EFFICIENT ACCESS TO 2-ARYL-3-SUBSTITUTED BENZO[*b*]THIOPHENES.

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General considerations. All reactants and solvents were commercially obtained. Tlcs were performed with silica gel plates. Flash chromatographies were performed with Si 60 (40-63 μm). Gas chromatographies were performed with an apolar column and a flame ionisation detector and with the following programming: 100°C (1 min) then +10°C/min then 300°C (1min). Mass spectra were performed with the same temperature program as described above. Melting points were measured on a Kfller bench.

Synthesis of 3-(2,2,2-trifluoroethoxy)benzo[*b*]thiophene (1): A solution of 2,2,2-trifluoroethanol (1.5 mL, 21 mmol) in anhydrous DMF (4 mL) was slowly added on NaH (505 mg, 21 mmol, 60% dispersion in mineral oil) at 0°C under inert atmosphere. After 20 min of stirring at room temperature, 3-bromobenzo[*b*]thiophene (3.19 g, 15 mmol) and CuI (143 mg, 0.75 mmol) were successively added. The mixture was heated at 100°C for 17 h. The resulting mixture was then cooled to room temperature, filtered on celite and rinsed with CH₂Cl₂. The organic layer was successively washed with water and with a saturated ammonium chloride solution, dried over MgSO₄, filtered and solvents were removed under reduced pressure. The crude product was purified by flash chromatography (cyclohexane) to afford **1** in 54% yield (1.73 g) as a yellow oil; *R*_f 0.1 (cyclohexane); ¹H NMR (CDCl₃, 300MHz) δ 4.49 (q, 2H, *J* = 8.1Hz), 6.39 (s, 1H), 7.42 (m, 2H), 7.78 (m, 1H), 7.88 (m, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ 149.5, 138.1, 131.8, 126.1, 124.6, 123.3, 121.4, 98.8, 67.7 (q, CH₂, *J* = 36 Hz); ¹⁹F NMR (CDCl₃, 188 MHz) δ -74.3 (s, 3F); Anal. Calcd for C₁₀H₇F₃OS: C, 51.72; H, 3.04. Found: C, 51.94; H, 2.82; MS (EI+) *m/z* 232 (M⁺).

Synthesis of 3-bromobenzo[*b*]thiophene 1-oxide (2):¹ To a stirred solution of 3-bromobenzo[*b*]thiophene (5 g, 23 mmol) in CH₂Cl₂ (40 mL) was added trifluoroacetic acid (40mL). After 5 min of stirring at room temperature, hydrogen peroxide (2.01 mL, 23 mmol, 35% aqueous solution) was added and the resulting mixture was stirred at room temperature.

The reaction was monitored by tlc's and stopped when the apparition of the corresponding sulfone was detected. The reaction mixture was then neutralized at 0°C with a saturated sodium carbonate solution and extracted with CH₂Cl₂. The combined organic layers were successively washed with a saturated sodium bicarbonate solution and water, dried over MgSO₄, filtered and solvents were removed under reduced pressure. The crude product was purified by flash chromatography (CH₂Cl₂/heptane: 9/1) to afford **2** in 85% yield (4.45 g) as a white solid; *R_f* 0.5 (CH₂Cl₂/EtOAc: 9/1); mp 152-154°C; ¹H NMR (CDCl₃, 300MHz) δ 7.28 (s, 1H), 7.61 (m, 3H), 7.92 (dd, 1H, *J* = 0.8, 7.5 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 144.1, 136.4, 135.4, 132.5, 130.1, 128.7, 126.0, 124.7; Anal. Calcd for C₈H₅BrOS: C, 41.94; H, 2.20; S, 14.00. Found: C, 42.10; H, 2.39; S, 14.27; MS *m/z* 230, 228 (M⁺).

General procedure for aromatic nucleophilic substitution reaction with phenols: To a stirred solution of 3-bromobenzo[*b*]thiophene 1-oxide **2** in anhydrous DMF at room temperature under inert atmosphere were successively added the phenol derivative (2 equivalents) and the carbonate potassium (2 equivalents). The suspension was heated. The resulting mixture was then cooled to room temperature, concentrated under vacuum and extracted with CH₂Cl₂. The combined organic layers were successively washed with water and brine, dried over MgSO₄, filtered and solvent was removed under reduced pressure.

