Regioselective Synthesis of 2-(Aryloxythio)benzoates by the First [3+3] Cyclizations of 3-Aryloxythio-1-silyloxybuta-1,3-dienes with 3-Alkoxy-2-en-1-ones

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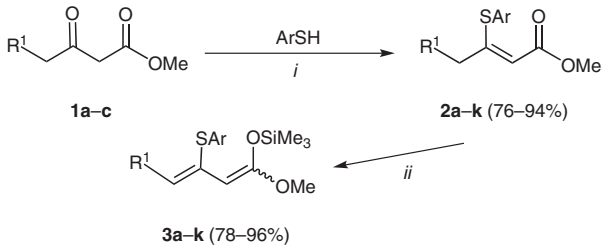
Abstract: Functionalized 2-(aryloxythio)benzoates were regioselectively prepared by the first [3+3] cyclizations of 3-aryloxythio-1-trimethylsilyloxybuta-1,3-dienes with 3-alkoxy-2-en-1-ones.

Key words: cyclizations, diaryl sulfides, regioselectivity, pyridines, silyl enol ethers

Diaryl sulfides are pharmacologically relevant compounds that occur in a number of natural products. Prominent examples include lissoclibadins, dibenzothiophenes, cyclic sulfides, varacins (lissoclinotoxins), and related natural products.[1] Classic syntheses of diaryl sulfides include, for example, reactions of arenes with sulfur[2] or sulfur dichloride,[3] condensations of Grignard or organolithium reagents with chlorophenyl sulfides[4] or base-mediated reactions of thiophenols with chloroarenes.[5] The formation of polysulfides and low regioselectivities are severe drawbacks of these methods. In contrast, transition-metal-catalyzed[6] and metal-free[7] C–S coupling reactions allow the synthesis of diaryl sulfides under relatively mild conditions. However, the scope of this approach is limited by the fact that reactions of sterically encumbered substrates are often difficult or not possible at all. In addition, the synthesis of the starting materials, substituted aryl halides or triflates, can be difficult and tedious.

An interesting alternative for the synthesis of diaryl sulfides is based on the use of appropriate sulfur-containing building blocks in cyclization reactions. Such reactions have only scarcely been reported to date. Hilt and coworkers reported the synthesis of diaryl sulfides by cobalt(I)-catalyzed [4+2] cycloaddition of alkynyl sulfides with buta-1,3-dienes.[8] Some years ago, Chan and coworkers developed[9] a convenient approach to salicylates based on formal [3+3] cyclizations[10] of 1,3-bis(silyloxy)buta-1,3-dienes[11] with 3-siloxy-2-en-1-ones. We have recently reported the application of this methodology to the synthesis of 3- and 5-(aryloxythio)salicylates.[12] Chan et al. developed an elegant synthesis of annulated cyclohexanones by conjugate addition of 1-methoxy-1-trimethylsilyloxy-3-phenoxythiobuta-1,3-diene to cyclohex-2-en-1-ones and subsequent base-mediated cyclization.[13] The synthesis of methyl 4,6-dimethyl-2-(phenoxythio)benzoate by cyclization of 1-methoxy-1-trimethylsilyloxy-3-phenoxythiobuta-1,3-diene with 4-(trimethylsilyloxy)pent-3-en-2-one has also been reported.[13] Recently, we have studied the synthesis of 2-aryloxythio-5-(haloethyl)benzoates by cyclization of 3-aryloxythio-1-silyloxybuta-1,3-dienes with 1,1-diacylcyclopropanes.[14] Herein we report what are, to the best of our knowledge, the first [3+3] cyclizations of 3-aryloxythio-1-silyloxybuta-1,3-dienes with 3-alkoxy-2-en-1-ones. These reactions provide a convenient and regioselective approach to sterically encumbered and functionalized 2-(aryloxythio)benzoates, which are not readily available by other methods. In contrast to the coupling reactions outlined above, our method relies on the assembly of one of the two arene moieties.

The reaction of β-keto esters **1a–c** with various thiophenols gave, following the procedure reported by Chan et al.,[13] the 3-(aryloxythio)alkanoates **2a–k** (Scheme 1). Deprotonation of **2a–k** (LDA) and subsequent addition of Me_3SiCl afforded, again following the procedure reported by Chan et al.,[13] the 3-aryloxythio-1-silyloxybuta-1,3-dienes **3a–k**. The synthesis of **2a** and **3a** has been previously reported.[13] Dienes **3a–k** proved to be unstable and had to be used directly after their preparation.



Scheme 1 Synthesis of **3a–k** (for R^1 and Ar, see Table 1). *Reagents and conditions*: (*i*) P_4O_{10}, CH_2Cl_2, 20 °C, 18 h; (*ii*) 1) LDA, THF, –78 °C, 1 h; 2) Me_3SiCl, –78 → 20 °C, 14 h.

The $TiCl_4$-mediated cyclization of 3-phenoxythio-1-silyloxybuta-1,3-diene (**3a**) with 1-(methoxy)but-1-en-3-one (**4a**) afforded methyl 6-methyl-2-(phenoxythio)benzoate (**5a**) with very good regioselectivity (Scheme 2). Notably, the formation of regioisomeric methyl 4-methyl-2-(phenoxythio)benzoate was *not* observed. The best yields were obtained when the reaction was carried out in a highly concentrated solution. The use of an excess (1.5 equiv) of

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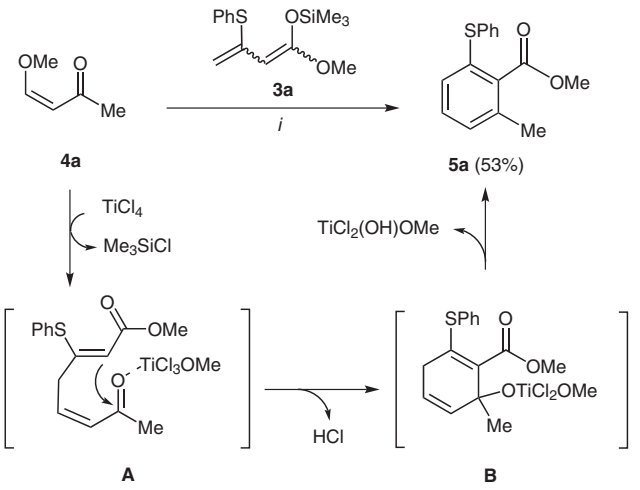
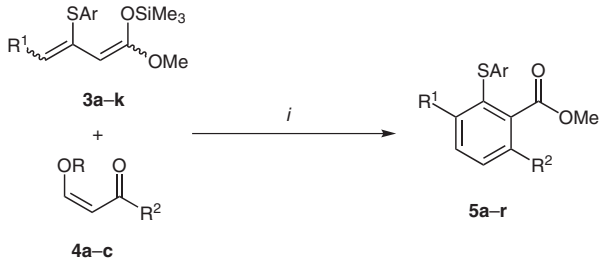


Scheme 2 Possible mechanism for the formation of **5a**. *Reagents and conditions*: (*i*) 1) $TiCl_4$, CH_2Cl_2, –78 → 20 °C, 20 h; 2) $NaHCO_3$, H_2O.

4a and of $TiCl_4$ also proved to be important. The formation of **5a** can be explained by $TiCl_4$-mediated conjugate addition of the terminal carbon atom of **3a** onto **4a** to give intermediate **A**, cyclization via the central carbon atom (intermediate **B**), and subsequent aromatization.



Scheme 3 Synthesis of **5a–r**. *Reagents and conditions*: (*i*) 1) $TiCl_4$, CH_2Cl_2, –78 → 20 °C, 20 h; 2) $NaHCO_3$, H_2O.

The cyclization of dienes **3a–k** with **4a** afforded the 2-aryloxythio-6-methylbenzoates **5a–j** (Scheme 3, Table 1). The cyclization of dienes **3** with 3-ethoxy-1-(aryl)prop-2-en-1-ones **4b**,**c**, readily available by Heck reaction of ethylvinyl ether with benzoyl chloride and 4-chlorobenzoyl chloride,[15] afforded the 6-aryl-2-(aryloxythio)benzoates **5k–r**. The relatively low yields might be explained by decomposition of the starting materials by HCl formed during the reaction.

