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Synthesis of 2-(arylthio)benzoates by [3+3] cyclocondensations of 3-arylthio-1-silyloxy-1,3-butadienes with 3-oxo-orthoesters, 1,1,3,3-tetramethoxypropane and 1,1-bis(methylthio)-1-en-3-ones

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ABSTRACT

A variety of 2-arylthio-4-methoxybenzoates are regioselectively prepared by $TiCl_4$-mediated [3+3] cyclocondensations of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes with 3-oxo-orthoesters. Unsubstituted 2-(arylthio)benzoates were prepared by Me_3SiOTf-catalyzed cyclization of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes with 1,1,3,3-tetramethoxypropane. The $TiCl_4$-mediated cyclization of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes with 1,1-bis(methylthio)-1-en-3-ones results in regioselective formation of 2-arylthio-6-(methylthio)benzoates.

1. Introduction

Diaryl sulfides occur in several pharmacologically relevant natural products (e.g., the lissoclibadins, dibenzothiophenes, cyclic sulfides, varacins).[1] Diaryl sulfides have been prepared by reaction of sulfur[2] or sulfur dichloride[3] with arenes, by reaction of organometallic reagents with chlorophenyl-sulfides[4] or by base-mediated reactions of thiophenols with chloroarenes.[5] The scope of these methods is limited by polysulfide formation and low regioselectivities. These problems can be successfully addressed by the application of novel transition metal-catalyzed[6] and metal-free[7] C–S coupling reactions. However, the synthesis of the starting materials, substituted aryl halides or triflates, can be a difficult and tedious task.

An alternative strategy relies on a building block approach. For example, diaryl sulfides have been prepared by cobalt(I)-catalyzed [4+2] cycloaddition of alkynyl sulfides with 1,3-butadienes.[8] 3- and 5-(Arylthio)salicylates have been prepared by $TiCl_4$-mediated formal [3+3] cyclizations of 1,3-bis(silyloxy)-1,3-butadienes with 3-silyloxy-2-en-1-ones.[9] Chan et al. reported the reaction of 1-methoxy-3-phenylthio-1-trimethylsilyloxy-1,3-butadiene with 3-silyloxy-2-en-1-ones and with enones.[10] We have reported the cyclization of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes with 1,1-diacylcyclopropanes,[11] 3-alkoxy-2-en-1-ones,[12] 1,1,3,3-tetramethoxypropane[13] and dimethyl acetylenedicarboxylate.[14] Recently, we have reported preliminary results related to the synthesis of 2-arylthio-4-methoxybenzoates by cyclocondensation of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes with 3-oxo-orthoesters.[15] Herein, we report full details of these studies. In addition, a full account of the cyclization of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes with 1,1,3,3,-tetramethoxypropane is included. We also report, for the first time, the synthesis of 2-arylthio-6-(methylthio)benzoates by cyclization of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes with 1,1-bis(methylthio)-1-en-3-ones.

The chemistry reported herein provides a regioselective approach to a wide range of novel diaryl sulfides, which are not readily available by other methods. In contrast to the C–S coupling reactions outlined above, our method relies on the assembly of one of the two arene moieties.

2. Results and discussion

The known 3-oxo-orthoesters **1a**,**b** were prepared, according to literature procedures,[16] by condensation of 1,1-dichloroethene with

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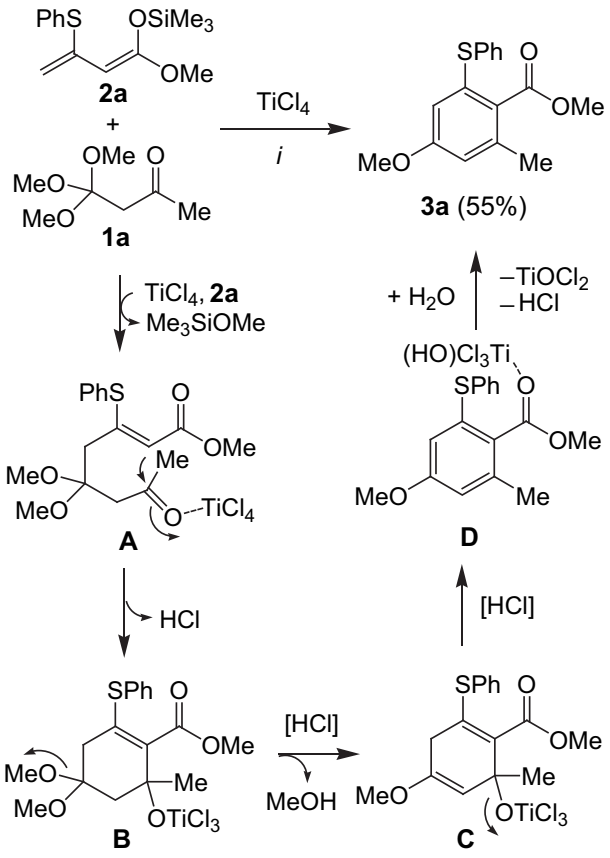
acetyl and propionyl chloride, respectively, to give 3,3,3-trichloroketones, which were subsequently transformed into the products by reaction with methanol. The known 3-arylthio-1-trimethylsilyloxy-1,3-butadienes **2a**–**m** were prepared from methyl acetoacetate, methyl 3-oxopentanoate and various thiophenols in two steps.[12]

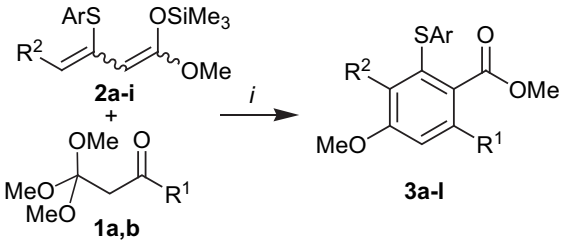
The $TiCl_4$-mediated cyclization of **1a** with 3-phenylthio-1-trimethylsilyloxy-1,3-butadiene **2a** afforded 2-phenylthio-4-methoxybenzoate **3a** (Scheme 1). The cyclization proceeded with very good regioselectivity. The formation of 2-phenylthio-6-methoxybenzoate, a regioisomer of **3a**, was not observed. The best yields were obtained when a stoichiometric ratio of **2a**/**1a**/$TiCl_4$=1.0:1.5:1.5 was used and when the reaction was carried out in a fairly concentrated solution (c(**1a**)=0.33 M). The relatively low yield (55%) can be explained by practical problems during the chromatographic purification and by partial hydrolysis of the starting materials.



Scheme 1. Possible mechanism of the formation of arene **3a**; i: (1) $TiCl_4$ (1.0 equiv), CH_2Cl_2, −78→20 °C, 20 h; (2) HCl (10%).

The formation of **3a** can be explained by the mechanism depicted in Scheme 1. The $TiCl_4$-mediated attack of diene **2a** to the orthoester gives intermediate **A**. The attack of carbon atom C-2 of **A** onto the carbonyl group results in cyclization (intermediate **B**). Aromatization (intermediates **C** and **D**) and hydrolysis (during the aqueous work-up) provide the final product. The cyclization might proceed also by $TiCl_4$-mediated extrusion of methanol from **1a** to give 4,4-dimethoxy-3-buten-2-one, conjugate addition of the terminal carbon atom of **2a** onto the latter and subsequent cyclization. This process would follow a mechanism earlier suggested for the cyclization of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes with 3-alkoxy-2-en-1-ones.[12]

The $TiCl_4$-mediated cyclization of 3-oxo-orthoesters **1a**,**b** with 3-arylthio-1-trimethylsilyloxy-1,3-butadienes **2a**–**i** gave the novel 2-arylthio-4-methoxybenzoates **3a**–**l** (Scheme 2, Table 1). Various substituents can be introduced at carbon atoms C3 and C6 of the benzoate moiety (substituents R^1 and R^2) and at the arylthio group. The yields of the products **3h**,**i**, derived from dienes **2h**,**i**, containing a substituent located at the terminal carbon atom, are lower than the yields of the other products. The yields of the products derived from **1a** are slightly higher than the yields of the products derived from **1b**. The substituents located at the aryl group of the diene seem to have no major influence on the yield. The moderate yields can be explained by problems during the chromatographic purification and by partial hydrolysis of the starting materials. In some reactions a small amount of hydrolyzed starting material was recovered.



