Novel Synthesis of Oxathiocine Derivatives by Wittig Olefination and Intramolecular Heck Reaction via an 8-*endo*-trig Cyclization

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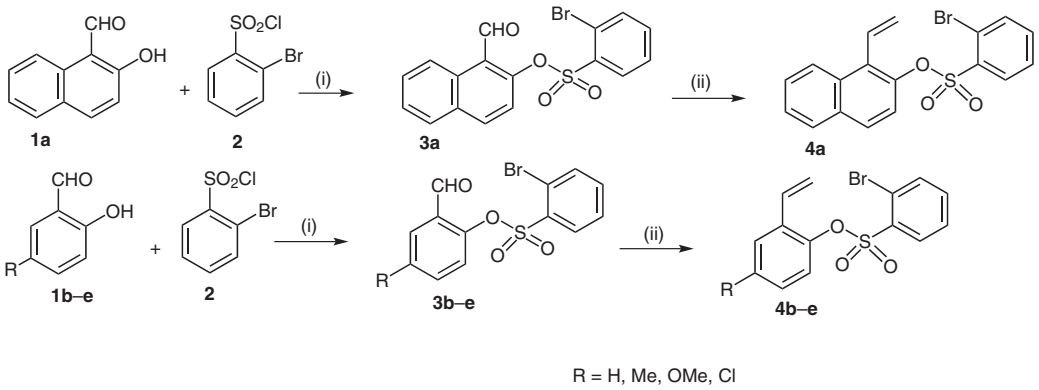
Abstract: Syntheses of hitherto unreported heterocycles, such as oxathiocine derivatives, in excellent yields, and a doubly cyclized oxathiocine derivative, through a Wittig olefination and intramolecular Heck reaction sequence via an unusual 8-*endo*-trig cyclization, are reported.

Key words: Wittig olefination, intramolecular Heck reaction, palladium catalyst, oxathiocine, 8-*endo*-trig

The importance of medium-sized rings in synthetic organic chemistry is exemplified by their presence as the structural core moiety in a large number of biologically important natural products.[1] Moreover, these units serve as target molecules in numerous synthetic studies.[2] Several excellent articles and monographs have documented such medium-ring syntheses well.[3] Though synthetic protocols for five- and six-membered ring systems are common, seven- and eight-membered ring formations are not abundant. The cyclization strategies for medium-sized rings are often restricted due to entropy factors and transannular interactions.[4] In general, the number of methods available for the synthesis of medium-sized heterocycles are relatively small. Among the various protocols, the palladium-catalyzed intramolecular Heck reaction has become a useful synthetic method due to its excellent functional group tolerance and high stereoselectivity. Recently, we have reported the synthesis of some interesting medium-ring heterocycles by the application of radical cyclization,[5] ring-closing metathesis[6] and the intramolecular Heck reaction.[7] Denieul and Skrydstrup recently showed that during the intramolecular Heck cyclization, the 7-*exo*-trig mode of cyclization of a compound having a vinyl group attached to an aromatic ring was favored over the 8-*endo*-trig mode.[8] Subsequently, Guy et al. supported this statement by synthesizing the 8-*endo* Heck products through a Heck reaction with the activated vinylic systems.[9] The same authors also synthesized eight-membered sulfur heterocycles via the 8-*endo*-trig mode of cyclization by the same protocol, starting from the highly activated vinylic double bond. These results prompted us to undertake a study on the intramolecular Heck reaction of different Heck precursors with a view to synthesizing eight-membered oxathio-heterocycles fused with diaryl moieties; synthetically, this is a challenge due to the presence of strain within such compounds. Additionally, we were interested in studying the Heck cyclization under ligand-free[10] conditions using aryl bromides in view of a recent finding that ligand-free approaches do not work for the usually preferred aryl bromides.[10] To our knowledge, the synthesis of oxathiocine heterocycles has not yet been reported.

The intramolecular Heck reaction, as stated earlier, can undergo ring-closure by two possible modes, namely *exo*- and *endo*-cyclization. Between these two possible modes, small to medium size (5–8) ring-formation is usually favored by an *exo*-mode,[11] since the *endo*-mode is sterically very demanding; the *endo*-mode requires that the olefinic system moves into the loop of the substrate, generating an



Scheme 1 *Reagents and conditions*: (i) anhyd CH_2Cl_2, Et_3N, DMAP, 0 °C→r.t., 2–3 h, stirring; (ii) PPh_3MeI, *n*-BuLi, THF, 0 °C→r.t., 1.5 h, stirring.