The structures of all products were established by spectroscopic methods. The structure of **5p** was independently confirmed by X-ray crystal structure analysis (Figure 1).[16]

Table 1 Synthesis of **5a–r**

3	4	5	R^1	Ar	R^2	R	Yield(%)[a] **2**	Yield (%)[a] **3**	Yield (%)[a] **5**
a	**a**	**a**	H	Ph	Me	Me	90	90	53
b	**a**	**b**	H	4-FC_6H_4	Me	Me	80	80	37
c	**a**	**c**	H	3-MeC_6H_4	Me	Me	82	87	50
d	**a**	**d**	H	3-ClC_6H_4	Me	Me	80	86	48
e	**a**	**e**	H	4-MeC_6H_4	Me	Me	85	88	51
f	**a**	**f**	H	2-naphthyl	Me	Me	75	79	33
g	**a**	**g**	Me	4-MeC_6H_4	Me	Me	85	83	37
h	**a**	**h**	Me	Ph	Me	Me	84	82	40
i	**a**	**i**	Me	4-FC_6H_4	Me	Me	74	78	34
j	**a**	**j**	Et	Ph	Me	Me	84	83	35
a	**b**	**k**	H	Ph	Ph	Et	90	90	40
k	**b**	**l**	H	4-ClC_6H_4	Ph	Et	87	84	37
a	**c**	**m**	H	Ph	4-ClC_6H_4	Et	90	90	47
k	**c**	**n**	H	4-ClC_6H_4	4-ClC_6H_4	Et	87	84	46
e	**c**	**o**	H	4-MeC_6H_4	4-ClC_6H_4	Et	85	88	47
b	**c**	**p**	H	4-FC_6H_4	4-ClC_6H_4	Et	80	80	35
h	**c**	**q**	Me	Ph	4-ClC_6H_4	Et	81	82	40
j	**c**	**r**	Et	Ph	4-ClC_6H_4	Et	84	83	36

[a] Isolated yields.

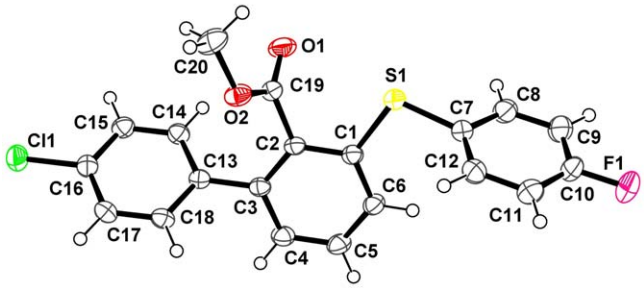


Figure 1 ORTEP plot of **5p** (50% probability level)

In conclusion, we have reported a convenient and regioselective approach to functionalized 2-(aryloxythio)benzoates by the first [3+3] cyclizations of 3-aryloxythio-1-trimethylsilyloxybuta-1,3-dienes with 3-alkoxy-2-en-1-ones.

All solvents were dried by standard methods and all reactions were carried out under an inert atmosphere. For ^{1}H and ^{13}C NMR spectra, the deuterated solvents indicated were used. Mass spectrometric data (MS) were obtained by electron ionization (EI, 70 eV), chemical ionization (CI, H_2O), or electrospray ionization (ESI). For preparative scale chromatography, silica gel (60–200 mesh) was used. Melting points are uncorrected.

Compounds 2a–k; General Procedure

To a CH_2Cl_2 solution (1 mL/mmol of **1**) of **1** (80.0 mmol) and the respective arylthiol (80.0 mmol) was added P_4O_{10} (80.0 mmol) at 20 °C and the mixture was stirred for 18 h. To the mixture was added 10% aq NaOH (80 mL). The aqueous and the organic layer were separated and the latter was washed with brine (100 mL). The aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layers were dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, EtOAc–heptanes, 1:4) (Table 1). The products were isolated as mixture of *E*/*Z* isomers. Only the signals of the major isomer are listed.

3-(Phenylsulfanyl)but-2-enoic Acid Methyl Ester (2a)

Starting from **1a** (9.3 g, 80 mmol), the respective arylthiol (8.80 g, 80.0 mmol), P_4O_{10} (22.60 g, 90.0 mmol), and CH_2Cl_2 (80 mL), **2a** was isolated as a highly viscous oil (14.50 g, 80%, isomeric ratio = 3:1).

IR (KBr): 3020 (w), 2980 (w), 2946 (w), 2920 (w), 2866 (w), 2838 (w), 1707 (s), 1604 (s), 1491 (m), 1431 (m), 1374 (w), 1335 (m), 1266 (w), 1175 (s), 1104 (s), 1038 (m), 1017 (m), 809 cm^{-1} (s).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.37 (s, 3 H, CH_3), 3.59 (s, 3 H, OCH_3), 5.21 (s, 1 H, CH), 7.31–7.54 (m, 5 H, Ar).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 19.9 (CH_3), 51.1 (OCH_3), 110.1 (CH), 128.3, 129.8, 129.9, 130.5, 135.6 (CH), 135.9, 160.7, 164.3 (C).

MS (EI, 70 eV): *m*/*z* (%) = 222 (M^+, 60), 191 (38), 164 (17), 163 (100), 148 (31), 124 (39), 123 (17), 91 (27), 79 (12), 77 (15), 59 (18), 45 (11), 39 (12).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{12}O_2S$ (M^+): 208.07097; found: 208.090604.

3-(4-Fluorophenylsulfanyl)but-2-enoic Acid Methyl Ester (2b)

Starting from **1a** (9.30 g, 80.0 mmol), the respective arylthiol (10.20 g, 80.0 mmol), P_4O_{10} (22.60 g, 80.0 mmol), and CH_2Cl_2 (80 mL), **2b** was isolated as a highly viscous oil (15.8 g, 80%, isomeric ratio = 3:1).

IR (KBr): 3022 (w), 2986 (w), 2949 (w), 2868 (w), 2839 (w), 1709 (s), 1604 (s), 1491 (m), 1431 (m), 1378 (w), 1335 (m), 1269 (w), 1175 (s), 1104 (s), 1038 (m), 1019 (m), 809 cm^{-1} (s).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.39 (s, 3 H, CH_3), 3.59 (s, 3 H, OCH_3), 5.11 (s, 1 H, CH), 6.85–7.44 (m, 4 H, Ar).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 19.8 (CH_3), 51.2 (OCH_3), 111.1 (CH), 128.3, 129.8, 129.9, 130.5, 135.6 (CH), 146.2, 160.7, 164.3 (C).

MS (EI, 70 eV): *m*/*z* (%) = 226 (M^+, 59), 191 (38), 169 (19), 163 (100), 148 (31), 124 (39), 123 (17), 91 (27), 79 (12), 77 (19), 59 (18), 45 (15), 39 (19).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{11}FO_2S$ (M^+): 226.06952; found: 222.059604.

3-(3-Methylphenylsulfanyl)but-2-enoic Acid Methyl Ester (2c)

Starting from **1a** (9.30 g, 80.0 mmol), the respective arylthiol (9.90 g, 80.0 mmol), P_4O_{10} (22.60 g, 80.0 mmol), and CH_2Cl_2 (80 mL), **2c** was isolated as a highly viscous oil (14.60 g, 82%, isomeric ratio = 3:1).

IR (KBr): 3021 (w), 2987 (w), 2946 (w), 2867 (w), 2838 (w), 1707 (s), 1608 (s), 1494 (m), 1433 (m), 1377 (w), 1335 (m), 1269 (w), 1104 (s), 1038 (m), 1019 (m), 807 cm^{-1} (s).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.38 (s, 3 H, CH_3), 2.47 (s, 3 H, CH_3), 3.58 (s, 3 H, OCH_3), 5.27 (s, 1 H, CH), 7.18–7.54 (m, 4 H, Ar).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 19.9 (CH_3), 21.7 (CH_3), 50.9 (OCH_3), 108.7 (CH), 129.8, 130.5, 130.6, 135.3, 135.7 (CH), 135.9, 160.7, 164.3 (C).

MS (EI, 70 eV): *m*/*z* (%) = 222 (M^+, 59), 193 (38), 169 (19), 163 (100), 148 (31), 124 (39), 123 (17), 91 (27), 79 (12), 77 (19), 59 (18), 45 (15), 39 (19).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{14}O_2S$ (M^+): 222.07090; found: 222.070604.

3-(3-Chlorophenylsulfanyl)but-2-enoic Acid Methyl Ester (2d)

Starting from **1a** (9.30 g, 80.0 mmol), the respective arylthiol (11.50 g, 80.0 mmol), P_4O_{10} (22.60 g, 90.0 mmol), and CH_2Cl_2 (80 mL), **2d** was isolated as a highly viscous oil (15.50 g, 80%, isomeric ratio = 3:1).

