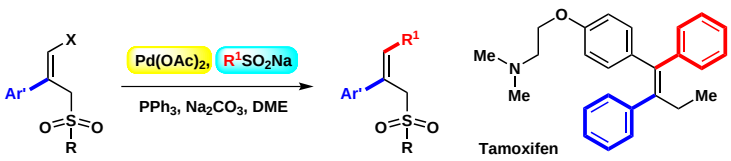
Synthesis M.-Y. Chang et al. Paper

Pd(OAc)$_2$-Catalyzed Desulfinative Cross-Coupling of Sodium Sulfinates with β-Bromostyrenes: Synthesis of Tamoxifen

Meng-Yang Chang[*a]
Yu- Chieh Cheng[a]
Pei- Pei Sun[b]

[a] Department of Medicinal and Applied Chemistry, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung 80708, Taiwan, ROC
mychang@kmu.edu.tw
[b] Department of Seafood Science, National Kaohsiung Marine University, Kaohsiung 81157, Taiwan, ROC



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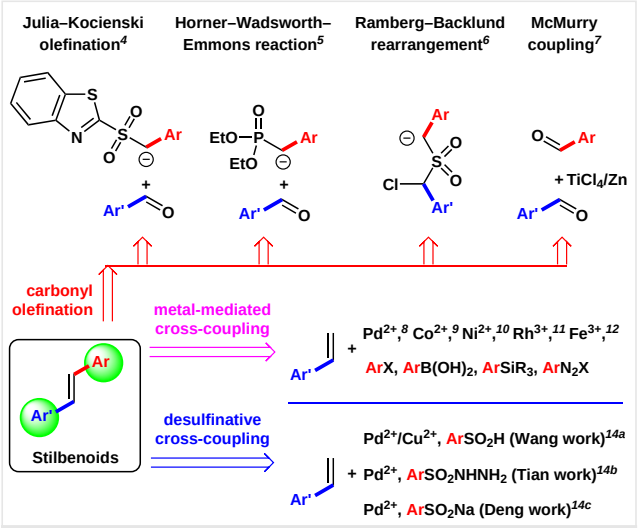
Abstract A Pd(OAc)$_2$-catalyzed desulfinative cross-coupling of (*Z*)-β-halostyrenes with sodium sulfinates in the presence of PPh_3 and Na_2CO_3 at reflux in good yields is reported. The stereocontrolled cross-coupling process provides a series of sulfonylmethyl (*Z*)-stilbenes. A synthesis of tamoxifen was studied.

Key words desulfinative cross coupling, halostyrenes, sodium sulfinates, stilbenes, tamoxifen

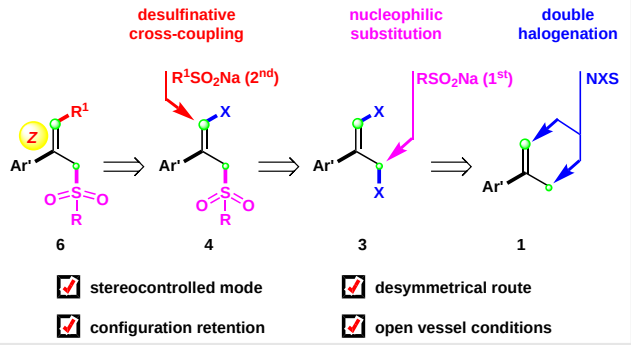
The expeditious, regioselective, and stereocontrolled synthesis of disubstituted olefins, including (*E*)- or (*Z*)-stilbenes, has provided an ongoing challenge for organic chemists.[1] Stilbene and its derivatives are ubiquitous in scientific applications of bioactive molecules[2] and functionalized materials.[3] Stilbenoid molecules can be obtained easily by some synthetic routes, including (i) carbonyl olefination type reactions (e.g., Julia–Kocienski olefination,[4] the Horner–Wadsworth–Emmons reaction,[5] Ramberg–Backlund rearrangement,[6] and McMurry coupling),[7] (ii) transition-metal-promoted (e.g., Pd^{2+},[8] Co^{2+},[9] Ni^{2+},[10] Rh^{3+},[11] and Fe^{3+})[12] cross-coupling of styrene with diversified aryl variants (e.g., aryl halides, arylboronic acids, aryl silanes, aryl diazonium salts), and (iii) photoisomerization.[13] Among these recent transition-metal-mediated syntheses of stilbenoids, the desulfinative cross-coupling strategy takes advantage of the tandem protocol that was established by Wang,[14a] Tian,[14b] and Deng[14c] (Scheme 1). In recent years, the development of palladium complex-mediated desulfinative carbon–carbon bond formation has been investigated via carbon–sulfur bond cleavage.[15] Despite remarkable advances in the types of desulfinative transformations (e.g., carbonylation,[16] conjugated addition,[17] arylation of heterocycles),[18] the continuing investigation for a new alternative route is still important. Sodium sulfinates (RSO_2Na) have been widely used as sulfonylating reagents for the formation of carbon–sulfur and heteroatom–sulfur bonds and have been demonstrated as electrophilic partners in transition-metal-catalyzed desulfinative cross-coupling.[19] Because of their readily availability, inexpensiveness, ease of operation and high air stability, sodium sulfinates are generally used more as arylating surrogates than other sulfonyl synthons, such as sulfonyl chlorides, sulfonyl acids, or sulfonyl hydrazines.[20]



Scheme 1 Synthetic routes of stilbenoids

Our interest in the utilization of facile and cascade protocols for sodium sulfinates-based synthesis of diverse scaffolds led us to explore protocols wherein stilbenoids were combined with a sulfonylmethyl substituent. As part of our efforts in the synthetic chemistry of β-ketosulfone,[21] we streamlined the stereocontrolled synthesis of sulfonyl-

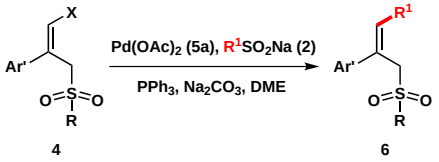
methyl (*Z*)-stilbenes **6** via $Pd(OAc)_2$ (**5a**)-mediated desulfinative cross-coupling of β-halovinyl sulfones **4** with sodium sulfinates (R^1SO_2Na), as shown in Scheme 2. The preparation of a range of β-halovinyl sulfones **4** in 85–90% yields via nucleophilic substitution of 1,3-dihalostyrenes **3** with a 1.1 equivalents of sodium sulfinates **2** (RSO_2Na; R = Tol, Ph, Me, 4-FC_6H_4, 4-$MeOC_6H_4$) in a co-solvent of 1,4-dioxane and H_2O (v/v =1:1) was first carried out. According to the known procedure, synthesis of 1,3-dihalostyrenes **3** (Ar′ = Ph, 4-FC_6H_4, 4-PhC_6H_4, 2-naphthyl; X = Br, Cl) was achieved by NXS-mediated double halogenation of α-methylstyrene (**1**) in the presence of *p*-TsOH in CH_2Cl_2 at reflux.[22] A structural template (such as tryptamines, pyrimidines, or chalcones) with a sulfonylmethyl motif could be found in a large number of biologically active molecules.[23]



