66, 30.51, 21.60.

*4.3.3. Compound (**5c**).* Yield=76% (321 mg); colorless solid; mp=104–106 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{25}H_{27}O_4S$ 423.1630, found 423.1632; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, *J*=8.4 Hz, 2H), 7.32 (d, *J*=8.4 Hz, 2H), 7.26–7.14 (m, 5H), 7.01 (d, *J*=8.0 Hz, 2H), 6.82 (d, *J*=8.8 Hz, 2H), 5.30 (d, *J*=15.6 Hz, 1H), 5.42 (dt, *J*=7.6, 15.6 Hz, 1H), 5.09 (d, *J*=8.8 Hz, 1H), 3.71 (s, 3H), 3.50–3.45 (m, 1H), 3.02 (br s, 1H), 2.48–2.41 (m, 1H), 2.41 (s, 3H), 2.22–2.15 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.67, 145.04, 136.62, 135.23, 132.10, 131.50, 129.78 (2×), 128.76 (2×), 128.52 (2×), 128.22 (2×), 127.15, 125.86 (2×), 124.57, 113.86 (2×), 72.66, 70.82, 55.08, 30.53, 21.50.

*4.3.4. Compound (**5d**).* Yield=80% (325 mg); colorless gum; HRMS (ESI, M^++1) calcd for $C_{25}H_{27}O_3S$ 407.1681, found 407.1686; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, *J*=8.4 Hz, 2H), 7.32 (d, *J*=8.4 Hz, 2H), 7.26–7.15 (m, 5H), 7.11 (d, *J*=8.0 Hz, 2H), 7.01 (d, *J*=8.4 Hz, 2H), 5.83 (d, *J*=16.0 Hz, 1H), 5.40 (dt, *J*=7.6, 15.6 Hz, 1H), 5.10 (d, *J*=8.8 Hz, 1H),

4.46 (s, 1H), 3.52–3.47 (m, 1H), 2.50–2.43 (m, 1H), 2.41 (s, 3H), 2.28 (s, 3H), 2.28–2.17 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.02, 138.40, 136.64, 136.39, 135.27, 132.14, 129.76 (2×), 129.18 (2×), 128.76 (2×), 128.22 (2×), 127.20 (2×), 127.14, 125.86 (2×), 124.58, 72.91, 70.73, 30.48, 21.51, 20.99.

*4.3.5. Compound (**5e**).* Yield=78% (365 mg); colorless solid; mp=166–168 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{30}H_{29}O_3S$ 469.1837, found 469.1838; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, J=8.4 Hz, 2H), 7.54–7.48 (m, 4H), 7.45–7.32 (m, 7H), 7.21–7.12 (m, 3H), 7.02–6.97 (m, 2H), 5.87 (d, J=16.0 Hz, 1H), 5.43 (dt, J=7.2, 16.0 Hz, 1H), 5.18 (d, J=8.4 Hz, 1H), 4.50 (br s, 1H), 3.56–3.51 (m, 1H), 2.58–2.51 (m, 1H), 2.41 (s, 3H), 2.31–2.24 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.16, 141.60, 140.46, 138.41, 136.61, 135.26, 132.52, 129.89 (2×), 128.84 (2×), 128.71 (2×), 128.35 (2×), 127.77 (2×), 127.43, 127.29 (3×), 127.06 (2×), 125.95 (2×), 124.54, 72.88, 70.75, 30.47, 21.60.

*4.3.6. Compound (**5f**).* Yield=80% (350 mg); colorless gum; HRMS (ESI, M^++1) calcd for $C_{24}H_{24}NO_5S$ 438.1375, found 438.1380; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.13 (t, J=2.0 Hz, 1H), 8.05–8.02 (m, 1H), 7.74–7.69 (m, 3H), 7.46 (t, J=8.0 Hz, 1H), 7.29 (d, J=8.4 Hz, 2H), 7.25–7.16 (m, 3H), 7.04–7.01 (m, 2H), 5.94 (d, J=16.0 Hz, 1H), 5.58 (dt, J=7.2, 16.0 Hz, 1H), 5.27 (d, J=7.6 Hz, 1H), 4.62 (br s, 1H), 3.59–3.54 (m, 1H), 2.64–2.57 (m, 1H), 2.40 (s, 3H), 2.38–2.30 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.17, 145.54, 141.75, 136.17, 134.95, 133.39, 133.24, 130.02 (2×), 129.44, 128.66 (2×), 128.46 (2×), 127.66, 125.92 (2×), 123.65, 123.32, 122.18, 71.87, 69.60, 30.21, 21.58.

*4.3.7. Compound (**5g**).* Yield=76% (350 mg); colorless solid; mp=126–128 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{25}H_{24}F_3O_3S$ 461.1398, found 461.1401; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, J=8.4 Hz, 2H), 7.52 (d, J=8.4 Hz, 2H), 7.43 (d, J=8.4 Hz, 2H), 7.28 (d, J=8.4 Hz, 2H), 7.25–7.16 (m, 3H), 7.04–7.01 (m, 2H), 5.95 (d, J=15.6 Hz, 1H), 5.49 (dt, J=7.6, 15.6 Hz, 1H), 5.21 (dd, J=3.6, 7.2 Hz, 1H), 4.56 (br d, J=3.6 Hz, 1H), 3.54–3.49 (m, 1H), 2.64–2.57 (m, 1H), 2.41 (s, 3H), 2.36–2.29 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.35, 143.52, 136.33, 135.16, 133.25, 129.93 (2×), 128.66 (2×), 128.45 (2×), 127.58 (2×), 127.55 (2×), 125.97 (2×), 125.47, 125.44, 125.38 (q, J=3.0 Hz), 123.95, 72.22, 70.09, 30.11, 21.56.

*4.3.8. Compound (**5h**).* Yield=82% (362 mg); colorless gum; HRMS (ESI, M^++1) calcd for $C_{28}H_{27}O_3S$ 443.1681, found 443.1688; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82–7.75 (m, 6H), 7.51–7.42 (m, 3H), 7.24 (d, J=8.4 Hz, 2H), 7.19–7.12 (m, 3H), 6.89–6.86 (m, 2H), 5.80 (d, J=16.0 Hz, 1H), 5.49 (dt, J=7.2, 16.0 Hz, 1H), 5.22 (d, J=8.4 Hz, 1H), 4.50 (br s, 1H), 3.70–3.61 (m, 1H), 2.56–2.49 (m, 1H), 2.36 (s, 3H), 2.34–2.28 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 145.05, 136.67, 136.48, 135.40, 133.35, 132.99, 132.72, 129.75 (2×), 128.71 (2×), 128.51, 128.22 (2×), 127.96, 127.59, 127.20, 126.77, 126.32, 126.30, 125.86 (2×), 124.39, 124.36, 73.13, 70.41, 30.43, 21.50.