IR (KBr): 3020 (w), 2982 (w), 2945 (w), 2920 (w), 2866 (w), 2838 (w), 1709 (s), 1605 (s), 1491 (m), 1431 (m), 1379 (w), 1335 (m), 1268 (w), 1175 (s), 1104 (s), 1036 (m), 1017 (m), 809 cm^{-1} (s).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.40 (s, 3 H, CH_3), 3.69 (s, 3 H, OCH_3), 5.41 (s, 1 H, CH), 6.71–7.34 (m, 4 H, Ar).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 23.3 (CH_3), 52.3 (OCH_3), 111.3 (CH), 128.3, 129.8, 129.9, 130.5, 135.6 (CH), 139.9, 160.7, 166.4 (C).

MS (EI, 70 eV): *m*/*z* (%) = 244 (M^+, ^{37}Cl, 16), 242 (M^+, ^{35}Cl, 71), 191 (38), 164 (17), 163 (100), 148 (31), 124 (39), 123 (17), 91 (27), 79 (12), 77 (15), 59 (18), 45 (11), 39 (12).

HRMS (EI): *m*/*z* calcd for $C_{11}H_{12}O_2S$ (M^+): 242.47097; found: 242.510684.

3-(4-Methylphenylsulfanyl)but-2-enoic Acid Methyl Ester (2e)

Starting from **1a** (9.30 g, 80.0 mmol), the respective arylthiol (9.90 g, 80.0 mmol), P_4O_{10} (22.60 g, 80.0 mmol), and CH_2Cl_2 (80 mL), **2e** was isolated as a highly viscous oil (15.30 g, 85%, isomeric ratio = 3:1).

IR (KBr): 3021 (w), 2987 (w), 2946 (w), 2867 (w), 2838 (w), 1707 (s), 1608 (s), 1494 (m), 1433 (m), 1377 (w), 1335 (m), 1269 (w), 1104 (s), 1038 (m), 1019 (m), 807 cm^{-1} (s).

^1H NMR (250 MHz, $CDCl_3$): δ = 2.38 (s, 3 H, CH_3), 2.47 (s, 3 H, CH_3), 3.58 (s, 3 H, OCH_3), 5.27 (s, 1 H, CH), 7.18–7.54 (m, 4 H, Ar).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 19.9 (CH_3), 21.7 (CH_3), 50.9 (OCH_3), 108.7 (CH), 129.8, 130.5, 130.6, 135.3, 135.7 (CH), 135.9, 160.7, 164.3 (C).

MS (EI, 70 eV): *m*/*z* (%) = 222 (M^+, 59), 193 (38), 169 (19), 163 (100), 148 (31), 124 (39), 123 (17), 91 (27), 79 (12), 77 (19), 59 (18), 45 (15), 39 (19).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{14}O_2S$ (M^+): 222.07090; found: 222.070604.

3-(Naphth-2-ylsulfanyl)but-2-enoic Acid Methyl Ester (2f)
Starting from **1a** (9.30 g, 80.0 mmol), the respective arylthiol (10.20 g, 80.0 mmol), P_4O_{10} (22.6 g, 80.0 mmol), and CH_2Cl_2 (80 mL), **2f** was isolated as a highly viscous oil (15.5 g, 75%, isomeric ratio = 3:1).

IR (KBr): 3021 (w), 2987 (w), 2946 (w), 2867 (w), 2838 (w), 1707 (s), 1608 (s), 1494 (m), 1433 (m), 1377 (w), 1335 (m), 1269 (w), 1104 (s), 1038 (m), 1019 (m), 807 cm^{-1} (s).

^1H NMR (250 MHz, $CDCl_3$): δ = 2.37 (s, 3 H, CH_3), 3.45 (s, 3 H, OCH_3), 5.17 (s, 1 H, CH), 7.38–7.94 (m, 7 H, Ar).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 19.9 (CH_3), 50.9 (OCH_3), 108.7 (CH), 129.8, 130.5, 130.6, 135.3, 135.7, 135.9, 140.5 (CH), 159.1, 159.8, 160.1, 160.7, 164.3 (C).

MS (EI, 70 eV): *m*/*z* (%) = 258 (M^+, 61), 193 (38), 169 (19), 163 (100), 148 (31), 124 (39), 123 (17), 91 (27), 79 (12), 77 (19), 59 (18), 45 (15), 39 (19).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{14}O_2S$ (M^+): 258.07090; found: 258.070604.

3-(4-Tolylsulfanyl)pent-2-enoic Acid Methyl Ester (2g)
Starting from **1a** (10.40 g, 80.0 mmol), the respective arylthiol (9.90 g, 80.0 mmol), P_4O_{10} (22.6 g, 80.0 mmol), and CH_2Cl_2 (80 mL), **2g** was isolated as a highly viscous oil (16.10 g, 85%, isomeric ratio = 3:1).

IR (KBr): 3021 (w), 2987 (w), 2946 (w), 2867 (w), 2838 (w), 1707 (s), 1608 (s), 1494 (m), 1433 (m), 1377 (w), 1335 (m), 1269 (w), 1104 (s), 1038 (m), 1019 (m), 807 cm^{-1} (s).

^1H NMR (250 MHz, $CDCl_3$): δ = 1.20 (t, *J* = 6.3 Hz, 3 H, CH_3), 2.08 (s, 3 H, CH_3), 2.41 (q, *J* = 6.3 Hz, 2 H, CH_2), 3.34 (s, 3 H, OCH_3), 5.21 (s, 1 H, CH), 6.81–7.12 (m, 4 H, Ar).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 19.9 (CH_3), 21.1 (CH_3), 29.3 (CH_3CH_2), 50.9 (OCH_3), 108.7 (CH), 129.8, 130.5, 135.3, 135.9 (CH), 159.1, 159.8, 160.7, 164.3 (C).

MS (EI, 70 eV): *m*/*z* (%) = 236 (M^+, 61), 193 (38), 169 (19), 161 (100), 148 (31), 124 (39), 123 (17), 91 (27), 79 (12), 77 (19), 59 (18), 45 (15), 39 (19).

HRMS (EI): *m*/*z* calcd for $C_{13}H_{16}O_2S$ (M^+): 236.07090; found: 236.070604.

3-(Phenylsulfanyl)pent-2-enoic Acid Methyl Ester (2h)
Starting from **1a** (10.40 g, 80.0 mmol), the respective arylthiol (8.80 g, 80.0 mmol), P_4O_{10} (22.60 g, 90.0 mmol), and CH_2Cl_2 (80 mL), **2h** was isolated as a highly viscous oil (14.90 g, 84%, isomeric ratio = 3:1).

IR (KBr): 3024 (w), 2985 (w), 2946 (w), 2867 (w), 2837 (w), 1707 (s), 1608 (s), 1494 (m), 1433 (m), 1377 (w), 1335 (m), 1267 (w), 1102 (s), 1038 (m), 1019 (m), 807 cm^{-1} (s).

^1H NMR (250 MHz, $CDCl_3$): δ = 1.22 (t, *J* = 6.3 Hz, 3 H, CH_3), 2.48 (q, *J* = 6.3 Hz, 2 H, CH_2), 3.35 (s, 3 H, OCH_3), 5.25 (s, 1 H, CH), 6.93–7.21 (m, 5 H, Ar).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 19.9 (CH_3), 21.9 (CH_3CH_2), 50.9 (OCH_3), 108.7 (CH), 129.8, 130.5, 130.6, 135.7, 140.1 (CH), 159.1, 159.8, 164.3 (C).

MS (EI, 70 eV): *m*/*z* (%) = 222 (M^+, 63), 195 (38), 169 (19), 163 (100), 148 (31), 124 (39), 123 (17), 91 (27), 79 (12), 77 (19), 59 (18), 45 (15), 39 (19).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{14}O_2S$ (M^+): 222.05090; found: 222.060602.

3-(4-Fluorophenylsulfanyl)pent-2-enoic Acid Methyl Ester (2i)
Starting from **1a** (10.40 g, 80.0 mmol), the respective arylthiol (10.20 g, 80.0 mmol), P_4O_{10} (22.60 g, 90.0 mmol), and CH_2Cl_2 (80 mL), **2i** was isolated as a highly viscous oil (14.10 g, 74%, isomeric ratio = 3:1).

IR (KBr): 3024 (w), 2985 (w), 2946 (w), 2867 (w), 2837 (w), 1707 (s), 1608 (s), 1494 (m), 1433 (m), 1377 (w), 1335 (m), 1267 (w), 1102 (s), 1038 (m), 1019 (m), 807 cm^{-1} (s).

