Tetrahedron 70 (2014) 1740–1747

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

One-pot synthesis of sulfonyl (*E*)-stilbenes by nitrobenzene-mediated dimerizative desulfonation of benzylic sulfones

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ARTICLE INFO

Article history:
Received 29 October 2013
Received in revised form 14 January 2014
Accepted 20 January 2014
Available online 27 January 2014

Keywords:
Sulfonyl stilbenes
Dimerizative desulfonation
Benzylic sulfones

ABSTRACT

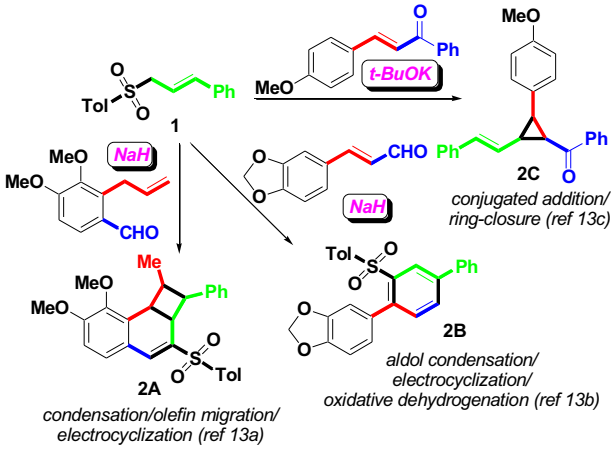
A facile one-pot synthetic route for preparing sulfonyl (*E*)-stilbenes **4** is developed. The efficient route is realized by a nitrobenzene ($PhNO_2$)-mediated dimerizative desulfonation of benzylic sulfones **3** in the presence of sodium hydride (NaH) in good yields. Some synthetic investigations of sulfonyl stilbenes **4** are also examined.

1. Introduction

The stilbene skeleton is a central pharmacophore for the construction of multi-functionalized structures possessing diversified potential biological activities[1] including anticancer,[2] antifungal,[3] antioxidant,[4] and anti-inflammatory;[5] it has also been applied to photo-responsive OLEDs or NLO materials[6] and photo-chemical or photo-physical cis–trans isomerization[7] in different technological fields. Accordingly, the well-designed synthetic pathway is an important tool to establish a stilbene skeleton. Some classical methods have adapted Perkin aldol-type condensation,[8] Wittig or Horner–Wadsworth–Emmons (HWE) olefination[9] and transition metal-mediated cross-couplings (for Pd: Heck, Negishi–Stille, Suzuki–Miyaura; for Ru, Grubbs metathesis; for Ti: McMurry).[10] Because the synthetic approaches for domino types are currently in vogue, many reagents mediated one-pot oxidative, reductive or eliminative dimerizations have been developed.[11] Many known drugs include the core structure of stilbene. Their biological activities and chemical properties have emerged as key targets due to the sulfonyl group being used as the main constituent of selective COX-2 inhibitors, such as DuP-697, HMN-214, rofecoxib, and etoricoxib.[12]

2. Results and discussion

In continuation of our recent investigation into the skeleton of cinnamyl sulfone (styrylmethyl sulfone) **1** for preparing tetrahydrocyclobuta[*a*]naphthalenes **2A**, *p*-terphenyls **2B**, and cyclopropanes **2C** using one-pot domino base-mediated annulation strategy (see Scheme 1),[13] one-pot base-mediated dimerizative desulfonation of benzylic sulfones **3** (the removal of olefinic motif) with $PhNO_2$ was examined. To explore the feasible transformation,[14,15] benzyl phenyl sulfone **3a** and different functionalized nitrobenzenes were chosen as the starting substrate under various basic conditions, as shown in Table 1.



Scheme 1. Application of cinnamyl sulfones **1**.

First, when NaH-mediated treatment of benzyl phenyl sulfone **3a** with 4-fluoronitrobenzene was screened in refluxing THF, **4a** with (*E*)-configuration was afforded in 78% yield. The ^1H NMR spectrum of **4a** exhibited one singlet at δ 7.97 for the proton of the

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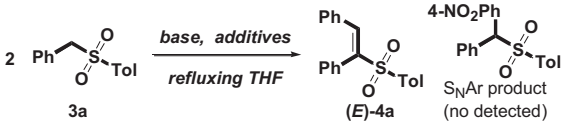
http://dx.doi.org/10.1016/j.tet.2014.01.045

Table 1
Reaction conditions of **3a**[a]



3a (*E*)-4a

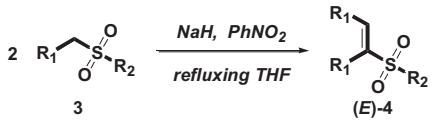
Entry	Additives (equiv), base (equiv), time (h)	**4a**, yield[b] (%)
1	4-F-1-NO_2Ph (1), NaH (5), 3	78
2	4-F-1-NO_2Ph (1), DMAP (5), 3	60[c]
3	4-F-1-NO_2Ph (1), *t*-BuOK (5), 3	34[d]
4	4-F-1-NO_2Ph (1), DBU (5), 3	55[e]
5	2-F-1-NO_2Ph (1), DBU (5), 3	60[f]
6	2,4-Cl_2-1-NO_2Ph (1), NaH (5), 3	70[g]
7	$PhNO_2$ (1), NaH (5), 3	82
8	*$PhNO_2$ (2), NaH (5), 3*	*86*
9	$PhNO_2$ (1), NaH (10), 3	82
10	$PhNO_2$ (1), NaH (5), 10	86
11	$PhNO_2$ (0.5), NaH (5), 10	80
12	$PhNO_2$ (0), NaH (10), 10	—[h]
13	$MeNO_2$ (1), NaH (5), 3	—[h]
14	$EtNO_2$ (1), NaH (5), 3	—[h]
15	$PhNO_2$ (0.5), NaH (5), 10	76[i]
16	TEMPO (1), NaH (5), 3	—[j]
17	$PhNO_2$ (2), TEMPO (1), NaH (5), 3	80

[a] The reactions were run on a 2.0 mmol scale with **3a** in refluxing THF (10 mL).
[b] The product was >95% pure as determined by ^{1}H NMR analysis.
[c] Compound **3a** of 18% was recovered.
[d] Compound **3a** of 28% was obtained.
[e] Compound **3a** of 26% was recovered.
[f] Compound **3a** of 25% was recovered.
[g] Unknown mixture of 16% was isolated.
[h] No reaction and **3a** was recovered.
[i] The reaction was treated with N_2 system.
[j] Compound of **3a** of 68% was recovered and 21% of unknown mixture was isolated.

β-vinylic position. The structure of **4a** was determined by single-crystal X-ray crystallography.[16] The resulting adduct replaced the expected S_NAr product. Experimental results are different from the literature reports.[17,18] Based on the results, various bases and additives of $PhNO_2$ derivatives were screened. Changing the base to NaH, *t*-BuOK or DBU in boiling THF solution for the one-pot reaction, we found that NaH was the optimal base to increase the yield of **4a** without the recovery of the starting material **3a** (entries 1–4). Next, when $PhNO_2$ was chosen as the promoter in the presence of NaH, the combination of NaH/$PhNO_2$ provided a better yield (entries 7–11). Interestingly, no reaction occurred even with a 5 equiv of NaH in the absence of $PhNO_2$ (entry 12). By changing from $PhNO_2$ to $MeNO_2$ or $EtNO_2$, no **4a** was observed under the same conditions (entries 13 and 14). Without the involvement of air, **4a** was still isolated in 76% yield in the presence of $PhNO_2$ (entry 15). It showed that the reaction procedure does not need oxygen (from air) as the oxidants. Furthermore, when $PhNO_2$ was changed to TEMPO (entry 16), **3a** was recovered (68%). To combine $PhNO_2$ and TEMPO (entry 17), **4a** was isolated in 80% yield. The reaction may not undergo a radical process. According to the above phenomenon, we envisioned that $PhNO_2$ is a key factor controlling high (*E*)-selectivity of **4a** during the dimerizative desulfonation.