Scheme 2 Synthetic analysis of sulfonylmethyl stilbenes

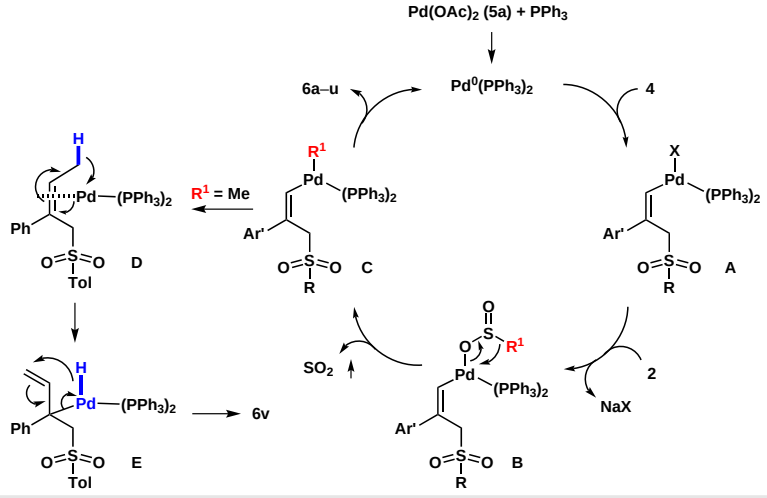
$Pd(OAc)_2$ (**5a**)-promoted desulfinative cross-coupling of model substrate **4a** (Ar′ = Ph, X = Br, R = Tol) with sodium sulfinate **2a** (R^1 = Ph) in 1,2-dimethoxyethane (DME) providing **6a** in 78% yield is shown in Table 1 (entry 1). The reactions were performed under EtOH and MeCN conditions, which gave **6a** in 51% and 30% yield, respectively. Next, some Pd-complexes were studied, such as $Pd(PPh_3)_4$ (**5b**), $Pd(MeCN)Cl_2$ (**5c**), and $PdCl_2$ (**5d**); however, none of these provided higher yields of **4a** than $Pd(OAc)_2$ (52% for **5b**; 42% for **5c**; 38% for **5d**). Changing the base from Na_2CO_3 to Cs_2CO_3 or K_2CO_3 provided 70% and 73% yield, respectively. Furthermore, different phosphine ligands were explored. We found that the use of PCy_3 (an alkyl ligand), dppp (an alkyl-aryl ligand) or BINAP (a bis-binaphthyl-type ligand) was not more effective than the PPh_3 (an aryl ligand) in the resulting transformation (57% for PCy_3; 68% for dppp; 52% for BINAP). Other catalytic amounts (1 and 10 mol%) of $Pd(OAc)_2$ were also examined; however, the isolated yields were similar (70% and 72%). From these observations, we concluded that $Pd(OAc)_2$, Na_2CO_3, and PPh_3 in refluxing DME provided optimal reaction conditions for desulfinative cross-coupling. For the groups of **4a–i** [Ar′ = Ph, 4-FC_6H_4, 4-PhC_6H_4, 2-naphthyl; X = Br, Cl; R = Tol, Ph, Me, 4-FC_6H_4, 4-$MeOC_6H_4$) and **2a–l** (R^1 = Ph, Tol, 4-FC_6H_4, 4-$MeOC_6H_4$, 3-MeC_6H_4, 4-$CF_3C_6H_4$, 4-$CHOC_6H_4$, 4-PhC_6H_4, 2-PhC_6H_4, 3,4-$(MeO)_2C_6H_3$, 3,4,5-$(MeO)_3C_6H_2$, Me], alkyl and aryl substituents (electron-withdrawing, electron-neutral, electron-donating groups) provided the desired products **6a–v** in good yields (67–78%) under the above-mentioned conditions, as shown in entries 1–23. The substituents on the scaffold **2** did not affect the *E*-configured outcome of the desulfinative cross-coupling procedure except that **6v** (R^1 = Me) was obtained as a mixture of stereoisomers (*E*/*Z* = 6:4, entry 22), and no obvious changes in yields were observed for the generation of **6a–v**. Stereocontrolled retention of all products **6a–u** was observed. The structures of **6n** and **6s** were determined by single-crystal X-ray crystallography.[24]

Table 1 Synthesis of **6**[a]



Entry	**4**, Ar′, X, R	**2**, R^1	**6**, (%)[b]
1	**4a**, Ph, Br, Tol	**2a**, Ph	**6a**, 78
2	**4a**, Ph, Br, Tol	**2b**, Tol	**6b**, 75
3	**4a**, Ph, Br, Tol	**2c**, 4-FC_6H_4	**6c**, 72
4	**4a**, Ph, Br, Tol	**2d**, 4-$MeOC_6H_4$	**6d**, 72
5	**4a**, Ph, Br, Tol	**2e**, 3-MeC_6H_4	**6e**, 74
6	**4a**, Ph, Br, Tol	**2f**, 4-$CF_3C_6H_4$	**6f**, 70
7	**4a**, Ph, Br, Tol	**2g**, 4-$CHOC_6H_4$	**6g**, 70
8	**4a**, Ph, Br, Tol	**2h**, 4-PhC_6H_4	**6h**, 74
9	**4a**, Ph, Br, Tol	**2i**, 2-PhC_6H_4	**6i**, 73
10	**4a**, Ph, Br, Tol	**2j**, 3,4-$(MeO)_2C_6H_3$	**6j**, 76
11	**4a**, Ph, Br, Tol	**2k**, 3,4,5-$(MeO)_3C_6H_2$	**6k**, 76
12	**4b**, Ph, Br, Ph	**2a**, Ph	**6l**, 78
13	**4b**, Ph, Br, Ph	**2c**, 4-FC_6H_4	**6m**, 74
14	**4b**, Ph, Br, Ph	**2d**, 4-$MeOC_6H_4$	**6n**, 74
15	**4b**, Ph, Br, Ph	**2h**, 4-PhC_6H_4	**6o**, 75
16	**4c**, Ph, Br, Me	**2a**, Ph	**6p**, 76
17	**4d**, Ph, Br, 4-FC_6H_4	**2a**, Ph	**6q**, 76
18	**4e**, Ph, Br, 4-$MeOC_6H_4$	**2a**, Ph	**6r**, 74
19	**4f**, 4-FC_6H_4, Br, Tol	**2a**, Ph	**6s**, 73
20	**4g**, 4-PhC_6H_4, Br, Tol	**2a**, Ph	**6t**, 73
21	**4h**, 2-naphthyl, Br, Tol	**2a**, Ph	**6u**, 72
22	**4a**, Ph, Br, Tol	**2l**, Me	**6v**, 67[c]
23	**4i**, Ph, Cl, Tol	**2a**, Ph	**6a**, 70

[a] The reactions were run on a 0.5 mmol scale with **4**, $Pd(OAc)_2$ (5 mol%), R^1SO_2Na (1.0 equiv), Na_2CO_3 (2.0 equiv), PPh_3 (1.2 equiv), DME (10 mL) for 5 h at reflux.
[b] Isolated yields.
[c] A mixture of stereoisomers (*E*/*Z* = 6:4) was isolated.

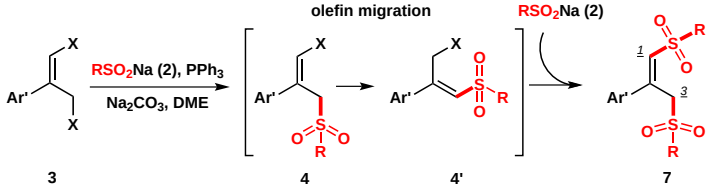


Scheme 3 Plausible mechanism

On the basis of the results, a plausible mechanism with the reasonable explanation is described in Scheme 3. At first, catalyst $Pd^0(PPh_3)_2$, is generated in situ from the reaction of $Pd(OAc)_2$ and phosphine (PPh_3). Initial oxidative addition of the Pd^0 complex into the vinyl–halide bond of **4** followed by a ligand exchange of **A** and **2** from halide to sulfinate produces Pd^{2+} sulfinic intermediate **B**. Next, **B** undergoes desulfination to yield **C** with a four-coordinate Pd^{2+} complex. At least, the catalytic cycle is completed by reductive elimination of **C**, generating the vinyl–aryl bond and $Pd^0(PPh_3)_2$. For the generation of **6v** (R^1 = Me), the possible reason could be that complexation of (*E*)-**6v** with $Pd^0(PPh_3)_2$ produces **D**. After intramolecular hydride shift and carbopalladation of **D**, the transformation from **D** to **E** is accomplished. Subsequently, $Pd^0(PPh_3)_2$ is regenerated and **6v** having two stereoisomers is obtained by the reductive elimination of **E** under the isomerization conditions.