^1H NMR (250 MHz, $CDCl_3$): δ = 1.30 (t, *J* = 6.3 Hz, 3 H, CH_3), 2.32 (q, *J* = 6.3 Hz, 2 H, CH_2), 3.40 (s, 3 H, OCH_3), 5.20 (s, 1 H, CH), 7.01–7.82 (m, 4 H, Ar).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 19.9 (CH_3), 21.9 (CH_3CH_2), 50.9 (OCH_3), 108.7 (CH), 129.8, 130.5, 135.7, 140.1 (CH), 159.1, 159.8, 160.5, 165.3 (C).

MS (EI, 70 eV): *m*/*z* (%) = 240 (M^+, 63), 195 (38), 169 (19), 163 (100), 148 (31), 124 (39), 123 (17), 91 (27), 79 (12), 77 (19), 59 (18), 45 (15), 39 (19).

HRMS (EI): *m*/*z* calcd for $C_{12}H_{13}FO_2S$ (M^+): 240.07280; found: 240.067602.

3-(Phenylsulfanyl)hex-2-enoic Acid Methyl Ester (2j)
Starting from **1a** (11.50 g, 80.0 mmol), the respective arylthiol (8.80 g, 80.0 mmol), P_4O_{10} (22.6 g, 90.0 mmol), and CH_2Cl_2 (80 mL), **2j** was isolated as a highly viscous oil (15.80 g, 84%, isomeric ratio = 3:1).

IR (KBr): 3024 (w), 2985 (w), 2946 (w), 2867 (w), 2837 (w), 1707 (s), 1608 (s), 1494 (m), 1433 (m), 1377 (w), 1335 (m), 1267 (w), 1102 (s), 1038 (m), 1019 (m), 807 cm^{-1} (s).

^1H NMR (250 MHz, $CDCl_3$): δ = 1.10 (t, *J* = 6.3 Hz, 3 H, CH_3), 1.70 (m, 2 H, CH_2), 2.30 (q, *J* = 6.3 Hz, 2 H, CH_2), 3.52 (s, 3 H, OCH_3), 5.30 (s, 1 H, CH), 6.80–7.30 (m, 5 H, Ar).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 19.9 (CH_3), 21.9 (CH_3CH_2), 22.9 (CH_2CH_2), 50.9 (OCH_3), 108.7 (CH), 129.8, 130.5, 130.9, 135.7, 140.1 (CH), 159.1, 160.5, 165.3 (C).

MS (EI, 70 eV): *m*/*z* (%) = 236 (M^+, 61), 193 (36), 167 (34), 161 (100), 148 (31), 124 (39), 123 (17), 91 (27), 79 (12), 77 (19), 59 (18), 45 (15), 39 (19).

HRMS (EI): *m*/*z* calcd for $C_{13}H_{16}O_2S$ (M^+): 236.06020; found: 240.065202.

3-(4-Chlorophenylsulfanyl)pent-2-enoic Acid Methyl Ester (2k)
Starting from **1a** (10.40 g, 80.0 mmol), the respective arylthiol (80.0 mmol), P_4O_{10} (22.60 g, 90.0 mmol), and CH_2Cl_2 (80 mL), **2k** was isolated as a highly viscous oil (3:1 isomeric ratio) (14.00 g, 70%, isomeric ratio = 3:1). The product was used directly after its preparation for the synthesis of **3k**.

Compounds 3a–k; General Procedure
To a THF solution (1.2 mL/mmol of **2**) of diisopropylamine (DIPA, 84.5 mmol) was added *n*-BuLi (84.5 mmol) at 0 °C. After stirring

for 45 min, **2** (65.0 mmol) was added at –78 °C. After stirring for 1 h, TMSCl (97.5 mmol) was added at –78 °C and the mixture was allowed to warm to 20 °C during 18 h with stirring. The solvent was removed in vacuo. To the residue was added heptane (100 mL) and the mixture was filtered under an inert atmosphere. The filtrate was concentrated in vacuo to give products **3**, which were used without further purification (Table 1). Due to their unstable nature, products **3** were used directly after their preparation and characterized only by ^{1}H NMR spectroscopy. The products were isolated as mixtures of *E*/*Z* isomers. Only the signals of the major isomer are listed.

[1-Methoxy-3-(phenylsulfanyl)buta-1,3-dienyloxy]trimethylsilane (3a)
Starting from **2a** (13.50 g, 65.0 mmol), DIPA (8.50 g, 84.5 mmol), *n*-BuLi (5.40 g, 84.5 mmol) and TMSCl (10.50 g, 97.5 mmol), **3a** was isolated as a highly viscous oil (16.30 g, 90%, isomeric ratio = 3:1).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.17 [s, 9 H, $Si(CH_3)_3$], 3.34 (s, 3 H, OCH_3), 3.47 (s, 2 H, CH_2), 5.29 (s, 1 H, CH), 7.02–7.31 (m, 5 H, Ar).

[1-Methoxy-3-(4-fluorophenylsulfanyl)buta-1,3-dienyloxy]trimethylsilane (3b)
Starting from **2b** (14.70 g, 65.0 mmol), DIPA (8.50 g, 84.5 mmol), *n*-BuLi (5.40 g, 84.5 mmol) and TMSCl (10.50 g, 97.5 mmol), **3b** was isolated as a highly viscous oil (15.50 g, 80%, isomeric ratio = 3:1).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.19 [s, 9 H, $Si(CH_3)_3$], 3.38 (s, 3 H, OCH_3), 3.49 (s, 2 H, CH_2), 5.34 (s, 1 H, CH), 7.08–7.51 (m, 4 H, Ar).

[1-Methoxy-3-(3-methylphenylsulfanyl)buta-1,3-dienyloxy)trimethylsilane (3c)
Starting from **2c** (14.40 g, 65.0 mmol), DIPA (8.50 g, 84.5 mmol), *n*-BuLi (5.40 g, 84.5 mmol) and TMSCl (10.50 g, 97.5 mmol), **3c** was isolated as a highly viscous oil (16.60 g, 87%, isomeric ratio = 3:1).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.16 [s, 9 H, $Si(CH_3)_3$], 2.12 (s, 3 H, CH_3), 3.35 (s, 3 H, OCH_3), 3.48 (s, 2 H, CH_2), 5.27 (s, 1 H, CH), 7.02–7.38 (m, 4 H, Ar).

[1-Methoxy-3-(3-chlorophenylsulfanyl)buta-1,3-dienyloxy]trimethylsilane (3d)
Starting from **2d** (15.70 g, 65.0 mmol), DIPA (8.50 g, 84.5 mmol), *n*-BuLi (5.40 g, 84.5 mmol) and TMSCl (10.50 g, 97.5 mmol), **3d** was isolated as a highly viscous oil (17.50 g, 86%, isomeric ratio = 3:1).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.21 [s, 9 H, $Si(CH_3)_3$], 3.49 (s, 2 H, CH_2), 5.32 (s, 1 H, CH), 7.04–7.37 (m, 4 H, Ar).

[1-Methoxy-3-(4-methylphenylsulfanyl)buta-1,3-dienyloxy]trimethylsilane (3e)
Starting from **2e** (14.40 g, 65.0 mmol), DIPA (8.50 g, 84.5 mmol), *n*-BuLi (5.40 g, 84.5 mmol) and TMSCl (10.50 g, 97.5 mmol), **3e** was isolated as a highly viscous oil (16.70 g, 88%, isomeric ratio = 3:1).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.16 [s, 9 H, $Si(CH_3)_3$], 2.14 (s, 3 H, CH_3), 3.37 (s, 3 H, OCH_3), 3.48 (s, 2 H, CH_2), 5.27 (s, 1 H, CH), 7.02–7.38 (m, 4 H, Ar).

[1-Methoxy-3-(naphth-2-ylsulfanyl)buta-1,3-dienyloxy)trimethylsilane (3f)
Starting from **2f** (10.40 g, 65.0 mmol), DIPA (8.50 g, 84.5 mmol), *n*-BuLi (5.40 g, 84.5 mmol) and TMSCl (10.50 g, 97.5 mmol), **3f** was isolated as a highly viscous oil (13.20 g, 79%, isomeric ratio = 3:1).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.19 [s, 9 H, $Si(CH_3)_3$], 3.32 (s, 3 H, OCH_3), 3.46 (s, 2 H, CH_2), 5.29 (s, 1 H, CH), 7.01–7.51 (m, 7 H, Ar).