As shown in Table 2, some compounds **4a**–**y** were efficiently constructed in good yields (57–88%) by the above one-pot cascade reaction of compounds **3a**–**y** (entries 1–25). Different substituents (R_1 and R_2), with diversified electron-withdrawing groups or electron-donating groups, were well-performed. Compounds **4a**,**b**, **4d**–**f**, and **4l** were determined by single-crystal X-ray crystallography.[16] But, when the R_1 group was a neopentyl, *n*-octyl or *n*-dodecyl aliphatic substituent, the starting material **3z**, **3aa** or **3ab** was recovered as a major product (entries 26–28). Similar results

Table 2
One-pot synthesis of sulfonyl (*E*)-stilbenes **4**[a,b]



3 (*E*)-4

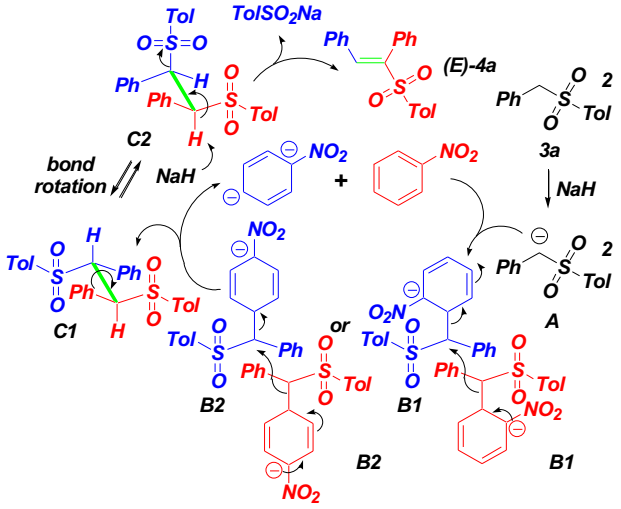
Entry	**3** (R_1, R_2)	**4**, yield (%)
1	**3a**, Ph, Tol	**4a**, 86
2	**3b**, 2-FPh, Tol	**4b**, 70
3	**3c**, 3-MeOPh, Tol	**4c**, 70
4	**3d**, 4-MeOPh, Tol	**4d**, 72
5	**3e**, 4-ClPh, Tol	**4e**, 70
6	**3f**, 4-FPh, Tol	**4f**, 73
7	**3g**, Ph, Me	**4g**, 85
8	**3h**, Ph, *n*-Bu	**4h**, 80
9	**3i**, 3,4-CH_2O_2Ph, Tol	**4i**, 72
10	**3j**, 3,5-$(MeO)_2$Ph, Tol	**4j**, 70
11	**3k**, 4-PhPh, Tol	**4k**, 78
12	**3l**, 1-Naphthalene, Tol	**4l**, 81
13	**3m**, 2-Naphthalene, Tol	**4m**, 78
14	**3n**, 1-Thiophene, Tol	**4n**, 62
15	**3o**, 3-Pyridine, Tol	**4o**, 57
16	**3p**, Ph, Ph	**4p**, 82
17	**3q**, Ph, 4-MeOPh	**4q**, 88
18	**3r**, Ph, 4-FPh	**4r**, 83
19	**3s**, Ph, 3-MePh	**4s**, 80
20	**3t**, Ph, 4-EtPh	**4t**, 86
21	**3u**, Ph, 4-*i*-PrPh	**4u**, 82
22	**3v**, Ph, 4-*n*-BuPh	**4v**, 80
23	**3w**, Ph, 4-*t*-BuPh	**4w**, 82
24	**3x**, (*E*)-CH=CHPh, Tol	**4x**, 62
25	**3y**, (*E*)-CH=CH-4-MeOPh, Tol	**4y**, 60
26	**3z**, *t*-BuCH_2, Tol	—[c]
27	**3aa**, *n*-C_8H_{17}, Tol	—[c]
28	**3ab**, *n*-$C_{12}H_{25}$, Tol	—[c]
29	**3ac**, 2,6-F_2Ph, Tol	—[d]
30	**3ad**, 9-Anthracene, Tol	—[d]
31	**3ae**, 4-NO_2Ph, Tol	—[e]

[a] The one-pot reaction was run on a 2.0 mmol scale with starting materials **3a**–**y** and $PhNO_2$ (4.0 mmol) in THF(10 mL).
[b] The isolated products **4a**–**y** was >95% pure as determined by ^{1}H NMR analysis.
[c] No reaction and **3z**, **3aa** or **3ab** was recovered.
[d] Trace unknown mixture was obtained and major **3ac** or **3ad** was recovered.
[e] Unknown mixture was obtained.

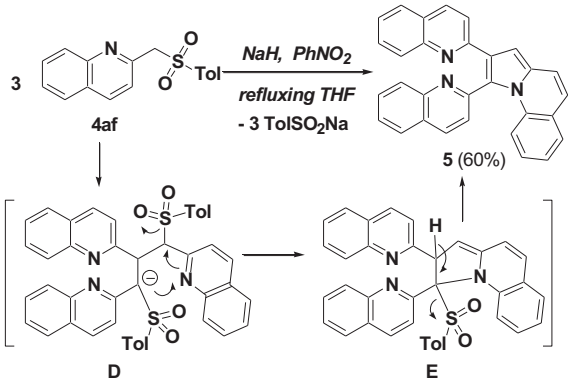
were also shown in the 2,6-difluorophenyl or 9-anthracenyl group (entries 29–30). These experimental results clearly show that the R_1 group of skeleton **3** must be an aromatic group with less steric hindrance due to (1) the benzylic α-position on the skeleton of sulfone **3** being more easily deprotonated than the aliphatic group (for **3aa** or **3ab**) by NaH and (2) the resulting delocalized α-carbanion with a bulky group (for **3ac** or **3ad**) being a stable nucleophile during the reversible equilibrium process. For 4-nitrobenzyl sulfone **3ae**, an unknown mixture was yielded (entry 31).

For the possible reaction mechanism, carbanion **A** was first proposed via NaH-mediated deprotonation of **3a** (see Scheme 2). After the representative S_NAr process of A and $PhNO_2$, self-dimerative cross-couplings of B1 and B2 were initiated. Subsequently, new single bond of C1 was formed via the removal of $PhNO_2$ and the dianion species. To achieve E2 process with stable conformation, the single bond of C1 was rotated. By the trans-configuration between proton and $TolSO_2$ group, deprotonation of C2 with NaH or dianion of $PhNO_2$ provided sole (*E*)-**4a** and $TolSO_2Na$. After work-up, the anion species of $PhNO_2$ could convert to $PhNO_2$ or other analogues.