*4.3.9. Compound (**5i**).* Yield=87% (329 mg); colorless solid; mp=141–142 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{23}H_{23}O_3S$ 379.1368, found 379.1369; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94–7.92 (m, 2H), 7.65–7.61 (m, 1H), 7.55–7.51 (m, 2H), 7.36–7.17 (m, 8H), 7.05–7.03 (m, 2H), 5.88 (d, J=15.6 Hz, 1H), 5.48 (dt, J=7.6, 15.6 Hz, 1H), 5.17 (d, J=8.4 Hz, 1H), 4.39 (br s, 1H), 3.59–3.54 (m, 1H), 2.53–2.45 (m, 1H), 2.32–2.25 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.30, 138.51, 136.51, 133.82, 132.69, 129.11 (2×), 128.65 (2×), 128.60, 128.52 (2×), 128.27 (2×), 127.27 (3×), 125.93 (2×), 124.39, 72.98, 70.61, 30.37.

*4.3.10. Compound (**5j**).* Yield=90% (284 mg); colorless solid; mp=152–153 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{18}H_{21}O_3S$ 317.1212, found 317.1215; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43–7.34 (m, 5H), 7.30–7.19 (m, 5H), 6.13 (d, J=15.6 Hz, 1H), 5.96 (dt, J=7.6, 15.6 Hz, 1H), 5.08 (d, J=8.4 Hz, 1H), 3.45 (br s, 1H), 3.38–3.34 (m, 1H), 3.01 (s, 3H), 2.59–2.55 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.02, 136.65, 133.45, 128.87, 128.85 (2×), 128.43 (2×), 127.43, 127.12 (2×), 126.13 (2×), 124.53, 73.16, 69.27, 43.93, 28.91.

*4.3.11. Compound (**5k**).* Yield=92% (304 mg); colorless solid; mp=107–109 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{19}H_{23}O_3S$ 331.1368, found 331.1370; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29–7.19 (m, 9H), 6.12 (d, J=15.6 Hz, 1H), 5.93 (dt, J=7.6, 15.6 Hz, 1H), 5.06 (d, J=8.8 Hz, 1H), 3.37–3.32 (m, 1H), 3.25 (br s, 1H), 3.02 (s, 3H), 2.59–2.56 (m, 2H), 2.34 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.86, 137.03, 136.73, 133.31, 129.56 (2×), 128.44 (2×), 127.40, 127.02 (2×), 126.12 (2×), 124.63, 73.10, 69.40, 43.94, 28.97, 21.12.

*4.3.12. Compound (**5l**).* Yield=90% (409 mg); colorless solid; mp=153–155 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{29}H_{27}O_3S$ 455.1681, found 455.1688; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, J=8.4 Hz, 2H), 7.66–7.62 (m, 1H), 7.57–7.35 (m, 11H), 7.22–7.15 (m, 3H), 7.04–7.02 (m, 2H), 5.92 (d, J=16.0 Hz, 1H), 5.51 (dt, J=7.2, 16.0 Hz, 1H), 5.23 (d, J=7.2 Hz, 1H), 4.46 (br s, 1H), 3.64–3.58 (m, 1H), 2.64–2.57 (m, 1H), 2.39–2.32 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.48, 140.34, 138.45, 138.33, 136.50, 135.26, 133.82, 132.68, 129.15 (2×), 128.68 (3×), 128.31 (2×), 127.67 (2×), 127.40, 127.27, 127.22 (2×), 126.99 (2×), 125.92 (2×), 124.39, 72.73, 70.66, 30.32.

*4.3.13. Compound (**5m**).* Yield=86% (341 mg); colorless gum; HRMS (ESI, M^++1) calcd for $C_{23}H_{22}FO_3S$ 397.1274, found 397.1278; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93–7.88 (m, 2H), 7.33–7.14 (m, 10H), 7.08–7.06 (m, 2H), 5.94 (d, J=15.6 Hz, 1H), 5.54 (dt, J=7.2, 16.0 Hz, 1H), 5.15 (d, J=8.4 Hz, 1H), 4.16 (br s, 1H), 3.57–3.52 (m, 1H), 2.54–2.47 (m, 1H), 2.38–2.30 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.76 (d, J=255.4 Hz), 139.35, 136.48, 134.94 (d, J=3.0 Hz), 133.00, 131.62 (d, J=9.9 Hz, 2×), 128.69, 128.64 (2×), 128.39 (2×), 127.45, 127.19 (2×), 125.98 (2×), 124.28, 116.40 (d, J=22.8 Hz, 2×), 73.00, 70.85, 30.40.

*4.3.14. Compound (**5n**).* Yield=85% (347 mg); colorless gum; HRMS (ESI, M^++1) calcd for $C_{24}H_{25}O_4S$ 409.1474, found 409.1477; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, J=8.8 Hz, 2H), 7.36–7.15 (m, 8H), 7.03–7.00 (m, 2H), 6.96 (d, J=8.8 Hz, 2H), 5.85 (d, J=16.0 Hz, 1H), 5.42 (dt, J=7.2, 16.0 Hz, 1H), 5.12 (d, J=8.4 Hz, 1H), 4.00 (br s, 1H), 3.82 (s, 3H), 3.55–3.46 (m, 1H), 2.48–2.41 (m, 1H), 2.25–2.18 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.88, 139.43, 136.62, 132.40, 131.04 (2×), 129.49, 128.60, 128.55 (2×), 128.27 (2×), 127.35 (2×), 127.24, 125.92 (2×), 124.63, 114.39 (2×), 73.14, 70.81, 55.61, 30.59.

*4.3.15. Compound (**5o**).* Yield=84% (365 mg); colorless gum; HRMS (ESI, M^++1) calcd for $C_{27}H_{31}O_3S$ 435.1994, found 435.1995; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, J=8.4 Hz, 2H), 7.51 (d, J=8.8 Hz, 2H), 7.38–7.14 (m, 8H), 7.00 (d, J=8.4 Hz, 2H), 5.88 (d, J=16.0 Hz, 1H), 5.41 (dt, J=7.6, 16.0 Hz, 1H), 5.17 (d, J=8.4 Hz, 1H), 4.55 (br s, 1H), 3.56–3.51 (m, 1H), 2.53–2.46 (m, 1H), 2.32–2.20 (m, 1H), 1.32 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.91, 139.43, 136.63, 135.37, 132.69, 128.65 (2×), 128.62, 128.58 (2×), 128.34 (2×), 127.33 (2×), 127.31, 126.22 (2×), 125.95 (2×), 124.57, 73.01, 70.63, 35.22, 30.94, 30.59 (3×).

*4.3.16. Compound (**5p**).* Yield=80% (347 mg); colorless gum; HRMS (ESI, M^++1) calcd for $C_{27}H_{31}O_3S$ 435.1994, found 435.1996; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 (d, J=8.8 Hz, 2H), 7.37–7.15 (m, 10H), 7.01 (d, J=8.4 Hz, 2H), 5.84 (d, J=15.6 Hz, 1H), 5.41 (dt, J=7.2, 15.6 Hz, 1H),

5.16 (d, J=8.8 Hz, 1H), 4.53 (br s, 1H), 3.54–3.49 (m, 1H), 2.67 (t, J=7.6 Hz, 2H), 2.50–2.43 (m, 1H), 2.27–2.20 (m, 1H), 1.63–1.56 (m, 2H), 1.41–1.31 (m, 2H), 0.95 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.94, 139.38, 136.59, 135.45, 132.57, 129.18 (2×), 128.81 (2×), 128.62, 128.55 (2×), 128.29 (2×), 127.35 (2×), 127.27, 125.93 (2×), 124.54, 73.06, 70.69, 35.54, 33.00, 30.54, 22.23, 13.82.