[1-Methoxy-3-(4-methylphenylsulfanyl)penta-1,3-dienyloxy]trimethylsilane (3g)
Starting from **2g** (15.30 g, 65.0 mmol), DIPA (8.50 g, 84.5 mmol), *n*-BuLi (5.40 g, 84.5 mmol) and TMSCl (10.50 g, 97.5 mmol), **3g** was isolated as a highly viscous oil (16.50 g, 83%, isomeric ratio = 3:1).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.04 [s, 9 H, $Si(CH_3)_3$], 1.72 (s, 3 H, CH_3), 2.08 (d, *J* = 5.5 Hz, 3 H, CH_3), 3.15 (s, 3 H, OCH_3), 6.03 (q, *J* = 5.5 Hz, 1 H, CH), 6.84 (s, 1 H, CH), 6.92–7.28 (m, 4 H, Ar).

[1-Methoxy-3-(phenylsulfanyl)penta-1,3-dienyloxy)]trimethylsilane (3h)
Starting from **2h** (14.40 g, 65.0 mmol), DIPA (8.50 g, 84.5 mmol), *n*-BuLi (5.40 g, 84.5 mmol) and TMSCl (10.50 g, 97.5 mmol), **3h** was isolated as a highly viscous oil (15.6 g, 82%, isomeric ratio = 3:1).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.04 [s, 9 H, $Si(CH_3)_3$], 2.12 (d, *J* = 5.5 Hz, 3 H, CH_3), 3.17 (s, 3 H, OCH_3), 6.06 (q, *J* = 5.5 Hz, 1 H, CH), 6.84 (s, 1 H, CH), 6.92–7.28 (m, 5 H, Ar).

[1-Methoxy-3-(4-fluorophenylsulfanyl)penta-1,3-dienyloxy]trimethylsilane (3i)
Starting from **2i** (15.60 g, 65.0 mmol), DIPA (8.50 g, 84.5 mmol), *n*-BuLi (5.40 g, 84.5 mmol) and TMSCl (10.50 g, 97.5 mmol), **3i** was isolated as a highly viscous oil (15.80 g, 78%, isomeric ratio = 3:1).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.04 [s, 9 H, $Si(CH_3)_3$], 2.08 (d, *J* = 5.5 Hz, 3 H, CH_3), 3.15 (s, 3 H, OCH_3), 6.05 (q, *J* = 5.5 Hz, 1 H, CH), 6.84 (s, 1 H, CH), 6.92–7.28 (m, 4 H, Ar).

[1-Methoxy-3-(phenylsulfanyl)hexa-1,3-dienyloxy]trimethylsilane (3j)
Starting from **2j** (15.30 g, 65.0 mmol), DIPA (8.50 g, 84.5 mmol), *n*-BuLi (5.40 g, 84.5 mmol) and TMSCl (10.50 g, 97.5 mmol), **3j** was isolated as a highly viscous oil (16.50 g, 83%, isomeric ratio = 3:1).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.04 [s, 9 H, $Si(CH_3)_3$], 2.08 (m, 2 H, CH_2), 2.6 (t, *J* = 5.5 Hz, 3 H, CH_3), 3.15 (s, 3 H, OCH_3), 6.05 (t, *J* = 5.5 Hz, 1 H, CH), 6.54 (s, 1 H, CH), 6.92–7.30 (m, 5 H, Ar).

[1-Methoxy-3-(4-chlorophenylsulfanyl)buta-1,3-dienyloxy]trimethylsilane (3k)
Starting from **2k** (15.70 g, 65.0 mmol), DIPA (8.50 g, 84.5 mmol), *n*-BuLi (5.40 g, 84.5 mmol) and TMSCl (10.50 g, 97.5 mmol), **3k** was isolated as a highly viscous oil (17.10 g, 84%, isomeric ratio = 3:1).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.04 [s, 9 H, $Si(CH_3)_3$], 3.49 (s, 2 H, CH_2), 5.32 (s, 1 H, CH), 7.04–7.39 (m, 4 H, Ar).

2-(Aryloxythio)benzoates 5a–r; General Procedure
To a CH_2Cl_2 solution (5 mL/mmol of **3**) of **3** (1.0 mmol) and the appropriate **4** (1.5 mmol) was added $TiCl_4$ (1.5 mmol) at –78 °C. The mixture was allowed to warm to 20 °C within 20 h. To the mixture was added sat. aq $NaHCO_3$ (15 mL). The organic and the aqueous layers were separated and the latter was extracted with Et_2O (3 × 20 mL). The combined organic layers were dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo. The residue was purified by chromatography (silica gel, EtOAc–*n*-heptane, 1:4) (Table 1).

Methyl 4-Methyl-2-phenylsulfanylbenzoate (5a)
Starting from **3a** (420 mg, 1.5 mmol), **4a** (0.23 mL, 2.25 mmol), $TiCl_4$ (0.25 mL, 2.25 mmol), and CH_2Cl_2 (9 mL), **5a** was isolated as a highly viscous oil (205 mg, 53%).

IR (KBr): 3056 (w), 2994 (w), 2948 (w), 2927 (w), 2857 (w), 1727 (s), 1606 (m), 1581 (m), 1476 (m), 1449 (s), 1437 (s), 1380 (w), 1266 (s), 1240 (s), 1188 (m), 1152 (m), 1105 (s), 1066 (s), 1023 (m), 954 (m), 738 (s), 688 cm^{-1} (s).

^1H NMR (250 MHz, $CDCl_3$): δ = 2.27 (s, 3 H, CH_3), 3.80 (s, 3 H, OCH_3), 7.05–7.24 (m, 8 H, Ar).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 18.6 (CH_3), 51.1 (OCH_3), 126.1, 128.1, 128.3, 128.9, 129.3, 130.1 (CH_{Ar}), 132.1, 134.7, 134.9, 135.6, 167.9 (C).

MS (EI, 70 eV): *m*/*z* (%) = 258 (M^+, 69), 227 (46), 226 (22), 225 (100), 197 (15), 184 (33), 165 (8), 152 (6), 63 (3).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{14}O_2S$ (M^+): 258.07090; found: 258.070766.

Methyl 2-(4-Fluorophenylsulfanyl)-4-methylbenzoate (5b)
Starting from **3b** (440 mg, 1.5 mmol), **4a** (0.23 mL, 2.25 mmol), $TiCl_4$ (0.25 mL, 2.25 mmol), and CH_2Cl_2 (9 mL), **5b** was isolated as a highly viscous oil (153 mg, 37%).

IR (KBr): 3091 (w), 3063 (w), 2950 (w), 2924 (w), 2853 (w), 1728 (s), 1712 (s), 1661 (m), 1588 (s), 1487 (s), 1434 (m), 1273 (s), 1220 (s), 1154 (s), 1107 (s), 1068 (s), 826 (s), 771 (s), 628 cm^{-1} (m).

^1H NMR (250 MHz, $CDCl_3$): δ = 2.26 (s, 3 H, CH_3), 3.83 (s, 3 H, OCH_3), 6.92–7.26 (m, 7 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.6 (CH_3), 52.1 (OCH_3), 116.1, 116.5, 129.1, 1295, 129.9 (CH_{Ar}), 130.4, 130.5 (C), 133.8, 133.9, 136.1 (CH_{Ar}), 160.4, 164.3, 168.8 (C).

MS (EI, 70 eV): *m*/*z* (%) = 276 (M^+, 74), 245 (49), 244 (22), 243 (100), 215 (15), 202 (38), 170 (5), 121 (5), 63 (3).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{13}FO_2S$ (M^+): 276.06148; found: 276.061483.

Methyl 4-Methyl-2-*m*-tolylsulfanylbenzoate (5c)
Starting from **3c** (441 mg, 1.5 mmol), **4a** (0.23 mL, 2.25 mmol), $TiCl_4$ (0.25 mL, 2.25 mmol), and CH_2Cl_2 (9 mL), **5c** was isolated as a highly viscous oil (204 mg, 50%).

IR (KBr): 3091 (w), 3063 (w), 2950 (w), 2924 (w), 2853 (w), 1728 (s), 1712 (s), 1661 (m), 1588 (s), 1487 (s), 1434 (m), 1273 (s), 1220 (s), 1154 (s), 1107 cm^{-1} (s).

^1H NMR (250 MHz, $CDCl_3$): δ = 2.22 (s, 3 H, CH_3), 2.27 (s, 3 H, CH_3), 3.82 (s, 3 H, OCH_3), 7.03–7.18 (m, 7 H, Ar).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 19.6 (CH_3), 21.27 (CH_3), 52.1 (OCH_3), 128.1, 128.5, 128.9, 129.0, 129.8, 129.9, 132.0 (CH_{Ar}), 135.1, 135.9, 136.2, 138.9, 168.9 (C).