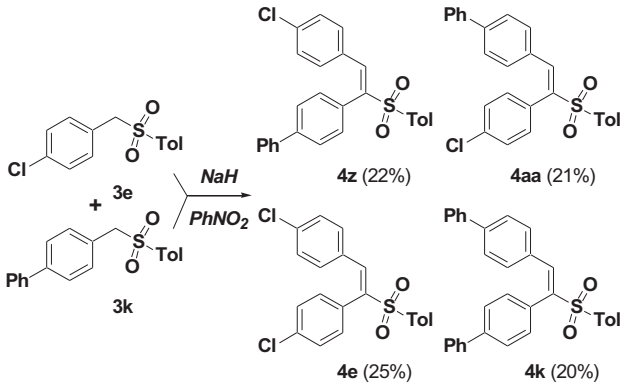
Under the same conditions, trimer **5** was observed by the treatment of **4af** with $PhNO_2$ via intermediates D and E (see Scheme 3).[16] Therefore, benzylic sulfone played a key role to initiate the formation of (*E*)-stilbene **4**. To extend this one-pot domino protocol for the cross-coupling, **3e** and **3k** were chosen as two starting materials (Scheme 4). Four sulfonyl stilbenes **4e**, **4k**, **4z**, and **4aa**



Scheme 2. Possible mechanism.

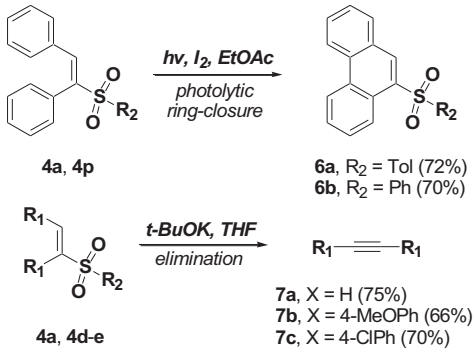


Scheme 3. Reaction of compound **4af** with $PhNO_2$.

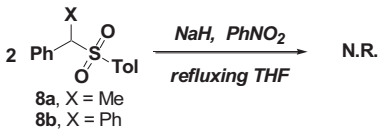


Scheme 4. Cross-coupling of compounds **3e** and **3k**.

were isolated in similar yields. From the observation of cross dimerizative desulfonation, we believe that $PhNO_2$ is the key factor affecting intermolecular aryl group exchanges. For exploring the synthetic application of skeleton **4**, photolytic ring-closure or reductive elimination was studied (Scheme 5). Two useful skeletons, sulfonyl phenanthrenes **6a**,**b** and diaryl alkynes **7a**–**c**, gave modest yields via photo-induced annulation[19] or base-promoted dehydrosulfonation. A two-step novel access to prepare **6** and **7** was described from skeleton **4**. The structures of **6a** and **7c** were determined by single-crystal X-ray crystallography.[16] By the above protocol, **8** (X=Me or Ph) was treated with $PhNO_2$,[15g] no reaction was observed (Scheme 6).



Scheme 5. Reactions of skeleton **4**.



Scheme 6. Reaction of skeleton **8** with $PhNO_2$.

After the examination for the proposed mechanism, we found that the formation of intermediates B1/B2 and C1/C2 should be the reasonable intermediates in the formation of skeleton **4** by $PhNO_2$-mediated dimerizative desulfonation of skeleton **3**. There are three points to support the possible mechanism: (1) only (*E*)-configurated **4a** is generated via the E2 process, (2) four sulfonyl (*E*)-stilbenes **4e**, **4k**, **4z**, **4aa** with the similar distribution of yields are observed by the intermolecular cross-couplings of intermediates B1 and B2 (in situ from **3e** and **3k**), and (3) no **4a** is isolated by only addition of TEMPO via a radical process.

3. Conclusion

In summary, we have successfully described the one-pot $PhNO_2$-mediated *E*-selective dimerizative desulfonation of benzylic sulfones **3** in the presence of NaH under boiling THF conditions. The structures of the key products **4** were confirmed by X-ray crystal analysis. This method represents good reactivity and tolerates an array of functionality. Two products, **6a**,**b** and **7a**–**c**, were obtained by photo-induced annulation or base-promoted dehydrosulfonation of skeleton **4**. The one-pot facile synthetic route begins with simple starting materials and reagents, and provides a potential methodology for synthetic research.

4. Experimental section

4.1. General

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 air with magnetic stirring. Products in organic solvents were dried with anhydrous $MgSO_4$ before concentration in vacuo. Melting points were determined with an SMP3 melting apparatus. ^1H 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). Elemental analyses were carried

out with Heraeus Vario III-NCSH, Heraeus CHN-OS-Rapid Analyzer or Elementar Vario EL III.

4.2. A representative synthetic procedure of compounds 4a–aa and 5

A representative synthetic procedure of compounds **4a**–**aa** and **5** is as follows: sodium hydride (NaH, 60% in oil, 400 mg, 10.0 mmol) was added to a stirred solution of skeleton **3** (2.0 mmol) in THF (8 mL) at 0 °C. The resulting solution was stirred at 0 °C for 5 min and warmed to rt for 5 min. A solution of nitrobenzene (490 mg, 4.0 mmol) in THF (2 mL) was slowly added to the reaction mixture at rt for 1 min. The reaction mixture was stirred at reflux for 3 h and cooled to rt. Water (1 mL) was added to the reaction mixture at 0 °C. The solvent was concentrated under reduced pressure. The resulting residue was diluted with water (10 mL) and the product 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=15:1 to 4:1) afforded compounds **4a**–**aa** and **5**.

*4.2.1. Compound (**4a**).*[20] Yield=86% (287 mg); colorless solid; mp=173–175 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3014, 2935, 1602, 1418, 1321, 1148, 913; HRMS (ESI, M^++1) calcd for $C_{21}H_{19}O_2S$ 335.1106, found 335.1112; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.94 (s, 1H), 7.50 (d, J=8.4 Hz, 2H), 7.38–7.12 (m, 8H), 7.07–7.02 (m, 4H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.09, 141.52, 137.26, 135.73, 132.86, 131.37, 130.74 (2×), 130.50 (2×), 129.94, 129.33 (2×), 129.08, 128.80 (2×), 128.64 (2×), 128.45 (2×), 21.59. Anal. Calcd for $C_{21}H_{18}O_2S$: C, 75.42; H, 5.42. Found: C, 75.63; H, 5.57. Single-crystal X-ray diagram: crystal of **4a** was grown by slow diffusion of EtOAc into a solution of **4a** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group $P121/n1$, a=12.3185(4) Å, b=5.8327(2) Å, c=24.3654(8) Å, V=1722.11(10) Å^3, Z=4, d_{calcd}=1.290 g/cm^3, $F(000)$=704, 2θ range 1.70–26.36°, R indices (all data) $R1$=0.0738, $wR2$=0.1668.

