Meta- and *Para*-Difunctionalization of Arenes via an *Ortho*-Magnesiation and a Subsequent Sulfoxide–Magnesium Exchange

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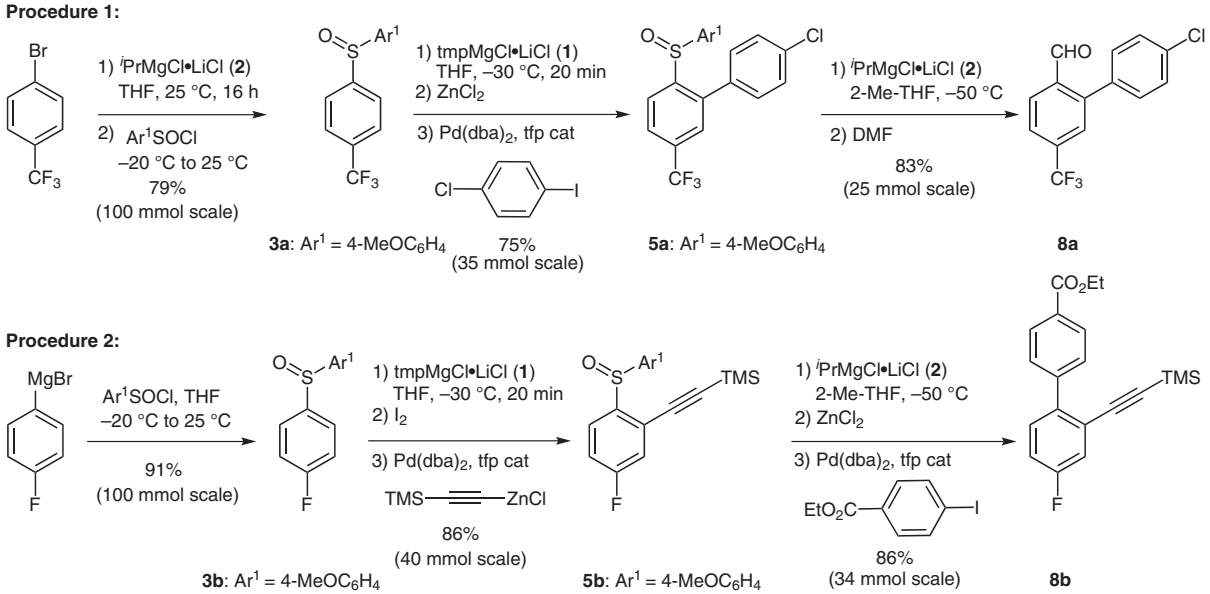
Abstract: Highly functionalized 1,2,4-trisubstituted arenes can be prepared on large scale by a two-step sequence, triggered by an aryl sulfoxide group. In the first step, the sulfoxide moiety acts as a metalation directing group, allowing a smooth magnesiation with tmpMgCl·LiCl. After a quenching reaction with an electrophile, the resulting sulfoxide is converted with *i*-PrMgCl·LiCl into a second magnesium reagent (sulfoxide–magnesium exchange), which can be trapped with various electrophiles. The highly chemoselective tmpMgCl·LiCl and *i*-PrMgCl·LiCl are compatible with a broad range of functional groups (FG = F, Cl, CF_3, CN, CO_2t-Bu, alkynyl).

Key words: metalation, *ortho*-magnesiation, sulfoxide–magnesium exchange, polyfunctional Grignard reagents



Scheme 1

Introduction

Highly functionalized arenes have found numerous applications in the preparation of pharmaceuticals and in materials science.[1] Arylorganometallic intermediates are especially versatile reagents for the functionalization of aromatics. They can be prepared by a directed *ortho*-metalation,[2] a metal insertion,[3] a halogen–metal exchange,[4] or a sulfoxide–metal exchange.[5–7] In this last approach the sulfoxide function may serve two purposes: (i) it may act as an *ortho*-directing group[8] using tmpMgCl·LiCl (**1**)[9] for ensuring a smooth magnesiation, and (ii) it may be the source of a carbon–metal bond by performing a sulfoxide–magnesium exchange using *i*-PrMgCl·LiCl[4b] (**2**). Both reagents tmpMgCl·LiCl (**1**) and *i*-PrMgCl·LiCl (**2**) have found to be compatible with a broad range of functional groups (FG = F, Cl, CF_3, CN, CO_2t-Bu, alkynyl, etc).

The sulfoxide–metal exchange has already been used in synthetic organic chemistry for performing a ligand exchange on pyridyl or quinolyl systems,[5] for generating various carbenoids starting from α-chlorosulfoxides or α-thiosulfoxides[6] and for racemic resolution.[7] Recently, we reported an efficient two-step synthesis for the generation of 1,2,4-trisubstituted arenes, starting from sulfoxides of type **3** (Scheme 2).[10]

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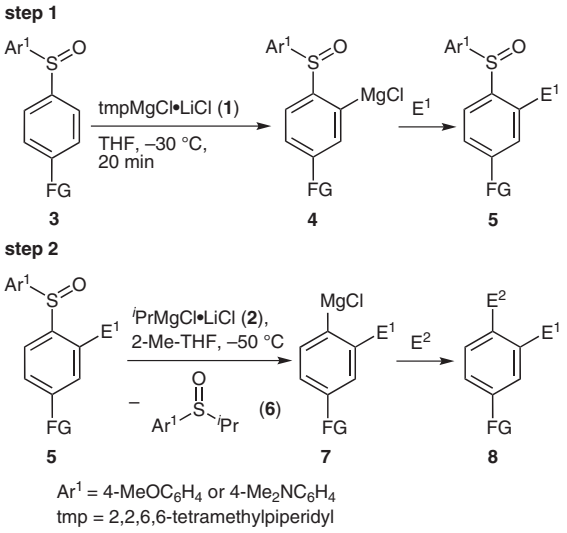


Scheme 2

Herein, we report an extension of this reaction sequence as well as its scale-up allowing a convenient synthesis of 1,2,4-trisubstituted arenes. Thus, by treating a diaryl sulfoxide of type **3** with tmpMgCl·LiCl (**1**; 1.1 equiv) at –30 °C for 20 minutes, a smooth *ortho*-magnesiation occurred and the intermediate magnesium reagent **4** was formed. Its quenching with an electrophile (E^1) led to functionalized sulfoxides of type **5**. Performing the sulfoxide–magnesium exchange with *i*-PrMgCl·LiCl (**2**; 1.1 equiv) at –50 °C for five minutes to seven hours furnished the magnesium reagent **7**. Remarkably, a selective cleavage of the carbon–sulfoxide bond occurs giving only (>95%) **7** and not Ar^1MgCl. This may be explained by the presence of the donor substituent (OMe or NMe_2) of Ar^1, which destabilizes Ar^1MgCl compared to the arylmagnesium compound **7**. The addition of a second electrophile (E^2) to the magnesium reagent **7** led to various polyfunctionalized arenes of type **8** (Table 1).