Scheme 2. Synthesis of arenes **3a**–**l**; conditions: i: (1) $TiCl_4$ (1.0 equiv), CH_2Cl_2, −78→20 °C, 20 h; (2) HCl (10%).

Table 1
Synthesis of **3a**–**l**

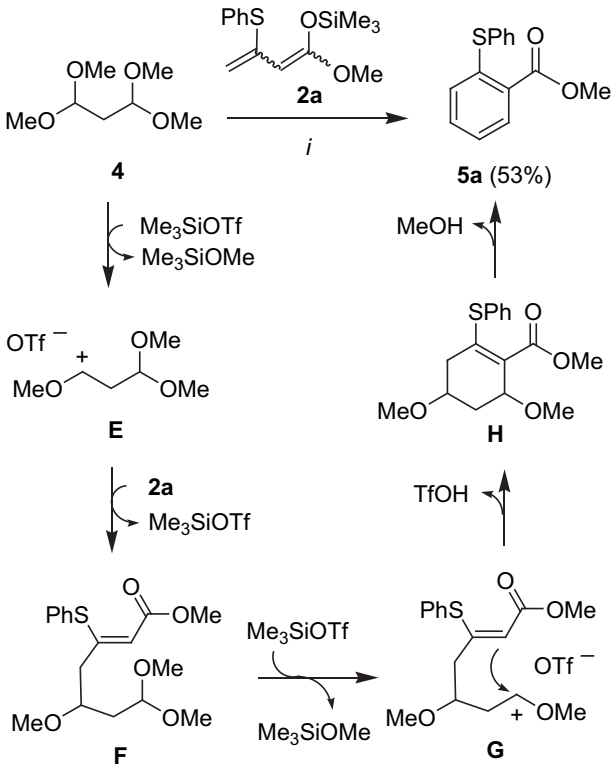
1	2	3	R^1	R^2	Ar	Yield[a] % (**3**)
a	**a**	**a**	Me	H	Ph	55
a	**b**	**b**	Me	H	3-MeC_6H_4	50
a	**c**	**c**	Me	H	3-ClC_6H_4	46
a	**d**	**d**	Me	H	4-MeC_6H_4	51
a	**e**	**e**	Me	H	4-EtC_6H_4	45
a	**f**	**f**	Me	H	4-FC_6H_4	40
a	**g**	**g**	Me	H	4-ClC_6H_4	46
a	**h**	**h**	Me	Me	Ph	37
a	**i**	**i**	Me	Me	4-EtC_6H_4	35
b	**c**	**j**	Et	H	3-ClC_6H_4	37
b	**d**	**k**	Et	H	4-MeC_6H_4	38
b	**g**	**l**	Et	H	4-ClC_6H_4	40

[a] Isolated yields.

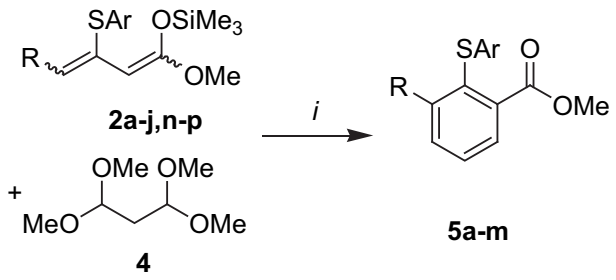
The reaction of 3-phenylthio-1-silyloxy-1,3-butadiene **2a** with 1,1,3,3-tetramethoxypropane (**4**), in the presence of catalytic amounts of Me_3SiOTf, afforded the 2-(phenylthio)benzoate **5a** (Scheme 3). The best yields were obtained when 0.1 equiv of Lewis acid was used. The use of 0.2 or 1.0 equiv of Me_3SiOTf did not result in an increase of the yield. The yields decreased when less than 0.1 equiv of Lewis acid was employed. The use of 1.0 equiv of $TiCl_4$ proved to be possible, but again did not increase the yield. The work-up procedure (diluted hydrochloric acid), the temperature (−78→20 °C, 20 h), and the concentration (ca. 2 mL of CH_2Cl_2 per **1** mmol of **4**) proved to be important parameters during the optimization. The high concentration is a significant difference to the procedure reported[17] for the Me_3SiOTf-catalyzed cyclization of 1,3-bis(silyloxy)-1,3-butadienes with **4**. The use of tetraethoxypropane rather than **4** proved to be unsuccessful. The use of trifluoroacetic acid or triflic acid (rather than Me_3SiOTf) failed to give the desired product.

The formation of **5a** can be explained by Me_3SiOTf-catalyzed formation of oxonium cation **E**, attack of the terminal carbon atom of **2a** onto **E** to give intermediate **F**, Me_3SiOTf-catalyzed formation of oxonium cation G, cyclization to give intermediate **H** and subsequent aromatization by extrusion of methanol. The suggested mechanism has not been experimentally proved.

The cyclization of dienes **2a**–**j**,**n**–**p** with **4** afforded the 2-(arylthio)benzoates **5a**–**m** in moderate yields (Scheme 4, Table 2). Comparable yields were obtained for products **5b**,**d**, which are derived from dienes containing an electron-withdrawing halogen atom located at the arylthio group, and for products **5a**,**c**,**e**.



Scheme 3. Possible mechanism of the formation of **5a**; conditions: i: (1) Me_3SiOTf (0.1 equiv), CH_2Cl_2, −78→20 °C, 20 h; (2) HCl, H_2O.



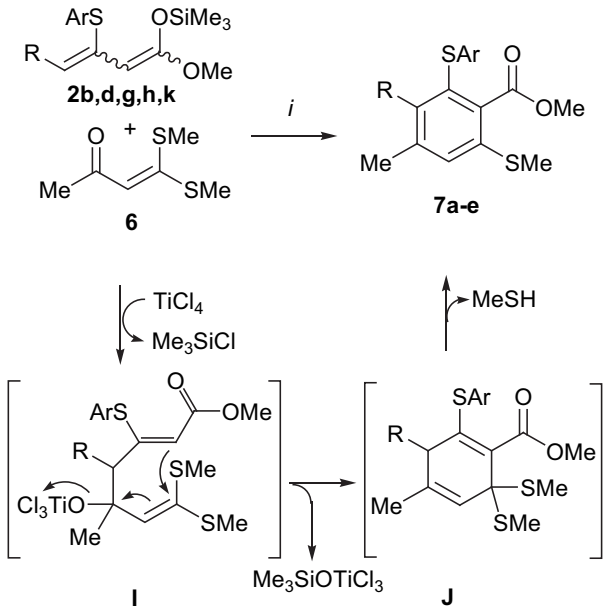
Scheme 4. Synthesis of **5a**–**m**; conditions: i: (1) Me_3SiOTf (0.1 equiv), CH_2Cl_2, −78→20 °C, 20 h; (2) HCl, H_2O.

Table 2
Synthesis of **5a**–**m**

2	5	R	Ar	Yield[a] % (**5**)
a	**a**	H	Ph	53
f	**b**	H	4-FC_6H_4	47
b	**c**	H	3-MeC_6H_4	54
c	**d**	H	3-ClC_6H_4	51
d	**e**	H	4-MeC_6H_4	53
j	**f**	H	2-Naph	33
k	**g**	Me	4-MeC_6H_4	46
h	**h**	Me	Ph	50
l	**i**	Me	4-FC_6H_4	44
m	**j**	Et	Ph	50
e	**k**	H	4-EtC_6H_4	55
i	**l**	Me	4-EtC_6H_4	45
n	**m**	Me	4-ClC_6H_4	48

[a] Isolated yields.

Recently, we have reported the synthesis of 6-(methylthio)salicylates by cyclization of 1,3-bis(trimethylsilyloxy)-1,3-butadienes with 1,1-bis(methylthio)-1-en-3-ones.[18] Based on these results we studied related cyclization reactions of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes. The cyclization of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes **2b**,**d**,**g**,**h**,**k** with 1,1-bis(methylthio)-1-en-3-one **6**[19] afforded the novel 2-arylthio-6-(methylthio)benzoates **7a**–**e** in 37–55% yield (Scheme 5, Table 3). The formation of products **7** might be explained by $TiCl_4$-mediated attack of the diene onto the carbonyl group of **4** to give intermediate **E**, formation of an allylic cation and cyclization (intermediate **F**). The extrusion of MeSH leads to the final product.



Scheme 5. Synthesis of arenes **7a**–**e**; conditions: i: (1) $TiCl_4$, −78→20 °C, 20 h; (2) HCl (10%).