*4.2.2. Compound (**4b**).* Yield=70% (259 mg); colorless solid; mp=135–137 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3045, 2953, 1621, 1425, 1334, 1156, 921; HRMS (ESI, M^++1) calcd for $C_{21}H_{17}F_2O_2S$ 371.0917, found 371.0922; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (s, 1H), 7.53 (d, J=8.4 Hz, 2H), 7.39–7.33 (m, 2H), 7.28–7.15 (m, 4H), 7.05 (dt, J=0.8, 10.0 Hz, 1H), 6.90–6.75 (m, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.29 (d, J=252.3 Hz), 159.71 (d, J=249.3 Hz), 144.37, 136.42, 136.81, 135.40, 132.69 (d, J=2.2 Hz), 131.93 (d, J=9.1 Hz), 131.75 (d, J=6.8 Hz), 131.63 (d, J=8.3 Hz), 129.42 (2×), 128.57 (2×), 124.42 (d, J=3.8 Hz), 123.96 (d, J=3.8 Hz), 121.08 (d, J=11.4 Hz), 118.77 (d, J=15.9 Hz), 115.80 (d, J=21.9 Hz), 115.76 (d, J=21.2 Hz), 21.61. Anal. Calcd for $C_{21}H_{16}F_2O_2S$: C, 68.09; H, 4.35. Found: C, 68.40; H, 4.68. Single-crystal X-ray diagram: crystal of **4b** was grown by slow diffusion of EtOAc into a solution of **4b** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the orthorhombic crystal system, space group $Pca21$, a=12.984(2) Å, b=8.6056(13) Å, c=15.989(3) Å, V=1786.5(5) Å^3, Z=4, d_{calcd}=1.377 g/cm^3, $F(000)$=768, 2θ range 2.55–26.39°, R indices (all data) $R1$=0.0577, $wR2$=0.1303.

*4.2.3. Compound (**4c**).* Yield=70% (276 mg); colorless solid; mp=73–75 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3034, 2953, 1611, 1388, 1139, 891; 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 7.89 (s, 1H), 7.54 (d, J=8.4 Hz, 2H), 7.20 (d, J=8.4 Hz, 2H), 7.17 (d, J=8.0 Hz, 1H), 7.11 (d, J=8.0 Hz, 1H), 6.89 (ddd, J=1.2, 2.4, 8.4 Hz, 1H), 6.90 (ddd, J=1.2, 2.4, 8.4 Hz, 1H), 6.78–6.76 (m, 1H), 6.59–6.56 (m, 3H), 3.65 (s, 3H), 3.47 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.69, 159.14, 144.06, 141.33, 137.05, 135.60, 133.86, 132.56, 129.76, 129.35, 129.27 (2×), 128.60 (2×), 123.57, 122.98, 116.78, 115.38, 115.30, 114.10, 55.12, 54.71, 21.47. Anal. Calcd for $C_{23}H_{22}O_4S$: C, 70.03; H, 5.62. Found: C, 70.30; H, 5.86.

*4.2.4. Compound (**4d**).*[15f] Yield=72% (284 mg); colorless solid; mp=125–126 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3055, 2948, 1602, 1377, 1141, 901; HRMS (ESI, M^++1) calcd for $C_{23}H_{23}O_4S$ 395.1317, found 395.1320; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (s, 1H), 7.50 (d, J=8.4 Hz, 2H), 7.18 (d, J=8.4 Hz, 2H), 7.04 (d, J=9.2 Hz, 2H), 6.95 (d, J=8.8 Hz, 2H), 6.82 (d, J=8.8 Hz, 2H), 6.70 (d, J=9.2 Hz, 2H), 3.82 (s, 3H), 3.75 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.89, 160.07, 143.71, 138.49, 137.04, 136.27, 132.22 (2×), 132.19 (2×), 129.26 (2×), 128.48 (2×), 125.64, 123.51, 114.36 (2×), 113.92 (2×), 55.23, 55.19, 21.55. Anal. Calcd for $C_{23}H_{22}O_4S$: C, 70.03; H, 5.62. Found: C, 70.25; H, 5.81. Single-crystal X-ray diagram: crystal of **4d** was grown by slow diffusion of EtOAc into a solution of **4d** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group $P121/c1$, a=14.6251(10) Å, b=5.8398(4) Å, c=24.7403(17) Å, V=2026.9(2) Å^3, Z=4, d_{calcd}=1.293 g/cm^3, $F(000)$=832, 2θ range 1.72–26.38°, R indices (all data) $R1$=0.0948, $wR2$=0.2201.

*4.2.5. Compound (**4e**).* Yield=70% (281 mg); colorless solid; mp >250 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3051, 2955, 1607, 1362, 1142, 909; HRMS (ESI, M^++1) calcd for $C_{21}H_{17}Cl_2O_2S$ 403.0326, found 403.0325; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (s, 1H), 7.49 (d, J=8.4 Hz, 2H), 7.28 (d, J=8.4 Hz, 2H), 7.21 (d, J=8.0 Hz, 2H), 7.17 (d, J=8.4 Hz, 2H), 7.01–6.96 (m, 4H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.47, 141.08, 136.38, 136.23, 135.30, 132.00 (2×), 131.56 (2×), 131.03, 129.55 (2×), 129.31 (2×), 128.90 (2×), 128.60 (2×), 128.52, 128.31, 21.61. Anal. Calcd for $C_{21}H_{16}Cl_2O_2S$: C, 62.54; H, 4.00. Found: C, 62.30; H, 4.29. Single-crystal X-ray diagram: crystal of **4e** was grown by slow diffusion of EtOAc into a solution of **4e** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group $P121/c1$, a=13.599(6) Å, b=5.740(3) Å, c=25.291(14) Å, V=1902.3(17) Å^3, Z=4, d_{calcd}=1.408 g/cm^3, $F(000)$=832, 2θ range 1.55–26.49°, R indices (all data) $R1$=0.0898, $wR2$=0.2142.

*4.2.6. Compound (**4f**).* Yield=73% (270 mg); colorless solid; mp=226–228 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3044, 2958, 1618, 1426, 1338, 1160, 922; HRMS (ESI, M^++1) calcd for $C_{21}H_{17}F_2O_2S$ 371.0917, found 371.0923; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (s, 1H), 7.49 (d, J=8.0 Hz, 2H), 7.20 (d, J=8.0 Hz, 2H), 7.07–7.00 (m, 6H), 6.90–6.56 (m, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.46 (d, J=250.9 Hz), 163.23 (d, J=247.9 Hz), 144.33, 136.42, 132.71 (d, J=8.3 Hz, 2×), 132.43 (d, J=8.4 Hz, 2×), 128.87 (d, J=3.0 Hz), 127.03 (d, J=3.8 Hz), 123.53, 123.37, 129.47 (2×), 128.58 (2×), 116.23 (d, J=21.2 Hz, 2×), 115.77 (d, J=21.2 Hz, 2×), 21.60. Anal. Calcd for $C_{21}H_{16}F_2O_2S$: C, 68.09; H, 4.35. Found: C, 68.20; H, 4.13. Single-crystal X-ray diagram: crystal of **4f** was grown by slow diffusion of EtOAc into a solution of **4f** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group $P121/n1$, a=12.3430(9) Å, b=5.7877(4) Å, c=25.3347(17) Å, V=1767.4(2) Å^3, Z=4, d_{calcd}=1.392 g/cm^3, $F(000)$=768, 2θ range 1.65–26.50°, R indices (all data) $R1$=0.0765, $wR2$=0.1066.

*4.2.7. Compound (**4g**).* Yield=85% (219 mg); colorless solid; mp=117–119 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3018, 2943, 1608, 1422, 1319, 1144, 917; HRMS (ESI, M^++1) calcd for $C_{15}H_{15}O_2S$ 259.0793, found 259.0780; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (s, 1H), 7.50–7.46 (m, 5H), 7.28–7.24 (m, 1H), 7.20–7.16 (m, 2H), 7.09–7.07 (m, 2H), 2.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 140.30, 137.82, 132.40, 131.37, 130.47 (2×),

130.34 (2×), 129.98, 129.55, 129.37 (2×), 128.41 (2×), 39.78. Anal. Calcd for $C_{15}H_{14}O_2S$: C, 69.74; H, 5.46. Found: C, 69.98; H, 5.38.