Scope and Limitations

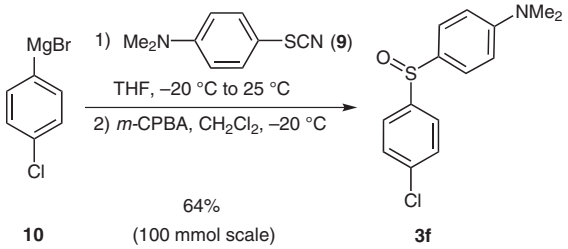
In all cases, the sulfoxides **3a–f** were metalated with tmpMgCl·LiCl (**1**, 1.1 equiv, –30 °C, 20 min) and functionalized by Negishi[11] cross-couplings. Thus, the trifluoromethyl-substituted sulfoxide **3a** (35 mmol scale) was deprotonated (–30 °C, 20 min) and after addition of zinc chloride coupled with 4-chloro-1-iodobenzene (1.2 equiv) in the presence of $Pd(dba)_2$ (1 mol%) and tfp (2 mol%; 7 h, 50 °C), furnishing the biphenyl **5a** in 75% yield (Table 1). The fluorinated sulfoxide **3b** (40 mmol scale) was metalated, trapped with iodine and reacted in situ with 2-(trimethylsilyl)ethynylzinc chloride[11c] in the presence of $Pd(PPh_3)_4$ (2 mol%; 2 h, 50 °C) giving the sulfoxide **5b** in 86% yield. The ester **3c** was deprotonated and underwent a similar Negishi cross-coupling, leading to the sulfoxide **5c** in 68% yield. Magnesiation of **3d**, transmetalation with zinc chloride and cross-coupling with 4-bromo-*N*,*N*-dimethylaniline gave **5d** in 84% yield. According to these expedient procedures the sulfoxides **5e**,**f** were prepared in 79–81% yield.

The third step of the synthetic sequence (Scheme 1), that is, the sulfoxide–magnesium exchange was >95% regioselective, providing only the desired functionalized aromatic magnesium reagents, and not the 4-methoxyphenylmagnesium chloride or 4-(dimethylamino)phenylmagnesium chloride.

Thus, sulfoxide **5a** (25 mmol) was treated with *i*-PrMgCl·LiCl (**2**; 1.1 equiv, –50 °C, 1.5 h) leading to the corresponding functionalized magnesium reagent, which reacted smoothly with DMF (0.8 equiv, –50 to 25 °C, 30 min) giving the aldehyde **8a** in 83% yield (Table 1, entry 1). The alkynyl substituted sulfoxide **5b** (34 mmol) displayed a higher reactivity, allowing to perform the sulfoxide–magnesium exchange within 5 minutes at –50 °C. The resulting magnesium compound provided after Negishi cross-coupling the biphenyl **8b** in 86% yield (entry 2). This high reactivity of the *ortho*-alkynated sulfoxides allows to perform the sulfoxide–magnesium exchange with the ester-functionalized sulfoxide **5c**, which after a subsequent reaction with DMF gave the aldehyde **9c** in 78% yield (entry 3). The cyano-substituted sulfoxide **5d** underwent a rapid sulfoxide–magnesium exchange (–50 °C, 5 min), leading to the aldehyde **8d** in 72% yield (entry 4). The bis-alkynylated sulfoxide **5e** led after a sulfoxide–magnesium exchange (–50 °C, 5 min) and after an addition to 3,4-dichlorobenzaldehyde to the alcohol **8e** in 72% yield (entry 5). In contrast, the sterically hindered sulfoxide **5f** required seven hours at –50 °C for completing the sulfoxide–magnesium exchange. Reaction with ethyl 2-(bromomethyl)acrylate[12] furnished the acrylate **8f** in 60% yield (entry 6).

Preparation of the Starting Sulfoxides

The starting functionalized diaryl sulfoxides **3a–f** were prepared by convenient one- or two-step syntheses. The reaction of arylmagnesium reagents, obtained by insertion[3] or halogen–magnesium exchange[4] with 4-methoxybenzenesulfinyl chloride[13] was performed on 15–100 mmol scale leading to the sulfoxides **3a–e** in 70–98% yield. Alternatively, the sulfoxide **3f** was prepared by the reaction of 4-(dimethylamino)phenyl thiocyanate[14] (**9**) with 4-chlorophenylmagnesium bromide (**10**). Subsequent oxidation of the resulting crude sulfide performed on large scale (100 mmol) provided the sulfoxide **3f** in 64% yield (Scheme 3).

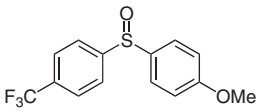
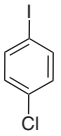
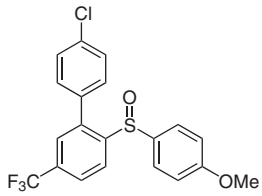
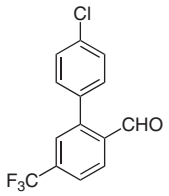
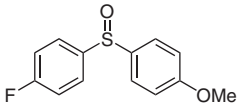
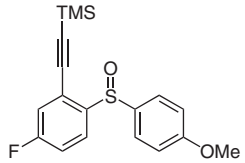
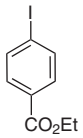
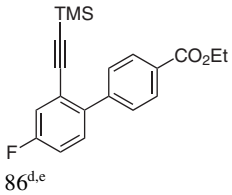
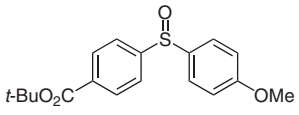
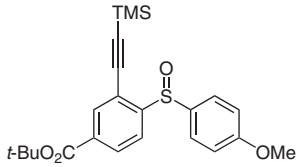
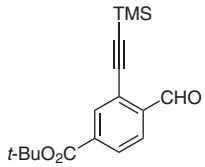
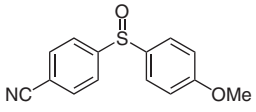
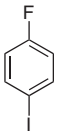
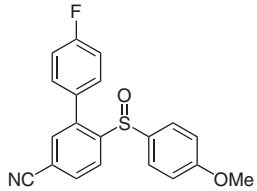
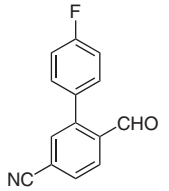
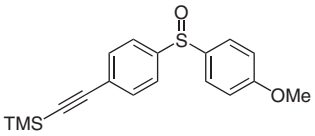
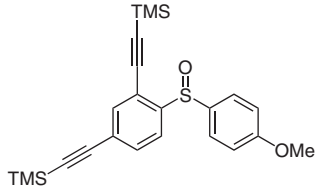
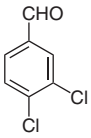
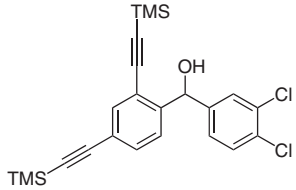
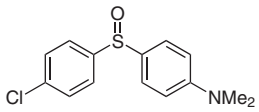
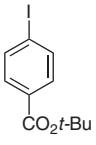
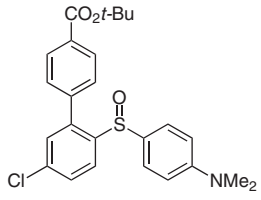
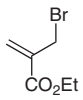
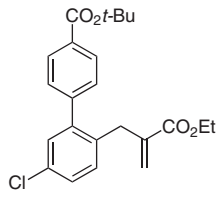


Scheme 3

Conclusion

In summary, we have developed an efficient protocol, on a multigram scale, for the preparation of polyfunctionalized diaryl sulfoxides and the consecutive sulfoxide–magnesium exchange leading to 1,2,4-trisubstituted arenes. The use of tmpMgCl·LiCl (**1**) and *i*-PrMgCl·LiCl (**2**) allows a compatibility with a wide range of functional groups (FG = F, Cl, CF_3 CN, CO_2t-Bu, alkynyl). Further extensions of this method are underway in our laboratories.