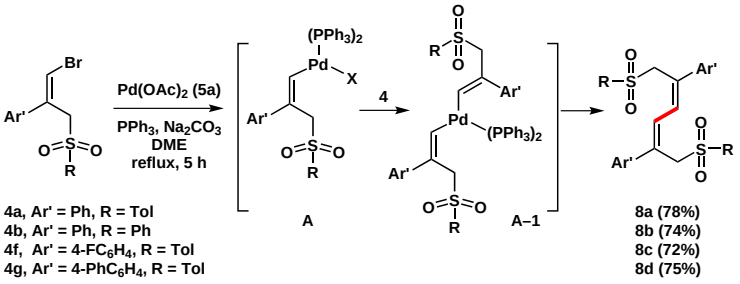
To explore the synthetic applications of the sodium sulfinate-based synthesis of diverse skeletons, the synthesis of β-sulfonyl styrenes was examined next by treatment of 1,3-dihalostyrene **3** with RSO_2Na. The effect of the removal of $Pd(OAc)_2$ (**5a**) on cross-coupling was investigated, as shown in Table 2. By increasing the equivalents of RSO_2Na **2** (R = Tol, Ph, Me, 4-FC_6H_4, 4-$MeOC_6H_4$) from 1.1 to 3.2 equiva-

Table 2 Synthesis of **7**[a]



Entry	**3**, Ar′, X	**2**, R	**7** (%)[b]
1	**3a**, Ph, Br	**2b**, Tol	**7a**, 86
2	**3a**, Ph, Br	**2a**, Ph	**7b**, 81
3	**3a**, Ph, Br	**2l**, Me	**7c**, 80
4	**3a**, Ph, Br	**2c**, 4-FC_6H_4	**7d**, 84
5	**3a**, Ph, Br	**2d**, 4-$MeOC_6H_4$	**7e**, 83
6	**3b**, 4-FC_6H_4, Br	**2b**, Tol	**7f**, 82
7	**3d**, 2-naphthyl, Br	**2b**, Tol	**7g**, 84
8	**3e**, Ph, Cl	**2b**, Tol	**7a**, 80 (86)[c]

[a] The reactions were run on a 0.5 mmol scale with **3**, RSO_2Na (3.2 equiv), Na_2CO_3 (2.0 equiv), PPh_3 (1.2 equiv), DME (10 mL) for 5 h at reflux.
[b] Isolated yields.
[c] Reaction time: 15 h.

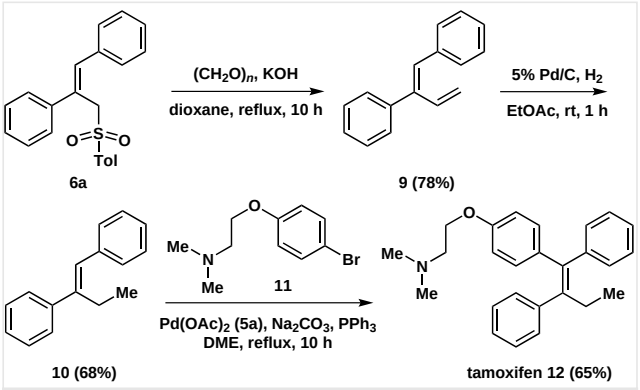


Scheme 4 Synthesis of **8**

lents, 1,3-disulfonylstyrenes **7a–g** were formed in 80–86% yields via double nucleophilic substitution of 1,3-dihalostyrene **3**. With these results in hand, we believe that the reasonable explanation should be that the key olefin migration from **4** to **4′** was first initiated during the non-desulfinative process. Then, another RSO_2Na reacted with the in situ formed **4′** to give **7** via an intermolecular S_N2 reaction. The structures of **7c** and **7g** were determined by single-crystal X-ray crystallography.[24]

In a different approach, the synthetic application of $Pd(OAc)_2$-catalyzed synthesis of symmetrical diaryl 1,3-dienes was demonstrated by the intermolecular cross coupling of β-bromostyenes in the presence of PPh_3 and Na_2CO_3 under the boiling DME conditions. In the absence of RSO_2Na **2**, $Pd(OAc)_2$-promoted self-dimerization of β-bromostyrenes **4** is shown in Scheme 4.[25,26] Under similar conditions, treatment of **4a**,**b**, **4f**, and **4g** (Ar′ = Ph, 4-FC_6H_4, 4-PhC_6H_4; R = Tol, Ph) with $Pd(OAc)_2$ (**5a**) afforded **8a–d** with self-coupling *Z*,*Z*-dimer in a yield range of 72–78%. Although the exact explanation of homocoupling reaction was not clear at this stage, on the basis of the results and the suggested pathways in the literature,[26] intermediate **A** should be first generated by complexation of **4** with $Pd^0(PPh_3)_2$ in the initial step. Following coordination of **A** with another **4**, **A-1** is formed. Subsequently, $Pd^0(PPh_3)_2$ is regenerated and **8** is obtained by the reductive elimination. The structure of **8a** was determined by single-crystal X-ray crystallography.[24]

Tamoxifen (**12**) is a therapeutic agent for the treatment of estrogen-dependent breast cancer and serves for other emerging clinical applications.[27] A number of novel and efficient synthetic routes have been developed.[28] On the basis of the $Pd(OAc)_2$-catalyzed desulfinative cross-coupling shown, synthesis of tamoxifen was investigated. By desulfonylative methylenation of **6a** with formaldehyde, vinyl stilbene **9** was isolated in 78% yield (Scheme 5). Controlling the hydrogenated time, terminal olefin of **9** was selectively hydrogenated to produce **10** in 68% yield. Finally, $Pd(OAc)_2$-catalyzed Heck-type cross-coupling of **10** with **11** [prepared by O-alkylation of 4-bromophenoxide with $Me_2N(CH_2)_2Cl{\cdot}HCl$] provided **12** in 65% yield.



Scheme 5 Synthesis of tamoxifen (**12**)

In summary, we have developed a $Pd(OAc)_2$ (**5a**)-catalyzed desulfinative cross coupling of (*Z*)-β-halostyrenes **4** with sodium sulfinates **2** in the presence of PPh_3 and Na_2CO_3 at reflux in good yields. The stereocontrolled cross-coupling process provides a series of sulfonylmethyl (*Z*)-stilbenes **6**. In the absence of the palladium catalyst or sodium sulfinate, two kinds of sulfonyl styrenes (1,3-disulfonyl styrenes **7** and self-homocoupling dimers **8**) have been observed in good yields under similar conditions. A synthesis of tamoxifen (**12**) was also studied. The structures of the key products were confirmed by X-ray crystallography. Further investigations regarding the synthetic application of sodium sulfinates will be conducted and published in due course.

All reagents and solvents were obtained from commercial sources and used without further purification. Reactions were routinely carried out under an atmosphere of dry air with magnetic stirring. Products in organic solvents were dried with anhyd $MgSO_4$ before concentration in vacuo. Melting points were determined with a 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. High-resolution mass spectra (HRMS) were recorded on Finnigan/Thermo Quest MAT 95XL mass spectrometer. 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.

β-Halovinyl Sulfones 4a–i; General Procedure

Sodium arenesulfinate **2** (1.1 mmol) was added to a solution of dihalide **3** (1.0 mmol) in a co-solvent of 1,4-dioxane and H_2O (1:1, 10 mL) at 25 °C. The reaction mixture was stirred at 25 °C for 5 min. Then, the mixture was stirred at reflux for 1 h. The mixture was cooled to 25 °C and concentrated. The residue was diluted with H_2O (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 under reduced pressure to afford the crude product. Purification on silica gel (hexanes–EtOAc, 4:1 to 1:1) afforded **4**.

Compound 4a

Yield: 315 mg (90%); colorless solid; mp 88–89 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 8.0 Hz, 2 H), 7.31–7.21 (m, 7 H), 6.65 (s, 1 H), 4.55 (s, 2 H), 2.40 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.75, 137.70, 135.84, 135.13, 129.49 (2 ×), 128.65 (2 ×), 128.56 (2 ×), 128.45, 126.68 (2 ×), 113.45, 59.94, 21.58.

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{16}H_{16}BrO_2S$: 351.0054; found: 351.0059.

Compound 4b

Yield: 296 mg (88%); colorless gum.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76–7.73 (m, 2 H), 7.55–7.51 (m, 1 H), 7.42–7.37 (m, 2 H), 7.26–7.19 (m, 5 H), 6.62 (s, 1 H), 4.54 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.76, 137.58, 134.98, 133.72, 128.87 (2 ×), 128.67 (2 ×), 128.55,

128.50 (2 ×), 126.63 (2 ×), 113.54, 59.85.

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{15}H_{14}BrO_2S$: 336.9898; found. 336.9896.

Compound 4c

Yield: 230 mg (84%); colorless solid; mp 109–110 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39 (br s, 5 H), 6.84 (s, 1 H), 4.47 (s, 2 H), 2.78 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 137.61, 135.54, 129.01, 128.99 (2 ×), 126.71 (2 ×), 113.21, 58.82, 41.48.

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{10}H_{12}BrO_2S$: 274.9741; found: 274.9745.