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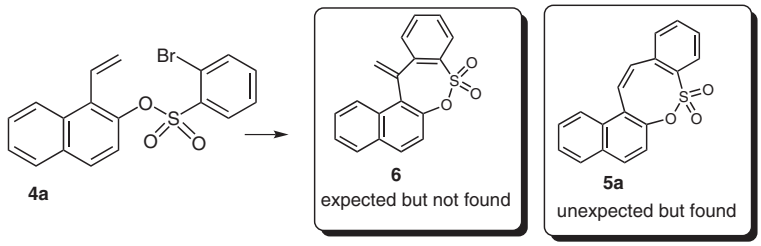


Scheme 2

energetically favorable substituted alkene product. Conversely, large ring (~20) formation with a flexible tether usually favors *endo*-cyclization.[12] To the best of our knowledge, only a limited number of examples of *endo*-cyclization for the formation of medium-sized rings have been reported.[9,13]

The required Heck precursors **4a–e** were synthesized in 88–95% yields by a Wittig olefination reaction of substrates **3a–e**. The Wittig reagent was prepared from Ph_3PMeI in anhydrous tetrahydrofuran in the presence of butyllithium, between 0 °C and room temperature, for 30 minutes. The substrates **3a–e** were synthesized in 74–90% yield by the reaction of hydroxyaldehydes **1a–e** with 2-bromobenzenesulfonyl chloride (**2**) in anhydrous dichloromethane in the presence of triethylamine and a catalytic amount of 4-(*N*,*N*-dimethylamino)pyridine (DMAP) at between 0 °C and room temperature for 2–3 hours (Scheme 1). Compounds **1a–e** were prepared in turn by the Reimer–Tiemann reaction of the corresponding phenolic compounds.

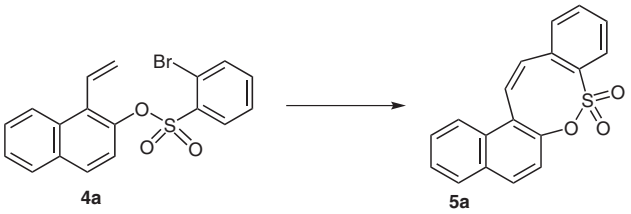
When the intramolecular Heck reaction was carried out with the substrate **4a** using the concept of Jeffery's two-phase protocol[14] in the presence of $Pd(OAc)_2$ as catalyst (which is mostly used in this type of intramolecular Heck reaction) in anhydrous *N*,*N*-dimethylformamide as solvent, potassium acetate as base and tetrabutylammonium bromide (TBAB) as additive for one hour under a nitrogen atmosphere, compound **5a**, the eight-membered *endo*-Heck product, was obtained in 90% yield (Scheme 2) without any contamination of the expected 7-*exo*-Heck product **6**. The *endo*-Heck product **5a** was easily characterized from its ^1H NMR spectrum, which indicated the presence of two olefinic protons belonging to the oxathiocine ring at δ = 7.20 (d, *J* = 12.2 Hz, 1 H) and 7.27 (d, *J* = 12.2 Hz, 1 H) ppm, with additional support from its ^{13}C NMR spectrum and other analytical data.

Optimum conditions for the cyclization were established through a series of experiments whereby various changes were made to the catalyst, base, additive and solvent (Table 1).

During the course of optimization of the reaction, we found that the catalyst, base, additive and solvent all have profound effects on the reaction yield (Table 1). It is important to note that aryl bromides are reported to usually undergo Heck cyclization in the presence of a ligand. However, in the present instance the reaction was achieved under ligand-free conditions.[10] TBAB plays an important role in the Heck cyclization because, in the absence of TBAB, the reaction did not proceed at all. Guy et al.[9] synthesized the *endo*-Heck product with a sophisticated catalytic combination system [$Pd(OAc)_2$, DMA, Et_4NCl, Cy_2NMe, 12 h, 100 °C], but our optimized condition are relatively simple [$Pd(OAc)_2$, DMF, KOAc, TBAB, 80 °C] and it takes only 45–70 min for complete conversion while their reaction required 12 hours. To test the generality of the reaction, substrates **4b–e** were also treated under the optimized conditions to afford the novel oxathiocine derivatives **5b–e** in 79–91% yield. The results are summarized in Table 2.

After achieving the synthesis of the *endo*-Heck products, we extended the reaction to the readily available, inexpensive starting material 2,7-dihydroxynaphthalene. 2,7-Di-

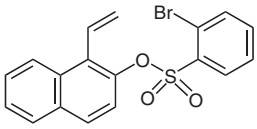
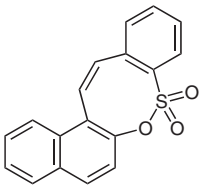
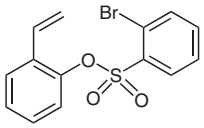
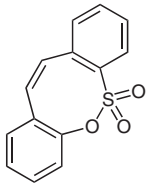
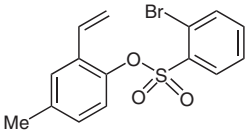
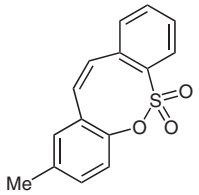
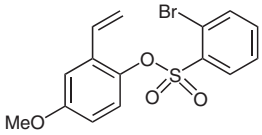
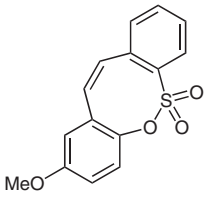
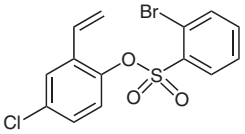
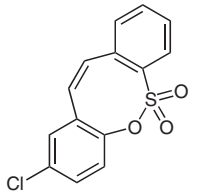
Table 1 Optimization of the Palladium-Catalyzed Intramolecular Heck Reaction[a]