Table 1 Functionalization of Diaryl Sulfoxides and Sulfoxide–Magnesium Exchange Followed by Reaction with an Electrophile

Sulfoxide	E^1	Sulfoxide, yield (%)[a]	E^2	Product, yield (%)[a]
3a 		**5a**  75[b,c,d]	DMF	**8a**  83[e]
3b 	i) I_2 ii) TMS—≡—ZnCl	**5b**  86[b,c]		**8b**  86[d,e]
3c 	i) I_2 ii) TMS—≡—ZnCl	**5c**  68	DMF	**8c**  78
3d 		**5d**  71[d]	DMF	**8d**  72
3e 	i) I_2 ii) TMS—≡—ZnCl	**5e**  81		**8e**  72
3f 		**5f**  79[b,d]		**8f**  60[f]

[a] Yield of analytically pure product.
[b] The starting material of type **1** was prepared on a 100 mmol scale.
[c] This functionalization was performed on a >35 mmol scale.
[d] A transmetalation using $ZnCl_2$ (1.0 M in THF) was performed.
[e] The sulfoxide–magnesium exchange was performed on a >25 mmol scale.
[f] CuCN·2LiCl (5 mol%, 1.0 M in THF) was used as catalyst.

Procedures

All reactions were carried out under argon in dried glassware. All starting materials were purchased from commercial suppliers and used without further purification, unless otherwise stated. THF was continuously refluxed and freshly distilled from sodium benzophenone ketyl under N_2. Yields refer to isolated compounds estimated to be >95% pure as determined by ^{1}H NMR and capillary GC analysis.

Sulfoxides of Type 3a–e; General Procedure (GP 1)

A dry and argon-flushed Schlenk flask, equipped with a magnetic stirrer and a septum, was charged with a solution (approx. 0.5 M, 10.0 mmol) of the appropriate magnesium reagent and cooled to –20 °C. 4-Methoxybenzenesulfinyl chloride (2.48 g, 13.0 mmol) was added slowly and the reaction mixture was allowed to warm to 25 °C. The mixture was quenched with sat. aq NH_4Cl (50 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration, the solvent was removed under reduced pressure. Flash chromatographic purification yielded the products **3a–e**.

Deprotonation of Sulfoxides and Negishi-Type Cross-Coupling; General Procedure (GP 2)

A dry and argon-flushed Schlenk flask, equipped with a magnetic stirrer and a septum, was charged with a sulfoxide of type **3** (1.00 mmol) dissolved in THF (2 mL). The reaction mixture was cooled to –30 °C and tmpMgCl·LiCl (920 μL, 1.1 mmol, 1.20 M in THF) was added dropwise. After stirring for 20 min at –30 °C, $ZnCl_2$ (1.00 mL, 1.00 mmol, 1.00 M in THF) was added, and the mixture was allowed to warm to 25 °C. A Pd catalyst and an electrophile were added and the mixture was stirred between 25 and 50 °C depending upon the substrate. The mixture was quenched with sat. aq NH_4Cl (50 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration, the solvent was removed under reduced pressure. Flash chromatographic purification yielded the products of type **5**.

Functionalization of Sulfoxides with Alkynyl Substrates; General Procedure (GP 3)

A dry and argon-flushed Schlenk flask, equipped with a magnetic stirrer and a septum, was charged with a sulfoxide of type **3** (10.0 mmol) dissolved in THF (20 mL). The reaction mixture was cooled to –30 °C and tmpMgCl·LiCl (9.20 mL, 11.0 mmol, 1.20 M in THF) was added dropwise. After stirring for 20 min at –30 °C, I_2 (3.05 g, 12.0 mmol) was added and the mixture was allowed to warm to 25 °C. The mixture was then diluted with EtOAc (200 mL) and washed with sat. aq $Na_2S_2O_3$ (100 mL). The organic layer was dried ($MgSO_4$) and after filtration, the solvent was removed under reduced pressure. The crude product was dried in high vacuum for 3 h and then dissolved in THF (20 mL). In a second dry and argon flushed Schlenk flask, equipped with a magnetic stirrer and a septum, the desired alkyne (11.0 mmol) was added slowly to *i*-PrMgCl·LiCl (8.80 mL, 10.5 mmol, 1.20 M in THF). After cessation of gas evolution, the mixture was heated to 60 °C for 5 min. After cooling to 25 °C, a $ZnCl_2$ solution (11.0 mL, 11.0 mmol, 1.0 M in THF) was added slowly. The resulting zinc reagent was transferred to the previously prepared crude sulfoxide and a Pd catalyst was added. The mixture was stirred at the given temperature and quenched with sat. aq NH_4Cl (50 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration, the solvent was removed under reduced pressure. Flash chromatographic purification yielded the products of type **5**.

Sulfoxide–Magnesium Exchange Leading to Arenes of Type 8; General Procedure (GP 4)

A dry and argon-flushed Schlenk flask, equipped with a magnetic stirrer and a septum, was charged with a solution of sulfoxide of type **5** (1.00 mmol) in 2-methyltetrahydrofuran (2 mL). The reaction mixture was cooled to –50 °C and *i*-PrMgCl·LiCl (920 μL, 1.10 mmol, 1.20 M in THF) was added dropwise. After stirring at –50 °C until GC analysis showed full conversion of the sulfoxide, the desired electrophile (0.8 mmol) was added and the mixture was stirred at the given temperature until GC analysis showed full conversion of the electrophile. The mixture was quenched with a sat. aq NH_4Cl (5 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were dried ($MgSO_4$) and after filtration, the solvent was removed under reduced pressure. Flash chromatographic purification yielded the products of type **8**.

Procedure 1

4-Methoxyphenyl 4-(Trifluoromethyl)phenyl Sulfoxide (3a)

According to **GP 1**, sulfoxide **3a** was prepared from 4-trifluoromethylphenylmagnesium bromide (100 mL, 100 mmol, 1.00 M in THF) and 4-methoxybenzenesulfinyl chloride (24.8 g, 130 mmol) and purified by flash chromatography (silica gel, pentane–Et_2O, 1:1), furnishing **3a** as a colorless solid; yield: 23.7 g (79%); mp 92–94 °C.