Compound 4d

Yield: 301 mg (85%); colorless gum.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79–7.76 (m, 2 H), 7.32–7.29 (m, 3 H), 7.25–7.22 (m, 2 H), 7.11–7.07 (m, 2 H), 6.67 (s, 1 H), 4.58 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.91 (d, *J* = 255.4 Hz), 137.45, 134.97, 134.74 (d, *J* = 3.8 Hz), 131.48 (d, *J* = 9.9 Hz, 2 ×), 128.77 (2 ×), 128.70, 126.62 (2 ×), 116.16 (d, *J* = 22.0 Hz, 2 ×), 113.65, 59.95.

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{15}H_{13}BrFO_2S$: 354.9804; found. 354.9808;

Compound 4e

Yield: 293 mg (80%); colorless solid; mp 107–108 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 8.8 Hz, 2 H), 7.31–7.23 (m, 5 H), 6.88 (d, *J* = 8.8 Hz, 2 H), 6.65 (s, 1 H), 4.55 (s, 2 H), 3.84 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.84, 137.75, 135.28, 130.75 (2 ×), 130.34, 128.68 (2 ×), 128.49, 126.68 (2 ×), 114.08 (2 ×), 113.36, 60.06, 55.62.

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{16}H_{16}BrO_3S$: 367.0004; found: 367.0010.

Compound 4f

Yield: 324 mg (88%); colorless solid; mp 110–111 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 8.4 Hz, 2 H), 7.30–7.25 (m, 4 H), 7.06–7.00 (m, 2 H), 6.66 (s, 1 H), 4.56 (s, 2 H), 2.45 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.75 (d, *J* = 247.1 Hz), 144.92, 135.85, 134.14, 133.86 (d, *J* = 3.8 Hz), 129.57 (2 ×), 128.55, 128.51 (2 ×), 128.47, 115.65 (d, *J* = 22.0 Hz, 2 ×), 113.42 (d, *J* = 1.5 Hz), 60.04, 21.56.

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{16}H_{15}BrFO_2S$: 368.9960; found: 368.9963.

Compound 4g

Yield: 358 mg (84%); colorless solid; mp 152–153 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 8.0 Hz, 2 H), 7.59–7.56 (m, 2 H), 7.52 (d, *J* = 8.4 Hz, 2 H), 7.47–7.43 (m, 2 H), 7.39–7.34 (m, 1 H), 7.32 (d, *J* = 8.4 Hz, 2 H), 7.22 (d, *J* = 8.0 Hz, 2 H), 6.73 (s, 1 H), 4.59 (s, 2 H), 2.38 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.80, 141.36, 140.16, 136.53, 135.97, 134.76, 129.53 (2 ×), 128.83 (2 ×), 128.63 (2 ×), 127.62, 127.32 (2 ×), 127.10 (2 ×), 126.95 (2 ×), 113.39, 59.90, 21.59.

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{22}H_{20}BrO_2S$: 427.0367; found: 427.0364.

Compound 4h

Yield: 332 mg (83%); colorless solid; mp 99–100 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80–7.75 (m, 1 H), 7.74 (s, 1 H), 7.72 (s, 1 H), 7.63–7.61 (m, 3 H), 7.51–7.46 (m, 2 H), 7.33 (dd, *J* = 1.6, 8.4 Hz, 1 H), 7.08 (d, *J* = 8.0 Hz, 2 H), 6.80 (s, 1 H), 4.67 (s, 2 H), 2.22 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.74, 135.86, 135.09, 134.79, 133.01, 132.91, 129.37 (2 ×), 128.49 (2 ×), 128.37, 128.13, 127.50, 126.54, 126.52, 126.22, 124.05, 113.73, 56.92, 21.35.

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{20}H_{18}BrO_2S$: 401.0211; found: 401.0215.

Compound 4i

Yield: 245 mg (80%); colorless gum.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 8.4 Hz, 2 H), 7.31–7.21 (m, 7 H), 6.46 (s, 1 H), 4.53 (s, 2 H), 2.40 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.72, 136.94, 135.95, 132.20, 129.49 (2 ×), 128.68 (2 ×), 128.53 (2 ×), 128.43, 126.70 (2 ×), 123.35, 57.78, 21.58.

HRMS (ESI): *m*/*z* [M⁺ + 1] calcd for $C_{16}H_{16}ClO_2S$: 307.0560: found: 307.0568.

Sulfonylmethyl (*Z*)-Stilbenes 6a–v; General Procedure

Na_2CO_3 (106 mg, 1.0 mmol) and PPh_3 (157 mg, 0.6 mmol) were added to a solution of vinyl halide **4** (0.5 mmol) in DME (10 mL) at 25 °C. The reaction mixture was stirred at 25 °C for 5 min. Then, sodium arenesulfinate **2** (0.5 mmol) was added to the mixture at 25 °C. The mixture was stirred at 25 °C for 5 min. $Pd(OAc)_2$ (11 mg, 0.05 mmol) was added to the mixture at 25 °C and the mixture was stirred at reflux for 5 h. The mixture was cooled to 25 °C and concentrated. The residue was diluted with H_2O (10 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with brine, dried, filtered, and evaporated under reduced pressure to afford the crude product. Purification on silica gel (hexanes–EtOAc, 4:1 to 1:1) afforded **6**.

Compound 6a

Yield: 136 mg (78%); colorless solid; mp 126–127 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 (d, *J* = 8.0 Hz, 2 H), 7.37–7.33 (m, 4 H), 7.28–7.21 (m, 6 H), 7.07 (d, *J* = 8.0 Hz, 2 H), 7.01 (s, 1 H), 4.56 (s, 2 H), 2.35 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.22, 140.29, 136.74, 136.40, 136.03, 130.37, 129.32 (2 ×), 128.58 (2 ×), 128.50 (2 ×), 128.32 (2 ×), 128.25 (2 ×), 127.73, 127.54, 126.74 (2 ×), 57.93, 21.48.

HRMS (ESI): *m*/*z* [M⁺ + 1] calcd for $C_{22}H_{21}O_2S$: 349.1262; found: 349.1266.

Compound 6b

Yield: 136 mg (75%); colorless solid; mp 130–131 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48 (d, *J* = 8.4 Hz, 2 H), 7.27–7.20 (m, 7 H), 7.17 (d, *J* = 7.6 Hz, 2 H), 7.06 (d, *J* = 8.4 Hz, 2 H), 6.98 (s, 1 H), 4.56 (s, 2 H), 2.38 (s, 3 H), 2.35 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.17, 140.47, 137.65, 136.82, 136.51, 133.18, 129.68, 129.28 (2 ×), 129.18 (2 ×), 128.53 (2 ×), 128.27 (4 ×), 127.39, 126.71 (2 ×), 58.03, 21.47, 21.21.

HRMS (ESI): *m*/*z* [M⁺ + 1] calcd for $C_{23}H_{23}O_2S$: 363.1419; found: 363.1425.

Compound 6c

Yield: 132 mg (72%); colorless solid; mp 103–104 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 (d, *J* = 8.0 Hz, 2 H), 7.39–7.36 (m, 2 H), 7.24–7.19 (m, 5 H), 7.08–7.03 (m, 4 H), 6.96 (s, 1 H), 4.50 (s, 2 H), 2.35 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.25 (d, *J* = 245.6 Hz), 144.34, 140.15, 136.39, 135.61, 132.08 (d, *J* = 3.8 Hz), 130.45 (d, *J* = 8.3 Hz, 2 ×), 129.49, 129.34 (2 ×), 128.33 (2 ×), 128.22 (2 ×), 127.57, 126.68 (2 ×), 115.47 (d, *J* = 21.9 Hz, 2 ×), 57.94, 21.46.

HRMS (ESI): *m*/*z* [M⁺ + 1] calcd for $C_{22}H_{20}FO_2S$: 367.1168; found: 367.1172.

Compound 6d

Yield: 136 mg (72%); colorless solid; mp 162–163 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48 (d, *J* = 8.0 Hz, 2 H), 7.36 (d, *J* = 8.0 Hz, 2 H), 7.23–7.17 (m, 5 H), 7.05 (d, *J* = 8.4 Hz, 2 H), 6.95 (s, 1 H), 6.90 (d, *J* = 8.4 Hz, 2 H), 4.56 (s, 2 H), 3.84 (s, 3 H), 2.34 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.26, 144.19, 140.62, 136.58, 136.54, 130.06 (2 ×), 129.28 (2 ×), 128.86, 128.63, 128.29 (2 ×), 128.26 (2 ×), 127.27 (2 ×), 126.65 (2 ×), 113.93, 58.16, 55.28, 21.47.