Entry	Catalyst[b]	Base[c]	Solvent	Yield (%)[d]
1	**$Pd(OAc)_2$**	**KOAc**	**DMF**	**90**
2	$Pd(OAc)_2$	K_2CO_3	DMF	81
3	$Pd(OAc)_2$	Et_3N	DMF	<5
4	$Pd(OAc)_2$	Ag_2CO_3	DMF	NR
5	$Pd(OAc)_2$	Cs_2CO_3	DMF	NR
6	$Pd(PPh_3)_2Cl_2$	KOAc	DMF	21
7	$PdCl_2$	KOAc	DMF	NR
8	$Pd(PPh_3)_4$	KOAc	DMF	NR
9	$Pd(OAc)_2$	KOAc	MeCN	NR
10	$Pd(OAc)_2$	KOAc	dioxane	NR
11	$Pd(OAc)_2$	KOAc	toluene	<5

[a] Reactions were carried out at 80 °C, TBAB used as additive.
[b] Catalyst used 5 mol%.
[c] 2.75 equivalents of base used.
[d] Isolated yield. NR indicates no reaction.

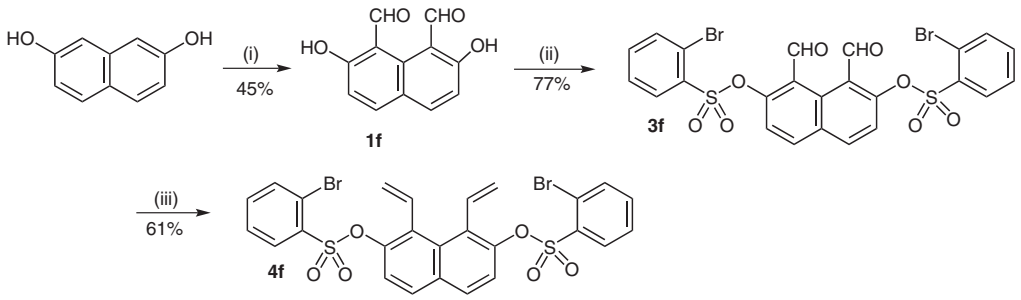
Table 2 Summarized Results of the Heck Reaction[a]

Entry	Substrate	Time (min)	Product	Yield (%)[b]
1	**4a** 	60	**5a** 	90
2	**4b** 	55	**5b** 	88
3	**4c** 	45	**5c** 	91
4	**4d** 	60	**5d** 	84
5	**4e** 	70	**5e** 	79

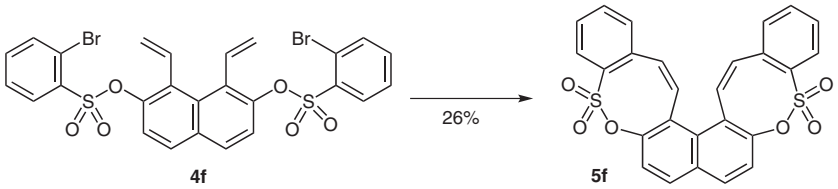
[a] All the reactions were performed under optimized reaction conditions [$Pd(OAc)_2$, DMF, KOAc, TBAB, 45–70 min, 80 °C].
[b] Isolated yield.

hydroxynaphthalene-1,8-dicarboxaldehyde (**1f**) was readily prepared from 2,7-dihydroxynaphthalene by a Reimer–Tiemann reaction. The hydroxyaldehyde **1f**, on reaction with 2-bromobenzenesulfonyl chloride (**2**), gave compound **3f** which, on treatment with Ph_3PMeI in the presence of *n*-BuLi in THF, afforded the corresponding di-Heck precursor **4f** (Scheme 3).

The substrate **4f** was reacted under the optimized reaction conditions (Table 1, entry 1) for 30 minutes at 120 °C to furnish the 8-*endo* double Heck product **5f** in only 26% yield along with unidentified products. Increasing the reaction time caused considerable decomposition of the doubly cyclized oxathiocine product. When the conditions described in Table 1 (except entry 1) were applied to



Scheme 3 *Reagents and conditions*: (i) $CHCl_3$, aq NaOH, 70 °C, srirring, 4 h, H_2SO_4; (ii) **2**, anhyd CH_2Cl_2, Et_3N, DMAP, 0 °C→r.t., 1 h; (iii) anhyd THF, PPh_3MeI, *n*-BuLi, stirring, 2 h.