Synthesis of 3-(*p*-methoxyphenoxy)benzo[*b*]thiophene 1-oxide (3a): 3-bromobenzo[*b*]thiophene 1-oxide **2** (500 mg, 2.18 mmol), 4-methoxyphenol (541 mg, 4.36 mmol) and potassium carbonate (603 mg, 4.36 mmol) in anhydrous DMF (4 mL). 70°C for 15 h. The crude product was purified by flash chromatography (CH₂Cl₂/EtOAc: 9/1) to afford **3a** in 80% yield (380 mg) as a white solid; *R_f* 0.2 (CH₂Cl₂/EtOAc: 9/1); mp 166-168°C; ¹H NMR (CDCl₃, 300 MHz) δ 3.83 (s, 3H), 5.73 (s, 1H), 6.95 (d, 2H, *J* = 9.0 Hz), 7.15 (d, 2H, *J* = 9.0 Hz), 7.58 (m, 2H), 7.74 (dd, 1H, *J* = 1.5, 7.0 Hz), 7.90 (dd, 1H, *J* = 1.9, 6.8 Hz); ¹³C

NMR (CDCl₃, 75 MHz) δ 162.1, 157.8, 147.7, 145.5, 133.3, 131.9, 130.3, 126.2, 122.0, 121.7, 115.1, 107.1, 55.8; Anal. Calcd for C₁₅H₁₂O₃S: C, 66.16; H, 4.44; S, 11.77. Found: C 65.60, H 4.70, S 10.88; MS (EI+) m/z 272 (M⁺).

Synthesis of 3-(*m*-dimethoxy-*p*-methoxy)phenoxybenzo[*b*]thiophene 1-oxide (3b): 3-bromobenzo[*b*]thiophene 1-oxide **2** (500 mg, 2.18 mmol), 3,4,5-trimethoxyphenol (803 mg, 4.36 mmol) and potassium carbonate (602 mg, 4.36 mmol) in anhydrous DMF (3 mL). 90°C for 17 h. The crude product was purified by flash chromatography (CH₂Cl₂/EtOAc: 9/1) to afford **3b** in 68% yield (492) as a white solid; R_f 0.1 (CH₂Cl₂/EtOAc: 9/1); mp 140-142°C; ¹H NMR (CDCl₃, 300 MHz) δ 3.84 (s, 9H), 5.86 (s, 1H), 6.48 (s, 2H), 7.59 (m, 2H), 7.73 (dd, 1H, J = 1.7, 6.8 Hz), 7.91 (dd, 1H, J = 1.8, 6.6 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 161.4, 154.1, 150.3, 145.5, 136.3, 133.2, 131.9, 130.3, 126.3, 121.9, 107.5, 98.3, 61.1, 56.4; Anal. Calcd for C₁₇H₁₆O₅S: C, 61.43; H, 4.85; S, 9.65. Found: C, 61.54; H, 4.93; S, 9.74; MS (EI+) m/z 332 (M⁺).

Synthesis of 3-phenoxybenzo[*b*]thiophene 1-oxide (3c): 3-bromobenzo[*b*]thiophene 1-oxide **2** (460 mg, 2 mmol), phenol (376 mg, 4 mmol) and potassium carbonate (553 mg, 4 mmol) in anhydrous DMF (3 mL). 70°C for 15 h. The crude product was purified by flash chromatography (CH₂Cl₂/EtOAc: 9/1) to afford **3c** in 70% yield (340 mg) as a white solid; R_f 0.3 (CH₂Cl₂/EtOAc: 9/1); mp 110-112°C; ¹H NMR (CDCl₃, 300 MHz) δ 5.78 (s, 1H), 7.29 (m, 3H), 7.48 (m, 2H), 7.61 (m, 2H), 7.77 (d, 1H, J = 7.5 Hz), 7.92 (d, 1H, J = 7.4 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 161.3, 154.2, 147.5, 145.5, 133.2, 131.9, 130.3, 126.6, 126.1, 122.0, 120.8, 107.5; Anal. Calcd for C₁₄H₁₀O₂S: C, 69.40; H, 4.16; S, 13.23. Found: C, 69.22; H, 4.55; S, 13.01; MS (EI+) m/z 242 (M⁺).