HRMS (ESI): *m*/*z* [M⁺ + 1] calcd for $C_{23}H_{23}O_3S$: 379.1368; found: 379.1362.

Compound 6e

Yield: 134 mg (74%); colorless solid; mp 130–131 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46 (d, *J* = 8.0 Hz, 2 H), 7.27–7.19 (m, 7 H), 7.12–7.09 (m, 2 H), 7.06 (d, *J* = 8.0 Hz, 2 H), 6.95 (s, 1 H), 4.53 (s, 2 H), 2.33 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.16, 140.27, 138.01, 136.79, 135.94, 136.34, 130.16, 129.27 (2 ×), 129.10, 128.43, 128.36, 128.27 (2 ×), 128.22 (2 ×), 127.48, 126.69 (2 ×), 125.53, 57.86, 21.45, 21.35.

HRMS (ESI): *m*/*z* [M⁺ + 1] calcd for $C_{23}H_{23}O_2S$: 363.1419; found: 363.1423.

Compound 6f

Yield: 146 mg (70%); colorless solid; mp 117–118 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, *J* = 8.0 Hz, 2 H), 7.48–7.44 (m, 4 H), 7.31–7.21 (m, 5 H), 7.06 (d, *J* = 8.0 Hz, 2 H), 7.01 (s, 1 H), 4.50 (s, 2 H), 2.35 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.49, 139.83, 139.61, 136.23, 134.92, 132.31, 129.43 (2 ×), 128.91 (2 ×), 128.67, 128.45 (2 ×), 128.21 (2 ×), 127.97 (2 ×), 126.77 (2 ×), 125.42 (q, *J* = 3.8 Hz), 113.47, 57.81, 21.47.

HRMS (ESI): *m*/*z* [M⁺ + 1] calcd for $C_{23}H_{20}F_3O_2S$: 417.1136; found: 417.1135.

Compound 6g

Yield: 132 mg (70%); colorless solid; mp 119–120 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 10.03 (s, 1 H), 7.88 (d, *J* = 8.4 Hz, 2 H), 7.55 (d, *J* = 8.0 Hz, 2 H), 7.46 (d, *J* = 8.0 Hz, 2 H), 7.29–7.22 (m, 5 H), 7.07 (d, *J* = 8.0 Hz, 2 H), 7.02 (s, 1 H), 4.52 (s, 2 H), 2.35 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.65, 144.53, 142.18, 139.83, 136.28, 135.39, 135.23, 132.67, 129.89 (2 ×), 129.44 (2 ×), 129.27 (2 ×), 128.45 (2 ×), 128.21 (2 ×), 128.02, 126.78 (2 ×), 57.99, 21.49.

HRMS (ESI): *m*/*z* [M⁺ + 1] calcd for $C_{23}H_{21}O_3S$: 377.1211; found: 377.1215.

Compound 6h

Yield: 157 mg (74%); colorless solid; mp 178–179 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 8.0 Hz, 2 H), 7.62 (d, *J* = 8.0 Hz, 2 H), 7.52–7.46 (m, 6 H), 7.41–7.38 (m, 1 H), 7.31–7.23 (m, 5 H), 7.07 (d, *J* = 8.0 Hz, 2 H), 7.05 (s, 1 H), 4.62 (s, 2 H), 2.35 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.24, 140.43, 140.36, 136.41, 136.29 (2 ×), 135.00, 130.37, 129.29 (2 ×), 129.07 (2 ×), 128.81 (2 ×), 128.30 (2 ×), 128.23 (2 ×), 127.51, 127.47, 127.08 (2 ×), 126.91 (2 ×), 126.71 (2 ×), 58.01, 21.46.

HRMS (ESI): *m*/*z* [M⁺ + 1] calcd for $C_{28}H_{25}O_2S$: 425.1575; found: 425.1580.

Compound 6i

Yield: 155 mg (73%); colorless solid; mp 84–85 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.27 (m, 12 H), 7.19–7.08 (m, 6 H), 6.77 (s, 1 H), 4.56 (s, 2 H), 2.35 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.17, 141.60, 140.55, 140.01, 136.85, 134.05, 130.03, 129.84, 129.61 (2 ×), 129.37 (2 ×), 129.31, 128.65, 128.57, 128.16 (2 ×), 128.08 (2 ×), 127.99 (2 ×), 127.38, 127.33, 127.16, 126.85 (2 ×), 57.86, 21.47.

HRMS (ESI): *m*/*z* [M⁺ + 1] calcd for $C_{28}H_{25}O_2S$: 425.1575; found: 425.1581.

Compound 6j

Yield: 155 mg (76%); colorless solid; mp 183–184 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45 (d, *J* = 8.4 Hz, 2 H), 7.22 (d, *J* = 2.0 Hz, 1 H), 7.18–7.12 (m, 5 H), 7.02 (d, *J* = 8.4 Hz, 2 H), 6.98 (d, *J* = 2.0 Hz, 1 H), 6.97 (s, 1 H), 6.88 (d, *J* = 8.4 Hz, 1 H), 4.58 (s, 2 H), 3.95 (s, 3 H), 3.92 (s, 3 H), 2.32 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.82, 148.77, 144.17, 140.51, 136.88, 136.60, 129.24 (2 ×), 128.99, 128.92, 128.21 (4 ×), 127.21, 126.58 (2 ×), 121.58, 111.88, 111.03, 58.36, 56.07, 55.87, 21.43.

HRMS (ESI): *m*/*z* [M⁺ + 1] calcd for $C_{24}H_{25}O_4S$: 409.1474; found: 409.1482.

Compound 6k

Yield: 166 mg (76%); colorless solid; mp 116–117 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43 (d, *J* = 8.4 Hz, 2 H), 7.16–7.12 (m, 5 H), 7.01 (d, *J* = 8.4 Hz, 2 H), 6.97 (s, 1 H), 6.84 (s, 2 H), 4.58 (s, 2 H), 3.90 (s, 6 H), 3.89 (s, 3 H), 2.31 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 153.18, 144.20, 140.21, 137.68, 137.01 (2 ×), 136.60, 131.56, 129.97, 129.25 (2 ×), 128.23 (2 ×), 128.13 (2 ×), 127.32, 126.57 (2 ×), 105.91 (2 ×), 60.85, 58.46, 56.23 (2 ×), 21.41.

HRMS (ESI): *m*/*z* [M⁺ + 1] calcd for $C_{25}H_{27}O_5S$: 439.1579; found: 439.1582.

Compound 6l

Yield: 130 mg (78%); colorless solid; mp 130–131 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62–7.59 (m, 2 H), 7.49–7.45 (m, 1 H), 7.37–7.21 (m, 12 H), 7.03 (s, 1 H), 4.58 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.15, 139.51, 136.89, 136.01, 133.29, 130.28, 128.71 (2 ×), 128.58 (4 ×), 128.39 (2 ×), 128.23 (2 ×), 127.77 (2 ×), 126.73 (2 ×), 57.89.

HRMS (ESI): *m*/*z* [M⁺ + 1] calcd for $C_{21}H_{19}O_2S$: 335.1106; found: 335.1112.

Compound 6m

Yield: 130 mg (74%); colorless solid; mp 115–116 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61–7.58 (m, 2 H), 7.49–7.44 (m, 1 H), 7.40–7.35 (m, 2 H), 7.32–7.18 (m, 7 H), 7.09–7.03 (m, 2 H), 6.97 (s, 1 H), 4.53 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.29 (d, *J* = 246.4 Hz), 140.02, 139.49, 135.77, 133.38, 132.06 (d, *J* = 3.0 Hz), 130.46 (d, *J* = 7.6 Hz, 2 ×), 128.76 (2 ×), 128.58, 128.40 (2 ×), 128.21 (2 ×), 127.83, 126.67 (2 ×), 115.57 (d, *J* = 21.2 Hz, 2 ×), 57.91.

HRMS (ESI): *m*/*z* [M⁺ + 1] calcd for $C_{21}H_{18}FO_2S$: 353.1012; found: 353.1015.

Compound 6n

Yield: 135 mg (74%); colorless solid; mp 130–131 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63–7.60 (m, 2 H), 7.47–7.43 (m, 1 H), 7.36 (d, *J* = 8.8 Hz, 2 H), 7.31–7.16 (m, 7 H), 6.96 (s, 1 H), 6.91 (d, *J* = 8.8 Hz, 2 H), 4.58 (s, 2 H), 3.84 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.28, 140.44, 139.60, 136.70, 133.26, 130.04 (2 ×), 128.75, 128.67 (2 ×), 128.57, 128.31 (2 ×), 128.23 (2 ×), 127.50, 126.61 (2 ×), 113.99 (2 ×), 58.07, 55.28.