MS (EI, 70 eV): *m*/*z* (%) = 272 (M^+, 100), 241 (54), 240 (16), 239 (72), 226 (16), 225 (73), 198 (22), 197 (35), 165 (11), 121 (9), 105 (5), 77 (6).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{16}O_2S$ (M^+): 272.08655; found: 272.086256.

Methyl 2-(3-Chlorophenylsulfanyl)-4-methylbenzoate (5d)
Starting from **3d** (470 mg, 1.5 mmol), **4a** (0.23 mL, 2.25 mmol), $TiCl_4$ (0.25 mL, 2.25 mmol), and CH_2Cl_2 (9 mL), **5d** was isolated as a highly viscous oil (210 mg, 48%).

IR (KBr): 3058 (w), 2996 (w), 2949 (w), 2927 (w), 2856 (w), 1729 (s), 1662 (w), 1574 (m), 1563 (m), 1459 (m), 1451 (m), 1435 (m), 1337 (w), 1267 (s), 1242 (s), 1189 (m), 1106 (s), 1067 (s), 955 (w), 773 (s), 678 (m), 663 cm^{-1} (w).

^1H NMR (250 MHz, $CDCl_3$): δ = 2.28 (s, 3 H, CH_3), 3.79 (s, 3 H, OCH_3), 7.08–7.17 (m, 7 H, Ar).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 19.6 (CH_3), 52.1 (OCH_3), 126.9, 128.3, 129.6, 130.0, 130.1, 130.2, 131.2 (CH_{Ar}), 131.4, 134.7, 136.3, 137.7, 138.5 (C).

MS (EI, 70 eV): *m*/*z* (%) = 294 (M^+, ^{37}Cl, 16), 292 (M^+, ^{35}Cl, 71), 261 (71), 260 (18), 259 (100), 226 (15), 225 (37), 198 (16), 197 (29), 165 (8), 152 (6), 121 (9), 63 (5).

HRMS (EI): *m*/*z* calcd for $C_{15}H_{13}ClO_2S$ (M^+, ^{35}Cl): 292.03193; found: 292.032372.

Methyl 4-Methyl-2-*p*-tolylsulfanylbenzoate (5e)
Starting from **3e** (350 mg, 1.2 mmol), **4a** (0.15 mL, 1.44 mmol), $TiCl_4$ (0.20 mL, 1.8 mmol), and CH_2Cl_2 (7 mL), **5e** was isolated as a highly viscous oil (166 mg, 51%).

IR (KBr): 3091 (w), 3063 (w), 2950 (w), 2924 (w), 2853 (w), 1728 (s), 1712 (s), 1661 (m), 1588 (s), 1485 (s), 1434 (m), 1272 (s), 1220 (s), 1154 (s), 1106 cm^{-1} (s).

^1H NMR (250 MHz, $CDCl_3$): δ = 2.25 (s, 3 H, CH_3), 2.26 (s, 3 H, CH_3), 3.83 (s, 3 H, OCH_3), 6.97–7.22 (m, 7 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.6 (CH_3), 21.1 (CH_3), 52.1 (OCH_3), 128.7, 129.1 (CH_{Ar}), 129.8 (C), 129.9, 132.0 (CH_{Ar}), 132.3, 134.6, 135.5, 135.9, 137.7 (C).

MS (EI, 70 eV): *m*/*z* (%) = 3272 (M^+, 100), 241 (50), 239 (64), 225 (56), 211 (11), 198 (20), 197 (30), 165 (10), 152 (4), 121 (10), 105 (85), 77 (6), 63 (4).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{16}O_2S$ (M^+): 272.08655; found: 272.086425.

Methyl 4-Methyl-2-(naphth-2-ylsulfanyl)benzoate (5f)
Starting from **3f** (660 mg, 2.0 mmol), **4a** (0.3 mL, 3.0 mmol), $TiCl_4$ (0.33 mL, 3.0 mmol), and CH_2Cl_2 (12 mL), **5f** was isolated as a highly viscous oil (203 mg, 33%).

IR (KBr): 3052 (w), 2991 (w), 2947 (w), 2952 (w), 2853 (w), 1727 (s), 1623 (w), 1584 (m), 1568 (m), 1499 (m), 1433 (m), 1379 (w), 1339 (w), 1264 (s), 1241 (s), 1189 (m), 1105 (s), 1066 (s), 1016 (m), 942 (m), 849 (m), 811 (s), 777 (s), 742 (s), 708 cm^{-1} (m).

^1H NMR (250 MHz, $CDCl_3$): δ = 2.29 (s, 3 H, CH_3), 3.80 (s, 3 H, OCH_3), 7.06–7.77 (m, 10 H, Ar).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 18.7 (CH_3), 51.1 (OCH_3), 125.2, 125.5, 126.7, 126.8, 127.8, 128.2, 128.9, 129.1, 129.2 (CH_{Ar}), 131.3, 131.9, 132.4, 132.6, 135.1, 135.3, 167.9 (C).

MS (EI, 70 eV): *m*/*z* (%) = 308 (M^+, 100), 277 (32), 276 (16), 275 (81), 248 (10), 234 (22), 117 (6), 115 (5), 69 (3).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{18}O_3S$ (M^+): 308.39414; found: 308.38943.

Methyl 3,4-Dimethyl-2-*p*-tolylsulfanyl)-3,4-dimethylbenzoate (5g)
Starting from **3e** (616 mg, 2.0 mmol), **4b** (0.3 mL, 3.0 mmol), $TiCl_4$ (0.33 mL, 3.0 mmol), and CH_2Cl_2 (12 mL), **5g** was isolated as a highly viscous oil (212 mg, 37%).

IR (KBr): 3017 (w), 2948 (w), 2921 (w), 2734 (w), 1731 (s), 1656 (w), 1490 (m), 1431 (m), 1280 (s), 1203 (s), 1111 (s), 1085 (m), 802 (s), 754 (w), 718 cm^{-1} (m).

^1H NMR (250 MHz, $CDCl_3$): δ = 2.14 (s, 3 H, CH_3), 2.18 (s, 3 H, CH_3), 2.22 (s, 3 H, CH_3), 3.76 (s, 3 H, OCH_3), 7.17 (m, 6 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.1 (CH_3), 20.5 (CH_3), 20.9 (CH_3), 52.1 (OCH_3), 127.7 CH_{Ar}), 128.5 (C), 129.6, 131.0, 131.4 (CH_{Ar}), 132.7, 133.4, 135.4, 140.7, 141.3 (C).

MS (EI, 70 eV): *m*/*z* (%) = 286 (M^+, 100), 255 (38), 254 (15), 253 (42), 240 (19), 239 (82), 225 (12), 212 (16), 211 (35), 193 (7), 178 (8), 91 (10).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{18}O_2S$ (M^+): 286.10220; found: 286.101482.

Methyl 3,4-Dimethyl-2-phenylsulfanylbenzoate (5h)
Starting from **3a** (440 mg, 1.5 mmol), **4b** (0.23 mL, 2.25 mmol), $TiCl_4$ (0.25 mL, 2.25 mmol), and CH_2Cl_2 (9 mL), **5h** was isolated as a highly viscous oil (163 mg, 40%).

IR (KBr): 2949 (w), 2922 (w), 2855 (w), 1729 (s), 1588 (m), 1487 (s), 1432 (m), 1386 (m), 1281 (s), 1203 (s), 156 (s), 1111 cm^{-1} (s).

^1H NMR (250 MHz, $CDCl_3$): δ = 2.19 (s, 3 H, CH_3), 2.23 (s, 3 H, CH_3), 3.75 (s, 3 H, OCH_3), 7.09–7.13 (m, 7 H, Ar).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 19.1 (CH_3), 20.5 (CH_3), 52.1 (OCH_3), 125.5, 127.3 (CH_{Ar}), 127.8 (C), 128.8, 131.2, 131.4 (CH_{Ar}), 132.8, 137.0, 140.7, 141.4 (C).

MS (EI, 70 eV): *m*/*z* (%) = 272 (M^+, 85), 241 (41), 240 (29), 239 (100), 211 (26), 197 (35), 179 (10), 135 (5).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{16}O_2S$ (M^+): 272.08655; found: 272.086221.

Methyl 2-(4-Fluorophenylsulfanyl)-3,4-dimenthylbenzoate (5i)
Starting from **3b** (620 mg, 2.0 mmol), **4b** (0.3 mL, 3.0 mmol), $TiCl_4$ (0.33 mL, 3.0 mmol), and CH_2Cl_2 (12 mL), **5i** was isolated as a highly viscous oil (197 mg, 34%).