Scheme 4

this reaction, no satisfactory results were obtained (Scheme 4).

The cyclization of substrates **4** with the sulfonate ester tether may occur via two alternative pathways – either an 8-*endo*-trig or a 7-*exo*-trig cyclization. It is interesting to note that we have observed only 8-*endo*-trig cyclization to afford, exclusively, the eight-membered oxathiocine derivatives.

Denieul and Skrydstrup have reported[8a] that the palladium-catalyzed cyclization of a similar substrate with an ester tether to give a mixture of three products: the 7-*exo*-trig cyclization product (i.e. seven-membered lactone, major product), the 8-*endo*-trig cyclization product (eight-membered lactone, minor product) and the biaryl coupling product (trace). The authors optimized the 7-*exo*-trig product with unactivated olefinic systems.[8a]

The exclusive formation of benzoxathiocine derivatives **5a–e** and **5f** via the 8-*endo*-mode of cyclization is quite unusual. Beletskaya and Cheprakov reported[15] that the *endo*-Heck cyclization can occur when the Heck precursor possesses a Michael-type olefinic fragment,[13] such as a highly activated double bond, otherwise exclusive *exo*-cyclization occurs. Subsequently, Guy et al. found that for 8-*endo*-Heck cyclization to occur, the substrate required an activated vinylic double bond. However, in our present work, the eight-membered oxathiocine derivatives were found to form exclusively via the unusual 8-*endo*-trig mode of cyclization without such requirements.

In conclusion, we have developed an efficacious, regioselective method for the construction of eight-membered oxathiocine derivatives (and a doubly Heck cyclized *endo*-Heck product) via an unusual 8-*endo*-trig cyclization using a Wittig reaction followed by intramolecular Heck cyclization as the key steps. The method represents a simple synthetic protocol for the formation of fused oxathiocine (and doubly cyclized oxathiocine) derivatives.

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded in KBr discs. NMR spectra were determined as solutions in $CDCl_3$ with TMS as internal standard. Silica gel (60–120 mesh) was used for chromatographic separation. Silica gel-G [Spectrochem (India)] was used for TLC. Petroleum ether (PE) refers to the fraction boiling between 60–80 °C. IR spectra were recorded on a Perkin-Elmer L 120-000A spectrophotometer. NMR spectra were recorded on a Bruker DPX-400 spectrometer. Mass spectra were recorded on Jeol JMS600 and QTOF Micro YA 263 instruments. Elemental analyses were carried out on a Perkin-Elmer 2400 series II CHN analyzer.

Preparation of 1a–f by Reimer–Tiemann Reaction; Typical Procedure

2-Naphthol (14 g, 0.1 mol) was added to a round-bottomed flask and a hot solution of NaOH (32 g, 0.8 mol) in H_2O (40 mL) was added. The reaction was heated to ~70 °C in an oil bath and $CHCl_3$ (16 mL) was added dropwise to it. The reaction mixture was stirred for 1 h at the same temperature and then allowed to cool to r.t. The reaction mixture was transferred to a 500 mL beaker with hot H_2O and subsequently acidified with H_2SO_4 (10N) and extracted with CH_2Cl_2 (3 × 75 mL), washed with H_2O (2 × 50 mL) and dried (Na_2SO_4). The organic layer was collected and the solvent was distilled off. The crude material was purified by column chromatography over silica gel (PE) to afford the product **1a**. Compounds **1b–f** were prepared in a similar manner.

Preparation of Compounds 3a–f; Typical Procedure

DMAP (10 mg) and Et_3N (2 mL) were added to a solution of **1a** (200 mg, 1.17 mmol) in anhydrous CH_2Cl_2 (20 mL) at 0 °C. 2-Bromobenzenesulfonyl chloride (**2**; 300 mg, 1.17 mmol) in anhydrous CH_2Cl_2 (10 mL) was added dropwise and reaction mixture and stirred for 2 h. The reaction mixture was washed with H_2O (3 × 10 mL) and brine (10 mL) and dried (Na_2SO_4). Evaporation of the CH_2Cl_2 gave a crude mass, which was purified by silica gel chromatography (EtOAc–PE, 10%) to afford product **3a**. Compounds **3b–f** were obtained in a similar manner.

3a

Yield: 83%; solid; mp 115–116 °C.

IR (KBr): 1697, 1371, 1197 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.34 (d, *J* = 9.2 Hz, 1 H, ArH), 7.45 (t, *J* = 6.8 Hz, 1 H, ArH), 7.56–7.58 (m, 2 H, ArH), 7.69 (t, *J* = 7.2 Hz, 1 H, ArH), 7.85–7.89 (m, 2 H, ArH), 8.00–8.05 (m, 2 H, ArH), 9.20 (d, *J* = 8.8 Hz, 1 H, ArH), 10.66 (s, 1 H, CHO).