*4.2.8. Compound (**4h**).* Yield=80% (240 mg); colorless gum; IR ($CHCl_3$): 3019, 2932, 1611, 1429, 1320, 1149, 918; HRMS (ESI, M^++1) calcd for $C_{18}H_{21}O_2S$ 301.1262, found 301.1266; ^1H NMR (400 MHz, $CDCl_3$): δ 7.78 (s, 1H), 7.47–7.43 (m, 5H), 7.27–7.24 (m, 1H), 7.20–7.16 (m, 2H), 7.09–7.07 (m, 2H), 2.84–2.80 (m, 2H), 1.79–1.71 (m, 2H), 1.42–1.32 (m, 2H), 0.88 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.90, 138.85, 132.59, 131.46, 130.48 (2×), 130.27 (2×), 129.92, 129.49, 129.30 (2×), 128.40 (2×), 50.66, 24.18, 21.41, 13.43.

*4.2.9. Compound (**4i**).* Yield=72% (304 mg); colorless solid; mp=195–197 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3049, 2952, 1610, 1360, 1148, 909; HRMS (ESI, M^++1) calcd for $C_{23}H_{19}O_6S$ 423.0902, found 423.0912; ^1H NMR (400 MHz, $CDCl_3$): δ 7.81 (s, 1H), 7.52 (d, J=8.8 Hz, 2H), 7.20 (d, J=8.4 Hz, 2H), 6.83 (dd, J=1.6, 8.4 Hz, 1H), 6.72 (s, 1H), 6.70 (s, 1H), 6.57 (d, J=1.6 Hz, 1H), 6.44 (d, J=1.6 Hz, 1H), 6.41 (dd, J=1.6, 8.0 Hz, 1H), 6.00 (s, 2H), 5.91 (s, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 149.23, 148.39, 148.05, 147.68, 143.96, 138.81, 137.33, 136.01, 129.36 (2×), 128.52 (2×), 127.23, 127.04, 124.80, 124.45, 111.00, 109.03, 108.85, 108.38, 101.42, 101.36, 21.60. Anal. Calcd for $C_{23}H_{18}O_6S$: C, 65.39; H, 4.29. Found: C, 65.58; H, 4.41.

*4.2.10. Compound (**4j**).* Yield=70% (318 mg); colorless solid; mp=144–146 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3052, 2958, 1610, 1365, 1145, 910; HRMS (ESI, M^++1) calcd for $C_{25}H_{27}O_6S$ 455.1528, found 455.1533; ^1H NMR (400 MHz, $CDCl_3$): δ 7.81 (s, 1H), 7.56 (d, J=8.0 Hz, 2H), 7.20 (d, J=8.0 Hz, 2H), 6.42 (t, J=2.0 Hz, 1H), 6.35 (t, J=2.0 Hz, 1H), 6.31 (d, J=2.0 Hz, 2H), 6.14 (d, J=2.0 Hz, 2H), 3.60 (s, 6H), 3.52 (s, 6H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.81 (2×), 160.27 (2×), 144.07, 141.52, 137.04, 135.58, 134.19, 133.08, 129.21 (2×), 128.66 (2×), 108.22 (2×), 108.06 (2×), 102.99, 101.66, 55.23 (2×), 55.93 (2×), 21.42. Anal. Calcd for $C_{25}H_{26}O_6S$: C, 66.06; H, 5.77. Found: C, 66.19; H, 6.02.

*4.2.11. Compound (**4k**).* Yield=78% (379 mg); colorless solid; mp=172–173 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3013, 2934, 1605, 1420, 1325, 1150, 913; HRMS (ESI, M^++1) calcd for $C_{33}H_{27}O_2S$ 487.1732, found 487.1733; ^1H NMR (400 MHz, $CDCl_3$): δ 8.04 (s, 1H), 7.65 (d, J=8.0 Hz, 2H), 7.59 (d, J=8.0 Hz, 2H), 7.58 (d, J=8.0 Hz, 2H), 7.54–7.32 (m, 9H), 7.22 (d, J=8.4 Hz, 4H), 7.17 (d, J=8.0 Hz, 2H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.08, 142.59, 141.64, 141.03, 139.94, 139.77, 137.01, 135.83, 131.77, 131.15 (2×), 131.00 (2×), 130.36, 129.38 (2×), 128.84 (2×), 128.79 (2×), 128.61 (2×), 127.82, 127.76, 127.37 (2×), 127.03 (2×), 126.96 (2×), 126.89 (2×), 21.57. Anal. Calcd for $C_{33}H_{26}O_2S$: C, 81.45; H, 5.39. Found: C, 81.60; H, 5.37.

*4.2.12. Compound (**4l**).* Yield=81% (352 mg); colorless solid; mp=211–213 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3022, 2937, 1617, 1424, 1330, 1149, 917; HRMS (ESI, M^++1) calcd for $C_{29}H_{23}O_2S$ 435.1419, found 435.1422; ^1H NMR (400 MHz, $CDCl_3$): δ 9.04 (s, 1H), 8.32 (d, J=8.4 Hz, 1H), 7.81 (d, J=8.4 Hz, 1H), 7.78 (d, J=8.0 Hz, 1H), 7.73 (d, J=8.0 Hz, 1H), 7.66 (d, J=8.0 Hz, 1H), 7.61 (d, J=8.4 Hz, 1H), 7.55–7.52 (m, 2H), 7.50 (d, J=8.4 Hz, 2H), 7.35–7.29 (m, 2H), 7.19 (d, J=7.6 Hz, 1H), 7.13 (d, J=7.6 Hz, 1H), 7.09 (d, J=8.0 Hz, 2H), 6.95–6.87 (m, 2H), 2.32 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.17, 141.80, 136.74, 135.38, 133.32, 133.29, 131.91, 131.86, 130.00, 129.92, 129.65, 129.34, 129.30 (2×), 128.87 (2×), 128.79, 128.33, 128.08, 126.98, 126.73, 126.42, 126.11, 125.88, 125.14, 124.92, 124.86, 123.35, 21.49. Anal. Calcd for $C_{29}H_{22}O_2S$: C, 80.15; H, 5.10. Found: C, 80.29; H, 5.31. Single-crystal X-ray diagram: crystal of **4l** was grown by slow diffusion of EtOAc into a solution of **4l** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group $P121/n1$, a=13.4592(15) Å, b=8.2686(9) Å, c=19.771(2) Å, V=2172.3(4) Å^3, Z=4, d_{calcd}=1.329 g/cm^3, $F(000)$=912, 2θ range 1.71–26.66°, R indices (all data) $R1$=0.1137, $wR2$=0.2331.

*4.2.13. Compound (**4m**).* Yield=78% (339 mg); colorless solid; mp=212–214 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3023, 2937, 1617, 1422, 1330, 1149, 916; HRMS (ESI, M^++1) calcd for $C_{29}H_{23}O_2S$ 435.1419, found 435.1422; ^1H NMR (400 MHz, $CDCl_3$): δ 8.23 (s, 1H), 7.86 (d, J=8.0 Hz, 1H), 7.78–7.73 (m, 4H), 7.67–7.63 (m, 2H), 7.57–7.49 (m, 4H), 7.45–7.39 (m, 3H), 7.16 (d, J=8.0 Hz, 2H), 7.11 (dd, J=1.6, 8.8 Hz, 1H), 6.96 (dd, J=1.6, 8.8 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.05, 141.46, 137.69, 135.88, 133.63, 133.20, 132.84, 132.24, 130.64, 130.46, 129.36 (2×), 128.80, 128.59 (2×), 128.51 (2×), 128.40, 127.99, 127.97 (2×), 127.72, 127.48, 127.39, 126.95, 126.46, 126.34, 125.94, 21.52. Anal. Calcd for $C_{29}H_{22}O_2S$: C, 80.15; H, 5.10. Found: C, 80.37; H, 5.23.