4.4. Representative procedure of skeletons 6 and 7

A representative procedure of skeletons **6** and **7** is as follows: *m*-CPBA (freshly purified *m*-chloroperoxybenzoic acid, 345 mg, 2.0 mmol) was added to a solution of **5** (1.0 mmol) in a co-solvent of CH_2Cl_2 (5 mL) and DMF (5 mL) at rt. The reaction mixture was refluxed for 3 h, cooled to rt, and the solvent was concentrated. The residue was diluted with water (10 mL) and the mixture was extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with brine, dried, filtered, and evaporated to afford crude product. Purification on silica gel (hexanes/EtOAc=8:1 to 3:1) afforded **6** and **7**.

*4.4.1. Compound (**6a**).* Yield=75% (306 mg); colorless solid; mp=169–170 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{24}H_{25}O_4S$ 409.1474, found 409.1477; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63–7.61 (m, 2H), 7.46–7.36 (m, 3H), 7.23–7.20 (m, 4H), 7.10–7.04 (m, 3H), 6.99 (d, J=8.0 Hz, 2H), 5.10 (d, J=2.8 Hz, 1H), 4.34 (dd, J=4.4, 8.8 Hz, 1H), 4.32–4.28 (m, 1H), 3.90 (dt, J=2.4, 5.2 Hz, 1H), 3.22–3.16 (m, 1H), 2.33 (s, 3H), 2.21–2.14 (m, 1H), 2.01 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.36, 139.07, 137.77, 136.95, 129.24 (2×), 128.62 (2×), 128.59, 127.80 (2×), 127.72 (2×), 127.68 (2×), 127.25, 125.96 (2×), 85.98, 77.93, 67.40, 64.74, 32.52, 21.44.

*4.4.2. Compound (**6b**).* Yield=78% (332 mg); colorless solid; mp=82–84 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{24}H_{24}FO_4S$ 427.1379, found 427.1382; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61–7.58 (m, 2H), 7.44–7.36 (m, 3H), 7.22 (d, J=8.4 Hz, 2H), 7.18–7.14 (m, 2H), 7.04 (d, J=8.0 Hz, 2H), 6.75–6.70 (m, 2H), 5.05 (d, J=2.0 Hz, 1H), 4.29 (dd, J=4.4, 8.8 Hz, 1H), 4.27 (br s, 1H), 3.87–3.84 (m, 1H), 3.17–3.12 (m, 1H), 2.37 (br s, 1H), 2.35 (s, 3H), 2.19–2.10 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.02 (d, J=244.8 Hz), 143.66, 139.04, 137.61, 132.72 (d, J=3.0 Hz), 129.21 (2×), 128.65 (2×), 127.68 (2×), 127.63, 127.58 (d, J=8.4 Hz, 2×), 127.52 (2×), 114.52 (d, J=21.2 Hz, 2×), 85.86, 77.19, 67.13, 64.66, 32.34, 21.37.

*4.4.3. Compound (**6c**).* Yield=85% (372 mg); colorless solid; mp=119–122 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{25}H_{27}O_5S$ 439.1579, found 439.1586; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62–7.60 (m, 2H), 7.45–7.35 (m, 3H), 7.23 (d, J=8.0 Hz, 2H), 7.11 (d, J=8.4 Hz, 2H), 7.01 (d, J=8.4 Hz, 2H), 6.56 (d, J=8.8 Hz, 2H), 5.05 (d, J=2.8 Hz, 1H), 4.31 (dd, J=4.4, 8.8 Hz, 1H), 4.27 (d, J=1.6 Hz, 1H), 3.87–3.81 (m, 1H), 3.73 (s, 3H), 3.20–3.15 (m, 1H), 2.34 (s, 3H), 2.19–2.11 (m, 1H), 1.93 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 158.84, 143.14, 139.17, 137.86, 129.09 (2×), 129.02, 128.55 (2×), 128.49, 127.71 (2×), 127.61 (2×), 127.00 (2×), 113.14 (2×), 85.88, 77.49, 67.35, 64.97, 55.11, 32.30, 21.41. Single-crystal X-ray diagram: crystal of compound **6c** was grown by slow diffusion of EtOAc into a solution of compound **6c** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the ortho-rhombic crystal system, space group $P2_12_12_1$, a=5.86780(10) Å, b=15.0626(5) Å, c=25.1038(7) Å, V=2218.78(10) Å^3, Z=4, d_{calcd}=1.313 g/cm^3, F(000)=928, 2θ range 1.577–26.387°, R indices (all data) $R1$=0.0632, $wR2$=0.1434.

*4.4.4. Compound (**6d**).* Yield=80% (338 mg); colorless solid; mp=174–177 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{25}H_{27}O_4S$ 423.1630, found 423.1633; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62–7.60 (m, 2H), 7.45–7.35 (m, 3H), 7.21 (d, J=8.0 Hz, 2H), 7.07 (d, J=8.0 Hz, 2H), 6.99 (d, J=8.0 Hz, 2H), 6.83 (d, J=8.4 Hz, 2H), 5.05 (d, J=2.0 Hz, 1H), 4.32 (dd, J=4.4, 8.8 Hz, 1H), 4.28 (d, J=1.6 Hz, 1H), 3.88–3.86 (m, 1H), 3.21–3.16 (m, 1H), 2.35 (s, 3H), 2.25 (s, 3H), 2.19–2.12 (m, 1H), 2.16 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.19, 139.17, 137.77, 136.89, 133.86, 129.02 (2×), 128.56 (2×), 128.51, 128.36 (2×), 127.72 (2×), 127.66 (2×), 125.72 (2×), 85.87, 77.74, 67.38, 64.90, 32.33, 21.46, 21.05.

*4.4.5. Compound (**6e**).* Yield=75% (363 mg); colorless solid; mp=190–193 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{30}H_{29}O_4S$ 485.1787, found 485.1786; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64–7.62 (m, 2H), 7.47–7.29 (m, 8H), 7.22–7.18 (m, 6H), 6.91 (d, J=8.0 Hz, 2H), 5.11 (d, J=2.8 Hz, 1H), 4.84 (br s, 1H), 4.33–4.29 (m, 2H), 3.95–3.91 (m, 1H), 3.28–3.23 (m, 1H), 2.35–2.23 (m, 1H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.14, 140.58, 140.02, 139.52, 137.80, 135.94, 129.08 (2×), 128.68 (2×), 128.41 (2×), 128.33, 127.75 (2×), 127.48 (2×), 127.24, 126.78 (2×), 126.30 (2×), 126.24 (2×), 85.87, 77.43, 67.07, 64.79, 32.47, 21.29.