HRMS (ESI): *m*/*z* [M⁺ + 1] calcd for $C_{22}H_{21}O_3S$: 365.1211; found: 365.1215.

X-ray Crystal Data[24]

Crystals of compound **6n** were 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 P 21/n, *a* = 9.4670(5) Å, *b* = 18.9214(9) Å, *c* = 10.2324(5) Å, *V* = 1831.17(16) Å^3, *Z* = 4, d_{calcd} = 1.322 g/cm^3, *F*(000) = 768, 2θ range 2.264–26.386°, *R* indices (all data) *R*1 = 0.0425, *wR*2 = 0.0921.

Compound 6o

Yield: 154 mg (75%); colorless solid; mp 197–198 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64–7.59 (m, 6 H), 7.50–7.44 (m, 5 H), 7.41–7.36 (m, 1 H), 7.32–7.27 (m, 4 H), 7.24–7.21 (m, 3 H), 7.05 (s, 1 H), 4.63 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.57, 140.43, 140.25, 139.54, 136.51, 135.01, 133.33, 130.31, 129.10 (2 ×), 128.86 (2 ×), 128.74 (2 ×), 128.42 (2 ×), 128.27 (2 ×), 127.80, 127.52, 127.23 (2 ×), 126.99 (2 ×), 126.74 (2 ×), 58.03.

HRMS (ESI): *m*/*z* [M⁺ + 1] calcd for $C_{27}H_{23}O_2S$: 411.1419; found: 411.1422.

Compound 6p

Yield: 103 mg (76%); colorless solid; mp 101–102 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54–7.50 (m, 4 H), 7.46–7.32 (m, 6 H), 7.12 (s, 1 H), 4.46 (s, 2 H), 2.49 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.71, 137.12, 135.86, 130.03, 128.93 (2 ×), 128.74 (2 ×), 128.68 (2 ×), 128.31, 128.05, 126.85 (2 ×), 57.03, 42.07.

HRMS (ESI): *m*/*z* [M⁺ + 1] calcd for $C_{16}H_{17}O_2S$: 273.0949; found: 273.0953.

Compound 6q

Yield: 134 mg (76%); colorless solid; mp 137–138 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59–7.54 (m, 2 H), 7.41–7.29 (m, 5 H), 7.26–7.22 (m, 5 H), 7.02 (s, 1 H), 6.95–6.89 (m, 2 H), 4.59 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.52 (d, *J* = 254.7 Hz), 140.06, 136.94, 135.89, 135.34, 131.11 (d, *J* = 9.1 Hz, 2 ×), 130.09, 128.61 (2 ×), 128.55 (2 ×), 128.44 (2 ×), 127.87, 127.82, 126.71 (2 ×), 115.88 (d, *J* = 22.8 Hz, 2 ×), 57.97.

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{21}H_{18}FO_2S$: 353.1012; found: 353.1015.

Compound 6r

Yield: 135 mg (74%); colorless solid; mp 99–100 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50 (d, *J* = 9.2 Hz, 2 H), 7.38 (br s, 2 H), 7.37 (br s, 2 H), 7.35–7.21 (m, 6 H), 7.01 (s, 1 H), 6.72 (d, *J* = 9.2 Hz, 2 H), 4.56 (s, 2 H), 3.81 (s, 3 H)…

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.40, 140.32, 136.62 (2 ×), 136.03, 130.90, 130.48, 130.35 (2 ×), 128.57 (2 ×), 128.49 (2 ×), 128.33 (2 ×), 127.71, 127.58, 126.71 (2 ×), 113.88, 57.97, 55.53.

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{22}H_{21}O_3S$: 365.1212; found 365.1215.

Compound 6s

Yield: 134 mg (73%); colorless solid; mp 156–157 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.47 (d, *J* = 8.4 Hz, 2 H), 7.38–7.30 (m, 5 H), 7.26–7.23 (m, 2 H), 7.11 (d, *J* = 8.0 Hz, 2 H), 6.96 (s, 1 H), 6.94–6.90 (m, 2 H), 4.51 (s, 2 H), 2.37 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.36 (d, *J* = 245.6 Hz), 144.45, 136.69, 136.48, 136.40, 135.86, 129.40 (2 ×), 128.54 (4 ×), 128.46 (d, *J* = 7.6 Hz, 2 ×), 128.21 (2 ×), 127.82 (2 ×), 115.19 (d, *J* = 22.0 Hz, 2 ×), 58.04, 21.46.

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{22}H_{20}FO_2S$: 367.1168; found: 367.1170.

X-ray Crystal Structure[24]

Crystals of compound **6s** were grown by slow diffusion of EtOAc into a solution of compound **6s** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group P 21, *a* = 9.060(2) Å, *b* = 5.6003(14) Å, *c* = 18.336(5) Å, *V* = 909.4(4) Å^3, *Z* = 2, d_{calcd} = 1.338 g/cm^3, *F*(000) = 384, 2θ range 1.136–26.516°, *R* indices (all data) *R*1 = 0.0416, *wR*2 = 0.0810.

Compound 6t

Yield: 155 mg (73%); colorless solid; mp 161–162 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58–7.55 (m, 2 H), 7.51–7.30 (m, 14 H), 7.08 (s, 1 H), 7.07–7.05 (m, 2 H), 4.59 (s, 2 H), 2.29 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.30, 140.50, 140.46, 139.19, 136.62, 136.58, 136.05, 129.99, 129.34 (2 ×), 128.81 (2 ×), 128.68 (2 ×), 128.57 (2 ×), 128.36 (2 ×), 127.82, 127.44, 127.19 (2 ×), 126.98 (2 ×), 126.91 (2 ×), 57.97, 21.48.

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{28}H_{25}O_2S$: 425.1575; found: 425.1577.

Compound 6u

Yield: 143 mg (72%); colorless solid; mp 146–147 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.79–7.77 (m, 1 H), 7.68 (d, *J* = 9.2 Hz, 1 H), 7.67 (d, *J* = 8.4 Hz, 1 H), 7.58 (d, *J* = 1.2 Hz, 1 H), 7.49–7.31 (m, 10 H), 7.15 (s, 1 H), 6.83 (d, *J* = 8.0 Hz, 2 H), 4.66 (s, 2 H), 2.06 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.31, 137.42, 137.10 (2 ×), 136.42, 136.04, 133.04, 132.65, 130.39, 129.10 (2 ×), 128.71 (2 ×), 128.58 (2 ×), 128.20 (2 ×), 127.99, 127.84, 127.37, 126.17, 126.05, 125.97, 124.72, 58.09, 21.14.

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{26}H_{23}O_2S$: 399.1419; found: 399.1428.

Compound 6v

Two isomers (ratio = 6:4); yield: 96 mg (67%); colorless gum.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62 (d, *J* = 8.0 Hz, 2 H), 7.23–7.16 (m, 6 H), 7.06–7.04 (m, 1 H), 6.09 (q, *J* = 7.2 Hz, 1 H), 4.34 (s, 2 H), 2.36 (s, 3 H), 1.67 (d, *J* = 7.2 Hz, 3 H).

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{17}H_{19}O_2S$: 287.1106; found: 287.1112.

1,3-Disulfonyl Styrenes 7a–g; General Procedure

Na_2CO_3 (106 mg, 1.0 mmol) and PPh_3 (157 mg, 0.6 mmol) were added to a solution of dihalide **3** (0.5 mmol) in DME (10 mL) at 25 °C. The reaction mixture was stirred at 25 °C for 5 min. Then, arenesulfinic acid sodium salt **2** (1.6 mmol) was added to the mixture at 25 °C. The mixture was stirred at 25 °C for 5 min and then stirred at reflux for 5 h. The mixture was cooled to 25 °C and concentrated. The residue was diluted with H_2O (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 under reduced pressure to afford the crude product. Purification on silica gel (hexanes–EtOAc, 4:1 to 1:1) afforded **7**.