Table 3
Synthesis of **7a**–**e**

2	7	R	Ar	Yield[a] % (**7**)
d	**a**	H	4-MeC_6H_4	55
b	**b**	H	3-MeC_6H_4	37
g	**c**	H	4-ClC_6H_4	49
h	**d**	Me	Ph	48
k	**e**	Me	4-MeC_6H_4	51

[a] Yields of isolated products.

The chromatographic purification of products **7a**–**e** proved to be rather difficult. A further variation of the diene and a variation of the 1,1-bis(methylthio)-1-en-3-one proved, in principle, to be possible. Inspection of the NMR spectra of the crude products showed that the expected products were formed. However, their isolation in pure form was not possible in many cases. Therefore, these experiments are not included herein.

In conclusion, we have reported the synthesis of 2-arylthio-4-methoxybenzoates by cyclocondensation of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes with 3-oxo-orthoesters. In addition, we have reported the synthesis of 2-arylthio-6-(methylthio)benzoates by cyclization of 3-arylthio-1-trimethylsilyloxy-1,3-butadienes with 1,1-bis(methylthio)-1-en-3-ones. The chemistry reported herein provides a regioselective approach to a wide range of novel diaryl sulfides, which are not readily available by other methods.

3. Experimental section

3.1. General comments

All solvents were dried by standard methods and all reactions were carried out under an inert atmosphere. For ^1H 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, isobutane) or electrospray ionization (ESI). For preparative scale chromatography silica gel 60 (0.063–0.200 mm, 70–230 mesh) was used.

3.2. General experimental procedure for the synthesis of diaryl sulfides 3a–l

To a dichloromethane solution (3 mL/mmol of **1**) of **2** (1.5 mmol) and of **1** (2.25 mmol) was added $TiCl_4$ (2.25 mmol) at −78 °C. The solution was allowed to warm to 20 °C within 20 h. To the solution was added hydrochloric acid (10%, 25 mL). The organic and the aqueous layers were separated and the latter was extracted with dichloromethane (3×20 mL). The combined organic layers were dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo and the residue was purified by chromatography (silica gel, EtOAc/*n*-heptane=1:9).

*3.2.1. Methyl 2-methoxy-4-methyl-6-phenylsulfanyl-benzoate (**3a**).* Starting with **2a** (420 mg, 1.5 mmol) and **1a** (364 mg, 2.25 mmol), **3a** was isolated as a highly viscous colourless oil (238 mg, 55%); ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.25 (s, 3H, CH_3), 3.57 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 6.44–7.22 (m, 7H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ=20.0 (CH_3), 50.7 (OCH_3), 51.0 (OCH_3), 110.2 ($2CH_{Ar}$), 129.1 (2C), 129.5, 130.7, 132.5 (CH_{Ar}), 135.9 ($2CH_{Ar}$), 139.6 (2C), 160.5, 165.8 (C); IR (KBr, cm^{-1}): ν=3400 (w), 3056 (w), 2992 (w), 2948 (w), 2922 (w), 2850 (w), 2664 (w), 1083 (m), 1738 (m), 1710 (s), 1650 (m), 1571 (m), 1473 (m), 1438 (s), 1303 (m), 1248 (m), 1195 (s), 1153 (s), 1099 (s), 1067 (m), 1022 (s), 1000 (m), 886 (m), 844 (m), 803 (m), 745 (s), 703 (s), 688 (s), 608 m; MS (EI, 70 eV): *m*/*z* (%)=289 (18), 288 (M$^+$, 100), 272 (12), 271 (61), 270 (21), 269 (86), 256 (18), 255 (49), 228 (17), 227 (13), 185 (10), 184 (17); HRMS (EI): calcd for $C_{16}H_{16}O_3S$ (M$^+$): 288.09612, found: 288.09715.

*3.2.2. Methyl 2-methoxy-4-methyl-6-(3-methylphenyl-sulfanyl)-benzoate (**3b**).* Starting with **2b** (441 mg, 1.5 mmol) and **1a** (364 mg, 2.25 mmol), **3b** was isolated as a highly viscous colourless oil (227 mg, 50%); ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.23 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 3.59 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 6.49–7.18 (m, 6H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ=20.3 (CH_3), 21.2 (CH_3), 51.9 (OCH_3), 52.2 (OCH_3), 114.1, 114.5, 128.5, 129.0, 129.3 (CH_{Ar}), 132.2 (C), 132 (CH_{Ar}), 134.4, 136.8, 138.3, 139.0, 160.2, 168.8 (C); IR (KBr, cm^{-1}): ν=3435 (w), 2998 (w), 2947 (w), 2834 (w), 2735 (w), 2664 (w), 1083 (m), 1738 (m), 1710 (s), 1650 (m), 1571 (m), 1473 (m), 1438 (s), 1303 (m), 1248 (m), 1195 (s), 1153 (s), 1099 (s), 1067 (m), 1022 (s), 1000 (m), 886 (m), 844 (m), 803 (m), 745 (s), 703 (s), 688 (s), 608 (m); MS (EI, 70 eV): *m*/*z* (%)=303 (19), 302 (M$^+$, 100), 272 (11), 271 (61), 270 (21), 269 (86), 256 (18), 255 (49), 228 (17), 227 (13), 186 (11), 184 (15); HRMS (EI): calcd for $C_{17}H_{18}O_3S$ (M$^+$): 302.09712, found: 302.09715.

*3.2.3. Methyl 2-methoxy-4-methyl-6-(3-chlorophenyl-sulfanyl)-benzoate (**3c**).* Starting with **2c** (471 mg, 1.5 mmol) and **1a** (364 mg, 2.25 mmol), **3c** was isolated as a highly viscous colourless oil (222 mg, 46%); ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.27 (s, 3H, CH_3), 3.64 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 6.58–7.23 (m, 6H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ=20.3 (CH_3), 52.0 (OCH_3), 55.3 (OCH_3), 115.6 ($2CH_{Ar}$), 127.2, 128.9, 130.0, 130.4 (CH_{Ar}), 134.1, 134.5, 134.7, 137.9, 138.5, 160.3, 168.6 (C); IR (KBr, cm^{-1}): ν=3055 (w), 2999 (w), 2947 (w), 2835 (w), 1725 (s), 1590 (s), 1562 (s), 1459 (s), 1427 (m), 1399 (m), 1304 (m), 1266 (s), 1218 (s), 1187 (m), 1137 (s), 1090 (m), 1071 (m), 1047 (s), 995 (m), 959 (m), 849 (m), 773 (s), 677 (s), 608 (m); MS (EI, 70 eV): *m*/*z* (%)=324 (26), 323 (13), 322 (M$^+$ 70), 293 (29), 292 (17), 291 (83), 290 (27), 289 (100), 255 (17), 185 (10), 184 (18); HRMS (EI): calcd for $C_{16}H_{15}O_3SCl$ (M$^+$): 322.04249, found: 322.04244.

*3.2.4. Methyl 2-methoxy-4-methyl-6-(4-methylphenyl-sulfanyl)-benzoate (**3d**).* Starting with **2d** (441 mg, 1.5 mmol) and **1a** (364 mg, 2.25 mmol), **3d** was isolated as a highly viscous colourless oil (231 mg, 51%); ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.24 (s, 3H, CH_3), 2.27 (s, 3H, CH_3), 3.59 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 6.49–7.18 (m, 6H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ=20.4 (CH_3), 21.1 (CH_3), 51.9 (OCH_3), 52.2 (OCH_3), 114.1, 114.5, 128.5, 129.0, 129.3 (CH_{Ar}), 132.2 (C), 132 (CH_{Ar}), 134.4, 136.8, 138.3, 139.0, 160.2, 168.8 (C); IR (KBr, cm^{-1}): ν=3434 (w), 2998 (w), 2947 (w), 2834 (w), 2735 (w), 2664 (w), 1083 (m), 1738 (m), 1710 (s), 1650 (m), 1572 (m), 1473 (m), 1438 (s), 1303 (m), 1248 (m), 1195 (s), 1153 (s), 1099 (s), 1067 (m), 1022 (s), 1000 (m), 886 (m), 844 (m), 803 (m), 745 (s), 703 (s), 688 (s), 608 (m); MS (EI, 70 eV): *m*/*z* (%)=303 (19), 302 (M$^+$, 100), 272 (11), 271 (61), 270 (21), 269 (86), 256 (18), 255 (49), 228 (17), 227 (13), 186 (11), 184 (15); HRMS (EI): calcd for $C_{17}H_{18}O_3S$ (M$^+$): 302.09712, found: 302.09715.