*4.2.14. Compound (**4n**).* Yield=62% (215 mg); brown viscous gum; IR ($CHCl_3$): 3034, 2942, 1617, 1433, 1342, 1161, 950; HRMS (ESI, M^++1) calcd for $C_{17}H_{15}O_2S_3$ 347.0234, found 347.0233; ^1H NMR (400 MHz, $CDCl_3$): δ 8.24 (s, 1H), 7.58 (d, J=8.4 Hz, 2H), 7.51 (dd, J=1.2, 4.8 Hz, 1H), 7.33 (dt, J=1.2, 5.2 Hz, 1H), 7.30 (dt, J=1.2, 5.2 Hz, 1H), 7.23 (d, J=8.4 Hz, 2H), 7.06 (dd, J=3.2, 4.8 Hz, 1H), 7.00 (dd, J=3.6, 4.8 Hz, 1H), 6.80 (dd, J=1.2, 3.6 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.20, 136.31, 135.45, 134.87, 134.19, 131.95, 131.54, 131.35, 130.09, 129.57, 129.40 (2×), 128.55 (2×), 127.71, 126.98, 21.60.

*4.2.15. Compound (**4o**).* Yield=57% (192 mg); colorless solid; mp=138–140 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3044, 2937, 1635, 1439, 1342, 1152, 941; HRMS (ESI, M^++1) calcd for $C_{19}H_{17}N_2O_2S$ 337.1011, found 337.1018; ^1H NMR (400 MHz, $CDCl_3$): δ 8.60 (dd, J=1.6, 5.2 Hz, 1H), 8.46 (dd, J=1.6, 4.8 Hz, 1H), 8.41 (d, J=2.0 Hz, 1H), 8.02 (s, 2H), 7.61 (dt, J=2.0, 8.0 Hz, 1H), 7.47 (d, J=8.4 Hz, 2H), 7.32 (ddd, J=0.8, 4.8, 8.0 Hz, 1H), 7.21–7.18 (m, 3H), 7.07 (dd, J=4.8, 8.4 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 151.51, 150.80, 150.49, 150.44, 144.97, 140.88, 138.27, 136.22, 135.14, 134.54, 129.74 (2×), 128.52 (2×), 128.35, 127.27, 123.67, 123.30, 21.57.

*4.2.16. Compound (**4p**).* Yield=82% (262 mg); colorless solid; mp=176–178 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3015, 2938, 1606, 1418, 1322, 1149, 913; HRMS (ESI, M^++1) calcd for $C_{20}H_{17}O_2S$ 321.0949, found 321.0952; ^1H NMR (400 MHz, $CDCl_3$): δ 7.98 (s, 1H), 7.64–7.62 (m, 2H), 7.55–7.51 (m, 1H), 7.40 (d, J=8.0 Hz, 2H), 7.38–7.34 (m, 1H), 7.30–7.23 (m, 3H), 7.18–7.15 (m, 2H), 7.09–7.06 (m, 2H), 7.04–7.02 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.28, 138.64, 137.57, 133.13, 132.72, 131.21, 130.70, 130.49 (2×), 130.02, 130.02, 129.13, 128.79 (2×), 128.64 (2×), 128.58 (2×), 128.44 (2×). Anal. Calcd for $C_{20}H_{16}O_2S$: C, 74.97; H, 5.03. Found: C, 75.30; H, 5.27.

*4.2.17. Compound (**4q**).* Yield=88% (308 mg); colorless solid; mp=157–159 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3038, 2958, 1619, 1384, 1142, 902; HRMS (ESI, M^++1) calcd for $C_{21}H_{19}O_3S$ 351.1055, found 351.1062; ^1H NMR (400 MHz, $CDCl_3$): δ 7.93 (s, 1H), 7.53 (d, J=9.2 Hz, 2H), 7.37–7.33 (m, 1H), 7.30–7.26 (m, 2H), 7.23–7.19 (m, 1H), 7.15–7.11 (m, 2H), 7.06–7.03 (m, 4H), 6.84 (d, J=9.2 Hz, 2H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 163.19, 141.63, 136.55, 132.65, 131.27, 130.55 (2×), 130.51 (2×), 130.24 (2×), 129.87, 129.72, 128.93, 128.62 (2×), 128.26 (2×), 113.76 (2×), 55.40. Anal. Calcd for $C_{21}H_{18}O_3S$: C, 71.98; H, 5.18. Found: C, 72.20; H, 5.33.

*4.2.18. Compound (**4r**).* Yield=83% (281 mg); colorless solid; mp=162–164 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3034, 2959, 1620, 1431, 1325, 1150, 911; HRMS (ESI, M^++1)

calcd for $C_{20}H_{16}FO_2S$ 339.0855, found 339.0853; ^1H NMR (400 MHz, $CDCl_3$): δ 7.97 (s, 1H), 7.65–7.60 (m, 2H), 7.40–7.36 (m, 1H), 7.33–7.22 (m, 3H), 7.17–7.14 (m, 2H), 7.09–7.02 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.34 (d, J=254.7 Hz), 140.97, 137.56, 134.58 (d, J=3.0 Hz), 132.48, 131.28 (d, J=9.8 Hz, 2×), 130.99, 130.62 (2×), 130.44 (2×), 130.08, 129.21, 128.84 (2×), 128.41 (2×), 115.88 (d, J=22.7 Hz, 2×). Anal. Calcd for $C_{20}H_{15}FO_2S$: C, 70.99; H, 4.47. Found: C, 71.18; H, 4.63.

*4.2.19. Compound (**4s**).* Yield=80% (267 mg); colorless solid; mp=130–132 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3013, 2935, 1602, 1416, 1320, 1148, 912; HRMS (ESI, M^++1) calcd for $C_{21}H_{19}O_2S$ 335.1106, found 335.1110; ^1H NMR (400 MHz, $CDCl_3$): δ 7.96 (s, 1H), 7.43–7.22 (m, 8H), 7.18–7.14 (m, 2H), 7.10–7.07 (m, 2H), 7.05–7.02 (m, 2H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.31, 138.80, 138.33, 137.32, 133.90, 132.71, 131.23, 130.66 (2×), 130.43 (2×), 129.94, 129.06, 128.82, 128.70 (2×), 128.45, 128.39 (2×), 125.70, 21.07. Anal. Calcd for $C_{21}H_{18}O_2S$: C, 75.42; H, 5.42. Found: C, 75.71; H, 5.71.

*4.2.20. Compound (**4t**).* Yield=86% (299 mg); colorless solid; mp=131–133 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3013, 2935, 1604, 1417, 1320, 1148, 912; HRMS (ESI, M^++1) calcd for $C_{22}H_{21}O_2S$ 349.1262, found 349.1267; ^1H NMR (400 MHz, $CDCl_3$): δ 7.95 (s, 1H), 7.52 (d, J=8.4 Hz, 2H), 7.39–7.14 (m, 8H), 7.08–7.09 (m, 4H), 2.68 (q, J=7.6 Hz, 2H), 1.22 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 150.22, 141.58, 137.23, 135.88, 132.86, 131.40, 130.74 (2×), 130.48 (2×), 129.92, 129.07, 128.77 (2×), 128.74 (2×), 128.43 (2×), 128.15 (2×), 28.80, 15.05. Anal. Calcd for $C_{22}H_{20}O_2S$: C, 75.83; H, 5.79. Found: C, 76.08; H, 5.88.