Synthesis of 3-(*p*-fluorophenoxy)benzo[*b*]thiophene 1-oxide (3d): 3-bromobenzo[*b*]thiophene 1-oxide **2** (500 mg, 2.18 mmol), 4-fluorophenol (489 mg, 4.36 mmol) and carbonate potassium (602 mg, 4.36 mmol) in anhydrous DMF (3 mL). 120°C for

16 h. The crude product was purified by flash chromatography (CH₂Cl₂) to afford **3d** in 72% yield (405 mg) as a colorless oil; *R_f* 0.4 (CH₂Cl₂/EtOAc: 9/1); ¹H NMR (CDCl₃, 300 MHz) δ 5.76 (s, 1H), 7.19 (m, 4H), 7.61 (m, 2H), 7.75 (d, 1H, *J* = 7.5 Hz), 7.92 (d, 1H, *J* = 7.4 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 161.5, 159.0, 150.0, 145.5, 133.1, 132.0, 130.4, 126.3, 122.5, 122.4, 122.0, 117.2, 116.9, 107.6; Anal. Calcd for C₁₄H₉FO₂S: C, 64.60; H, 3.49; F, 7.30; S, 12.29. Found: C, 64.35; H, 3.64; F, 7.14; S, 12.54; MS (EI+) *m/z* 260 (M⁺).

Synthesis of 3-(*p*-chlorophenoxy)benzo[*b*]thiophene 1-oxide (3e): 3-bromobenzo[*b*]thiophene 1-oxide **2** (458 mg, 2 mmol), 4-chlorophenol (514 mg, 4 mmol) and carbonate potassium (552 mg, 4 mmol) in anhydrous DMF (4 mL). 110°C for 15 h. The crude product was purified by flash chromatography (CH₂Cl₂) to afford **3e** in 58% yield (320 mg) as a pink oil; *R_f* 0.4 (CH₂Cl₂/EtOAc: 9/1); ¹H NMR (CDCl₃, 300 MHz) δ 5.78 (s, 1H), 7.20 (d, 2H, *J* = 9.0 Hz), 7.43 (d, 2H, *J* = 9.0 Hz), 7.60 (m, 2H), 7.72 (d, 1H, *J* = 6.8 Hz), 7.91 (d, 1H, *J* = 6.6 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 182.0, 168.7, 161.7, 153.2, 133.6, 132.6, 131.0, 126.9, 122.9, 122.6, 108.5; Anal. Calcd for C₁₄H₉ClO₂S: C, 60.76; H, 3.28; S, 11.59; Found: C, 60.68; H, 3.49; S, 11.64; MS (EI+) *m/z* 277 (M⁺).

Synthesis of 3-(*p*-cyanophenoxy)benzo[*b*]thiophene 1-oxide (3f): 3-bromobenzo[*b*]thiophene 1-oxide **2** (1.5 g, 7 mmol), 4-hydroxybenzonitrile (1.56 g, 14.0 mmol) and potassium carbonate (1.9 g, 14.0 mmol) in anhydrous DMF (5 mL). 110°C for 15 h. The crude product was purified by flash chromatography (cyclohexane/EtOAc: 7/3) to afford **3f** in 68% yield (1.28 g) as a colorless oil; *R_f* 0.3 (CH₂Cl₂/EtOAc: 8/2); ¹H NMR (CDCl₃, 300 MHz) δ 5.89 (s, 1H), 7.40 (d, 2H, *J* = 8.9 Hz), 7.62 (m, 2H), 7.72 (dd, 1H, *J* = 2.3, 6.5 Hz), 7.79 (d, 2H, *J* = 8.9 Hz), 7.93 (dd, 1H, *J* = 2.4, 7.5 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 159.8, 157.3, 145.4, 134.7, 132.7, 132.1, 130.7, 126.5, 122.0, 121.9, 117.9, 110.6, 109.1; Anal. Calcd for C₁₅H₉NO₂S: C, 67.40; H, 3.39; N, 5.24; S, 12.00. Found: C, 67.65; H, 4.63; N, 4.71; S, 11.20; MS (EI+) *m/z* 251 (M⁺-16).