*3.2.5. Methyl 2-methoxy-4-methyl-6-(4-ethylphenyl-sulfanyl)-benzoate (**3e**).* Starting with **2e** (462 mg, 1.5 mmol) and **1a** (364 mg, 2.25 mmol), **3e** was isolated as a highly viscous colourless oil (213 mg, 45%); ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.14 (t, J=7.6 Hz, 3H, CH_3), 2.25 (s, 3H, CH_3), 2.54 (q, J=7.6 Hz, 2H, CH_2), 3.56 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 6.39–7.26 (m, 6H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ=14.3 (CH_3), 19.4 (CH_3), 27.2 (CH_2CH_3), 50.9 (OCH_3), 54.1 (OCH_3), 112.6, 113.0 (CH_{Ar}), 125.9 (C), 127.8 ($2CH_{Ar}$), 129.9 (C), 131.9 ($2CH_{Ar}$), 136.8, 137.4, 143.3, 159.2, 167.7 (C); IR (KBr, cm^{-1}): ν=3070 (w), 3023 (w), 2959 (w), 2930 (w), 2870 (w), 1911 (w), 1083 (m), 1738 (m), 1710 (s), 1650 (m), 1572 (m), 1473 (m), 1438 (s), 1303 (m), 1248 (m), 1195 (s), 1153 (s), 1099 (s), 1067 (m), 1022 (s), 1000 (m), 886 (m), 844 (m), 803 (m), 745 (s), 703 (s), 688 (s), 608 (m); MS (EI, 70 eV): *m*/*z* (%)=317 (20), 316 (M$^+$, 100), 285 (45), 284 (17), 283 (51), 269 (13), 256 (10), 255 (40), 121 (26), 186 (11), 184 (15); HRMS (EI): calcd for $C_{18}H_{20}O_3S$ (M$^+$): 316.11277, found: 316.11293.

*3.2.6. Methyl 2-methoxy-4-methyl-6-(4-flourophenyl-sulfanyl)-benzoate (**3f**).* Starting with **2f** (447 mg, 1.5 mmol) and **1a** (364 mg, 2.25 mmol), **3f** was isolated as a highly viscous colourless oil (183 mg, 40%); ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.27 (s, 3H, CH_3), 3.59 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 6.37–7.29 (m, 6H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ=20.4 (CH_3), 51.9 (OCH_3), 55.2 (OCH_3), 113.8, 114.4, 116.2, 116.6 (CH_{Ar}), 127.1, 129.7, 129.8 (C), 134.7, 134.9 (CH_{Ar}), 137.2, 138.6, 160.3, 168.6 (C); IR (KBr, cm^{-1}): ν=3055 (w), 2999 (w), 2947 (w), 2835 (w), 1725 (s), 1590 (s), 1562 (s), 1459 (s), 1427 (m), 1399 (m), 1304 (m), 1266 (s), 1218 (s), 1187 (m), 1137 (s), 1090 (m), 1071 (m), 1047 (s), 995 (m), 959 (m), 849 (m), 773 (s), 677 (s), 608 (m); MS (EI, 70 eV): *m*/*z* (%)=307 (14), 306 (M$^+$ 79), 276 (10), 275 (57), 274 (30), 273 (100), 260 (12), 232 (14), 203 (10), 202 (10), 189 (10), 185 (10), 184 (18); HRMS (EI): calcd for $C_{16}H_{15}O_3SF$ (M$^+$): 306.04622, found: 306.046232.

*3.2.7. Methyl 2-methoxy-4-methyl-6-(4-chlorophenyl-sulfanyl)-benzoate (**3g**).* Starting with **2g** (471 mg, 1.5 mmol) and **1a** (364 mg, 2.25 mmol), **3g** was isolated as a highly viscous colourless oil (222 mg, 46%); ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.28 (s, 3H, CH_3), 3.65 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 6.58–7.23 (m, 6H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ=20.3 (CH_3), 52.0 (OCH_3), 55.3 (OCH_3), 115.6 ($2CH_{Ar}$), 127.2, 128.9, 130.0, 130.4 (CH_{Ar}), 134.1, 134.5, 134.7, 137.9, 138.5, 160.3, 168.6 (C); IR (KBr, cm^{-1}): ν=3055 (w), 2999 (w), 2947 (w), 2835 (w), 1725 (s), 1590 (s), 1561 (s), 1459 (s), 1427 (m), 1399 (m), 1304 (m), 1266 (s), 1218 (s), 1187 (m), 1137 (s), 1090 (m), 1071 (m), 1047 (s), 995 (m), 959 (m), 849 (m), 773 (s), 677 (s), 608 (m); MS (EI, 70 eV): *m*/*z* (%)=324 (26), 323 (13), 322 (M$^+$ 70), 293 (29),

292 (17), 291 (83), 290 (27), 289 (100), 255 (17), 185 (10), 184 (18); HRMS (EI): calcd for $C_{16}H_{15}O_3SCl$ (M^+): 322.04249, found: 322.04244.

*3.2.8. Methyl 6-methoxy-3,4-dimethyl-2-phenylsulfanyl-benzoate (**3h**).* Starting with **2h** (441 mg, 1.5 mmol) and **1a** (364 mg, 2.25 mmol), **3h** was isolated as a highly viscous colourless oil (167 mg, 37%); ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.11 (s, 3H, CH_3), 2.25 (s, 3H, CH_3), 3.72 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 6.66–7.18 (m, 6H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ=13.3 (CH_3), 19.7 (CH_3), 52.0 (OCH_3), 55.6 (OCH_3), 112.9, 125.3 (CH_{Ar}), 127.2, 128.7 ($2CH_{Ar}$), 129.3, 129.5, 129.9, 133.5, 137.3, 158.4, 169.6 (C); IR (KBr, cm^{-1}): ν=3434 (w), 2998 (w), 2947 (w), 2834 (w), 2735 (w), 2664 (w), 1083 (m), 1738 (m), 1710 (s), 1650 (m), 1572 (m), 1473 (m), 1438 (s), 1303 (m), 1248 (m), 1195 (s), 1153 (s), 1099 (s), 1067 (m), 1022 (s), 1000 (m), 886 (m), 844 (m), 803 (m), 745 (s), 703 (s), 688 (s), 608 (m); MS (EI, 70 eV): *m*/*z* (%)=303 (13), 302 (M^+, 70), 272 (11), 271 (61), 270 (21), 269 (100), 256 (18), 255 (49), 228 (17), 227 (13), 186 (11), 184 (15); HRMS (EI): calcd for $C_{17}H_{18}O_3S$ (M^+): 302.09712, found: 302.09713.

*3.2.9. Methyl 6-methoxy-3,4-dimethyl-2-(4-ethylphenyl-sulfanyl)-benzoate (**3i**).* Starting with **2i** (483 mg, 1.5 mmol) and **1a** (364 mg, 2.25 mmol), **3i** was isolated as a highly viscous colourless oil (173 mg, 35%); ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.10 (t, *J*=7.6 Hz, 3H, CH_3), 2.11 (s, 3H, CH_3), 2.25 (s, 3H, CH_3), 2.48 (q, *J*=7.6 Hz, 2H, CH_2), 3.73 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 6.94–7.18 (m, 5H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ=12.3 (CH_3), 14.4 (CH_3), 18.7 (CH_3), 27.3 (CH_2), 51.0 (OCH_3), 54.6 (OCH_3), 111.7 (CH_{Ar}), 126.6, 127.3 ($2CH_{Ar}$), 127.5, 128.3, 128.6, 132.3, 132.8, 134.9, 157.3, 168.5 (C); IR (KBr, cm^{-1}): ν=2962 (w), 2928 (w), 2872 (w), 2735 (w), 2664 (w), 1083 (m), 1738 (m), 1710 (s), 1650 (m), 1572 (m), 1473 (m), 1438 (s), 1303 (m), 1248 (m), 1195 (s), 1153 (s), 1099 (s), 1067 (m), 1022 (s), 1000 (m), 886 (m), 844 (m), 803 (m), 745 (s), 703 (s), 688 (s), 608 (m); MS (EI, 70 eV): *m*/*z* (%)=331 (20), 330 (M^+, 98), 272 (11), 271 (61), 270 (21), 269 (100), 256 (18), 255 (49), 228 (17), 227 (13), 186 (11), 184 (15); HRMS (EI): calcd for $C_{19}H_{22}O_3S$ (M^+): 330.12842, found: 330.12824.