IR (ATR): 1592 (s), 1575 (m), 1491 (s), 1398 (m), 1319 (s), 1305 (s), 1245 (vs), 1183 (s), 1172 (s), 1167 (s), 1141 (s), 1128 cm^{-1} (vs).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.78 (s, 3 H), 6.93–6.95 (m, 2 H), 7.54–7.57 (m, 2 H), 7.67–7.71 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.4 (CH_3), 115.0 (CH), 123.4 (q, *J* = 274.3 Hz, CF_3), 124.7 (CH), 126.1 (q, *J* = 3.8 Hz, CH), 127.3 (CH), 132.4 (q, *J* = 32.6 Hz), 135.9, 150.2, 162.4.

MS (EI, 70 eV): *m*/*z* (%) = 300 (24), 284 (11), 253 (16), 252 (100), 237 (12), 155 (95), 139 (29), 123 (59), 92 (10).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{11}F_3O_2{}^{32}S$: 300.0432; found: 300.0427.

4′-Chloro-5-(trifluoromethyl)biphenyl-2-yl 4-Methoxyphenyl Sulfoxide (5a)

According to **GP 2**, sulfoxide **5a** was prepared starting from sulfoxide **3a** (35.0 mmol, 10.5 g), using $Pd(dba)_2$ (201 mg, 350 μmol), tri-2-furylphosphine (tfp, 162 mg, 700 μmol) and 4-chloro-1-iodobenzene (10.02 g, 42.0 mmol) for the cross-coupling. The reaction mixture was stirred for 7 h at 50 °C. Flash chromatographic purification (silica gel, pentane–Et_2O, 1:1) afforded a colorless solid; yield: 10.8 g (75%); mp 113–115 °C.

IR (ATR): 1594 (m), 1578 (w), 1412 (m), 1327 (s), 1307 (m), 1292 (m), 1253 (s), 1240 (m), 1174 (s), 1135 (vs), 1089 (s), 1075 (s), 1044 (s), 1023 (s), 1012 cm^{-1} (s).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 3.74 (s, 3 H), 6.71 (d, *J* = 8.6 Hz, 2 H), 6.95 (d, *J* = 8.6 Hz, 2 H), 7.05 (d, *J* = 8.6 Hz, 2 H), 7.34 (d, *J* = 8.6 Hz, 2 H), 7.41 (s, 1 H), 7.86–7.87 (m, 1 H), 8.37 (d, *J* = 8.11 Hz, 1 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 55.4 (CH_3), 114.5 (CH), 123.5 (q, *J* = 272.9 Hz, CF_3), 124.6 (CH), 125.4 (q, *J* = 3.9 Hz, CH), 127.1 (q, *J* = 3.7 Hz, CH), 128.1 (CH), 128.8 (CH), 130.6 (CH), 132.6 (q, *J* = 32.9 Hz), 134.7, 135.0, 135.2, 139.7, 148.2, 162.1.

MS (EI, 70 eV): *m*/*z* (%) = 412 (9), 410 (23), 394 (7), 362 (9), 251 (6), 157 (5), 156 (8), 155 (100), 139 (20), 124 (30), 123 (28).

HRMS (EI): *m*/*z* calcd for $C_{20}H_{14}{}^{35}ClF_3O_2{}^{32}S$: 410.0355; found: 410.0355.

4′-Chloro-5-(trifluoromethyl)biphenyl-2-carbaldehyde (8a)

According to **GP 4**, the sulfoxide **5a** (10.3 g, 25.0 mmol) was treated with *i*-PrMgCl·LiCl (**2**; 17.3 mL, 27.5 mmol, 1.59 M in THF) at –50 °C for 30 min. DMF (1.47 g, 1.56 mL, 20.0 mmol) was then added and the reaction mixture was allowed to warm to 25 °C and stirred for an additional 4 h. Flash chromatographic purification

(silica gel, pentane– Et_2O, 17:1) gave a colorless solid; yield: 4.74 g (83%); mp 58–60 °C.

IR (ATR): 2860 (w), 1696 (s), 1484 (m), 1418 (m), 1390 (m), 1332 (s), 1298 (m), 1278 (m), 1246 (s), 1200 (m), 1168 (s), 1120 (vs), 1106 (s), 1092 (s), 1074 cm^{-1} (vs).

^1H NMR (300 MHz $CDCl_3$): δ = 7.31–7.35 (m, 2 H), 7.47–7.51 (m, 2 H), 7.68 (s, 1 H), 7.74–7.77 (m, 1 H), 8.12 (d, *J* = 8.2 Hz, 1 H), 9.99 (s, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 123.3 (q, *J* = 272.0 Hz, CF_3), 124.9 (q, *J* = 3.6 Hz, CH), 127.7 (q, *J* = 3.7 Hz, CH), 128.7 (CH), 129.1 (CH), 131.2 (CH), 134.8, 134.9 (q, *J* = 32.9 Hz), 135.4, 136.0, 144.8, 190.7 (CH).

MS (EI, 70 eV): *m*/*z* (%) = 286 (22), 285 (21), 284 (67), 283 (41), 249 (100), 220 (23), 201 (29), 152 (32).

HRMS (EI): *m*/*z* calcd for $C_{14}H_8{}^{35}ClF_3O$: 284.0216; found: 284.0212.

Procedure 2

4-Fluorophenyl 4-Methoxyphenyl Sulfoxide (3b)

According to **GP 1**, sulfoxide **3b** was prepared from 4-fluorophenylmagnesium bromide (100 mL, 100 mmol, 1.00 M in THF), and 4-methoxybenzenesulfinyl chloride (24.8 g, 130 mmol) and recrystallized from pentane furnishing **3b** as a colorless solid; yield: 22.9 g (91%); mp 83–84 °C.

IR (ATR): = 2836 (w), 1592 (s), 1577 (s), 1496 (s), 1436 (m), 1410 (m), 1311 (m), 1303 (m), 1254 (s), 1215 (s), 1154 (m), 1089 (s), 1076 (s), 1035 (s), 855 (s), 828 cm^{-1} (vs).

^1H NMR (300 MHz, $CDCl_3$): δ = 3.79 (s, 3 H), 6.92–6.95 (m, 2 H), 7.09–7.15 (m, 2 H), 7.51–7.60 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.4 (CH_3), 114.8 (CH), 116.4 (d, *J* = 22.67 Hz, CH), 126.9 (d, *J* = 8.85 Hz, CH), 127.0 (CH), 136.5, 141.4 (d, *J* = 3.04 Hz), 162.1, 164.0 (d, *J* = 251.2 Hz, CF).

MS (EI, 70 eV): *m*/*z* (%) = 251 (8), 250 (49), 233 (8), 203 (13), 202 (100), 187 (17), 154 (43), 139 (23), 123 (60), 101 (8).

HRMS (EI): *m*/*z* calcd for $C_{13}H_{11}FO_2{}^{32}S$: 250.0464; found: 250.0470.

({5-Fluoro-2-[(4-methoxyphenyl)sulfinyl]phenyl}ethynyl)(trimethyl)silane (5b)

According to **GP 3**, sulfoxide **5b** was prepared starting from sulfoxide **3b** (10.0 g, 40.0 mmol), using $Pd(PPh_3)_4$ (880 mg, 800 μmol) and trimethylethynylsilane (5.88 g, 8.52 mL, 60.0 mmol) for the cross-coupling. The reaction mixture was stirred for 2 h at 50 °C. Flash chromatographic purification (silica gel, pentane– Et_2O, 1:1) afforded a colorless solid; yield: 12.0 g (86%); mp 83–85 °C.