MS: *m*/*z* = 390 [M^+], 392 [M^+ + 2].

Anal. Calcd for $C_{17}H_{11}BrO_4S$: C, 52.19; H, 2.83. Found: C, 52.03; H, 2.97.

3b

Yield: 81%; solid; mp 97–98 °C.

IR (KBr): 1693, 1378, 1160 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.15 (dd, *J* = 8.4, 1.2 Hz, 1 H, ArH), 7.37 (t, *J* = 7.6 Hz, 1 H, ArH), 7.43 (dt, *J* = 7.6, 1.2 Hz, 1 H, ArH), 7.50–7.54 (m, 2 H, ArH), 7.84 (dd, *J* = 7.6, 1.2 Hz, 1 H, ArH), 7.91 (dd, *J* = 8.0, 1.6 Hz, 1 H, ArH), 7.98 (dd, *J* = 8.0, 2.0 Hz, 1 H, ArH), 10.27 (s, 1 H, CHO).

MS: *m*/*z* = 340 [M^+], 342 [M^+ + 2].

Anal. Calcd for $C_{13}H_9BrO_4S$: C, 45.76; H, 2.66. Found: C, 45.79; H, 2.54.

3c

Yield: 90%; solid; mp 90–91 °C.

IR (KBr): 1694, 1372, 1195 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.37 (s, 3 H, CH_3), 7.03 (d, *J* = 8.4 Hz, 1 H, ArH), 7.32 (d, *J* = 8.4 Hz, 1 H, ArH), 7.45 (t, *J* = 7.6 Hz, 1 H, ArH), 7.54 (t, *J* = 7.6 Hz, 1 H, ArH), 7.71 (s, 1 H, ArH), 7.87 (d, *J* = 8.0 Hz, 1 H, ArH), 7.97 (dd, *J* = 7.6, 1.2 Hz, 1 H, ArH), 10.26 (s, 1 H, CHO).

MS: *m*/*z* = 354 [M$^+$], 356 [M$^+$ + 2].

Anal. Calcd for $C_{14}H_{11}BrO_4S$: C, 47.34; H, 3.12. Found: C, 47.63; H, 2.99.

3d

Yield: 77%; solid; mp 78–79 °C.

IR (KBr): 1691, 1375, 1199 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 3.83 (s, 3 H, OCH_3), 7.04 (d, *J* = 2.0 Hz, 1 H, ArH), 7.37–7.38 (m, 2 H, ArH), 7.45 (dt, *J* = 7.6, 1.6 Hz, 1 H, ArH), 7.55 (dt, *J* = 7.6, 1.6 Hz, 1 H, ArH), 7.88 (dd, *J* = 8.0, 1.2 Hz, 1 H, ArH), 7.98 (dd, *J* = 7.6, 1.6 Hz, 1 H, ArH), 10.25 (s, 1 H, CHO).

MS: *m*/*z* = 370 [M$^+$], 372 [M$^+$ + 2].

Anal. Calcd for $C_{14}H_{11}BrO_5S$: C, 45.30; H, 2.99. Found: C, 45.53; H, 3.13.

3e

Yield: 74%; solid; mp 108–109 °C.

IR (KBr): 1694, 1378, 1169 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.15 (d, *J* = 8.8 Hz, 1 H, ArH), 7.50–7.55 (m, 2 H, ArH), 7.58 (dt, *J* = 7.6, 1.6 Hz, 1 H, ArH), 7.88–7.89 (m, 2 H, ArH), 8.02 (dt, *J* = 8.0, 1.6 Hz, 1 H, ArH), 10.23 (s, 1 H, CHO).

MS: *m*/*z* = 374 [M$^+$], 376 [M$^+$ + 2].

Anal. Calcd for $C_{13}H_8BrClO_4S$: C, 41.57; H, 2.15. Found: C, 41.73; H, 1.96.

3f

Yield: 77%; solid; mp 134–135 °C.

IR (KBr): 1395, 1371, 1195 cm^{-1}.

^{1}H NMR (DMSO-d_6, 400 MHz): δ = 7.39 (d, *J* = 8.5 Hz, 2 H, ArH), 7.51–7.89 (m, 8 H, ArH), 8.13 (m, 2 H, ArH), 10.53 (s, 2 H, CHO).

MS: *m*/*z* = 652, 654, 656.

Anal. Calcd for $C_{24}H_{14}Br_2O_8S_2$: C, 44.06; H, 2.16. Found: C, 43.91; H, 1.99.