*3.2.10. Methyl 2-(3-chlorophenylsulfanyl)-4-ethyl-6-methoxybenzoate (**3j**).* Starting with **2c** (471 mg, 1.5 mmol) and **1b** (396 mg, 2.25 mmol), **3j** was isolated as a highly viscous colourless oil (186 mg, 37%); ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.55 (t, *J*=7.6 Hz, 3H, CH_3), 2.56 (q, *J*=7.6 Hz, 2H, CH_2), 3.65 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 6.58–7.23 (m, 6H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ=15.3 (CH_3), 27.1 (CH_2), 52.0 (OCH_3), 55.3 (OCH_3), 114.4, 115.8, 127.1, 128.6 (CH_{Ar}), 129.7 (C), 130.0, 130.1 (CH_{Ar}), 134.1, 135.6, 138.1, 144.4, 160.5, 168.7 (C); IR (KBr, cm^{-1}): ν=3055 (w), 2999 (w), 2947 (w), 2835 (w), 1725 (s), 1590 (s), 1562 (s), 1459 (s), 1427 (m), 1399 (m), 1304 (m), 1266 (s), 1218 (s), 1187 (m), 1137 (s), 1090 (m), 1071 (m), 1047 (s), 995 (m), 959 (m), 849 (m), 773 (s), 677 (s), 608 (m); MS (EI, 70 eV): *m*/*z* (%)=338 (26), 337 (13), 336 (M^+ 70), 293 (29), 292 (17), 291 (83), 290 (27), 289 (100), 255 (17), 185 (10), 184 (18); HRMS (EI): calcd for $C_{17}H_{17}O_3SCl$ (M^+): 336.05814, found: 336.057409.

*3.2.11. Methyl 2-(4-methylphenylsulfanyl)-4-ethyl-6-methoxybenzoate (**3k**).* Starting with **2d** (441 mg, 1.5 mmol) and **1b** (396 mg, 2.25 mmol), **3k** was isolated as a highly viscous colourless oil (180 mg, 38%); ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.14 (t, *J*=7.6 Hz, 3H, CH_3), 2.26 (s, 3H, CH_3), 2.57 (q, *J*=7.6 Hz, 2H, CH_2), 3.59 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 6.41–7.25 (m, 6H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ=14.3 (CH_3), 20.1 (CH_3), 26.1 (CH_2), 50.9 (OCH_3), 54.1 (OCH_3), 111.8, 112.6 (CH_{Ar}), 126.0 (C), 128.8, 131.7 ($2CH_{Ar}$), 132.3, 136.1, 136.9, 143.3, 159.3, 167.9 (C); IR (KBr, cm^{-1}): ν=3055 (w), 2999 (w), 2947 (w), 2835 (w), 1725 (s), 1590 (s), 1562 (s), 1459 (s), 1427 (m), 1399 (m), 1304 (m), 1266 (s), 1218 (s), 1187 (m), 1137 (s), 1090 (m), 1071 (m), 1047 (s), 995 (m), 959 (m), 849 (m), 773 (s), 677 (s), 608 (m); MS (EI, 70 eV): *m*/*z* (%)=316 (M^+, 45), 285 (23), 284 (20), 383 (100), 269 (31), 255 (17), 185 (10), 184 (18); HRMS (EI): calcd for $C_{18}H_{20}O_3S$ (M^+): 316.11277, found: 316.11268.

*3.2.12. Methyl 2-(4-chlorophenylsulfanyl)-4-ethyl-6-methoxybenzoate (**3l**).* Starting with **2g** (471 mg, 1.5 mmol) and **1b** (396 mg, 2.25 mmol), **3l** was isolated as a highly viscous colourless oil (201 mg, 40%); ^{1}H NMR (250 MHz, $CDCl_3$): δ=1.55 (t, *J*=7.6 Hz, 3H, CH_3), 2.56 (q, *J*=7.6 Hz, 2H, CH_2), 3.65 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 6.58–7.23 (m, 6H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ=15.3 (CH_3), 27.1 (CH_2), 52.0 (OCH_3), 55.3 (OCH_3), 114.4, 115.8, 127.1, 128.6 (CH_{Ar}), 129.7 (C), 130.0, 130.1 (CH_{Ar}), 134.1, 135.6, 138.1, 144.4, 160.5, 168.7 (C); IR (KBr, cm^{-1}): ν=3055 (w), 2999 (w), 2947 (w), 2835 (w), 1725 (s), 1590 (s), 1562 (s), 1459 (s), 1427 (m), 1399 (m), 1304 (m), 1266 (s), 1218 (s), 1187 (m), 1137 (s), 1090 (m), 1071 (m), 1047 (s), 995 (m), 959 (m), 849 (m), 773 (s), 677 (s), 608 (m); MS (EI, 70 eV): *m*/*z* (%)=338 (26), 337 (13), 336 (M^+ 70), 293 (29), 292 (17), 291 (83), 290 (27), 289 (100), 255 (17), 185 (10), 184 (18); HRMS (EI): calcd for $C_{17}H_{17}O_3SCl$ (M^+): 336.05814, found: 336.05741.

3.3. General procedure for the synthesis of diaryl sulfides 5a–m

To a dichloromethane solution (2 mL/mmol of **6**) of **6** (1.5 mmol) and of 1,1,3,3-tetramethoxypropane (1.0 mmol) was added TMSOTf (0.1 mmol) at −78 °C. The solution was allowed to warm to 20 °C within 20 h. To the solution was added a diluted aqueous solution of HCl (15 mL). The organic and the aqueous layers were separated and the latter was extracted with dichloromethane (3×15 mL). The combined organic layers were dried (Na_2SO_4), filtered and the filtrate was concentrated in vacuo. The residue was purified by chromatography.

*3.3.1. Methyl 2-(phenylsulfanyl)benzoate (**5a**).* Starting with tetramethoxypropane (0.33 mL, 2.0 mmol), **2a** (843 mg, 3.0 mmol), TMSOTf (0.036 mL, 0.2 mmol) and CH_2Cl_2 (4 mL), **7a** was isolated as a highly viscous colourless oil (275 mg, 53%); ^{1}H NMR (250 MHz, $CDCl_3$): δ=3.66 (s, 3H, OCH_3), 6.75 (dd, 1H, ^3J=7.2, ^4J=1.87 Hz, ArH), 7.06 (ddd, 1H, ^3J=7.2, ^4J=1.87, ^5J=0.92 Hz, ArH), 7.16 (m, 2H, ArH), 7.36 (m, 3H, ArH), 7.48 (m, 2H, ArH); ^{13}C NMR (62 MHz, $CDCl_3$): δ=52.1 (OCH_3), 124.2 (ArCH), 126.7 (C), 127.4, 129.0 (ArCH), 129.7 (2C, ArCH), 131.1, 132.2 (ArCH), 124.6 (C), 135.5 (2C, ArCH), 143.1, 166.8 (C); IR (neat): $\tilde{\nu}$=3056 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1433 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s), 530 (m) cm^{-1}; GC–MS (EI, 70 eV): *m*/*z* (%): 244 (100), 213 (76), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI, 70 eV): calcd for $C_{14}H_{12}O_2S$ [M^{++}]: 244.05525, found: 244.05570.

*3.3.2. Methyl 2-(4-fluorophenylsulfanyl)-benzoate (**5b**).* Starting with 1,1,3,3-tetramethoxypropane (0.25 mL, 1.5 mmol), **2f** (447 mg, 1.5 mmol), and TMSOTf (0.02 mL, 0.12 mmol), and CH_2Cl_2 (7 mL), **5b** was isolated as a highly viscous colourless oil (184 mg, 47%); ^{1}H NMR (250 MHz, CDCl3): δ=3.89 (s, 3H, OCH_3), 6.69–7.89 (m, 8H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ=52.0 (OCH_3), 123.9 (CH_{Ar}), 126.3 (C_{Ar}), 127.0 (CH_{Ar}), 128.6 (C_{Ar}), 130.6 (2C, CH_{Ar}), 131.0, 132.2 (CH_{Ar}), 135.7 (2C, CH_{Ar}), 139.4, 143.9 (C_{Ar}), 166.8 (C); IR (neat): $\tilde{\nu}$=3056 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1433 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s), 530 (m) cm^{-1}; GC–MS (EI, 70 eV): *m*/*z* (%): 263 (17), 262 (M^+ 100), 232 (12), 231 (77), 228 (14), 227 (87), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI): calcd for $C_{14}H_{11}O_2FS$ [M^+]: 262.04583, found: 262.046008.