*4.4.6. Compound (**6f**).* Yield=70% (317 mg); colorless solid; mp=172–174 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{24}H_{24}NO_6S$ 454.1324, found 454.1326; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (dd, J=2.0, 8.0 Hz, 1H), 7.87 (d, J=7.6 Hz, 1H), 7.73 (br s, 1H), 7.63–7.60 (m, 2H), 7.49–7.37 (m, 4H), 7.24 (d, J=8.4 Hz, 2H), 7.02 (d, J=8.0 Hz, 2H), 5.17 (d, J=2.8 Hz, 1H), 4.39–4.31 (m, 2H), 4.01–3.99 (m, 1H), 3.23–3.18 (m, 1H), 2.30 (s, 3H), 2.24–2.17 (m, 1H), 1.80 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.19, 139.08, 138.52, 137.39, 132.50, 129.58 (2×), 129.03, 128.85, 128.77 (2×), 127.70 (3×), 127.44 (2×), 122.33, 120.92, 86.13, 76.92, 67.03, 63.84, 32.16, 21.28.

*4.4.7. Compound (**6g**).* Yield=66% (314 mg); colorless solid; mp=189–190 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{25}H_{24}F_3O_4S$ 477.1347, found 477.1352; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64–7.62 (m, 2H), 7.47–7.37 (m, 3H), 7.30–7.24 (m, 4H), 7.17 (d, J=8.4 Hz, 2H), 6.97 (d, J=8.4 Hz, 2H), 5.12 (d, J=1.6 Hz, 1H), 4.39–4.29 (m, 2H), 3.95–3.92 (m, 1H), 3.32–3.27 (m, 1H), 2.32 (s, 3H), 2.24–2.16 (m, 1H), 1.78 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.83, 140.85, 138.80, 137.39, 129.34 (2×), 128.72, 128.68 (2×), 127.73 (2×), 127.43 (2×), 126.31 (2×), 124.65, 124.61, 124.58, 124.54, 85.01, 77.17, 67.18, 64.15, 32.17, 21.25.

*4.4.8. Compound (**6h**).* Yield=78% (357 mg); colorless gum; HRMS (ESI, M^++1) calcd for $C_{28}H_{27}O_4S$ 459.1630, found 458.1633; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69–7.62 (m, 5H), 7.49–7.38 (m, 6H), 7.15 (d, J=8.4 Hz, 1H), 7.04 (d, J=8.4 Hz, 2H), 6.52 (d, J=8.0 Hz, 2H), 5.24 (d, J=2.0 Hz, 1H), 4.43–4.33 (m, 2H), 4.00–3.98 (m, 1H), 3.37–3.32 (m, 1H), 2.27–2.20 (m, 1H), 2.08 (s, 3H), 1.99 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.17, 139.18, 137.36, 134.05, 132.75, 128.64 (2×), 128.62 (2×), 128.57 (2×), 127.94, 127.83 (2×), 127.37, 127.32 (2×), 127.21, 125.84, 125.81, 125.04, 123.50, 86.01, 77.75, 67.37, 64.55, 32.18, 21.09.

*4.4.9. Compound (**6i**).* Yield=80% (315 mg); colorless solid; mp=150–152 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{23}H_{23}O_4S$ 395.1317, found 395.1322; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64–7.61 (m, 2H), 7.46–7.30 (m, 6H), 7.22–7.17 (m, 4H), 7.07–7.02 (m, 3H), 5.09 (d, J=2.8 Hz, 1H), 4.34–4.24 (m, 2H), 3.95–3.92 (m, 1H), 3.25–3.20 (m, 1H), 2.23–2.14 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.75, 139.08, 136.75, 132.41, 128.58 (4×), 128.53, 127.81 (2×), 127.71 (2×), 127.52 (2×), 127.43, 125.94 (2×), 85.88, 77.72, 67.40, 64.69, 32.36.

*4.4.10. Compound (**6j**).* Yield=74% (246 mg); colorless solid; mp=164–165 °C (recrystallized from hexanes and EtOAc); HRMS

(ESI, M^++1) calcd for $C_{18}H_{21}O_4S$ 333.1161, found 333.1163; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59–7.55 (m, 4H), 7.44–7.30 (m, 6H), 5.19 (d, J=2.4 Hz, 1H), 4.31 (d, J=9.2 Hz, 1H), 4.22–4.15 (m, 1H), 3.56–3.54 (m, 1H), 3.22 (ddd, J=2.4, 4.8, 14.4 Hz, 1H), 2.19–2.09 (m, 1H), 2.01 (s, 3H), 1.92 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.88, 137.54, 128.73, 128.61 (4×), 128.41, 127.68 (2×), 126.27 (2×), 85.91, 77.79, 67.04, 64.78, 43.07, 31.36.

*4.4.11. Compound (**6k**).* Yield=74% (256 mg); colorless solid; mp=191–193 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{19}H_{23}O_4S$ 347.1317, found 347.1315; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59–7.56 (m, 2H), 7.44–7.33 (m, 5H), 7.20 (d, J=8.0 Hz, 2H), 5.15 (d, J=2.4 Hz, 1H), 4.29 (d, J=9.2 Hz, 1H), 4.20–4.13 (m, 1H), 3.53–3.51 (m, 1H), 3.19 (ddd, J=2.4, 4.8, 14.4 Hz, 1H), 2.34 (s, 3H), 2.18–2.09 (m, 1H), 2.04 (s, 3H), 2.00 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.98, 138.15, 134.48, 129.34 (2×), 128.56 (2×), 128.54, 127.68 (2×), 126.11 (2×), 85.86, 77.72, 67.05, 64.83, 43.14, 31.33, 21.16.

*4.4.12. Compound (**6l**).* Yield=78% (367 mg); colorless solid; mp=235–237 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{29}H_{27}O_4S$ 471.1630, found 471.1635; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67–7.65 (m, 2H), 7.49–7.32 (m, 10H), 7.24–7.21 (m, 5H), 7.16–7.12 (m, 2H), 5.14 (d, J=2.4 Hz, 1H), 4.39–4.32 (m, 2H), 4.01–3.98 (m, 1H), 3.37–3.32 (m, 1H), 2.27–2.17 (m, 1H), 1.84 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.81, 140.74, 140.17, 139.02, 135.82, 132.20, 129.09, 128.81 (2×), 128.65 (2×), 128.55 (2×), 127.75 (2×), 127.51 (2×), 127.33, 126.90 (2×), 126.48 (2×), 126.39 (2×), 85.96, 77.48, 67.46, 64.93, 32.16.

*4.4.13. Compound (**6m**).* Yield=75% (309 mg); colorless gum; HRMS (ESI, M^++1) calcd for $C_{23}H_{22}FO_4S$ 413.1223, found 413.1226; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61–7.59 (m, 2H), 7.44–7.34 (m, 3H), 7.29–7.24 (m, 2H), 7.18–7.17 (m, 2H), 7.10–7.03 (m, 3H), 6.85–6.79 (m, 2H), 5.08 (d, J=2.8 Hz, 1H), 4.28 (d, J=7.6 Hz, 1H), 4.27 (d, J=8.0 Hz, 1H), 3.90–3.88 (m, 1H), 3.28–3.23 (m, 1H), 2.21–2.14 (m, 1H), 2.02 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.80 (d, J=253.2 Hz), 139.00, 136.80, 136.75, 130.36 (d, J=9.1 Hz, 2×), 128.58 (2×), 128.56, 127.88 (2×), 127.68 (2×), 127.48, 125.92 (2×), 115.74 (d, J=22.7 Hz, 2×), 85.88, 77.55, 67.35, 64.95, 32.30.