IR (ATR): 2956 (w), 1738 (m), 1591 (m), 1576 (m), 1495 (m), 1457 (s), 1249 (vs), 1217 (m), 1148 (m), 1083 (s), 1058 (s), 1037 (s), 952 (s), 846 (vs), 833 (vs), 821 cm^{-1} (vs).

^1H NMR (300 MHz, $CDCl_3$): δ = 0.26 (s, 9 H), 3.80 (s, 3 H), 6.89–6.92 (m, 2 H), 7.13 (dd, *J* = 8.8, 2.4 Hz, 1 H), 7.20–7.24 (m, 1 H), 7.59–7.63 (m, 2 H), 8.02 (dd, *J* = 8.8, 5.7 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –0.42 ($SiCH_3$), 55.4 (CH_3), 99.9 (d, *J* = 2.7 Hz), 104.9, 114.5 (CH), 117.0 (d, *J* = 22.2 Hz, CH), 120.0 (d, *J* = 24.1 Hz, CH), 122.2 (d, *J* = 10.3 Hz, CH), 125.8 (d, *J* = 9.3 Hz), 127.8 (CH), 136.3 (d, *J* = 1.2 Hz), 143.1 (d, *J* = 3.1 Hz), 162.0, 163.3 (d, *J* = 251.4 Hz, CF).

MS (EI, 70 eV): *m*/*z* (%) = 346 (40), 332 (24), 331 (100), 330 (14), 316 (14), 245 (13), 155 (14), 139 (14), 123 (15), 73 (88).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{19}FO_2{}^{32}S^{28}Si$: 346.0859; found: 346.0863.

Ethyl 4′-Fluoro-2′-[(trimethylsilyl)ethynyl]biphenyl-4-carboxylate (8b)

According to **GP 4**, the sulfoxide **5b** (11.7 g, 34.0 mmol) was treated with *i*-PrMgCl·LiCl (**2**; 33.7 mL, 37.4 mmol, 1.11 M in THF) at –50 °C for 5 min. $ZnCl_2$ (37.4 mL, 37.4 mmol, 1.00 M in THF) was then added and the reaction mixture was allowed to warm to 25 °C. Ethyl 4-iodobenzoate (7.51 g, 4.52 mL, 27.2 mmol) and $Pd(PPh_3)_4$ (750 mg, 680 μmol) were added and the mixture was stirred for an additional 4 h. Flash chromatographic purification (silica gel, pentane–Et_2O, 50:1) gave a yellow oil; yield: 8.09 g (86%).

IR (ATR): 2898 (w), 1475 (m), 1367 (w), 1269 (vs), 1250 (s), 1180 (m), 1156 (m), 1099 (s), 1026 (m), 959 (s), 840 (vs), 775 (s), 758 (s), 704 cm^{-1} (s).

^1H NMR (300 MHz, $CDCl_3$): δ = 0.11 (s, 9 H), 1.38 (t, *J* = 7.1 Hz, 3 H), 4.38 (q, *J* = 7.1 Hz, 2 H), 7.00–7.07 (m, 1 H), 7.22–7.30 (m, 2 H), 7.57–7.61 (m, 2 H), 8.03–8.07 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –0.56 ($SiCH_3$), 14.3 (CH_3), 60.9 (CH_2), 99.3, 102.8, 116.1 (d, *J* = 21.4 Hz, CH), 119.7 (d, *J* = 22.7 Hz, CH), 123.1 (d, *J* = 9.54 Hz, CH), 129.0 (CH), 129.2 (CH), 129.4, 130.9 (d, *J* = 8.8 Hz), 139.2 (d, *J* = 3.4 Hz), 143.8, 161.6 (d, *J* = 248.2 Hz, CF), 166.3.

MS (EI, 70 eV): *m*/*z* (%) = 341 (16), 340 (61), 325 (37), 297 (28), 295 (19), 282 (24), 280 (100), 189 (16), 140 (28), 75 (17).

HRMS (EI): *m*/*z* calcd for $C_{20}H_{21}FO_2{}^{28}Si$: 340.1295; found: 340.1295.

***tert*-Butyl 4-[(4-Methoxyphenyl)sulfinyl]benzoate (3c)**

According to **GP 1**, sulfoxide **3c** was prepared from 4-(*tert*-butoxycarbonyl)phenylmagnesium chloride (33.7 mL, 30.0 mmol, 0.89 M in THF) and 4-methoxybenzenesulfinyl chloride (6.27 g, 33.0 mmol), and purified by flash chromatography (silica gel, pentane–Et_2O, 1:1) to give **3c** as a colorless solid; yield: 9.01 g (90%); mp 73–75 °C.

IR (ATR): 2978 (m), 1705 (vs), 1594 (s), 1576 (m), 1366 (s), 1301 (s), 1290 (s), 1246 (vs), 1167 (s), 1121 (s), 1087 (s), 1040 (s), 1023 (s), 1011 (s), 827 cm^{-1} (m).

^1H NMR (300 MHz, $CDCl_3$): δ = 1.36 (s, 9 H), 3.55 (s, 3 H), 6.73 (d, *J* = 9.0 Hz, 2 H), 7.38 (d, *J* = 9.0 Hz, 2 H), 7.48 (d, *J* = 8.8 Hz, 2 H), 7.86 (d, *J* = 8.8 Hz, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 27.5 (CH_3), 54.9 (CH_3), 80.9, 114.4 (CH), 123.5 (CH), 126 (CH), 129.6 (CH), 133.4, 135.8, 150.0, 161.7, 163.9.

MS (EI, 70 eV): *m*/*z* (%) = 332 (11), 284 (30), 260 (7), 259 (6), 229 (13), 228 (100), 155 (34), 139 (45), 123 (59), 57 (7).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{20}O_4{}^{32}S$: 332.1082; found: 322.1066.

4-[(4-Methoxyphenyl)sulfinyl]benzonitrile (3d)

According to **GP 1**, sulfoxide **3d** was prepared from 4-cyanophenylmagnesium bromide (51.0 mL, 50.0 mmol, 0.98 M in THF) and 4-methoxybenzenesulfinyl chloride (10.5 g, 55.0 mmol), and purified by flash chromatography (silica gel, Et_2O), furnishing **3d** as a colorless solid; yield: 9.01 g (70%); mp 121–123 °C.

IR (ATR): 2228 (s), 1590 (s), 1575 (s), 1495 (s), 1258 (s), 1184 (w), 1174 (m), 1086 (s), 1039 (vs), 1024 (s), 1013 (s), 828 cm^{-1} (s).

^1H NMR (300 MHz, $CDCl_3$): δ = 3.80 (s, 3 H), 6.93–6.98 (m, 2 H), 6.52–6.57 (m, 2 H), 7.67–7.76 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.5 (CH_3), 114.3, 115.2 (CH), 117.7, 124.9 (CH), 127.4 (CH), 132.8 (CH), 135.5, 151.5, 162.6.