*3.3.3. Methyl 2-(m-tolylsulfanyl)-benzoate (**5c**).* Starting with 1,1,3,3-tetramethoxypropane (0.25 mL, 1.5 mmol), **2b** (441 mg, 1.5 mmol), and TMSOTf (0.02 mL, 0.12 mmol), and CH_2Cl_2 (7 mL), **5c** was isolated as a highly viscous colourless oil (208 mg, 54%); ^{1}H

NMR (250 MHz, CDCl3): δ=2.33 (s, 3H, CH_3), 3.91 (s, 3H, OCH_3), 6.72–7.41 (m, 8H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ=21.3 (CH_3), 52.0 (OCH_3), 123.9 (CH_{Ar}), 126.3 (C_{Ar}), 127.0 (CH_{Ar}), 128.6 (C_{Ar}), 130.6 (2C, CH_{Ar}), 131.0, 132.2 (CH_{Ar}), 135.7 (2C, CH_{Ar}), 139.4, 143.9 (C_{Ar}), 166.8 (C); IR (neat): $\tilde{\nu}$=3056 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1433 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s), 530 (m) cm^{-1}; GC–MS (EI, 70 eV): *m*/*z* (%): 259 (34), 258 (M^+ 100), 228 (14), 227 (87), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI): calcd for $C_{15}H_{14}O_2S$ [M^+]: 258.05525, found: 258.05570.

*3.3.4. Methyl 2-(3-chlorophenylsulfanyl)-benzoate (**5d**).* Starting with 1,1,3,3-tetramethoxypropane (0.25 mL, 1.5 mmol), **2c** (471 mg, 1.5 mmol), and TMSOTf (0.02 mL, 0.12 mmol), and CH_2Cl_2 (7 mL), **5d** was isolated as a highly viscous colourless oil (212 mg, 51%); ^{1}H NMR (250 MHz, CDCl3): δ=3.87 (s, 3H, OCH_3), 6.77–7.92 (m, 8H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ=51.2 (OCH_3), 123.9 (CH_{Ar}), 126.3 (C_{Ar}), 127.0 (CH_{Ar}), 128.6 (C_{Ar}), 130.6 (2C, CH_{Ar}), 131.0, 132.2 (CH_{Ar}), 135.7 (2C, CH_{Ar}), 139.4, 143.9 (C_{Ar}), 166.8 (C); IR (neat): $\tilde{\nu}$=3056 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1432 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s), 530 (m) cm^{-1}; GC–MS (EI, 70 eV): *m*/*z* (%): 280 (31), 279 (12), 278 (M^+ 100), 249 (18), 247 (54), 227 (87), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI): calcd for $C_{14}H_{11}O_2ClS$ [M^+]: 278.01628, found: 278.016068.

*3.3.5. Methyl 2-(p-tolylsulfanyl)-benzoate (**5e**).* Starting with 1,1,3,3-tetramethoxypropane (0.25 mL, 1.5 mmol), **2d** (441 mg, 1.5 mmol), and TMSOTf (0.02 mL, 0.12 mmol), and CH_2Cl_2 (7 mL), **5e** was isolated as a highly viscous colourless oil (205 mg, 53%); ^{1}H NMR (250 MHz, CDCl3): δ=2.34 (s, 3H, CH_3), 3.90 (s, 3H, OCH_3), 6.72–7.94 (m, 8H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ=21.3 (CH_3), 52.1 (OCH_3), 123.9 (CH_{Ar}), 126.3 (C_{Ar}), 127.0 (CH_{Ar}), 128.6 (C_{Ar}), 130.6 (2C, CH_{Ar}), 131.0, 132.2 (CH_{Ar}), 135.7 (2C, CH_{Ar}), 139.4, 143.9 (C_{Ar}), 166.8 (C); IR (neat): $\tilde{\nu}$=3056 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1433 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s), 530 (m) cm^{-1}; GC–MS (EI, 70 eV): *m*/*z* (%): 259 (34), 258 (M^+ 100), 228 (14), 227 (87), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI): calcd for $C_{15}H_{14}O_2S$ [M^+]: 258.05525, found: 258.05570.

*3.3.6. Methyl 2-(naphth-2-ylsulfanyl)-benzoate (**5f**).* Starting with 1,1,3,3-tetramethoxypropane (0.25 mL, 1.5 mmol), **2j** (495 mg, 1.5 mmol), and TMSOTf (0.02 mL, 0.12 mmol), and CH_2Cl_2 (7 mL), **5f** was isolated as a highly viscous colourless oil (145 mg, 33%); ^{1}H NMR (250 MHz, CDCl3): δ=3.91 (s, 3H, OCH_3), 6.72–8.01 (m, 11H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ=52.2 (OCH_3), 124.4, 126.7 (CH_{Ar}), 126.8 (C_{Ar}), 127.0, 127.7, 127.8, 127.9, 129.4 (CH_{Ar}), 129.9 (C_{Ar}), 131.0, 131.8, 132.3 (CH_{Ar}), 133.2, 13.9 (C_{Ar}), 135.2 (CH_{Ar}), 143.0 (C_{Ar}), 166.8 (C); IR (neat): $\tilde{\nu}$=3055 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1433 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s), 530 (m) cm^{-1}; GC–MS (EI, 70 eV): *m*/*z* (%): 296 (17), 294 (M^+ 100), 228 (14), 227 (87), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI): calcd for $C_{18}H_{14}O_2S$ [M^+]: 294.05525, found: 294.05570.

*3.3.7. Methyl 3-methyl-2-(4-methylcyclohexa-1,5-dienylsulfanyl)-benzoate (**5g**).* Starting with 1,1,3,3-tetramethoxypropane (0.25 mL, 1.5 mmol), **2k** (462 mg, 1.5 mmol), and TMSOTf (0.02 mL, 0.12 mmol), and CH_2Cl_2 (7 mL), **5g** was isolated as a highly viscous colourless oil (187 mg, 46%); ^{1}H NMR (250 MHz, CDCl3): δ=2.12 (s, 3H, CH_3), 2.25 (s, 3H, CH_3), 3.78 (s, 3H, OCH_3), 6.82–7.44 (m, 7H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ=19.9, 20.1 (CH_3), 51.3 (OCH_3), 125.2 (CH_{Ar}), 126.9 (2C, CH_{Ar}), 127.5 (CH_{Ar}), 128.7 (2C, CH_{Ar}), 131.8 (CH_{Ar}), 136.3, 138.4, 143.0, 144.6, 144.9 (C_{Ar}), 167.9 (C); IR (neat): $\tilde{\nu}$=3055 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1433 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s), 530 (m) cm^{-1}; GC–MS (EI, 70 eV): *m*/*z* (%): 273 (18), 272 (M^+ 100), 241 (29), 240 (22), 239 (15), 227 (42), 226 (39), 225 (55), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI): calcd for $C_{16}H_{16}O_2S$ [M^+]: 272.08655, found: 272.086163.

*3.3.8. Methyl 2-(cyclohexa-1,5-dienylsufanyl)-3-methyl-benzoate (**5h**).* Starting with 1,1,3,3-tetramethoxypropane (0.25 mL, 1.5 mmol), **2h** (441 mg, 1.5 mmol), and TMSOTf (0.02 mL, 0.12 mmol), and CH_2Cl_2 (7 mL), **5h** was isolated as a highly viscous colourless oil (193 mg, 50%); ^{1}H NMR (250 MHz, CDCl3): δ=2.30 (s, 3H, CH_3), 3.86 (s, 3H, OCH_3), 7.12–7.74 (m, 8H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ=21.2 (CH_3), 52.3 (OCH_3), 124.5 (C_{Ar}), 125.5, 126.4 (CH_{Ar}), 127.5, 128.8 (2C, CH_{Ar}), 129.1, 132.9 (CH_{Ar}), 136.3, 138.4, 143.0 (C_{Ar}), 167.9 (C); IR (neat): $\tilde{\nu}$=3056 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1433 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s), 530 (m) cm^{-1}; GC–MS (EI, 70 eV): *m*/*z* (%): 259 (17), 258 (M^+ 100), 227 (42), 226 (39), 225 (55), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI): calcd for $C_{15}H_{14}O_2S$ [M^+]: 258.07090, found: 258.070812.