Compound 7a

Yield: 183 mg (86%); colorless solid; mp 128–129 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 8.4 Hz, 2 H), 7.72 (d, *J* = 8.4 Hz, 2 H), 7.37–7.30 (m, 7 H), 7.26 (d, *J* = 8.4 Hz, 2 H), 6.53 (s, 1 H), 5.20 (s, 2 H), 2.44 (s, 3 H), 2.42 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.90, 144.81, 141.84, 137.64, 137.52, 136.43, 132.65, 130.06, 129.96 (2 ×), 129.61 (2 ×), 128.76 (2 ×), 128.49 (2 ×), 127.94 (2 ×), 127.21 (2 ×), 55.44, 21.64, 21.60.

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{23}H_{23}O_4S_2$: 427.1038; found: 427.1041.

Compound 7b

Yield: 161 mg (81%); colorless solid; mp 73–74 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03–8.00 (m, 2 H), 7.87–7.84 (m, 2 H), 7.68–7.55 (m, 4 H), 7.50–7.46 (m, 2 H), 7.39–7.31 (m, 5 H), 6.55 (s, 1 H), 5.24 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.25, 140.50, 139.28, 137.37, 133.85, 133.84, 132.39, 130.30, 129.38 (2 ×), 129.06 (2 ×), 128.86 (2 ×), 128.48 (2 ×), 127.89 (2 ×), 127.21 (2 ×), 55.44.

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{21}H_{19}O_4S_2$: 399.0725; found: 399.0726.

Compound 7c

Yield: 110 mg (80%); colorless solid; mp 139–140 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55–7.52 (m, 2 H), 7.49–7.45 (m, 3 H), 6.74 (s, 1 H), 5.04 (s, 2 H), 3.20 (s, 3 H), 2.92 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.95, 137.64, 131.40, 130.78, 129.31 (2 ×), 127.12 (2 ×), 54.33, 43.85, 42.70.

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{11}H_{15}O_4S_2$: 275.0412; found: 275.0419.

X-ray Crystal Data[24]

Crystals of compound **7c** were grown by slow diffusion of EtOAc into a solution of compound **7c** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group C2/c, *a* = 19.862(4) Å, *b* = 8.7119(16) Å, *c* = 16.377(3) Å, *V* = 2517.1(9) Å^3, *Z* = 8, d_{calcd} = 1.448 g/cm^3, *F*(000) = 1152, 2θ range 2.607–26.418°, *R* indices (all data) *R*1 = 0.0536, *wR*2 = 0.1151.

Compound 7d

Yield: 182 mg (84%); colorless solid; mp 133–134 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.09–8.04 (m, 2 H), 7.86–7.81 (m, 2 H), 7.40–7.29 (m, 5 H), 7.27–7.22 (m, 2 H), 7.15–7.09 (m, 2 H), 6.54 (s, 1 H), 5.22 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 165.95 (d, *J* = 255.5 Hz), 165.91 (d, *J* = 255.4 Hz), 142.16, 137.15, 136.46 (d, *J* = 3.0 Hz), 135.23 (d, *J* = 3.0 Hz), 132.26, 131.39 (d, *J* = 9.9 Hz, 2 ×), 130.92 (d, *J* = 9.9 Hz, 2 ×), 130.44, 128.94 (2 ×), 127.17 (2 ×), 116.73 (d, *J* = 22.8 Hz, 2 ×), 116.34 (d, *J* = 22.7 Hz, 2 ×), 55.56.

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{21}H_{17}F_2O_4S_2$: 435.0536; found: 435.0539.

Compound 7e

Yield: 190 mg (83%); colorless solid; mp 143–144 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 8.8 Hz, 2 H), 7.73 (d, *J* = 9.2 Hz, 2 H), 7.35–7.29 (m, 5 H), 7.01 (d, *J* = 9.2 Hz, 2 H), 6.89 (d, *J* = 8.8 Hz, 2 H), 6.51 (s, 1 H), 5.19 (s, 2 H), 3.86 (s, 3 H), 3.84 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.85, 163.77, 141.33, 137.48, 132.79, 132.00, 130.84, 130.60 (2 ×), 130.14 (2 ×), 129.97, 128.71 (2 ×), 127.14 (2 ×), 114.52 (2 ×), 114.14 (2 ×), 55.64, 55.61, 55.45.

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{23}H_{23}O_6S_2$: 459.0936; found: 459.0939.

Compound 7f

Yield: 182 mg (82%); colorless solid; mp 103–104 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 8.4 Hz, 2 H), 7.72 (d, *J* = 8.4 Hz, 2 H), 7.36 (d, *J* = 8.0 Hz, 2 H), 7.39–7.29 (m, 2 H), 7.28 (d, *J* = 8.0 Hz, 2 H), 7.02–6.97 (m, 2 H), 6.50 (s, 1 H), 5.17 (s, 2 H), 2.44 (s, 3 H), 2.43 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.74 (d, *J* = 250.2 Hz), 144.98, 140.63, 137.47, 136.37, 133.52 (d, *J* = 3.1 Hz), 132.57, 129.99 (2 ×), 129.66 (2 ×), 129.50, 129.28 (d, *J* = 8.3 Hz, 2 ×), 128.41 (2 ×), 127.92 (2 ×), 115.85 (d, *J* = 21.9 Hz, 2 ×), 55.43, 21.61, 21.56.

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{23}H_{22}FO_4S_2$: 445.0944; found: 445.0948.

Compound 7g

Yield: 200 mg (84%); colorless solid; mp 156–160 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 8.4 Hz, 2 H), 7.78–7.70 (m, 4 H), 7.64 (d, *J* = 8.0 Hz, 2 H), 7.51–7.45 (m, 2 H), 7.37 (d, *J* = 8.0 Hz, 2 H), 7.33 (dd, *J* = 2.0, 8.4 Hz, 1 H), 7.07 (d, *J* = 8.4 Hz, 2 H), 6.66 (s, 1 H), 5.33 (s, 2 H), 2.44 (s, 3 H), 2.23 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.88, 144.72, 141.89, 137.63, 136.29, 134.35, 133.63, 132.70, 132.66, 129.96 (2 ×), 129.40 (2 ×), 128.56, 128.46, 128.32 (2 ×), 127.96 (2 ×), 127.47 (2 ×), 127.31, 126.70, 123.89, 55.37, 21.60, 21.34.

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{27}H_{25}O_4S_2$: 477.1194; found: 477.1198.

X-ray Crystal Data[24]

Crystals of compound **7g** were grown by slow diffusion of EtOAc into a solution of compound **7g** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the monoclinic crystal system, space group P 21/c, *a* = 14.3518(12) Å, *b* = 11.3055(9) Å, *c* = 15.0648(13) Å, *V* = 2301.5(3) Å^3, *Z* = 4, d_{calcd} = 1.375 g/cm^3, *F*(000) = 1000, 2θ range 2.304–26.397°, *R* indices (all data) *R*1 = 0.0430, *wR*2 = 0.0884.

Sulfonyl Dimers 8a–d; General Procedure

Na_2CO_3 (106 mg, 1.0 mmol) and PPh_3 (157 mg, 0.6 mmol) were added to a solution of vinyl halide **4** (0.5 mmol) in DME (10 mL) at 25 °C. The reaction mixture was stirred at 25 °C for 5 min. Then, $Pd(OAc)_2$ (11 mg, 0.05 mmol) was added to the mixture at 25 °C. The mixture was stirred at 25 °C for 5 min and then stirred at reflux for 5 h. The mixture was cooled to 25 °C and concentrated. The residue was diluted with H_2O (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 under reduced pressure to afford the crude product. Purification on silica gel (hexanes–EtOAc, 4:1 to 1:1) afforded **8**.

Compound 8a

Yield: 211 mg (78%); colorless solid; mp 180–181 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63 (d, *J* = 8.0 Hz, 4 H), 7.23 (br s, 10 H), 7.10 (d, *J* = 8.0 Hz, 4 H), 6.77 (s, 2 H), 4.47 (s, 4 H), 2.27 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.76 (2 ×), 140.37 (2 ×), 135.48 (2 ×), 131.32 (2 ×), 129.92 (2 ×), 129.58 (4 ×), 128.59 (4 ×), 128.36 (4 ×), 127.85 (2 ×), 126.53 (4 ×), 57.95 (2 ×), 21.47 (2 ×).

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{32}H_{31}O_4S_2$: 543.1664; found: 543.1669.