Synthesis of Heck Precursors 4a–f by Wittig Olefination; Typical Procedure

Wittig salt PPh_3MeI (403 mg, 0.99 mmol) in anhydrous THF (25 mL) was added to a 25 mL round-bottomed flask. *n*-BuLi (1.6 M in hexane, 1.2 mL) was added at 0 °C under a nitrogen atmosphere. Compound **3a** (300 mg, 0.76 mmol) in anhydrous THF (5 mL) was added to the reaction mixture at 0 °C and stirring was continued at r.t. for 1.5 h. THF was removed under reduced pressure and aq NH_4Cl (10 mL) was added, and the mixture was extracted with CH_2Cl_2 (3 × 30 mL), washed with H_2O (2 × 20 mL) and dried (Na_2SO_4). CH_2Cl_2 was evaporated and the crude product was purified by column chromatography over silica gel (EtOAc–PE, 5%) to give **4a**. Compounds **4b–f** were prepared in a similar manner.

4a

Yield: 88%; solid; mp 122–123 °C.

IR (KBr): 1372, 1165 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.53 (dd, *J* = 11.2, 1.6 Hz, 1 H, =C*H*$_a$H$_b$), 5.62 (dd, *J* = 17.6, 1.6 Hz, 1 H, =CH$_a$*H*$_b$), 6.82–6.89 (m, 1 H, CH_2=C*H*), 7.16 (d, *J* = 8.8 Hz, 1 H, ArH), 7.42 (dt, *J* = 6.4, 1.2 Hz, 1 H, ArH), 7.48–7.53 (m, 3 H, ArH), 7.69 (d, *J* = 9.2 Hz, 1 H, ArH), 7.81–7.82 (m, 1 H, ArH), 7.48 (dd, *J* = 6.8, 1.2 Hz, 1 H, ArH), 7.93 (dd, *J* = 7.6, 1.6 Hz, 1 H, ArH), 8.11–8.13 (m, 1 H, ArH).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 121.4, 122.0, 123.7, 126.1, 126.7, 127.3, 128.0, 128.7, 129.2, 129.5, 132.5, 132.6, 132.7, 132.8, 135.3, 136.3, 137.2, 144.7.

HRMS: *m*/*z* calcd for $C_{18}H_{13}BrO_3S$: 410.9666 [M + Na], 412.9666 [M + 2 + Na]; found: 410.9666 [M + Na], 412.9647 [M + 2 + Na].

Anal. Calcd for $C_{18}H_{13}BrO_3S$: C, 55.54; H, 3.37. Found: C, 55.61; H, 3.31.

4b

Yield: 89%; solid; mp 69–70 °C.

IR (KBr): 1379, 1193 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.24 (dd, *J* = 11.2, 1.6 Hz, 1 H, =C*H*$_a$H$_b$), 5.67 (dd, *J* = 17.6, 1.6 Hz, 1 H, =CH$_a$*H*$_b$), 6.79–6.81 (m, 1 H, CH_2=C*H*), 6.92–6.97 (m, 2 H, ArH), 7.13–7.17 (m, 2 H, ArH), 7.40–7.52 (m, 2 H, ArH), 7.85 (dd, *J* = 6.8, 1.2 Hz, 1 H, ArH), 7.96 (dd, *J* = 6.4, 1.6 Hz, 1 H, ArH).

MS: *m*/*z* = 338 [M$^+$], 340 [M$^+$ + 2].

Anal. Calcd for $C_{14}H_{11}BrO_3S$: C, 49.57; H, 3.27. Found: C, 49.37; H, 3.07.

4c

Yield: 92%; solid; mp 77–78 °C.

IR (KBr): 1362, 1170 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.40 (s, 3 H, CH_3), 5.20 (dd, *J* = 11.2, 1.6 Hz, 1 H, =C*H*$_a$H$_b$), 5.63 (dd, *J* = 17.6, 1.6 Hz, 1 H, =CH$_a$*H*$_b$), 6.73–6.78 (m, 1 H, CH_2=C*H*), 6.90 (s, 1 H, ArH), 6.93 (d, *J* = 7.2 Hz, 1 H, ArH), 7.06 (d, *J* = 3.0 Hz, 1 H, ArH), 7.51 (dt, *J* = 7.8, 1.7 Hz, 1 H, ArH), 7.58 (dt, *J* = 7.6, 1.7 Hz, 1 H, ArH), 7.89 (dd, *J* = 7.7, 1.2 Hz, 1 H, ArH), 7.99 (dd, *J* = 8.2, 1.2 Hz, 1 H, ArH).

MS: *m*/*z* = 352 [M$^+$], 354 [M$^+$ + 2].

Anal. Calcd for $C_{15}H_{13}BrO_3S$: C, 51.00; H, 3.71. Found: C, 50.87; H, 3.89.

4d

Yield: 95%; solid; mp 81–82 °C.