IR (KBr): 2949 (w), 2922 (w), 2855 (w), 1729 (s), 1588 (m), 1487 (s), 1432 (m), 1386 (m), 1281 (s), 1203 (s), 156 (s), 1111 (s), 1084 (m), 1010 (m), 813 (s), 790 (m), 626 cm^{-1} (s).

^1H NMR (250 MHz, $CDCl_3$): δ = 2.18 (s, 3 H, CH_3), 2.22 (s, 3 H, CH_3), 3.77 (s, 3 H, OCH_3), 6.98–7.11 (m, 6 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.0 (CH_3), 19.4 (CH_3), 51.1 (OCH_3), 114.7, 115.1 (CH_{Ar}), 127.2 (C), 128.5, 128.6, 130.3, 130.5 (CH_{Ar}), 131.8, 139.5, 140.3, 158.3, 162.2, 168.4 (C).

MS (EI, 70 eV): *m*/*z* (%) = 290 (M^+ 90), 259 (45), 258 (25), 257 (100), 229 (34), 216 (19), 215 (38), 197 (8), 77 (6), 51 (3).

HRMS (EI): *m*/*z* calcd for $C_{16}H_{15}FO_2S$ (M^+): 290.07713; found: 290.077573.

Methyl 3-Ethyl-4-methyl-2-phenylsulfanylbenzoate (5j)
Starting from **3b** (460 mg, 1.5 mmol), **4c** (0.23 mL, 2.25 mmol), $TiCl_4$ (0.25 mL, 2.25 mmol), and CH_2Cl_2 (9 mL), **5j** was isolated as a highly viscous oil (150 mg, 35%).

IR (KBr): 3055 (w), 2965 (w), 2948 (w), 2928 (w), 2870 (w), 2738 (w), 1729 (s), 1580 (m), 1477 (m), 1432 (m), 1393 (w), 1323 (w), 1271 (s), 1200 (s), 1157 (m), 1111 (s), 1080 (m), 1058 (m), 1023 (m), 1013 (m), 959 (m), 893 (w), 826 (m), 790 (m), 736 (s), 688 (s), 636 cm^{-1} (m).

^1H NMR (250 MHz, $CDCl_3$): δ = 1.00 (t, ^2J = 7.5 Hz, 3 H, CH_2CH_3), 2.23 (s, 3 H, CH_3), 2.63 (q, ^2J = 7.5 Hz, 2 H, CH_2), 3.71 (s, 3 H, OCH_3), 7.08–7.17 (m, 7 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.8, 19.1 (CH_3), 26.7 (CH_3CH_2), 52.0 (OCH_3), 125.3, 127.0, 128.7, 129.8, 131.6 (CH_{Ar}), 132.8, 137.9, 141.7, 146.5, 169.3 (C).

MS (EI, 70 eV): *m*/*z* (%) = 286 (M^+, 100), 255 (22), 254 (23), 253 (59), 239 (47), 227 (12), 225 (16), 211 (26), 197 (19), 184 (14), 178 (14), 105 (30), 77 (10).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{18}O_2S$ (M^+): 286.10220; found: 286.102040.

Methyl 3-Phenylsulfanylbiphenyl-4-carboxylate (5k)
Starting from **3a** (420 mg, 1.5 mmol), **4d** (0.18 mL, 1.8 mmol), $TiCl_4$ (0.25 mL, 2.25 mmol), and CH_2Cl_2 (9 mL), **5k** was isolated as a highly viscous oil (192 mg, 40%).

IR (KBr): 3056 (w), 3029 (w), 2992 (w), 2946 (w), 2838 (w), 1730 (s), 1711 (s), 1638 (w), 1597 (m), 1577 (m), 1556 (w), 1526 (m), 1475 (m), 1438 (s), 1415 (w), 1373 (w), 136 (w), 1258 (s), 1191 (s), 111 (s), 1060 (s), 1034 (m), 1017 (m), 999 (m), 955 (m), 888 (m), 846 (w), 750 (s), 732 (s), 688 (s), 650 (m), 632 cm^{-1} (m).

^1H NMR (250 MHz, $CDCl_3$): δ = 3.53 (s, 3 H, OCH_3), 7.16–7.32 (m, 13 H, Ar).

^{13}C NMR (MHz, $CDCl_3$): δ = 52.1 (OCH_3), 127.5, 127.7, 128.2, 128.4, 128.5, 129.2, 129.9, 130.7, 131.9 (CH_{Ar}), 132.6, 134.5, 135.0, 139.9, 140.9 (C).

MS (EI, 70 eV): *m*/*z* (%) = 320 (M^+, 100), 290 (19), 289 (87), 271 (15), 261 (10), 260 (14), 240 (25), 163 (18), 152 (11), 131 (15), 110 (13), 105 (17), 77 (17), 69 (5).

HRMS (EI): *m*/*z* calcd for $C_{20}H_{16}O_2S$ (M^+): 320.08655; found: 320.086676.

Methyl 3-(4-Chlorophenylsulfanyl)biphenyl-4-carboxylate (5k)
Starting from **3g** (370 mg, 1.2 mmol), **4d** (0.22 mL, 1.3 mmol), $TiCl_4$ (0.2 mL, 1.7mmol), and CH_2Cl_2 (7 mL), **5k** was isolated as a highly viscous oil (157 mg, 37%).

IR (KBr): 3058 (w), 2996 (w), 2949 (w), 2927 (w), 2856 (w), 1729 (s), 1662 (w), 1574 (m), 1563 (m), 1459 (m), 1451 (m), 1435 (m), 1337 (w), 1267 (s), 1242 (s), 1189 (m), 1106 (s), 1067 (s), 955 (w), 773 (s), 678 (m), 663 cm^{-1} (w).

^1H NMR (250 MHz, $CDCl_3$): δ = 3.53 (s, 3 H, OCH_3), 7.18–7.32 (m, 12 H, Ar).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 52.1 (OCH_3), 127.8, 128.2, 128.4, 129.0, 129.4, 130.1, 131.2, 132.8 (CH_{Ar}), 133.6, 133.6, 133.9, 135.7, 139.81, 141.1, 168.6 (C).

MS (EI, 70 eV): *m*/*z* (%) = 356 (M^+, ^{37}Cl, 39), 354 (M^+, ^{35}Cl, 100), 323 (36), 244 (15), 91 (7), 77 (5).

HRMS (EI): *m*/*z* calcd for $C_{20}H_{15}ClO_2S$ (M^+): 354.06323; found: 354.063118.

Methyl 4′-Chloro-3-phenylsulfanylbiphenyl-2-carboxylate (5m)
Starting from **3a** (400 mg, 1.5 mmol), **4e** (0.37 mL, 1.8 mmol), $TiCl_4$ (0.25 mL, 2.25 mmol), and CH_2Cl_2 (9 mL), **5m** was isolated as a highly viscous oil (250 mg, 47%).

IR (KBr): 3057 (w), 2997 (w), 2947 (w), 2852 (w), 1728 (s), 1676 (w), 1596 (w), 1580 (m), 1573 (m), 1493 (m), 1438 (s), 1260 (s), 1192 (m), 1152 (w), 1115 (s), 1090 (s), 1061 (m), 1023 (m), 1012 (m), 900 (m), 836 (m), 741 (s), 688 cm^{-1} (s).

^1H NMR (250 MHz, $CDCl_3$): δ = 3.56 (s, 3 H, OCH_3), 7.21–7.32 (m, 12 H, Ar).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 52.2 (OCH_3), 127.7, 128.3, 128.6, 129.3, 129.6, 130.0, 131.1, (CH_{Ar}), 133.9, 134.7, 134.9, 135.0, 138.4, 139.6, 168.4 (C).

MS (EI, 70 eV): *m*/*z* (%) = 356 (M^+, ^{37}Cl, 39), 354 (M^+, ^{35}Cl, 100), 323 (46), 287 (13), 260 (18), 259 (12), 258 (23).

HRMS (EI): *m*/*z* calcd for $C_{20}H_{15}ClO_2S$ (M^+): 354.06323; found: 354.063118.

Methyl 4′-Chloro-3-(4-chlorophenylsulfanyl)biphenyl-2-carboxylate (5n)
Starting from **3g** (470 mg, 1.5 mmol), **4e** (0.37 mL, 1.8 mmol), $TiCl_4$ (0.25 mL, 2.25 mmol), and CH_2Cl_2 (9 mL), **5n** was isolated as a highly viscous oil (268 mg, 46%).