X-ray Crystal Data[24]

Crystals of compound **8a** were grown by slow diffusion of EtOAc into a solution of compound **8a** in CH_2Cl_2 to yield colorless prisms. The compound crystallizes in the tetragonal crystal system, space group I 41/a, *a* = 20.4669(8) Å, *b* = 20.4669(8) Å, *c* = 13.5548(6) Å, *V* = 5678.0(5) Å^3, *Z* = 16, d_{calcd} = 1.270 g/cm^3, *F*(000) = 2288, 2θ range 1.802–26.411°, *R* indices (all data) *R*1 = 0.0573, *wR*2 = 0.1170.

Compound 8b

Yield: 190 mg (74%); colorless solid; mp 165–166 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 8.4 Hz, 4 H), 7.45–7.41 (m, 2 H), 7.34–7.30 (m, 4 H), 7.22 (br s, 10 H), 6.86 (s, 2 H), 4.51 (s, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.29 (2 ×), 138.53 (2 ×), 133.67 (2 ×), 131.29 (2 ×), 130.25 (2 ×), 128.91 (4 ×), 128.64 (4 ×), 128.46 (4 ×), 128.02 (2 ×), 126.53 (4 ×), 57.89 (2 ×).

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{30}H_{27}O_4S_2$: 515.1351; found: 515.1356.

Compound 8c

Yield: 208 mg (72%); colorless solid; mp 211–212 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 8.4 Hz, 4 H), 7.24–7.20 (m, 4 H), 7.15 (d, *J* = 8.0 Hz, 4 H), 6.95–6.91 (m, 4 H), 6.77 (s, 2 H), 4.43 (s, 4 H), 2.31 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 162.51 (d, *J* = 247.1 Hz, 2 ×), 144.97 (2 ×), 136.64 (d, *J* = 3.0 Hz, 2 ×), 135.57 (2 ×), 130.28 (2 ×), 130.00 (2 ×), 129.68 (4 ×), 128.60 (4 ×), 128.37 (d, *J* = 8.3 Hz, 4 ×), 115.33 (d, *J* = 21.2 Hz, 4 ×), 58.16 (2 ×), 21.50 (2 ×).

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{32}H_{29}F_2O_4S_2$: 579.1475; found: 579.1481.

Compound 8d

Yield: 260 mg (75%); colorless solid; mp 201–202 °C (hexanes–EtOAc).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 (d, *J* = 8.0 Hz, 4 H), 7.59 (d, *J* = 8.0 Hz, 4 H), 7.50–7.45 (m, 10 H), 7.32 (d, *J* = 8.8 Hz, 4 H), 7.13 (d, *J* = 8.0 Hz, 4 H), 6.89 (s, 2 H), 4.53 (s, 4 H), 2.25 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.85 (2 ×), 140.77 (2 ×), 140.32 (2 ×), 139.21 (2 ×), 135.69 (2 ×), 130.94 (2 ×), 129.78 (2 ×), 129.65 (4 ×), 128.87 (4 ×), 128.70 (4 ×), 127.58 (2 ×), 127.11 (4 ×), 127.04 (4 ×), 126.99 (4 ×), 57.94 (2 ×), 21.53 (2 ×).

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{44}H_{39}O_4S_2$: 695.2290; found: 695.2296.

Compound 9

KOH (112 mg, 2.0 mmol) was added to a solution of **6a** (350 mg, 1.0 mmol) in 1,4-dioxane (10 mL) at 25 °C. Formaldehyde (37% in H_2O, 2 mL) was added and the reaction mixture was stirred at 25 °C for 5 min. The mixture was stirred at reflux for 10 h, cooled to 25 °C, and concentrated. The residue was diluted with H_2O (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 under reduced pressure to afford the crude product. Purification on silica gel (hexanes–EtOAc, 100:1 to 50:1) afforded **9**; yield: 161 mg (78%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42–7.33 (m, 3 H), 7.20–7.17 (m, 2 H), 7.13–7.09 (m, 3 H), 6.93–6.90 (m, 2 H), 6.76 (dd, *J* = 10.4, 17.2 Hz, 1 H), 6.62 (s, 1 H), 5.17 (d, *J* = 10.8 Hz, 1 H), 4.86 (d, *J* = 17.2 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 141.73, 137.88 (2 ×), 136.65, 131.46, 129.59 (2 ×), 129.40 (2 ×), 128.74 (2 ×), 127.93 (2 ×), 127.27, 126.88, 116.40.

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{16}H_{15}$: 207.1174; found: 207.1179.

Compound 10

Pd/C (5%, 10 mg) was added to a solution of **9** (173 mg, 0.8 mmol) in EtOAc (10 mL) at 25 °C. H_2 was bubbled through the reaction mixture at 25 °C and stirred for 1 h. The mixture was filtered and concentrated. Purification on silica gel (hexanes–EtOAc, 10:1 to 1:1) afforded **10**; yield: 113 mg (68%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64–7.61 (m, 2 H), 7.53–7.48 (m, 4 H), 7.45–7.37 (m, 4 H), 6.86 (s, 1 H), 2.91 (q, *J* = 7.6 Hz, 2 H), 1.23 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.41, 142.65, 138.26, 128.68 (2 ×), 128.30 (2 ×), 128.10 (2 ×), 127.58, 127.11, 126.75 (2 ×), 126.48, 23.22, 13.45.

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{16}H_{17}$: found: 244.0339.

Compound 11

K_2CO_3 (276 mg, 2.0 mmol) was added to a solution of 4-bromophenol (173 mg, 1.0 mmol) in acetone (10 mL) at 25 °C. $Me_2NCH_2CH_2Cl{\cdot}HCl$ (173 mg, 1.2 mmol) was added and the reaction mixture was stirred at 25 °C for 5 min. The mixture was stirred at reflux for 10 h, cooled to 25 °C, and concentrated. The residue was diluted with H_2O (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 under reduced pressure to afford the crude product. Purification on silica gel (hexanes–EtOAc, 10:1 to 1:1) afforded **11**; yield: 214 mg (88%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35 (d, *J* = 8.8 Hz, 2 H), 6.79 (d, *J* = 8.8 Hz, 2 H), 4.03 (t, *J* = 5.6 Hz, 2 H), 2.74 (t, *J* = 5.6 Hz, 2 H), 2.35 (s, 6 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.86, 132.19 (2 ×), 116.36 (2 ×), 112.94, 66.10, 58.09, 45.77 (2 ×).

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{10}H_{15}BrNO$: 244.0337; found 244.0335.

Tamoxifen (12)

Na_2CO_3 (106 mg, 1.0 mmol) and PPh_3 (157 mg, 0.6 mmol) were added to a solution of **10** (62 mg, 0.3 mmol) in DME (10 mL) at 25 °C and the reaction mixture was stirred at 25 °C for 5 min. Then, $Pd(OAc)_2$ (11 mg, 0.05 mmol) was added at 25 °C and the mixture was stirred at 25 °C for 5 min. Compound **11** (122 mg, 0.5 mmol) in DME (1 mL) was added to the mixture at 25 °C and stirred at reflux for 5 h. The mixture was cooled to 25 °C and concentrated. The residue was diluted with H_2O (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 under reduced pressure to afford the crude product. Purification on silica gel (hexanes–EtOAc, 4:1 to 1:1) afforded **12**; yield: 76 mg (65%); colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37–7.33 (m, 2 H), 7.28–7.23 (m, 3 H), 7.20–7.16 (m, 2 H), 7.13–7.09 (m, 3 H), 6.77 (d, *J* = 9.2 Hz, 2 H), 6.56 (d, *J* = 9.2 Hz, 2 H), 3.98 (t, *J* = 6.4 Hz, 2 H), 3.73 (t, *J* = 6.4 Hz, 2 H), 2.46 (q, *J* = 7.6 Hz, 2 H), 2.36 (s, 6 H), 0.92 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.53, 143.76, 142.38, 141.40, 138.20, 135.72, 131.84 (2 ×), 129.67 (2 ×), 129.43 (2 ×), 128.08 (2 ×), 127.84 (2 ×), 126.49, 126.00, 113.38 (2 ×), 65.30, 58.06, 45.57 (2 ×), 28.98, 13.54.

HRMS (ESI): *m*/*z* [M$^+$ + 1] calcd for $C_{26}H_{30}NO$: 372.2327; found: 372.2331.

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0036-1588705. Scanned photocopies of

NMR ($CDCl_3$) spectral data for all compounds and X-ray crystal structure analysis data of **6n**, **6s**, **7c**, **7g** and **8a** are included.

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