MS (EI, 70 eV): *m*/*z* (%) = 257 (15), 210 (14), 209 (56), 194 (10), 166 (7), 154 (100), 139 (21), 123 (40), 92 (7), 64 (7).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{11}NO_2{}^{32}S$: 257.0510; found: 257.0500.

({4-[(4-Methoxyphenyl)sulfinyl]phenyl}ethynyl)(trimethyl)silane (3e)

A dry and argon-flushed Schlenk flask, equipped with a magnetic stirrer and a septum, was charged with ethynyl(trimethyl)silane (1.96 g, 2.84 mL, 20.0 mmol), and *i*-PrMgCl·LiCl (15.2 mL, 19.0 mmol, 1.25 M in THF) was added at 25 °C. After cessation of gas evolution, the reaction mixture was heated to 60 °C for 5 min. After cooling to 25 °C, a $ZnCl_2$ solution (20.0 mL, 20.0 mmol, 1.00 M in THF) was slowly added. The resulting mixture was stirred for 30 min at 25 °C, then 4-iodophenyl-4′-methoxyphenyl sulfoxide[10] (15.0 mmol, 5.37 g), $Pd(dba)_2$ (173 mg, 300 μmol), and tri-2-furylphosphine (139 mg, 600 mol) were added and the mixture was stirred for 14 h at 25 °C. The mixture was quenched with sat. aq NH_4Cl (50 mL) and extracted with EtOAc (3 × 50 mL). The combined organic layers were dried ($MgSO_4$) and after filtration, the solvents were removed under reduced pressure. Flash chromatographic purification (silica gel, pentane–EtOAc, 2:1) afforded **3e** as a colorless solid; yield: 4.85 g (98%); mp 122–124 °C.

IR (ATR): 1591 (s), 1576 (m), 1491 (s), 1245 (vs), 1187 (m), 1171 (m), 1086 (s), 845 (m), 835 (s), 829 (s), 816 cm^{-1} (s).

^1H NMR (600 MHz, $CDCl_3$): δ = 0.21 (9 H), 3.78 (3 H), 6.90–6.93 (m, 2 H), 7.49–7.52 (m, 6 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = –0.3 ($SiCH_3$), 55.4 (CH_3), 96.7, 103.6, 114.8 (CH), 124.3 (CH), 125.6, 127.3 (CH), 132.5 (CH), 136.4, 145.7, 162.2.

MS (EI, 70 eV): *m*/*z* (%) = 328 (12), 313 (17), 312 (18), 297 (26), 281 (20), 280 (100), 266 (17), 265 (84), 158 (23), 155 (16), 143 (12), 139 (50), 123 (25).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{20}O_2{}^{32}S^{28}Si$: 328.0953; found: 328.0945.

{4-[(4-Chlorophenyl)sulfinyl]phenyl}dimethylamine (3f)

In a dry and argon-flushed Schlenk flask, equipped with a magnetic stirrer and a septum, 4-(dimethylamino)phenyl thiocyanate (17.8 g 100 mmol) was dissolved in THF (100 mL) and cooled to –20 °C. A solution of 4-chlorophenylmagnesium bromide (125 mL, 110 mmol, 0.88 M in THF) was added and the reaction mixture was allowed to warm to 25 °C. The mixture was quenched with sat. aq NH_4Cl (100 mL) and extracted with EtOAc (3 × 200 mL). The combined organic layers were dried ($MgSO_4$) and after filtration, the solvent was removed under reduced pressure. The crude sulfide was dissolved in CH_2Cl_2 (100 mL) and cooled to –20 °C. MCPBA (27.0 g, 110 mmol, 70% in H_2O) dissolved in CH_2Cl_2 (100 mL) was added slowly. After stirring for 1 h at –20 °C, the mixture was quenched with sat. aq $Na_2S_2O_3$ (50 mL) and extracted with EtOAc (3 × 200 mL). The combined organic layers were dried ($MgSO_4$) and after filtration, the solvent was removed under reduced pressure. Flash chromatographic purification (silica gel, pentane–EtOAc, 1:1) furnished **3f** as a colorless solid; yield: 17.9 g (64%); mp 128–129 °C.

IR (ATR): 1596 (s), 1509 (m), 1091 (s), 1083 (s), 1060 (m), 1045 (vs), 1010 (s), 826 (s), 807 (s), 738 cm^{-1} (s).

^1H NMR (300 MHz, $CDCl_3$): δ = 2.99 (s, 6 H), 6.65–6.70 (m, 2 H), 7.38–7.46 (m, 4 H), 7.49–7.54 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 40.1 (CH_3), 112.0 (CH), 126.0 (CH), 127.7 (CH), 129.2 (CH), 130.3, 136.3, 144.8, 152.5.

MS (EI, 70 eV): *m*/*z* (%) = 279 (19), 263 (34), 233 (25), 232 (23), 231 (80), 230 (30), 168 (100), 152 (25), 136 (30), 44 (19).

HRMS (EI): *m*/*z* calcd for $C_{14}H_{14}{}^{35}ClNO^{32}S$: 279.0485; found: 279.0479.

***tert*-Butyl 4-[(4-Methoxyphenyl)sulfinyl]-3-[(trimethylsilyl)ethynyl]benzoate (5c)**

According to **GP 3**, sulfoxide **5c** was prepared starting from sulfoxide **3c** (3.32 g, 10.0 mmol), using $Pd(PPh_3)_4$ (0.22 g, 0.20 mmol) and trimethylethynylsilane (1.47 g, 2.13 mL, 15.0 mmol) for the cross-coupling. The reaction mixture was stirred for 2 h at 50 °C. Flash chromatographic purification (silica gel, pentane–Et_2O, 1:1) afforded a colorless solid; yield: 2.91 g (68%); mp 134–135 °C.

IR (ATR): 1713 (vs), 1590 (m), 1495 (m), 1457 (m), 1368 (m), 1300 (s), 1250 (vs), 1160 (s), 1036 (s), 841 (vs), 833 (vs), 762 cm^{-1} (s).

^1H NMR (300 MHz, $CDCl_3$): δ = 0.23 (s, 9 H), 1.53 (s, 9 H), 3.74 (s, 3 H), 6.86 (d, *J* = 8.8 Hz, 2 H), 7.59 (d, *J* = 8.6 Hz, 2 H), 7.96–7.99 (m, 1 H), 8.08–8.12 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –0.5 ($SiCH_3$), 27.9 (CH_3), 55.3 (CH_3), 81.8, 99.4, 104.4, 114.4 (CH), 120.0, 123.1 (CH), 128.1 (CH), 129.9 (CH), 133.8, 134.1 (CH), 135.7, 151.4, 162.0, 163.9.

MS (EI, 70 eV): *m*/*z* (%) = 412 (16), 373 (20), 372 (60), 358 (27), 357 (98), 356 (35), 254 (50), 139 (21), 73 (100), 43 (24).

HRMS (EI): *m*/*z* calcd for $C_{23}H_{28}O_4SSi$: 428.1478; found: 428.1468.