General procedure for aromatic nucleophilic substitution reaction with amines: The amine was added at room temperature under inert atmosphere to a stirred suspension of 3-bromobenzo[*b*]thiophene 1-oxide **2** in anhydrous toluene. The mixture was heated at 80°C. After cooled at room temperature, the resulting mixture was extracted with CH₂Cl₂. The combined organic layers were then washed with water until neutral pH, dried over MgSO₄, filtered and solvents were removed under reduced pressure.

Synthesis of 3-piperidinobenzo[*b*]thiophene 1-oxide (4a): 3-bromobenzo[*b*]thiophene 1-oxide **2** (458 mg, 2 mmol) and piperidine (400 μ L, 4 mmol) in anhydrous toluene (2 mL). 80°C for 2 h. **4a** was obtained in 94% yield (440 mg) as an off-white solid; *R_f* 0.3 (CH₂Cl₂/EtOAc: 8/2); mp 144-146°C; ¹H NMR (CDCl₃, 300 MHz) δ 1.74 (m, 6H), 3.25 (m, 4H), 5.89 (s, 1H), 7.50 (m, 3H), 7.88 (dd, 1H, *J* = 1.4, 6.3 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 156.2, 147.3, 134.8, 130.6, 128.6, 125.7, 123.1, 108.6, 51.0, 25.0, 23.8; Anal. Calcd for C₁₃H₁₅NOS: C, 66.92; H, 6.48; N, 6.00; S, 13.74. Found: C, 66.58; H, 6.69; N, 6.06; S, 13.81. MS (EI+) *m/z* 217 (M⁺-16).

Synthesis of 3-*N*-morpholinobenzo[*b*]thiophene 1-oxide (4b): 3-bromobenzo[*b*]thiophene 1-oxide **2** (230 mg, 1 mmol) and morpholine (180 μ L, 2 mmol) in anhydrous toluene (1 mL). 80°C for 3 h. The crude product was purified by passivated flash chromatography (CH₂Cl₂/AcOEt: 9/1) to afford **4b** in 85% yield (440 mg) as a brown solid; *R_f* 0.2 (EtOAc/CH₂Cl₂: 6/4); mp 192-194°C; ¹H NMR (CDCl₃, 300 MHz) δ 3.10 (m, 2H), 3.27 (m, 2H), 3.80 (m, 4H), 5.90 (s, 1H), 7.42 (m, 3H), 7.80 (m, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ 156.3, 147.8, 135.0, 131.6, 129.7, 126.8, 123.7, 111.2, 66.6, 60.0; Anal. Calcd for C₁₂H₁₃NO₂S: C, 61.25; H, 5.57; N, 5.95; S, 13.63. Found: C, 61.42; H, 5.44; N, 5.57; S, 13.88; MS (EI+) *m/z* 219 (M⁺-16).

Synthesis of 3-*N*-(*N*'-methyl)piperazinobenzo[*b*]thiophene 1-oxide (4c): 3-bromobenzo[*b*]thiophene 1-oxide **2** (458 mg, 2 mmol) and *N*-methylpiperazine (450 μ L, 4

mmol) in anhydrous toluene (2 mL). 80°C for 2 h. The crude product was purified by flash chromatography (EtOAc/Et₃N: 8/2) to afford **4c** in 86% (430 mg) yield as a brown oil; *R_f* 0.3 (MeOH); ¹H NMR (CDCl₃, 300 MHz) δ 2.37 (s, 3H), 2.61 (m, 4H), 3.23 (m, 2H), 3.39 (m, 2H), 5.94 (s, 1H), 7.49 (m, 3H), 7.88 (m, 1H); ¹³C NMR (CDCl₃, 75 MHz) δ 156.1, 147.8, 135.1, 131.2, 129.4, 126.6, 123.5, 110.5, 54.5, 50.3, 46.2; Anal. Calcd for C₁₃H₁₆N₂OS, H₂O: C, 58.62; H, 6.81; N, 10.52. Found: C, 58.90; H, 6.77; N, 10.18; MS (EI+) *m/z* 232 (M⁺-16).