*4.4.14. Compound (**6n**).* Yield=78% (331 mg); colorless solid; mp=121–123 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{24}H_{25}O_5S$ 425.1423, found 425.1426; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62–7.60 (m, 2H), 7.45–7.35 (m, 3H), 7.27–7.21 (m, 4H), 7.10–7.08 (m, 3H), 6.67–6.63 (m, 2H), 5.09 (d, J=2.8 Hz, 1H), 4.32 (dd, J=4.4, 8.8 Hz, 1H), 4.28 (d, J=2.0 Hz, 1H), 3.89–3.86 (m, 1H), 3.79 (s, 3H), 3.21–3.16 (m, 1H), 2.20–2.13 (m, 1H), 2.09 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.72, 139.15, 137.04, 132.36, 129.79 (2×), 128.55 (2×), 128.50, 127.83 (2×), 127.71 (2×), 127.30, 125.91 (2×), 113.86 (2×), 85.91, 77.86, 67.37, 64.80, 55.55, 32.63. Single-crystal X-ray diagram: crystal of compound **6n** was grown by slow diffusion of EtOAc into a solution of compound **6n** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group *Pc*, a=10.3109(3) Å, b=12.0886(3) Å, c=8.5131(2) Å, V=1060.59(5) Å^3, Z=2, d_{calcd}=1.329 g/cm^3, F(000)=448, 2θ range 1.685–26.395°, R indices (all data) $R1$=0.0474, $wR2$=0.1379.

*4.4.15. Compound (**6o**).* Yield=80% (360 mg); colorless gum; HRMS (ESI, M^++1) calcd for $C_{27}H_{31}O_4S$ 451.1943, found 451.1946; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64–7.61 (m, 2H), 7.45–7.35 (m, 3H), 7.25–7.22 (m, 3H), 7.19–7.16 (m, 3H), 7.03–6.98 (m, 3H), 5.09 (d, J=2.8 Hz, 1H), 4.33 (dd, J=4.4, 8.8 Hz, 1H), 4.31 (br s, 1H), 3.93–3.91 (m, 1H), 3.28 (ddd, J=2.4, 4.0, 13.6 Hz, 1H), 2.22 (br s, 1H), 2.19–2.14 (m, 1H), 1.29 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.00, 139.15, 137.54, 136.79, 128.55 (2×), 128.50, 127.73 (4×), 127.39 (2×), 127.29, 125.88 (2×), 125.59 (2×), 85.92, 77.72, 67.37, 64.46, 34.95, 32.31, 30.94 (3×).

*4.4.16. Compound (**6p**).* Yield=81% (365 mg); colorless solid; mp=184–187 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{27}H_{31}O_4S$ 451.1943, found 451.1948; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63–7.61 (m, 2H), 7.47–7.35 (m, 3H), 7.24–7.20 (m, 4H), 7.08–7.01 (m, 3H), 6.98 (d, J=8.4 Hz, 2H), 5.09 (d, J=2.8 Hz, 1H), 4.35–4.27 (m, 2H), 3.92–3.90 (m, 1H), 3.24–3.20 (m, 1H), 2.57 (t, J=7.6 Hz, 2H), 2.31 (s, 1H), 2.21–2.14 (m, 1H), 1.62–1.52 (m, 2H), 1.39–1.24 (m, 2H), 0.95 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.13, 139.12, 137.88, 136.88, 128.61 (2×), 128.56 (2×), 128.52, 127.76 (2×), 127.72 (2×), 127.59 (2×), 127.30, 125.93 (2×), 85.91, 77.80, 67.38, 64.63, 35.41, 33.15, 32.44, 22.18, 13.82.

*4.4.17. Compound (**7a**).* Yield=12% (49 mg); colorless solid; mp=157–159 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{24}H_{25}O_4S$ 409.1474, found 409.1476; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54–7.50 (m, 4H), 7.36–7.25 (m, 8H), 7.20 (d, J=8.4 Hz, 2H), 5.28 (d, J=4.8 Hz, 1H), 4.51 (d, J=7.6 Hz, 1H), 3.93 (dt, J=4.8, 10.8 Hz, 1H), 3.88 (dd, J=4.8, 7.6 Hz, 1H), 2.67 (dt, J=8.8, 10.8 Hz, 1H), 2.55 (dt, J=4.8, 8.8 Hz, 1H), 2.45 (s, 3H), 2.25 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.58, 137.79, 135.73, 135.66, 129.65 (2×), 129.34 (2×), 128.74 (2×), 128.46 (2×), 128.28 (2×), 128.15 (2×), 127.15 (2×), 77.26, 73.46, 69.57, 63.69, 28.46, 21.58.

*4.4.18. Compound (**7b**).* Yield=12% (51 mg); colorless solid; mp=164–166 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{24}H_{24}FO_4S$ 427.1379, found 427.1388; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55–7.51 (m, 3H), 7.33–7.22 (m, 8H), 6.98–6.94 (m, 2H), 5.25 (d, J=4.8 Hz, 1H), 4.44 (d, J=7.6 Hz, 1H), 3.93–3.81 (m, 2H), 2.65–2.44 (m, 2H), 2.45 (br s, 1H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.52 (d, J=246.3 Hz), 144.79, 137.65, 135.53, 131.65 (d, J=3.8 Hz), 131.11 (d, J=8.4 Hz, 2×), 129.67 (2×), 128.66 (2×), 128.40, 128.33 (2×), 127.11 (2×), 114.98 (d, J=21.2 Hz, 2×), 77.32, 72.63, 69.28, 63.45, 28.33, 21.51.

*4.4.19. Compound (**7d**).* Yield=15% (63 mg); colorless solid; mp=159–161 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{25}H_{27}O_4S$ 423.1630, found 423.1633; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, J=8.0 Hz, 2H), 7.40 (d, J=8.0 Hz, 2H), 7.34–7.28 (m, 5H), 7.20 (d, J=8.0 Hz, 2H), 7.07 (d, J=8.0 Hz, 2H), 5.24 (d, J=4.8 Hz, 1H), 4.52 (d, J=7.6 Hz, 1H), 3.94–3.86 (m, 2H), 2.71–2.63 (m, 1H), 2.57–2.51 (m, 1H), 2.42 (s, 3H), 2.34 (s, 3H), 1.80 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.50, 138.14, 137.86, 135.70, 132.70, 129.56 (2×), 129.32 (2×), 128.81 (2×), 128.74 (2×), 128.49 (2×), 128.43, 127.17 (2×), 77.11, 73.32, 69.66, 63.77, 28.42, 21.59, 21.13.