*4.2.21. Compound (**4u**).* Yield=82% (297 mg); colorless solid; mp=120–122 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3013, 2934, 1602, 1416, 1321, 1149, 912; HRMS (ESI, M^++1) calcd for $C_{23}H_{23}O_2S$ 363.1419, found 363.1425; ^1H NMR (400 MHz, $CDCl_3$): δ 7.95 (s, 1H), 7.54 (d, J=8.4 Hz, 2H), 7.38–7.34 (m, 1H), 7.30–7.21 (m, 5H), 7.17–7.13 (m, 2H), 7.08–7.02 (m, 4H), 2.96–2.89 (m, 1H), 1.22 (d, J=6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.73, 141.55, 137.12, 135.88, 132.75, 131.31, 130.62 (2×), 130.37 (2×), 129.84, 129.00, 128.67 (4×), 128.35 (2×), 126.69 (2×), 34.03, 23.50 (2×). Anal. Calcd for $C_{23}H_{22}O_2S$: C, 76.21; H, 6.12. Found: C, 76.40; H, 6.27.

*4.2.22. Compound (**4v**).* Yield=80% (301 mg); colorless solid; mp=99–100 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3015, 2935, 1602, 1417, 1320, 1150, 913; HRMS (ESI, M^++1) calcd for $C_{24}H_{25}O_2S$ 377.1575, found 377.1576; ^1H NMR (400 MHz, $CDCl_3$): δ 7.94 (s, 1H), 7.51 (d, J=8.4 Hz, 2H), 7.38–7.34 (m, 1H), 7.29–7.14 (m, 7H), 7.08–7.05 (m, 2H), 7.03–7.01 (m, 2H), 2.63 (t, J=7.2 Hz, 2H), 1.61–1.53 (m, 2H), 1.39–1.26 (m, 2H), 0.91 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.96, 141.60, 137.12, 135.77, 132.85, 131.40, 130.73 (2×), 130.48 (2×), 129.92, 129.05, 128.74 (2×), 128.70 (2×), 128.67 (2×), 128.43 (2×), 35.50, 33.05, 22.10, 13.82.

*4.2.23. Compound (**4w**).* Yield=82% (308 mg); colorless solid; mp=117–119 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3015, 2935, 1605, 1416, 1320, 1150, 912; HRMS (ESI, M^++1) calcd for $C_{24}H_{25}O_2S$ 377.1575, found 377.1581; ^1H NMR (400 MHz, $CDCl_3$): δ 7.95 (s, 1H), 7.54 (d, J=8.4 Hz, 2H), 7.40 (d, J=8.8 Hz, 2H), 7.37–7.34 (m, 1H), 7.31–7.22 (m, 3H), 7.18–7.14 (m, 2H), 7.08–7.02 (m, 4H), 1.30 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 157.08, 141.58, 137.24, 135.59, 132.83, 131.37, 130.70 (2×), 130.45 (2×), 129.90, 129.05, 128.72 (2×), 128.45 (2×), 128.41 (2×), 125.64 (2×), 35.11, 31.00 (3×). Anal. Calcd for $C_{24}H_{24}O_2S$: C, 76.56; H, 6.42. Found: C, 76.80; H, 6.53.

*4.2.24. Compound (**4x**).* Yield=62% (239 mg); yellow viscous gum; IR ($CHCl_3$): 3582, 2938, 1598, 1401, 1302, 1144, 931; HRMS (ESI, M^++1) calcd for $C_{25}H_{23}O_2S$ 387.1419, found 387.1423; ^1H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, J=8.0 Hz, 2H), 7.58 (d, J=6.8 Hz, 1H), 7.50–7.28 (m, 12H), 7.16 (d, J=6.8 Hz, 1H), 7.10 (d, J=15.6 Hz, 1H), 7.06 (d, J=16.4 Hz, 1H), 6.89 (d, J=16.4 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 143.98, 142.78, 137.93, 137.52, 137.47, 137.11, 136.34, 135.88, 129.68 (2×), 129.44, 128.87 (2×), 128.73 (3×), 127.74 (2×), 127.42 (2×), 126.86 (2×), 122.18, 117.37, 21.53.

*4.2.25. Compound (**4y**).* Yield=60% (268 mg); yellowish viscous gum; IR ($CHCl_3$): 3586, 2942, 1602, 1401, 1312, 1147, 928; HRMS (ESI, M^++1) calcd for $C_{27}H_{27}O_4S$ 447.1630, found 447.1633; ^1H NMR (400 MHz, $CDCl_3$): δ 7.77 (d, J=8.4 Hz, 2H), 7.50 (dd, J=4.4, 6.8 Hz, 1H), 7.43 (d, J=8.8 Hz, 2H), 7.36 (d, J=8.4 Hz, 2H), 7.27 (d, J=8.0 Hz, 2H), 7.03–7.00 (m, 3H), 6.89 (d, J=8.8 Hz, 2H), 6.88 (d, J=9.2 Hz, 2H), 6.73 (d, J=16.4 Hz, 1H), 3.83 (s, 3H), 3.82 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.69, 160.08, 143.77, 142.15, 137.86, 137.33, 136.76, 136.16, 129.62 (2×), 128.94 (2×), 128.86, 128.18 (2×), 127.67 (2×), 127.03, 120.24, 115.33, 114.35 (2×), 114.17 (2×), 55.35 (2×), 21.54.

*4.2.26. Compound (**4z**).* Colorless solid; mp=112–114 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3048, 2959, 1611, 1365, 1142, 915; HRMS (ESI, M^++1) calcd for $C_{27}H_{22}ClO_2S$ 445.1029, found 445.1033; ^1H NMR (400 MHz, $CDCl_3$): δ 8.01 (s, 1H), 7.65–7.30 (m, 11H), 7.21 (d, J=8.4 Hz, 2H), 7.20 (d, J=8.4 Hz, 2H), 7.14 (d, J=8.4 Hz, 2H), 2.39 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.12, 142.65, 141.68, 141.05, 140.02, 139.85, 137.06, 135.87, 131.20, 131.04, 129.42 (2×), 128.89 (2×), 128.83 (2×), 128.67 (2×), 127.42 (2×), 127.09 (2×), 127.02 (2×), 126.95 (2×), 21.61.

*4.2.27. Compound (**4aa**).* Colorless solid; mp=130–132 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3048, 2959, 1611, 1365, 1142, 915; HRMS (ESI, M^++1) calcd for $C_{27}H_{22}ClO_2S$ 445.1029, found 445.1032; ^1H NMR (400 MHz, $CDCl_3$): δ 7.98 (s, 1H), 7.52–7.50 (m, 4H), 7.44–7.27 (m, 9H), 7.20 (d, J=8.4 Hz, 2H), 7.01 (d, J=8.4 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.31, 142.82, 140.11, 139.70, 137.42, 135.57, 135.44, 132.17 (2×), 131.43, 130.96 (2×), 129.99, 129.49 (2×), 129.24 (2×), 128.85 (2×), 128.55 (2×), 127.93, 127.13 (2×), 126.92 (2×), 21.60.