General procedure for the reduction of sulfoxides: To a stirred solution of the sulfoxide derivative in anhydrous toluene was added dropwise at 0°C under inert atmosphere Dibal-H (1.25 equivalents). Then, the mixture was heated at 65°C for 5 h for phenol derivative **3a-e** and at room temperature for amine derivatives **4a-c**. The resulting mixture was cooled to 0°C, hydrolyzed with a sodium hydroxide 2M solution and extracted with CH₂Cl₂. The combined organic layers were washed with water until neutral pH, dried over MgSO₄, filtered and solvents were removed under reduced pressure.

Synthesis of 3-(*p*-methoxyphenoxy)benzo[*b*]thiophene (5a): 3-(*p*-methoxyphenoxy)benzo[*b*]thiophene 1-oxide **3a** (400mg, 1.5 mmol) and Dibal-H (2.17 mL, 3.7 mmol, 20% wt in toluene) in anhydrous toluene (3 mL). **5a** was obtained in 81% yield (312 mg) as a yellow solid; *R_f* 0.3 (heptane/CH₂Cl₂: 6/4); mp 100-102°C; ¹H NMR (CDCl₃, 300 MHz) δ 3.82 (s, 3H), 6.45 (s, 1H), 6.90 (d, 2H, *J* = 9.0 Hz), 7.11 (d, 2H, *J* = 9.0 Hz), 7.39 (m, 2H), 7.81 (m, 2H); ¹³C NMR (CDCl₃, 75 MHz) δ 156.2, 151.0, 149.7, 138.1, 132.2, 125.3, 124.2, 123.2, 121.2, 120.1, 115.0, 104.4, 55.8; Anal. Calcd for C₁₅H₁₂O₂S: C, 70.29; H, 4.72; S, 12.51. Found: C, 69.21; H, 5.16; S, 12.54; MS (EI+) *m/z* 256 (M⁺).

Synthesis of 3-(*m*-dimethoxy-*p*-methoxy)benzo[*b*]thiophene (5b): 3-(*m*-dimethoxy-*p*-methoxy)phenoxybenzo[*b*]thiophene 1-oxide **3b** (360 mg, 1.1 mmol) and Dibal-H (2.25 mL, 2.7 mmol, 20% wt in toluene). The crude product was purified by flash chromatography

(heptane/EtOAc: 8/2) to afford **5b** in 63% yield (216 mg) as a pink solid; R_f 0.8 (heptane/CH₂Cl₂: 5/5); mp 152-154°C; ¹H NMR (CDCl₃, 300 MHz) δ 3.79 (s, 6H), 3.85 (s, 3H), 6.41 (s, 2H), 6.62 (s, 1H), 7.39 (m, 2H), 7.80 (m, 2H); ¹³C NMR (CDCl₃, 75 MHz) δ 154.2, 153.8, 151.2, 148.7, 138.2, 132.4, 125.6, 124.5, 123.4, 121.3, 105.9, 96.5, 61.3, 56.5; Anal. Calcd for C₁₇H₁₆O₄S: C, 64.54; H, 5.10; S, 10.13. Found: C, 64.20; H, 5.05; S, 10.64; MS (EI+) m/z 316 (M⁺).