*4.4.20. Compound (**7e**).* Yield=11% (53 mg); colorless solid; mp=123–125 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{30}H_{29}O_4S$ 485.1787, found 485.1789; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61–7.29 (m, 16H), 7.16 (d, J=8.0 Hz, 2H), 5.31 (d, J=4.8 Hz, 1H), 4.65 (d, J=7.2 Hz, 1H), 4.41 (br s, 1H), 4.00–3.93 (m, 2H), 2.77 (dt, J=8.8, 10.8 Hz, 1H), 2.58 (dt, J=4.8, 8.8 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.45, 140.91, 140.36, 137.67, 134.74, 133.59, 129.57 (2×), 129.45 (2×), 128.76 (2×), 128.71 (2×), 128.34, 128.31 (2×), 127.45, 127.09 (2×), 126.94 (2×), 126.66 (2×), 77.53, 72.86, 68.93, 63.55, 29.31, 21.49.

*4.4.21. Compound (**7f**).* Yield=15% (68 mg); colorless gum; HRMS (ESI, M^++1) calcd for $C_{24}H_{24}NO_6S$ 454.1324, found 454.1328; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12 (s, 1H), 8.11 (d, J=8.0 Hz, 1H), 8.05 (d, J=8.0 Hz, 1H), 7.54–7.50 (m, 1H), 7.49 (d, J=8.8 Hz, 2H), 7.39–7.26

(m, 5H), 7.19 (d, *J*=8.0 Hz, 2H), 5.30 (d, *J*=4.8 Hz, 1H), 4.72 (d, *J*=5.6 Hz, 1H), 4.14–4.07 (m, 1H), 3.91–3.87 (m, 1H), 2.77 (dt, *J*=8.8, 10.8 Hz, 1H), 2.51 (dt, *J*=4.8, 8.8 Hz, 1H), 2.38 (s, 3H), 1.75 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.99, 138.30, 136.80, 135.68, 134.52, 129.86 (2×), 129.25, 128.96 (2×), 128.83, 128.56, 128.12 (2×), 126.81 (2×), 123.35, 123.04, 78.84, 71.51, 67.37, 62.43, 28.07, 21.47.

*4.4.22. Compound (**7g**).* Yield=16% (76 mg); colorless solid; mp=150–153 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{25}H_{24}F_3O_4S$ 477.1347, found 477.1354; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, *J*=8.0 Hz, 2H), 7.46–7.41 (m, 4H), 7.37–7.27 (m, 5H), 7.15 (d, *J*=8.4 Hz, 2H), 5.25 (d, *J*=4.4 Hz, 1H), 4.71 (d, *J*=5.6 Hz, 1H), 4.11–4.07 (m, 1H), 3.88–3.84 (m, 1H), 2.80 (dt, *J*=8.0, 14.0 Hz, 1H), 2.52 (dt, *J*=4.4, 14.0 Hz, 1H), 2.39 (s, 3H), 1.95 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.72, 140.09, 137.08, 135.73, 129.71 (2×), 128.92 (2×), 128.77 (2×), 128.65 (2×), 128.46, 128.09 (2×), 126.85 (2×), 124.50, 124.97 (q, *J*=3.0 Hz), 78.66, 71.88, 67.55, 62.76, 28.02, 21.44.

*4.4.23. Compound (**7h**).* Yield=10% (46 mg); colorless solid; mp=204–205 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{28}H_{27}O_4S$ 459.1630, found 459.1633; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (s, 1H), 7.80–7.78 (m, 2H), 7.64 (d, *J*=8.8 Hz, 1H), 7.51–7.48 (m, 2H), 7.40 (d, *J*=8.4 Hz, 2H), 7.39–7.36 (m, 1H), 7.32–7.26 (m, 5H), 6.94 (d, *J*=8.0 Hz, 2H), 5.39 (d, *J*=4.8 Hz, 1H), 4.67 (d, *J*=6.8 Hz, 1H), 4.07–4.02 (m, 1H), 4.00–3.96 (m, 1H), 2.87 (dt, *J*=8.8, 10.8 Hz, 1H), 2.62 (dt, *J*=4.8, 8.8 Hz, 1H), 2.26 (s, 3H), 1.96 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.44, 137.58, 135.63, 133.09, 132.97, 132.73, 129.37 (2×), 128.81 (2×), 128.47, 128.38, 128.27 (2×), 128.11, 127.86, 127.32, 127.04 (2×), 126.43, 126.31, 126.11, 78.00, 72.95, 68.65, 63.53, 28.31, 21.41.

*4.4.24. Compound (**7i**).* Yield=10% (39 mg); colorless solid; mp=99–101 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{23}H_{23}O_4S$ 395.1317, found 395.1318; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63–7.50 (m, 5H), 7.42–7.39 (m, 2H), 7.34–7.24 (m, 8H), 5.27 (d, *J*=5.2 Hz, 1H), 4.54 (d, *J*=7.2 Hz, 1H), 3.98–3.89 (m, 2H), 2.70 (dt, *J*=4.8, 14.8 Hz, 1H), 2.55 (dt, *J*=5.6, 14.8 Hz, 1H), 2.40 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.64, 137.68, 135.64, 133.48, 129.23 (2×), 129.01 (2×), 128.74 (2×), 128.43, 128.39 (3×), 128.18 (2×), 127.11 (2×), 77.33, 73.30, 69.32, 63.57, 28.38.

*4.4.25. Compound (**7j**).* Yield=10% (32 mg); colorless solid; mp=205–207 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{18}H_{21}O_4S$ 333.1161, found 333.1168; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, *J*=7.2 Hz, 2H), 7.45–7.29 (m, 8H), 5.18 (d, *J*=3.6 Hz, 1H), 5.09 (d, *J*=3.6 Hz, 1H), 4.33 (dd, *J*=4.0, 8.4 Hz, 1H), 3.48 (dd, *J*=4.8, 9.2 Hz, 1H), 2.91 (dt, *J*=4.8, 14.8 Hz, 1H), 2.68 (br s, 1H), 2.48 (dt, *J*=5.6, 14.8 Hz, 1H), 2.24 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 137.01, 136.98, 128.99 (2×), 128.77 (2×), 128.66, 128.15, 127.56 (2×), 126.63 (2×), 79.60, 71.30, 65.35, 62.57, 41.61, 27.28.

*4.4.26. Compound (**7k**).* Yield=14% (48 mg); colorless solid; mp=187–189 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{19}H_{23}O_4S$ 347.1317, found 347.1319; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44–7.30 (m, 7H), 7.22 (d, *J*=8.0 Hz, 2H), 4.74 (d, *J*=9.6 Hz, 1H), 4.28 (d, *J*=9.2 Hz, 1H), 3.80 (ddd, *J*=4.8, 9.2, 14.0 Hz, 1H), 3.43 (ddd, *J*=4.0, 10.0, 14.0 Hz, 1H), 2.86 (dt, *J*=4.0, 14.0 Hz, 1H), 2.35 (s, 3H), 2.14 (dt, *J*=10.8, 14.0 Hz, 1H), 2.04 (s, 3H), 1.80 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 139.53, 137.94, 135.01, 129.73 (2×), 128.70 (2×), 128.69, 128.09 (2×), 127.25 (2×), 84.79, 80.24, 71.10, 64.94, 41.41, 30.10, 21.25.