*4.2.28. Compound (**5**).* Brown solid; mp=192–194 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3547, 3052, 2946, 2847, 1624, 1435, 1366, 1169, 915, 875; HRMS (ESI, M^++1) calcd for $C_{30}H_{20}N_3$ 422.1657, found 422.1658; ^1H NMR (400 MHz, $CDCl_3$): δ 8.21 (d, J=8.4 Hz, 1H), 8.16 (dd, J=0.4, 8.4 Hz, 1H), 7.94 (dd, J=1.2, 8.4 Hz, 1H), 7.83 (d, J=8.4 Hz, 1H), 7.80–7.76 (m, 2H), 7.67–7.55 (m, 5H), 7.44 (d, J=9.2 Hz, 1H), 7.40 (dt, J=0.8, 6.8 Hz, 1H), 7.28 (d, J=8.4 Hz, 1H), 7.25 (br s, 1H), 7.19 (dt, J=1.6, 6.8 Hz, 1H), 7.09 (d, J=9.2 Hz, 1H), 6.97–6.90 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.75, 154.51, 148.21, 148.07, 136.38, 135.39, 134.29, 132.76, 129.82, 129.78, 129.58, 129.26, 129.12, 128.63, 127.68, 127.33, 127.23, 127.07, 127.00, 126.79, 126.49, 125.69 (2×), 125.29, 123.63, 121.54, 120.69, 119.15, 117.48, 104.26. Anal. Calcd for $C_{30}H_{19}N_3$: C, 85.49; H, 4.54. Found: C, 85.65; H, 4.73. Single-crystal X-ray diagram: crystal of compound **5** was grown by slow diffusion of EtOAc into a solution of compound **5** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group $P121/c1$, a=15.0399(13) Å, b=6.2472(6) Å, c=22.3520(19) Å, V=2097.3(3) Å^3, Z=4, d_{calcd}=1.335 g/cm^3, $F(000)$=880, 2θ range 1.82–26.51°, R indices (all data) $R1$=0.1152, $wR2$=0.1350.

4.3. A representative synthetic procedure of compounds 6a,b

A representative synthetic procedure of compounds **6a**,**b** is as follows: compound **4a** or **4p** (0.2 mmol) and I_2 (100 mg, 0.4 mmol)

were dissolved in EtOAc (15 mL) at rt. Then, 1,2-epoxybutane (440 mg, 6.0 mmol) was added to the reaction mixture and irradiated under a nitrogen atmosphere with a lamp (λ=2540 Å), using a Pyrex glass filter at rt for 80 h. The solvent was evaporated to afford crude product. Purification on silica gel (hexanes/EtOAc=8:1 to 2:1) afforded compounds **6a**,**b**.

*4.3.1. Compound (**6a**).* Yield=72% (48 mg); colorless solid; mp=170–171 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3533, 3023, 2946, 1614, 1427, 1320, 1142, 923; HRMS (ESI, M^++1) calcd for $C_{21}H_{17}O_2S$ 333.0949, found 333.0952; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.90 (s, 1H), 8.71–8.64 (m, 3H), 8.09 (dd, J=2.4, 8.0 Hz, 1H), 7.88 (d, J=8.4 Hz, 2H), 7.83 (dt, J=1.6, 8.4 Hz, 1H), 7.71 (dt, J=0.8, 8.0 Hz, 1H), 7.66 (dt, J=1.6, 8.0 Hz, 1H), 7.60 (dt, J=1.6, 8.4 Hz, 1H), 7.25 (d, J=8.4 Hz, 2H), 2.35 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.02, 138.62, 134.57, 132.70, 131.25, 130.74, 129.99, 129.75 (3×), 129.35, 127.62 (2×), 127.46 (3×), 126.00, 125.45, 123.27, 122.74, 21.51. Anal. Calcd for $C_{21}H_{16}O_2S$: C, 75.88; H, 4.85. Found: C, 76.03; H, 4.98. Single-crystal X-ray diagram: crystal of **6a** was grown by slow diffusion of EtOAc into a solution of **6a** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the triclinic crystal system, space group P-1, a=8.9084(9) Å, b=9.2635(9) Å, c=10.4687(9) Å, V=783.84(13) Å^3, Z=2, d_{calcd}=1.408 g/cm^3, F(000)=348, 2θ range 2.07–26.39°, R indices (all data) $R1$=0.0533, $wR2$=0.1554.

*4.3.2. Compound (**6b**).* Yield=70% (45 mg); colorless solid; mp=159–161 °C (recrystallized from hexanes and EtOAc); IR ($CHCl_3$): 3533, 3023, 2946, 1615, 1427, 1323, 1142, 922; HRMS (ESI, M^++1) calcd for $C_{20}H_{15}O_2S$ 319.0793, found 319.0785; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.92 (s, 1H), 8.71 (dd, J=0.8, 8.8 Hz, 1H), 8.69 (d, J=8.4 Hz, 1H), 8.63 (dd, J=0.8, 8.4 Hz, 1H), 8.11 (dd, J=0.8, 8.4 Hz, 1H), 8.02–7.99 (m, 2H), 7.83 (dt, J=1.6, 8.4 Hz, 1H), 7.74–7.58 (m, 3H), 7.55–7.44 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.62, 134.21, 133.67, 133.09, 132.79, 131.28, 130.80, 130.12, 129.14 (2×), 128.63, 127.69 (2×), 127.54, 127.37 (2×), 125.99, 125.42, 123.32, 122.78. Anal. Calcd for $C_{20}H_{14}O_2S$: C, 75.45; H, 4.43. Found: C, 75.62; H, 4.70.

4.4. A representative synthetic procedure of compounds 7a–c

A representative synthetic procedure of compounds **7a**–**c** is as follows: *t*-BuOK (224 mg, 2.0 mmol) was added to a stirred solution of compounds **4a**, **4d**,**e** (0.5 mmol) in THF (15 mL) at rt. The reaction mixture was stirred at reflux for 1 h. The reaction mixture was cooled to rt, concentrated, and extracted with CH_2Cl_2 (3×30 mL). The combined organic layers were washed with brine, dried, filtered, and evaporated to afford crude products under reduced pressure. Purification on silica gel (hexanes/EtOAc=100:1 to 50:1) afforded compounds **7a**–**c**.

*4.4.1. Compound (**7a**).*[21] Yield=75% (67 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.54–7.50 (m, 4H), 7.32–7.28 (m, 6H).

*4.4.2. Compound (**7b**).*[22] Yield=66% (79 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, J=8.8 Hz, 4H), 6.85 (d, J=8.8 Hz, 4H), 3.78 (s, 6H).

*4.4.3. Compound (**7c**).*[23] Yield=70% (86 mg); colorless solid; mp=175–177 °C (recrystallized from hexanes and EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (d, J=8.4 Hz, 4H), 7.33 (d, J=8.4 Hz, 4H). Single-crystal X-ray diagram: crystal of **7c** was grown by slow diffusion of EtOAc into a solution of **7c** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group P121/c1, a=9.9057(9) Å, b=4.8954(5) Å, c=11.1324(11) Å, V=538.53(9) Å^3, Z=2, d_{calcd}=1.524 g/cm^3, F(000)=252, 2θ range 2.06–26.28°, R indices (all data) $R1$=0.0429, $wR2$=0.1089.

Acknowledgements

The authors would like to thank the National Science Council of the Republic of China for its financial support (NSC 102-2113-M-037-005-MY2).

Supplementary data

Scanned photocopies of ^{1}H and ^{13}C NMR 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.2014.01.045.

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