IR (KBr): 1363, 1169 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 3.78 (s, 3 H, OCH_3), 5.23 (dd, *J* = 11.2, 1.6 Hz, 1 H, =C*H*$_a$H$_b$), 5.61 (dd, *J* = 17.6, 1.6 Hz, 1 H, =CH$_a$*H*$_b$), 6.67–6.70 (m, 1 H, CH_2=C*H*), 6.85 (s, 1 H, ArH), 6.90 (d, *J* = 6.8 Hz, 1 H, ArH), 7.02 (d, *J* = 3.2 Hz, 1 H, ArH), 7.42 (dt, *J* = 8.0, 1.2 Hz, 1 H, ArH), 7.51 (dt, *J* = 7.6, 1.6 Hz, 1 H, ArH), 7.83 (dd, *J* = 7.6, 1.2 Hz, 1 H, ArH), 7.94 (dd, *J* = 8.0, 1.6 Hz, 1 H, ArH).

MS: *m*/*z* = 368 [M$^+$], 370 [M$^+$ + 2].

Anal. Calcd for $C_{15}H_{13}BrO_4S$: C, 48.79; H, 3.55. Found: C, 48.61; H, 3.74.

4e

Yield: 91%; solid; mp 76–77 °C.

IR (KBr): 1365, 1169 cm^{-1}.

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 5.25 (dd, *J* = 11.2, 1.6 Hz, 1 H, =C*H*$_a$H$_b$), 5.69 (dd, *J* = 17.6, 1.6 Hz, 1 H, =CH$_a$*H*$_b$), 6.76–6.83 (m, 1 H, CH_2=C*H*), 6.92 (s, 1 H, ArH), 6.96 (d, *J* = 7.4 Hz, 1 H, ArH), 7.11 (d, *J* = 2.3 Hz, 1 H, ArH), 7.39–7.56 (m, 2 H, ArH), 7.91 (dd, *J* = 8.1, 1.0 Hz, 1 H, ArH), 8.01 (dd, *J* = 7.9, 1.0 Hz, 1 H, ArH).

MS: *m*/*z* = 372 [M$^+$], 374 [M$^+$ + 2].

Anal. Calcd for $C_{14}H_{10}BrClO_3S$: C, 45.00; H, 2.70. Found: C, 45.23; H, 2.66.

4f
Yield: 61%; solid; mp 143–144 °C.

IR (KBr): 1373, 1171 cm^{-1}.

^1H NMR (DMSO-d_6, 400 MHz): δ = 5.59 (dd, *J* = 11.2, 1.6 Hz, 2 H, =CH_aH$_b$), 5.69 (dd, *J* = 17.6, 1.6 Hz, 2 H, =CH$_a$$H_b$), 6.99–7.11 (m, 2 H, CH_2=C*H*), 7.19 (d, *J* = 7.9 Hz, 2 H, ArH), 7.45–7.59 (m, 8 H, ArH), 8.19 (dd, *J* = 7.2, 1.6 Hz, 2 H, ArH).

MS: *m*/*z* = 648, 650, 652.

Anal. Calcd for $C_{26}H_{18}Br_2O_6S_2$: C, 48.02; H, 2.79. Found: C, 48.19; H, 2.91.

Synthesis of Compounds 5a–f by the Heck Reaction; Typical Procedure
A mixture of **4a** (50 mg, 0.13 mmol), TBAB (50 mg, 0.15 mmol) and anhydrous KOAc (34.6 mg, 0.35 mmol) was taken in anhydrous DMF (10 mL) under a nitrogen atmosphere. $Pd(OAc)_2$ (5 mol%, 1.43 mg) was added and the reaction mixture was stirred at 80 °C for 60 min. The reaction mixture was cooled, and H_2O (10 mL) was added, the mixture was extracted with EtOAc (3 × 30 mL) and the combined organic layer was washed with H_2O (2 × 40 mL), followed by brine (30 mL). The organic layer was dried (Na_2SO_4), and the solvent was distilled off to furnish a viscous mass, which was purified by column chromatography over silica gel (EtOAc–PE, 4%) to give **5a**. Substrates **4b–f** were treated similarly to give products **5b–f**.

5a
Yield: 90%; solid; mp 200–201 °C.

IR (KBr): 1350, 1180 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 7.20 (d, *J* = 12.2 Hz, 1 H, =CH_a), 7.27 (d, *J* = 12.2 Hz, 1 H, =CH_b), 7.28–7.30 (m, 2 H, ArH), 7.41–7.52 (m, 3 H, ArH), 7.62 (d, *J* = 9.0 Hz, 1 H, ArH), 7.81 (m, 3 H, ArH), 8.01 (dd, *J* = 5.7, 3.0 Hz, 1 H, ArH).

^{13}C NMR ($CDCl_3$, 125 MHz): δ = 121.0, 125.3, 127.0, 127.2, 127.6, 128.5, 128.8, 129.9, 130.0, 130.6, 131.5, 131.6, 131.7, 132.2, 133.2, 134.6, 135.3, 145.4.

HRMS: *m*/*z* calcd for $C_{18}H_{12}O_3S$: 331.0405 [M + Na]; found: 331.0405 [M + Na].