*4.4.27. Compound (**7l**).* Yield=13% (61 mg); colorless solid; mp=160–161 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{29}H_{27}O_4S$ 471.1630, found 471.1635; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62–7.27 (m, 19H), 5.31 (d, *J*=4.8 Hz, 1H), 4.66 (d, *J*=6.8 Hz, 1H), 4.02–3.95 (m, 2H), 2.82–2.74 (m, 1H), 2.62–2.57 (m, 1H), 1.80 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.00, 140.44, 138.70, 137.60, 134.71, 133.34, 129.46 (2×), 128.98 (2×), 128.83 (2×), 128.81 (2×), 128.44, 128.35 (2×), 127.50, 127.08 (2×), 127.01 (2×), 126.79 (2×), 77.63, 72.85, 68.93, 63.58, 28.30.

*4.4.28. Compound (**7m**).* Yield=11% (45 mg); colorless solid; mp=157–159 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{23}H_{22}FO_4S$ 413.1223, found 413.1228; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.57–7.53 (m, 2H), 7.46–7.44 (m, 2H), 7.35–7.22 (m, 8H), 7.06–7.00 (m, 2H), 5.24 (d, *J*=4.8 Hz, 1H), 4.61 (d, *J*=6.8 Hz, 1H), 3.99–3.90 (m, 2H), 2.75–2.67 (m, 1H), 2.59–2.53 (m, 1H), 1.86 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.56 (d, *J*=254.7 Hz), 137.55, 135.64, 134.54, 131.24 (d, *J*=9.1 Hz, 2×), 129.06, 128.77 (2×), 128.62, 128.42 (2×), 128.21 (2×), 127.05 (2×), 116.22 (d, *J*=22.8 Hz, 2×), 77.53, 73.05, 68.86, 63.67, 28.34.

*4.4.29. Compound (**7n**).* Yield=12% (51 mg); colorless gum; HRMS (ESI, M^++1) calcd for $C_{24}H_{25}O_5S$ 425.1423, found 425.1424; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54–7.51 (m, 4H), 7.33–7.25 (m, 8H), 6.85 (d, *J*=8.4 Hz, 2H), 5.26 (d, *J*=4.8 Hz, 1H), 4.51 (d, *J*=7.6 Hz, 1H), 3.95–3.80 (m, 2H), 3.85 (s, 3H), 2.69–2.52 (m, 2H), 2.26 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.59, 137.82, 135.74, 130.62 (2×), 129.37 (2×), 128.71 (2×), 128.57, 128.41, 128.30, 128.15 (2×), 127.15 (2×), 114.21 (2×), 77.11, 73.49, 69.55, 63.81, 55.65, 28.52.

*4.4.30. Compound (**7o**).* Yield=12% (54 mg); colorless solid; mp=130–132 °C (recrystallized from hexanes and EtOAc); HRMS (ESI, M^++1) calcd for $C_{27}H_{31}O_4S$ 451.1943, found 450.1948; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53–7.47 (m, 4H), 7.38 (d, *J*=8.8 Hz, 2H), 7.34–7.20 (m, 8H), 5.28 (d, *J*=4.8 Hz, 1H), 4.57 (d, *J*=7.2 Hz, 1H), 3.96–3.91 (m, 2H), 2.71 (dt, *J*=8.8, 10.8 Hz, 1H), 2.56 (dt, *J*=4.8, 8.8 Hz, 1H), 2.02 (br s, 1H), 1.33 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.32, 137.77, 135.77, 135.49, 129.15 (2×), 128.74 (2×), 128.40, 128.25, 128.22 (2×), 128.13 (2×), 127.11 (2×), 126.01 (2×), 77.44, 73.26, 69.22, 63.50, 35.16, 31.00 (3×), 28.43. Single-crystal X-ray diagram: crystal of compound **7o** was grown by slow diffusion of EtOAc into a solution of compound **7o** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the orthorhombic crystal system, space group *P*-1, *a*=11.8674(6) Å, *b*=13.6155(7) Å, *c*=16.9842(7) Å, *V*=2535.9(2) Å^3, *Z*=2, d_{calcd}=1.291 g/cm^3, *F*(000)=1044, 2θ range 1.565–26.412°, *R* indices (all data) *R*1=0.1141, *wR*2=0.2228.

*4.4.31. Compound (**7p**).* Yield=8% (36 mg); colorless gum; HRMS (ESI, M^++1) calcd for $C_{27}H_{31}O_4S$ 451.1943, found 451.1950; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52–7.50 (m, 4H), 7.32–7.23 (m, 8H), 7.19 (d, *J*=8.4 Hz, 2H), 5.27 (d, *J*=5.2 Hz, 1H), 4.54 (d, *J*=7.6 Hz, 1H), 3.97–3.89 (m, 2H), 2.73–2.53 (m, 5H), 1.64–1.56 (m, 2H), 1.42–1.32 (m, 2H), 0.95 (t, *J*=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.40, 137.76, 135.74, 129.28 (2×), 129.15, 129.02 (2×), 128.74 (2×), 128.60, 128.44 (2×), 128.30, 128.15 (2×), 127.13 (2×), 77.32, 73.39, 69.43, 63.61, 35.54, 33.16, 28.43, 22.22, 13.83.

4.5. Synthetic procedure of 8 and 9

A synthetic procedure of **8** and **9** is as follows: excess Jones reagent was added to a solution of **6a** (1.0 mmol) in acetone (20 mL) at 0 °C. The reaction mixture was stirred at rt for 2 h and the solvent was concentrated. The residue was diluted with water (10 mL) and the mixture was extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with brine, dried, filtered and evaporated to afford crude product. Purification on silica gel (hexanes/EtOAc=8:1 to 3:1) afforded **8** and **9**.

*4.5.1. Compound (**8**).* Yield=46% (115 mg); colorless gum; HRMS (ESI, M^++1) calcd for $C_{17}H_{15}O_2$ 251.1072, found 251.1077; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49–7.34 (m, 10H), 7.12 (dd, J=2.0, 10.0 Hz, 1H), 6.33 (dd, J=2.4, 10.0 Hz, 1H), 5.59 (dd, J=2.4, 4.0 Hz, 1H), 5.21 (d, J=2.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 194.11, 150.78, 138.78, 135.71, 128.85 (2×), 128.68, 128.42, 128.26 (2×), 127.88 (2×), 127.07 (2×), 126.96, 83.22, 77.13.

*4.5.2. Compound (**9**).*[8] Yield=25% (59 mg); colorless oil; HRMS (ESI, M^++1) calcd for $C_{17}H_{15}O$ 235.1123, found 235.1132; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64–7.61 (m, 2H), 7.37–7.20 (m, 8H), 6.56 (d, J=3.6 Hz, 1H), 6.06 (dt, J=0.8, 3.2 Hz, 1H), 4.04 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.34, 152.90, 138.06, 131.06, 128.74 (2×), 128.58 (2×), 128.51, 126.91 (2×), 126.50, 123.45 (2×), 108.44, 105.76, 34.66.