IR (KBr): 3445 (w), 3056 (w), 2947 (w), 2385 (w), 2075 (w), 1900 (w), 1728 (s), 1679 (m), 1572 (m), 1493 (m), 1474 (s), 1446 (m), 1388 (m), 1260 (s), 1190 (m), 1116 (m), 1090 (s), 1011 (s), 818 (s), 790 (s), 743 (m), 715 cm^{-1} (m).

^1H NMR (250 MHz, $CDCl_3$): δ = 3.56 (s, 3 H, OCH_3), 7.15–7.32 (m, 11 H, Ar).

MS (EI, 70 eV): *m*/*z* (%) = 392 (M^+, $^{37}Cl^{37}Cl$, 8), 390 (M^+, $^{35}Cl^{37}Cl$, 23), 388 (M^+, $^{35}Cl^{35}Cl$, 100), 359 (26), 357 (38), 321 (14), 294 (15), 258 (26), 151 (5), 159 (5), 129 (10), 75 (4).

HRMS (EI): *m*/*z* calcd for $C_{20}H_{14}Cl_2O_2S$ (M^+, $^{35}Cl^{35}Cl$): 388.00861; found: 388.008235.

Methyl 4′-Chloro-3-*p*-tolylsulfanylbiphenyl-2-carboxylate (5o)
Starting from **3e** (400 mg, 1.5 mmol), **4e** (0.37 mL, 1.8 mmol), $TiCl_4$ (0.25 mL, 2.25 mmol), and CH_2Cl_2 (9 mL), **5o** was isolated as a highly viscous oil (260 mg, 47%).

IR (KBr): 3021 (w), 2947 (w), 2920 (w), 2853 (w), 1903 (w), 1728 (s), 1650 (m), 1587 (m), 1546 (m), 1490 (s), 1445 (s), 1390 (m), 1256 (s), 1191 (m), 1115 (s), 1089 (s), 1061 (s), 1012 (s), 806 (s), 789 (s), 742 (m), 684 (m), 533 cm^{-1} (m).

^1H NMR (250 MHz, $CDCl_3$): δ = 2.27 (s, 3 H, CH_3), 3.58 (s, 3 H, OCH_3), 7.06–7.29 (m, 11 H, Ar).

^{13}C NMR (63 MHz, $CDCl_3$): δ = 18.2 (CH_3), 52.1 (OCH_3), 128.5, 128.8, 129.4, 129.8, 130.5, 131.4, 133.0 (CH_{Ar}), 133.7, 134.0, 135.5, 136.2, 138.2, 139.7, 168.3 (C).

MS (EI, 70 eV): *m*/*z* (%) = 370 (M^+, ^{37}Cl, 39), 368 (M^+, ^{35}Cl, 100), 339 (14), 337 (36), 301 (8), 274 (10), 258 (12), 150 (6), 129 (4).

HRMS (EI): *m*/*z* calcd for $C_{21}H_{17}ClO_2S$ (M^+): 368.06323; found: 368.063118.

Methyl 4′-Chloro-3-(4-fluorophenylsulfanyl)biphenyl-2-carboxylate (5p)
Starting from **3b** (440 mg, 1.5 mmol), **4e** (0.37 mL, 1.8 mmol), $TiCl_4$ (0.25 mL, 2.25 mmol), and CH_2Cl_2 (9 mL), **5p** was isolated as a colorless solid (195 mg, 35%).

IR (KBr): 3091 (w), 3065 (w), 2992 (w), 2948 (w), 2851 (w), 1892 (w), 1711 (m), 1678 (m), 1587 (s), 1488 (s), 1445 (m), 1435 (m), 1397 (m), 1337 (m), 1272 (m), 1221 (s), 1193 (s), 1153 (s), 1105 (m), 1088 (s), 1012 (m), 898 (m), 829 (s), 813 (s), 790 (m), 733 (m), 637 cm^{-1} (m).

^1H NMR (250 MHz, $CDCl_3$): δ = 3.57 (s, 3 H, OCH_3), 6.99–7.27 (m, 11 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 51.2 (OCH_3), 115.4, 115.7, 127.2 (CH_{Ar}), 127.6, 128.5, 129.1, 129.2, 132.7, 133.7, 133.9 (CH_{Ar}), 134.4, 134.5, 136.6, 136.7, 137.3, 138.7, 167.4 (C).

MS (EI, 70 eV): *m*/*z* (%) = 374 (M^+, ^{37}Cl, 40), 372 (M^+, ^{35}Cl, 100), 343 (16), 341 (42), 305 (14), 278 (16), 276 (20), 168 (8), 152 (6), 138 (9).

HRMS (EI): *m*/*z* calcd for $C_{20}H_{14}ClFO_2S$ (M^+): 372.063816; found: 372.038069.

Methyl 4′-Chloro-4-methyl-3-phenylsulfanylbiphenyl-2-carboxylate (5q)
Starting from **3a** (400 mg, 1.5 mmol), **4f** (0.37 mL, 1.8 mmol), $TiCl_4$ (0.25 mL, 2.25 mmol), and CH_2Cl_2 (9 mL), **5q** was isolated as a highly viscous oil (220 mg, 40%).

IR (KBr): 3055 (w), 2947 (w), 2920 (w), 2851 (w), 2735 (w), 2660 (w), 2112 (w), 1907 (w), 1730 (s), 1673 (m), 1581 (m), 1476 (m), 1459 (m), 1431 (m), 1400 (m), 1277 (s), 1221 (s), 1189 (m), 1118 (s), 1092 (s), 1011 (s), 971 (m), 890 (m), 842 (m), 816 (s), 734 (s), 715 (m), 688 (s), 627 cm^{-1} (m).

^1H NMR (250 MHz, $CDCl_3$): δ = 2.27 (s, 3 H, CH_3), 3.54 (s, 3 H, OCH_3), 7.04–7.29 (m, 11 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.8 (CH_3), 51.1 (OCH_3), 124.7, 126.6, 127.5, 127.9, 128.8, 129.7, 130.7 (CH_{Ar}), 132.8, 135.6, 135.8, 137.0, 139.5, 142.0, 167.8 (C).

MS (EI, 70 eV): *m*/*z* (%) = 370 (M^+, ^{37}Cl, 39), 368 (M^+, ^{35}Cl, 100), 337 (52), 336 (23), 335 (60), 309 (13), 307 (27), 301 (23), 271 (13), 258 (18), 165 (13), 152 (10), 51 (4).

HRMS (EI): *m*/*z* calcd for $C_{21}H_{17}ClO_2S$ (M^+): 368.06323; found: 368.062687.

Methyl 4′-Chloro-4-ethyl-3-phenylsulfanylbiphenyl-2-carboxylate (5r)
Starting from **3a** (440 mg, 1.5 mmol), **4g** (0.37 mL, 1.8 mmol), $TiCl_4$ (0.25 mL, 2.25 mmol), and CH_2Cl_2 (9 mL), **5r** was isolated as a highly viscous oil (206 mg, 36%).

IR (KBr): 3055 (w), 2965 (w), 2947 (w), 2931 (w), 2870 (w), 1730 (s), 1673 (w), 1581 (m), 1496 (w), 1477 (m), 1459 (m), 1431 (m), 1403 (w), 1385 (w), 1271 (s), 1229 (m), 1214 (s), 1118 (s), 1092 (s), 1067 (m), 1023 (m), 1012 (s), 959 (m), 900 (m), 823 (s), 737 (s), 688 (s), 539 cm^{-1} (m).

^1H NMR (250 MHz, $CDCl_3$): δ = 1.05 (t, 2*J* = 0.03 Hz, 3 H, CH_3), 2.71 (q, 2*J* = 0.03 Hz, 2 H, CH_2), 3.49 (s, 3 H, OCH_3), 7.02–7.17 (m, 11 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.7 (CH_3), 27.0 (CH_3CH_2), 52.1 (OCH_3), 125.6, 127.39 (CH_{Ar}), 128.2 (C), 128.6, 128.8, 129.8, 130.1, 131.1 (CH_{Ar}), 133.1, 136.7, 137.4, 138.0, 140.9, 148.6, 168.8 (C).

MS (EI, 70 eV): *m*/*z* (%) = 384 (M^+, ^{37}Cl, 39), 382 (M^+, ^{35}Cl, 100), 350 (27), 349 (35), 335 (18), 315 (12), 307 (13), 297 (31), 271 (26), 258 (18), 245 (27), 237 (22), 178 (16), 165 (12), 105 (24).

HRMS (EI): *m*/*z* calcd for $C_{22}H_{19}ClO_2S$ (M^+): 382.07888; found: 382.079023.

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