4′-Fluoro-6-[(4-methoxyphenyl)sulfinyl]biphenyl-3-carbonitrile (5d)

According to **GP 2**, sulfoxide **5d** was prepared starting from sulfoxide **3d** (1.29 g, 5.00 mmol), using $Pd(PPh_3)_4$ (110 mg, 100 μmol) and 1-fluoro-4-iodobenzene (1.33 g, 6.00 mmol) for the cross-coupling. The reaction mixture was stirred for 2 h at 50 °C. Flash chromatographic purification (silica gel, pentane–Et_2O, 3:7) gave a colorless solid; yield: 1.25 g (71%); mp 121–122 °C.

IR (ATR): 1591 (vs), 1577 (m), 1509 (vs), 1494 (vs), 1460 (s), 1249 (vs), 1220 (s), 1159 (m), 1083 (s), 1042 (vs), 1026 (vs), 825 cm^{-1} (vs).

^1H NMR (300 MHz, $CDCl_3$): δ = 3.75 (s, 3 H), 6.68–6.72 (m, 2 H), 6.88–6.93 (m, 2 H), 7.05–7.08 (m, 4 H), 7.44 (dd, *J* = 1.7, 0.5 Hz, 1 H), 7.89 (d, *J* = 8.1, 1.7 Hz, 1 H), 8.38 (dd, *J* = 8.11, 0.48 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.3 (CH_3), 114.3, 114.4 (CH), 115.7 (d, *J* = 21.72 Hz, CH), 117.5, 124.5 (CH), 127.9 (CH), 130.8 (d, *J* = 8.48 Hz, CH), 131.8 (CH), 131.9 (d, *J* = 2.39 Hz), 133.3 (CH), 134.1, 140.1, 149.6, 162.0, 162.8 (d, *J* = 249.8 Hz, CF).

MS (EI, 70 eV): *m*/*z* (%) = 352 (25), 351 (9), 303 (14), 156 (10), 155 (100), 139 (20), 124 (26), 123 (36), 114 (12), 44 (7).

HRMS (EI): *m*/*z* calcd for $C_{20}H_{14}FNO_2{}^{32}S$: 351.0729; found: 351.0717.

[{4-[(4-Methoxyphenyl)sulfinyl]-1,3-phenylene}bis(ethyne-2,1-diyl)]bis(trimethylsilane) (5e)

According to **GP 3**, sulfoxide **5e** was prepared starting from sulfoxide **3e** (657 mg, 2.00 mmol), using $Pd(dba)_2$ (23.0 mg, 40.0 μmol), tri-2-furylphosphine (19.0 mg, 80.0 μmol) and trimethylethynylsilane (393 mg, 4.00 mmol) for the cross-coupling. The reaction mixture was stirred for 2 h at 50 °C. Flash chromatographic purification (silica gel, pentane–EtOAc, 9:2) gave **5e** as a yellow oil; yield: 610 mg (72%).

IR (ATR): 2958 (m), 2151 (m), 1738 (w), 1592 (m), 1578 (m), 1495 (m), 1460 (m), 1378 (w), 1302 (m), 1248 (s), 1036 (m), 950 (m), 836 (vs), 825 cm^{-1} (vs).

^1H NMR (600 MHz, $CDCl_3$): δ = 0.22 (s, 9 H), 0.25 (s, 9 H), 3.80 (s, 3 H), 6.89–6.90 (m, 2 H), 7.53 (s, 1 H), 7.59–7.61 (m, 3 H), 8.00 (d, *J* = 8.4 Hz, 1 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = –0.4 (Si CH_3), –0.3 ($SiCH_3$), 55.5 (CH_3), 97.3, 99.3, 102.9, 104.2, 114.5 (CH), 120.3, 123.4 (CH), 125.5, 128.2 (CH), 132.6 (CH), 136.1, 136.4 (CH), 147.1, 162.1.

MS (EI, 70 eV): *m*/*z* (%) = 425 (17), 424 (51), 411 (11), 410 (33), 409 (100), 408 (13), 381 (7), 336 (8), 323 (9), 287 (9), 273 (6).

HRMS (EI): *m*/*z* calcd for $C_{23}H_{28}O_2{}^{32}S^{28}Si_2$: 424.1349; found: 424.1336.

***tert*-Butyl 5′-Chloro-2′-{[4-(dimethylamino)phenyl]sulfinyl}biphenyl-4-carboxylate (5f)**

According to **GP 2**, sulfoxide **5f** was prepared starting from sulfoxide **3f** (2.80 g, 10.0 mmol), using $Pd(dba)_2$ (120 mg, 200 μmol), tri-2-furylphosphine (93.0 mg, 400 μmol), and *tert*-butyl 4-iodobenzoate (3.65 g 12.0 mmol) for the cross-coupling. The reaction mixture was stirred for 15 min at 50 °C. Flash chromatographic purification (silica gel, pentane–EtOAc, 1:1) furnished **5f** as a colorless solid; yield: 3.61 g (79%); mp 137–139 °C.

IR (ATR): 1712 (vs), 1592 (vs), 1516 (s), 1366 (vs), 1294 (vs), 1282 (s), 1170 (s), 1120 (s), 1092 (s), 1086 (s), 1066 (s), 1040 (vs), 1024 (s), 1012 (s), 802 cm^{-1} (vs).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.62 (s, 9 H), 2.92 (s, 6 H), 6.40–6.45 (m, 2 H), 6.85–6.90 (m, 2 H), 7.14–7.18 (m, 3 H), 7.57 (dd, *J* = 8.4, 2.21 Hz, 1 H), 7.91–7.95 (m, 2 H), 8.18 (d, *J* = 8.6 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 28.2 (CH_3), 40.1 (CH_3), 81.4, 111.6 (CH), 125.6 (CH), 127.8 (CH), 128.7 (CH), 129.2 (CH), 129.3, 129.4 (CH), 130.0 (CH), 131.8, 136.3, 140.9, 141.1, 142.9, 152.1, 165.3.

MS (EI, 70 eV): *m*/*z* (%) = 457 (22), 456 (17), 455 (67), 384 (20), 383 (42), 382 (27), 351 (28), 170 (19), 169 (40), 168 (100), 152 (31), 136 (83), 119 (15).

HRMS (EI): *m*/*z* calcd for $C_{25}H_{26}{}^{35}ClNO_3{}^{32}S$: 455.1322; found: 455.1319.

***tert*-Butyl 4-Formyl-3-[(trimethylsilyl)ethynyl]benzoate (8c)**

According to **GP 4**, the sulfoxide **5c** (429 mg, 1.00 mmol) was treated with *i*-PrMgCl·LiCl (**2**; 920 μL, 1.10 mmol, 1.20 M in THF) at –50 °C for 15 min. DMF (62.0 μL, 800 μmol) was then added and the reaction mixture was allowed to warm to 25 °C. Flash chromatographic purification (silica gel, pentane–Et_2O, 20:1) afforded a colorless solid; yield. 189 mg (78%); mp 116–118 °C.