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Supplementary data

Experimental procedure and scanned photocopies of NMR ($CDCl_3$) spectral data were supported. Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2015.01.016.

References and notes

1. For synthesis of the biological active THP derivatives, see: (a) Umamatheswari, S.; Balaji, B.; Ramanathan, M.; Kabilan, S. *Eur. J. Med. Chem.* **2011**, *46*, 1415; (b) Fakler, T. M.; Berlin, K. D. *Org. Prep. Proced. Int.* **1989**, *21*, 327; (c) Parthiban, P.; Aridoss, G.; Rathika, P.; Ramkumar, V.; Kabilan, S. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 2981; (d) El-Subbagh, H. I.; Abu-Zaid, S. M.; Mahran, M. A.; Badria, F. A.; Alofaid, A. M. *J. Med. Chem.* **2000**, *43*, 2915.
2. For synthesis of THP derivatives, see: (a) Ramachandran, P. V.; Gagare, P. D. *Tetrahedron Lett.* **2011**, *52*, 4378; (b) Mahmood, A.; Suarez, J. R.; Thomas, S. P.; Aggarwal, V. K. *Tetrahedron Lett.* **2013**, *54*, 49; (c) Ghosh, A. K.; Keyes, C.; Veitschegger, A. M. *Tetrahedron Lett.* **2014**, *55*, 4251; (d) Yang, X.-F.; Wang, M.; Zhang, Y.; Li, C.-J. *Synlett* **2005**, 1912; (e) Olier, C.; Kaafarani, M.; Gastaldi, S.; Bertrand, M. P. *Tetrahedron* **2010**, *66*, 413; (f) Crosby, S. R.; Harding, J. R.; King, C. D.; Parker, G. D.; Willis, C. L. *Org. Lett.* **2002**, *4*, 577; (g) Hiebel, M. A.; Pelotier, B.; Piva, O. *Tetrahedron* **2007**, *63*, 7874; (h) Yadav, J. S.; Reddy, B. V. S.; Maity, T.; Kumar, G. G. K. S. *Tetrahedron Lett.* **2007**, *48*, 8874; (i) Chan, K. P.; Seow, A. H.; Loh, T. P. *Tetrahedron Lett.* **2007**, *48*, 37; (j) Barry, C. St J.; Crosby, S. R.; Harding, J. R.; Hughes, R. A.; King, C. D.; Parker, G. D.; Willis, C. L. *Org. Lett.* **2003**, *5*, 2429; (k) Jasti, R.; Vitale, J.; Rychnovsky, S. D. *J. Am. Chem. Soc.* **2004**, *126*, 9904; (l) Cossey, K. N.; Funk, R. L. *J. Am. Chem. Soc.* **2004**, *126*, 12216; (m) Yadav, V. K.; Kumar, N. V. *J. Am. Chem. Soc.* **2004**, *126*, 8652; (n) Bunt, A. J.; Bailey, C. D.; Cons, B. D.; Edwards, S. J.; Elsworth, J. D.; Pheko, T.; Willis, C. L. *Angew. Chem., Int. Ed.* **2012**, *51*, 3901; (o) Bolla, M. L.; Patterson, B.; Rychnovsky, S. D. *J. Am. Chem. Soc.* **2005**, *127*, 16044; (p) Epstein, O. L.; Rovis, T. *J. Am. Chem. Soc.* **2006**, *128*, 16480.
3. For synthesis of natural products with a THP skeleton, see: (a) Watson, A. A.; Fleet, G. W. J.; Asano, N.; Molyneux, R. J.; Nugh, R. J. *Phytochemistry* **2001**, *56*, 265; (b) Reddy, U. C.; Bondalapati, S.; Saikia, A. K. *J. Org. Chem.* **2009**, *74*, 2605; (c) Clarke, P. A.; Santos, S. *Eur. J. Org. Chem.* **2006**, 2045; (d) Tian, X. T.; Jaber, J. J.; Rychnovsky, S. D. *J. Org. Chem.* **2006**, *71*, 3176; (e) Miles, R. B.; Davis, C. E.; Coates, R. M. *J. Org. Chem.* **2006**, *71*, 1493; (f) Class, Y. J.; DeShong, P. *Chem. Rev.* **1995**, *95*, 1843; (g) Crane, E. A.; Scheidt, K. A. *Angew. Chem., Int. Ed.* **2010**, *49*, 8316; (h) Woo, S. K.; Kwon, M. S.; Lee, E. *Angew. Chem., Int. Ed.* **2008**, *47*, 3242; (i) Gesinski, M. R.; Tadpetch, K.; Rychnovsky, S. D. *Org. Lett.* **2009**, *11*, 5342; (j) Wender, P. A.; DeChristopher, B. A.; Schrier, A. J. *J. Am. Chem. Soc.* **2008**, *130*, 6658.
4. For reviews on the synthesis of THP skeleton, see: (a) Pastor, I. M.; Yus, M. *Curr. Org. Chem.* **2007**, *11*, 925; (b) Smith, A. B., III; Fox, R. J.; Razler, T. M. *Acc. Chem. Res.* **2008**, *41*, 675; (c) Nasir, N. M.; Ermanis, K.; Clarke, P. A. *Org. Biomol. Chem.* **2014**, *12*, 3323.
5. (a) Chang, M.-Y.; Chen, Y.-C.; Chan, C.-K. *Tetrahedron* **2014**, *70*, 8908; (b) Chang, M.-Y.; Chen, Y.-C.; Chan, C.-K. *Synlett* **2014**, 1739; (c) Chang, M.-Y.; Tsai, C.-Y. *Tetrahedron Lett.* **2014**, *55*, 5548; (d) Chang, M.-Y.; Chan, C.-K.; Chen, Y.-C. *Heterocycles* **2014**, *89*, 1229; (e) Chang, M.-Y.; Cheng, Y.-C.; Lu, Y.-R. *Org. Lett.* **2014**, *16*, 6252.
6. CCDC 1034482 (**5a**), 1034485 (**6c**), 1034483 (**6n**), and 1034484 (**7o**) contain the supplementary crystallographic data for this paper. This data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).
7. (a) Mengel, A.; Reser, O. *Chem. Rev.* **1999**, *99*, 1191; (b) Gung, B. W. *Tetrahedron* **1996**, *52*, 5263; (c) Ager, D. J.; East, M. B. *Tetrahedron* **1992**, *48*, 2803.
8. (a) Imagawa, H.; Kurisaki, T.; Nishizawa, M. *Org. Lett.* **2004**, *6*, 3679; (b) Yuguchi, M.; Tokuda, M.; Orito, K. *J. Org. Chem.* **2004**, *69*, 908; (c) Chang, S.; Desai, S.; Leznoff, D. B.; Merbouh, N.; Britton, R. *Eur. J. Org. Chem.* **2013**, *16*, 3219.