Anal. Calcd for $C_{18}H_{12}O_3S$: C, 70.11; H, 3.92. Found: C, 70.09; H, 4.02.

5b
Yield: 88%; solid; mp 120–121 °C.

IR (KBr): 1354, 1163 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 6.86 (d, *J* = 12.2 Hz, 1 H, =CH_a), 7.01 (d, *J* = 12.2 Hz, 1 H, =CH_b), 7.13–7.21 (m, 2 H, ArH), 7.27–7.34 (m, 3 H, ArH), 7.47–7.51 (m, 2 H, ArH), 8.02 (d, *J* = 8.0 Hz, 1 H, ArH).

MS: *m*/*z* = 258 [M^+].

Anal. Calcd for $C_{14}H_{10}O_3S$: C, 65.10; H, 3.90. Found: C, 65.31; H, 4.11.

5c
Yield: 91%; solid; mp 132–133 °C.

IR (KBr): 1354, 1164 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 2.30 (s, 3 H, CH_3), 6.81 (d, *J* = 12.2 Hz, 1 H, =CH_a), 6.93 (s, 1 H, ArH), 7.00 (d, *J* = 12.2 Hz, 1 H, =CH_b), 7.08 (dd, *J* = 8.4, 1.8 Hz, 1 H, ArH), 7.30 (d, *J* = 6.9 Hz, 1 H, ArH), 7.32 (dd, *J* = 7.2, 1.3 Hz, 1 H, ArH), 7.35 (d, *J* = 8.3 Hz, 1 H, ArH), 7.49 (dt, *J* = 6.4, 1.2 Hz, 1 H, ArH), 8.02 (dd, *J* = 8.1, 1.0 Hz, 1 H, ArH).

MS: *m*/*z* = 272 [M^+].

Anal. Calcd for $C_{15}H_{12}O_3S$: C, 66.16; H, 4.44. Found: C, 66.30; H, 4.29.

5d
Yield: 84%; solid; mp 142–143 °C.

IR (KBr): 1355, 1162 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 3.71 (s, 3 H, OCH_3), 6.61 (d, *J* = 3.0 Hz, 1 H, ArH), 6.78 (dd, *J* = 7.6, 1.6 Hz, 1 H, ArH), 6.82 (d, *J* = 12.2 Hz, 1 H, =CH_a), 7.02 (d, *J* = 12.2 Hz, 1 H, =CH$_b$), 7.30 (s, 1 H, ArH), 7.33 (t, *J* = 7.3 Hz, 1 H, ArH), 7.40 (d, *J* = 9.0 Hz, 1 H, ArH), 7.50 (dt, *J* = 7.5, 1.0 Hz, 1 H, ArH), 8.02 (dd, *J* = 7.9, 1.2 Hz, 1 H, ArH).

MS: *m*/*z* = 288 [M^+].

Anal. Calcd for $C_{15}H_{12}O_4S$: C, 62.49; H, 4.20. Found: C, 62.61; H, 4.03.

5e
Yield: 79%; solid; mp 122–123 °C.

IR (KBr): 1334, 1167 cm^{-1}.

^1H NMR ($CDCl_3$, 400 MHz): δ = 6.64 (d, *J* = 2.8 Hz, 1 H, ArH), 6.79 (d, *J* = 6.9 Hz, 1 H, ArH), 6.83 (d, *J* = 12.2 Hz, 1 H, =CH_a), 7.04 (d, *J* = 12.2 Hz, 1 H, =CH_b), 7.31 (s, 1 H, ArH), 7.36 (dd, *J* = 7.6, 1.2 Hz, 1 H, ArH), 7.44–7.48 (m, 2 H, ArH), 8.04 (dd, *J* = 8.1, 1.7 Hz, 1 H, ArH).

MS: *m*/*z* = 292 [M^+].

Anal. Calcd for $C_{14}H_9ClO_3S$: C, 57.44; H, 3.10. Found: C, 57.61; H, 2.97.

5f
Yield: 26%; solid; mp 211–212 °C.

IR (KBr): 1352, 1183 cm^{-1}.

^1H NMR (DMSO-d_6, 400 MHz): δ = 7.24 (d, *J* = 12.2 Hz, 2 H, =CH_a), 7.29 (d, *J* = 12.2 Hz, 2 H, =CH_b), 7.31 (d, *J* = 7.4 Hz, 2 H, ArH), 7.44–7.56 (m, 6 H, ArH), 7.61 (dd, *J* = 6.9, 1.0 Hz, 2 H, ArH), 8.07 (dd, *J* = 8.2, 1.7 Hz, 2 H, ArH).

MS: *m*/*z* = 488 [M^+].

Anal. Calcd for $C_{26}H_{16}O_6S_2$: C, 63.92; H, 3.30. Found: C, 63.71; H, 3.13.

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