Synthesis of 3-phenoxybenzo[*b*]thiophene (5c): 3-phenoxybenzo[*b*]thiophene 1-oxide **3c** (300 mg, 1.2 mmol) and Dibal-H (2.5 mL, 3.0 mmol, 20% wt in toluene). **5c** was obtained in 85% yield (231 mg) as a yellow oil; R_f 0.5 (heptane/ CH₂Cl₂: 7/3); ¹H NMR (CDCl₃, 300 MHz) δ 6.70 (s, 1H), 7.15 (m, 3H), 7.39 (m, 4H), 7.76 (dd, 1H, J = 1.9, 7.3 Hz), 7.83 (dd, 1H, J = 1.7, 7.4 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 155.7, 148.0, 138.1, 132.4, 129.9, 125.3, 124.3, 123.6, 123.2, 121.3, 118.1, 107.2; Anal. Calcd for C₁₄H₁₀OS: C, 74.31; H, 4.45; S, 14.17. Found: C, 74.08; H, 4.86; S, 13.98; MS (EI+) m/z 226 (M⁺).

Synthesis of 3-(*p*-fluorophenoxy)benzo[*b*]thiophene (5d): 3-(*p*-fluorophenoxy)benzo[*b*]thiophene 1-oxide **3d** (200 mg, 0.8 mmol) and Dibal-H (1.63 mL, 1.9 mmol, 20% wt in toluene) in anhydrous toluene (1 mL). The crude product was purified by flash chromatography (CH₂Cl₂) to afford **5d** in 72% yield (202 mg) as a yellow oil; R_f 0.7 (heptane/CH₂Cl₂: 5/5); ¹H NMR (CDCl₃, 300 MHz) δ 6.58 (s, 1H), 7.08 (m, 4H), 7.40 (m, 2H), 7.80 (m, 2H); ¹³C NMR (CDCl₃, 75 MHz) δ 160.7, 153.4, 148.6, 138.2, 132.1, 125.4, 124.3, 123.2, 121.2, 119.9, 119.8, 116.6, 116.3, 106.2; Anal. Calcd for C₁₄H₉FOS: C, 68.83; H, 3.71. Found: C, 68.47; H, 4.07; MS (EI+) m/z 244 (M⁺).

Synthesis of 3-(*p*-chlorophenoxy)benzo[*b*]thiophene (5e): 3-(*p*-chlorophenoxy)benzo[*b*]thiophene 1-oxide **3e** (260 mg, 0.9 mmol) and Dibal-H (2.07 mL, 2.5 mmol, 20% wt in toluene) in anhydrous toluene (1 mL). **5e** was obtained in 76% yield (185 mg) as a yellow oil; R_f 0.8 (heptane/CH₂Cl₂: 5/5); ¹H NMR (CDCl₃, 300 MHz) δ 6.72 (s, 1H),

7.05 (d, 2H, $J = 9.0$ Hz), 7.29 (d, 2H, $J = 9.0$ Hz), 7.41 (m, 2H), 7.69 (dd, 1H, $J = 2.5, 7.4$ Hz), 7.91 (dd, 1H, $J = 2.0, 7.5$ Hz); ^{13}C NMR (CDCl_3 , 75 MHz) δ 156.6, 147.7, 138.4, 130.1, 128.8, 125.7, 124.6, 123.5, 121.4, 119.5, 113.8, 108.1; Anal. Calcd for $\text{C}_{14}\text{H}_9\text{ClOS}$: C, 64.49; H, 3.48. Found: C, 64.20; H, 3.77; MS (EI+) m/z 261 (M^+).

Synthesis of 3-(*p*-carboxaldehydophenoxy)benzo[*b*]thiophene (6) and 3-(*p*-methylaminephenoxy)benzo[*b*]thiophene (7): 3-(*p*-cyanophenoxy)benzo[*b*]thiophene 1-oxide **3f** (300 mg, 1.1 mmol) and Dibal-H (3.5 mL, 4.5 mmol, 20% wt in toluene). The crude product was purified by flash chromatography (cyclohexane/EtOAc: 9/1 then EtOAc/ MeOH: 8/2) to afford successively compounds **6** and **7**.