*3.3.9. Methyl 2-(4-fluorocyclohexa-1,5-dienylsulfanyl)-3-methyl-benzoate (**5i**).* Starting with 1,1,3,3-tetramethoxypropane (0.25 mL, 1.5 mmol), **2l** (468 mg, 1.5 mmol), and TMSOTf (0.02 mL, 0.12 mmol), and CH_2Cl_2 (7 mL), **5i** was isolated as a highly viscous colourless oil (182 mg, 44%); ^{1}H NMR (250 MHz, CDCl3): δ=2.25 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3), 6.72–7.54 (m, 7H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ=20.2 (CH_3), 51.3 (OCH_3), 114.8, 115.1 (CH_{Ar}), 124.5 (C_{Ar}), 125.4, 128.0, 128.7, 128.8 (CH_{Ar}), 129.1, 129.9 (C_{Ar}), 132.0 (CH_{Ar}), 143.1, 144.2 (C_{Ar}), 167.9 (C); IR (neat): $\tilde{\nu}$=3056 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1433 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s), 530 (m) cm^{-1}; GC–MS (EI, 70 eV): *m*/*z* (%): 277 (16), 276 (M^+ 100), 345 (40), 244 (24), 243 (60), 225 (55), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI): calcd for $C_{15}H_{13}O_2FS$ [M^+]: 276.06148, found: 276.061274.

*3.3.10. Methyl (3-ethyl-2-phenylsulfanyl)-benzoate (**5j**).* Starting with 1,1,3,3-tetramethoxypropane (0.25 mL, 1.5 mmol), **2m** (462 mg, 1.5 mmol), and TMSOTf (0.02 mL, 0.12 mmol), and CH_2Cl_2 (7 mL), **5j** was isolated as a highly viscous colourless oil (204 mg, 50%); ^{1}H NMR (250 MHz, CDCl3): δ=1.06 (t, *J*=7.5 Hz, 3H, CH_2CH_3), 2.72 (q, *J*=7.5 Hz, 2H, CH_2CH_3), 3.66 (s, 3H, OCH_3), 6.98–7.34 (m, 8H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ=14.9 (CH_3), 27.3 (CH_2), 52.2 (OCH_3), 125.4 (CH_{Ar}), 126.3 (C_{Ar}), 126.4 (CH_{Ar}), 127.3, 128.8 (2C, CH_{Ar}), 129.0 (C_{Ar}), 129.2, 131.1 (CH_{Ar}), 139.4, 143.9 (C_{Ar}), 166.8 (C); IR (neat): $\tilde{\nu}$=3056 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1433 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s), 530 (m) cm^{-1}; GC–MS (EI, 70 eV): *m*/*z* (%): 273 (18), 272 (M^+ 100), 228 (14), 227 (87), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI): calcd for $C_{16}H_{16}O_2S$ [M^+]: 272.05025, found: 258.050701.

*3.3.11. Methyl 2-(4-ethylcyclohexa-1,5-dienylsulfanyl)-benzoate (**5k**).* Starting with 1,1,3,3-tetramethoxypropane (0.25 mL, 1.5 mmol), **2e** (462 mg, 1.5 mmol), and TMSOTf (0.02 mL, 0.12 mmol), and CH_2Cl_2 (7 mL), **5k** was isolated as a highly viscous colourless oil (224 mg, 55%); ^{1}H NMR (250 MHz, CDCl3): δ=1.11 (t, *J*=7.5 Hz, 3H, CH_2CH_3), 2.71 (q, *J*=7.5 Hz, 2H, CH_2CH_3), 3.86 (s, 3H, OCH_3), 6.73–7.94 (m, 8H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ=15.3 (CH_3), 28.5 (CH_2), 52.1 (OCH_3), 124.4 (CH_{Ar}), 126.3 (C_{Ar}), 126.6 (CH_{Ar}), 128.5 (2C, CH_{Ar}), 129.0 (C_{Ar}), 130.5, 132.2 (CH_{Ar}), 135.8 (2C, CH_{Ar}), 139.4, 143.9 (C_{Ar}), 166.8 (C); IR (neat): $\tilde{\nu}$=3056 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1433 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s), 530 (m) cm^{-1}; GC–MS (EI, 70 eV): *m*/*z* (%): 273 (19), 272 (M^+ 100), 228 (14), 227 (87), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI): calcd for $C_{16}H_{16}O_2S$ [M^+]: 272.05025, found: 258.050701.

*3.3.12. Methyl 2-(4-ethylcyclohexa-1,5-dienylsulfanyl)-4-methyl-benzoate (**5l**).* Starting with 1,1,3,3-tetramethoxypropane (0.25 mL, 1.5 mmol), **2i** (483 mg, 1.5 mmol), and TMSOTf (0.02 mL, 0.12 mmol), and CH_2Cl_2 (7 mL), **5l** was isolated as a highly viscous

colourless oil (193 mg, 45%); ^{1}H NMR (250 MHz, CDCl3): δ=1.09 (t, J=7.5 Hz, 3H, CH_2CH_3), 2.28 (s, 3H, CH_3), 2.42 (q, J=7.5 Hz, 2H, CH_2CH_3), 3.78 (s, 3H, OCH_3), 6.90–7.34 (m, 7H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ=14.4 (CH_2CH_3), 20.3 (CH_3), 27.3 (CH_2CH_3), 51.3 (OCH_3), 125.2 (CH_{Ar}), 126.9, 127.4 (2C, CH_{Ar}), 127.6 (CH_{Ar}), 129.7 (C_{Ar}), 131.1 (CH_{Ar}), 132.7, 138.2, 140.8, 142.8 (C_{Ar}), 168.0 (C); IR (neat): $\tilde{\nu}$=3056 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1433 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s), 530 (m) cm^{-1}; GC–MS (EI, 70 eV): m/z (%): 287 (18), 286 (M$^+$ 100), 271 (17), 227 (87), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI): calcd for $C_{17}H_{18}O_2S$ [M$^+$]: 286.10220, found: 286.102313.

*3.3.13. Methyl 2-(3-chlorocyclohexa-1,5-dienylsulfanyl)-3-methyl-benzoate (**5m**).* Starting with 1,1,3,3-tetramethoxypropane (0.25 mL, 1.5 mmol), **2n** (492 mg, 1.5 mmol), and TMSOTf (0.02 mL, 0.12 mmol), and CH_2Cl_2 (7 mL), **5m** was isolated as a highly viscous colourless oil (210 mg, 48%); ^{1}H NMR (250 MHz, CDCl3): δ=2.33 (s, 3H, CH_3), 3.85 (s, 3H, OCH_3), 6.82–7.53 (m, 7H, ArH); ^{13}C NMR (63 MHz, $CDCl_3$): δ=20.2 (CH_3), 51.3 (OCH_3), 124.5 (C_{Ar}), 125.5 (CH_{Ar}), 126.5 (C_{Ar}), 127.6, 128.0 (2C, CH_{Ar}), 128.3, 132.0 (CH_{Ar}), 136.3, 138.4, 143.0 (C_{Ar}), 167.9 (C); IR (neat): $\tilde{\nu}$=3056 (w), 2948 (w), 1711 (s), 1585 (m), 1562 (m), 1433 (s), 1246 (s), 1189 (m), 1056 (s), 738 (s), 688 (s), 530 (m) cm^{-1}; GC–MS (EI, 70 eV): m/z (%): 294 (39), 293 (17), 292 (M$^+$ 100), 261 (35), 260 (15), 227 (42), 226 (39), 225 (55), 184 (55), 152 (16), 139 (10), 108 (8); HRMS (EI): calcd for $C_{15}H_{13}O_2ClS$ [M$^+$]: 292.03193, found: 292.032066.

3.4. General procedure for the synthesis of diaryl sulfides 7a–e

To a dichloromethane solution (6 mL/mmol of **6**) of **2** (1.5 mmol) and of **6** (1.5 mmol) was added $TiCl_4$ (2.25 mmol) at −78 °C. The solution was allowed to warm to 20 °C within 20 h. To the solution was added a hydrochloric acid (10%, 25 mL). The organic and the aqueous layers were separated and the latter was extracted with dichloromethane (3×20 mL). The combined organic layers were dried (Na_2SO_4), filtered, and the filtrate was concentrated in vacuo and the residue was purified by chromatography (silica gel, EtOAc/n-heptane=1:9).