IR (ATR): 2977 (w), 1716 (s), 1693 (s), 1600 (w), 1390 (m), 1087 (w), 941 (w), 842 (vs), 758 cm^{-1} (s).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.27 (s, 9 H), 1.59 (s, 9 H), 7.91 (dd, *J* = 8.2, 0.7 Hz, 1 H), 7.98 (ddd, *J* = 8.2, 1.7, 0.8 Hz, 1 H), 8.13 (dd, *J* = 1.7, 0.7 Hz, 1 H), 10.56 (d, *J* = 0.8 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –0.3 ($SiCH_3$), 28.1 (CH_3), 82.3, 99.3, 103.3, 126.6, 126.8 (CH), 129.3 (CH), 134.5 (CH), 136.4, 138.3, 164.0, 191.3 (CH).

MS (EI, 70 eV): *m*/*z* (%) = 246 (57), 233 (21), 232 (100), 231 (24), 229 (83), 201 (93), 186 (19), 107 (26), 73 (23), 57 (49).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{22}O_3{}^{28}Si$: 302.1338; found: 302.1344.

4′-Fluoro-6-formylbiphenyl-3-carbonitrile (8d)

According to **GP 4**, the sulfoxide **5d** (351 mg, 1.00 mmol) was treated with *i*-PrMgCl·LiCl (**2**; 920 μL, 1.10 mmol, 1.20 M in THF) at –50 °C for 15 min. DMF (62.0 μL, 800 μmol) was then added and the reaction mixture was allowed to warm to 25 °C. Flash chromatographic purification (silica gel, pentane–Et_2O, 10:1) furnished a colorless solid; yield: 0.129 g (72%); mp 116–118 °C.

IR (ATR): 1691 (vs), 1602 (s), 1507 (s), 1415 (m), 1390 (m), 1259 (m), 1226 (s), 1197 (s), 832 cm^{-1} (vs).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.21–7.29 (m, 2 H), 7.36–7.42 (m, 2 H), 7.77–7.78 (m, 1 H), 7.79–7.82 (m, 1 H), 8.12 (dd, *J* = 8.0, 0.5 Hz, 1 H), 10.01 (d, *J* = 0.7 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 116.1 (d, *J* = 22.01 Hz, CH), 116.9, 117.6, 128.6 (CH), 131.1 (CH), 131.5 (d, *J* = 3.4 Hz, CH), 131.6 (d, *J* = 8.5 Hz, CH), 134.5 (d, *J* = 1.0 Hz), 136.2, 145.0, 163.3 (d, *J* = 250 Hz, CF), 190.4 (CH).

MS (EI, 70 eV): *m*/*z* (%) = 226 (10), 225 (93), 224 (100), 197 (20), 196 (26), 195 (19), 170 (7), 169 (15), 168 (6), 129 (8).

HRMS (EI): *m*/*z* calcd for $C_{14}H_8FNO$: 225.0590; found: 225.0585.

{2,4-Bis[(trimethylsilyl)ethynyl]phenyl}(3,4-dichlorophenyl)methanol (8e)

According to **GP 4**, the sulfoxide **5e** (425 mg, 1.00 mmol) was treated with *i*-PrMgCl·LiCl (**2**; 920 μL, 1.10 mmol, 1.20 M in THF) at –50 °C for 5 min. 3,4-Dichlorobenzaldehyde (140 mg, 800 μmol) was then added and the reaction mixture was allowed to warm to 25 °C. Flash chromatographic purification (silica gel, pentane–Et_2O, 4:1) gave a colorless oil; yield: 257 mg (72%).

IR (ATR): 2150 (m), 1483 (w), 1469 (m), 1389 (m), 1248 (s), 1186 (m), 1031 (m), 956 (m), 836 (vs), 797 (m), 757 cm^{-1} (s).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 0.24 (s, 18 H), 2.60 (s, 1 H), 6.17 (s, 1 H), 7.20 (dd, *J* = 8.3, 2.1 Hz, 1 H), 7.37 (d, *J* = 8.7 Hz, 1 H), 7.41 (s, 1 H), 7.42 (s, 1 H), 7.53 (d, *J* = 1.8 Hz, 1 H), 7.57–7.58 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = –0.3 ($SiCH_3$), –0.1 ($SiCH_3$), 72.6 (CH), 95.5, 101.4, 110.8, 103.5, 121.2, 122.9, 125.9 (CH), 126.1 (CH), 128.1 (CH), 130.3 (CH), 131.5, 132.3 (CH), 132.4, 136.3 (CH), 142.8, 144.8.

MS (EI, 70 eV): *m*/*z* (%) = 446 (11), 444 (14), 429 (19), 409 (16), 375 (15), 374 (17), 373 (73), 372 (25), 371 (100), 358 (26), 357 (15), 356 (38), 336 (16), 75 (12).

HRMS (EI): *m*/*z* calcd for $C_{23}H_{26}{}^{35}ClO^{28}Si_2$: 444.0899; found: 444.0887.

***tert*-Butyl 5′-Chloro-2′-[2-(ethoxycarbonyl)prop-2-en-1-yl]biphenyl-4-carboxylate (8f)**

According to **GP 4**, the sulfoxide **5f** (456 mg, 1.00 mmol) was treated with *i*-PrMgCl·LiCl (**2**; 850 μL, 1.10 mmol, 1.30 M in THF) at –50 °C for 7 h. CuCN·2LiCl (50.0 μL, 5.00 mol%, 1.00 M in THF) and ethyl 2-(bromomethyl)acrylate (154 mg, 800 μmol) were then added and the reaction mixture was allowed to warm to 25 °C. Flash chromatographic purification (silica gel, pentane–Et_2O, 12:1) furnished a colorless liquid; yield: 193 mg (60%).

IR (ATR): 1709 (vs), 1367 (m), 1308 (m), 1293 (s), 1252 (m), 1162 (m), 1142 (m), 1115 (s), 1099 (m), 846 cm^{-1} (m).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.21 (t, *J* = 7.17 Hz, 3 H), 1.60 (s, 9 H), 3.52 (s, 2 H), 4.12 (q, *J* = 7.2 Hz, CH_2), 5.19 (s, 1 H), 6.19 (s, 1 H), 7.18 (d, *J* = 8.3 Hz, 1 H), 7.22 (d, *J* = 2.2 Hz, 1 H), 7.28 (d, *J* = 2.2 Hz, 1 H), 7.30–7.33 (m, 2 H), 7.98–8.02 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 14.1 (CH_3), 28.2 (CH_3), 34.7 (CH_2), 60.8 (CH_2), 81.1, 126.5 (CH_2), 127.9 (CH), 128.8 (CH), 129.4 (CH), 129.7 (CH), 131.2, 131.4 (CH), 132.2, 134.4, 139.9, 143.1, 144.3, 165.5, 166.5.

MS (EI, 70 eV): *m*/*z* (%) = 400 (0.5), 344 (31), 328 (42), 327 (71), 326 (100), 300 (38), 299 (34), 298 (91), 270 (39), 253 (28),

HRMS (EI): *m*/*z* calcd for $C_{23}H_{25}{}^{35}ClO_4$: 400.1441; found: 400.1442.

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