*3.4.1. Methyl 4-methyl-2-methylsulfanyl-6-(4-tolylsulfanyl)-benzoate (**7a**).* Starting with **2d** (441 mg, 1.5 mmol), **6** (243 mg, 1.5 mmol), $TiCl_4$ (0.25 mL, 2.25 mmol) and CH_2Cl_2 (9 mL), **7a** was isolated as a highly viscous oil (262 mg, 55%); ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.21 (s, 3H, CH_3), 2.23 (s, 3H, CH_3), 2.39 (s, 3H, SCH_3), 3.82 (s, 3H, OCH_3), 6.80–7.19 (m, 6H, Ar); ^{13}C NMR (63 MHz, $CDCl_3$): δ=17.4 (CH_3), 21.2 (CH_3), 21.3 (Sme), 52.2 (Ome), 127.4, 128.3, 128.8, 129.0, 130.2, 132.2 (CH_{Ar}), 133.6, 134.6, 134.7, 136.8, 139.0, 140.5 (C_{Ar}), 167.7 (CO); IR (KBr, cm^{-1}): ν=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 (s); MS (EI, 70 eV): m/z (%)=319 (20), 318 (M$^+$ 100), 287 (33), 272 (16), 271 (25), 212 (16), 211 (16), 195 (17), 63 (3); HRMS (EI): calcd for $C_{17}H_{18}O_2S_2$ (M$^+$): 318.07427, found: 318.07489.

*3.4.2. Methyl 3-methyl-2-methylsulfanyl-6-(4-tolylsulfanyl)-benzoate (**7b**).* Starting with **2b** (441 mg, 1.5 mmol), **6** (243 mg, 1.5 mmol), $TiCl_4$ (0.25 mL, 2.25 mmol) and CH_2Cl_2 (9 mL), **7b** was isolated as a highly viscous oil (248 mg, 52%); ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.22 (s, 3H, CH_3), 2.24 (s, 3H, CH_3), 2.39 (s, 3H, SCH_3), 3.82 (s, 3H, OCH_3), 6.80–7.20 (m, 6H, Ar); ^{13}C NMR (63 MHz, $CDCl_3$): δ=17.4 (CH_3), 21.1 (CH_3), 21.3 (SMe), 52.2 (Ome), 127.4, 128.3, 128.8, 129.0, 130.2, 132.2 (CH_{Ar}), 133.6, 134.6, 134.7, 136.8, 139.0, 140.5 (C_{Ar}), 167.7 (CO); IR (KBr, cm^{-1}): ν=3055 (w), 2994 (w), 2948 (w), 2927 (w), 2857 (w), 1726 (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 (s); MS (EI, 70 eV): m/z (%)=319 (20), 318 (M$^+$ 100), 287 (33), 272 (16), 271 (25), 212 (16), 211 (14), 195 (17), 63 (7); HRMS (EI): calcd for $C_{17}H_{18}O_2S_2$ (M$^+$): 318.07427, found: 318.07489.

*3.4.3. Methyl 4-chloro-2-methylsulfanyl-6-(4-tolylsulfanyl)-benzoate (**7c**).* Starting with **2g** (472 mg, 1.5 mmol), **6** (243 mg, 1.5 mmol), $TiCl_4$ (0.25 mL, 2.25 mmol) and CH_2Cl_2 (9 mL), **7c** was isolated as a highly viscous oil (244 mg, 45%); ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.22 (s, 3H, CH_3), 2.39 (s, 3H, SCH_3), 3.85 (s, 3H, OCH_3), 6.80–7.30 (m, 6H, Ar); ^{13}C NMR (63 MHz, $CDCl_3$): δ=21.1 (CH_3), 21.3 (SMe), 52.3 (OMe), 127.4, 128.3, 128.8, 129.0, 130.2, 132.2 (CH_{Ar}), 133.6, 134.6, 134.7, 136.8, 139.0, 140.5 (C_{Ar}), 167.7 (CO); IR (KBr, cm^{-1}): ν=3055 (w), 2994 (w), 2948 (w), 2927 (w), 2857 (w), 1726 (s), 1608 (m), 1581 (m), 1475 (m), 1449 (s), 1437 (s), 1380 (w), 1266 (s), 1240 (s), 1188 (m), 1152 (m), 1105 (s), 1066 (s), 1023 (m), 957 (m), 738 (s), 688 (s); MS (EI, 70 eV): m/z (%)=340 (24), 338 (M$^+$, 71), 287 (33), 272 (16), 271 (25), 212 (16), 211 (14), 195 (17), 63 (7); HRMS (EI): calcd for $C_{16}H_{15}O_2S_2Cl$ (M$^+$): 338.3496, found: 338.33908.

*3.4.4. Methyl 3,4-dimethyl-6-methylsulfanyl-2-phenylsulfanyl-benzoate (**7d**).* Starting with **2h** (441 mg, 1.5 mmol), **6** (243 mg, 1.5 mmol), $TiCl_4$ (0.25 mL, 2.25 mmol) and CH_2Cl_2 (9 mL), **7d** was isolated as a highly viscous oil (190 mg, 40%); ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.21 (s, 3H, CH_3), 2.22 (s, 3H, CH_3), 2.39 (s, 3H, SCH_3), 3.85 (s, 3H, OCH_3), 6.91–7.30 (m, 6H, Ar); ^{13}C NMR (63 MHz, $CDCl_3$): δ=21.0 (CH_3), 21.1 (CH_3), 21.3 (SMe), 52.3 (OMe), 127.4, 128.3, 128.8, 129.0, 130.2, 132.2 (CH_{Ar}), 133.6, 134.6, 134.7, 136.8, 139.0, 140.5 (C_{Ar}), 167.8 (CO); IR (KBr, cm^{-1}): ν=3055 (w), 2994 (w), 2948 (w), 2927 (w), 2857 (w), 1726 (s), 1608 (m), 1581 (m), 1475 (m), 1449 (s), 1437 (s), 1380 (w), 1266 (s), 1240 (s), 1188 (m), 1152 (m), 1105 (s), 1066 (s), 1023 (m), 957 (m), 738 (s), 688 (s); MS (EI, 70 eV): m/z (%)=319 (21), 318 (M$^+$ 100), 287 (33), 272 (16), 271 (25), 212 (16), 211 (14), 195 (17), 63 (7); HRMS (EI): calcd for $C_{17}H_{18}O_2S_2$ (M$^+$): 318.07427, found: 318.075053.

*3.4.5. Methyl 3,4-dimethyl-6-methylsulfanyl-2-(4-tolylsulfanyl)-benzoate (**7e**).* Starting with **2k** (462 mg, 1.5 mmol), **6** (243 mg, 1.5 mmol), $TiCl_4$ (0.25 mL, 2.25 mmol) and CH_2Cl_2 (9 mL), **7e** was isolated as a highly viscous oil (184 mg, 37%); ^{1}H NMR (250 MHz, $CDCl_3$): δ=2.20 (s, 3H, CH_3), 2.22 (s, 3H, CH_3), 2.39 (s, 3H, SCH_3), 3.85 (s, 3H, OCH_3), 6.91–7.30 (m, 5H, Ar); ^{13}C NMR (63 MHz, $CDCl_3$): δ=21.0 (CH_3), 21.0 (CH_3), 21.3 (SMe), 52.3 (OMe), 127.3, 128.6, 128.9, 129.0, 130.2, 132.2 (CH_{Ar}), 133.6, 134.6, 134.7, 136.8, 139.0, 140.5 (C_{Ar}), 167.8 (CO); IR (KBr, cm^{-1}): ν=3055 (w), 2994 (w), 2948 (w), 2927 (w), 2857 (w), 1726 (s), 1608 (m), 1581 (m), 1475 (m), 1449 (s), 1437 (s), 1380 (w), 1266 (s), 1240 (s), 1188 (m), 1152 (m), 1105 (s), 1066 (s), 1023 (m), 957 (m), 738 (s), 688 (s); MS (EI, 70 eV): m/z (%)=333 (21), 332 (M$^+$ 100), 287 (33), 272 (16), 271 (25), 212 (16), 211 (14), 195 (17), 63 (7); HRMS (EI): calcd for $C_{17}H_{18}O_2S_2$ (M$^+$): 332.08992, found: 332.090382.

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