6 was obtained in 39% yield (104 mg) as a yellow solid; R_f 0.4 (cyclohexane/EtOAc: 9/1); mp 124-126°C; ^1H NMR (CDCl_3 , 300 MHz) δ 7.00 (s, 1H), 7.15 (d, 2H, $J = 8.7$ Hz), 7.38 (m, 2H), 7.57 (d, 1H, $J = 8.3$ Hz), 7.85 (m, 3H), 9.93 (s, 1H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 190.8, 163.1, 145.5, 138.2, 132.1, 131.9, 131.7, 125.6, 124.6, 123.4, 121.1, 117.0, 111.2; Anal. Calcd for $\text{C}_{15}\text{H}_{10}\text{O}_2\text{S}$: C, 70.85; H, 3.96; S, 12.61; Found: C, 70.89; H, 4.48; S, 12.89; MS (EI+) m/z 254 (M^+).

7 was obtained in 33% yield (91 mg) as a colorless oil; R_f 0.1 (EtOAc/MeOH: 8/2); ^1H NMR (CD_3OD , 300 MHz) δ 3.79 (s, 2H), 6.78 (s, 1H), 7.06 (d, 2H, $J = 8.7$ Hz), 7.35 (m, 4H), 7.63 (d, 1H, $J = 7.9$ Hz), 7.83 (d, 1H, $J = 8.3$ Hz); ^{13}C NMR (CD_3OD , 75 MHz) δ 158.2, 149.1, 139.5, 132.0, 131.2, 130.2, 126.3, 125.2, 124.2, 121.9, 119.0, 108.4, 45.9; Anal. Calcd for $\text{C}_{15}\text{H}_{13}\text{NOS}$: C, 70.56; H, 5.13; N, 5.49. Found: C, 70.50; H, 5.33; N, 4.79; MS (EI+) m/z 255 (M^+).

Synthesis of 3-piperidinobenzo[*b*]thiophene (5g):² 3-piperidinobenzo[*b*]thiophene 1-oxide **4a** (880 mg, 3.77 mmol) and Dibal-H (6.3 mL, 9.42 mmol, 1.5 M in toluene) in anhydrous toluene (4 mL). Room temperature for 2 h. The crude product was purified by flash chromatography (Heptane/ CH_2Cl_2 : 9/1) to afford **5g** in 72% yield (597 mg) as a off-white

solid; R_f 0.3 (heptane/ CH_2Cl_2 : 5/5); mp 68-70°C; ^1H NMR (CDCl_3 , 300 MHz) δ 1.71 (m, 2H), 1.89 (m, 4H), 3.15 (m, 4H), 6.63 (s, 1H), 7.43 (m, 2H), 7.89 (m, 2H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 148.2, 139.3, 134.9, 124.4, 123.5, 123.2, 122.1, 106.4, 53.8, 26.3, 24.5; Anal. Calcd for $\text{C}_{13}\text{H}_{15}\text{NS}$: C, 71.85; H, 6.96; N, 6.44; S, 14.75. Found: C, 71.75; H, 6.92; N, 6.57; S, 14.76; MS (EI+) m/z 217 (M^+).

Synthesis of 3-*N*-morpholinobenzo[*b*]thiophene (5h):² 3-*N*-morpholinobenzo[*b*]thiophene 1-oxide **4b** (300 mg, 1.27 mmol) and Dibal-H (2.12 mL, 3.18 mmol, 1.5 M in toluene) in anhydrous toluene (1.5 mL). Room temperature for 30 min. The crude product was purified by flash chromatography (Heptane/EtOAc: 9/1) to afford **5h** in 75 % yield (210 mg) as a pink solid; R_f 0.2 (heptane/EtOAc: 7/3); mp 64-66°C; ^1H NMR (CDCl_3 , 300 MHz) δ 3.13 (m, 4H), 9.95 (m, 4H), 6.62 (s, 1H), 7.37 (m, 2H), 7.78 (dd, 1H, J = 2.9, 6.3 Hz), 7.82 (dd, 1H, J = 2.7, 6.3 Hz); ^{13}C NMR (CDCl_3 , 75 MHz) δ 146.8, 139.4, 134.4, 124.7, 123.7, 123.4, 121.8, 107.3, 67.1, 52.8; Anal. Calcd for $\text{C}_{12}\text{H}_{13}\text{NOS}$: C, 65.72; H, 5.97; N, 6.39; S, 14.62. Found: C, 65.66; H, 5.98; N, 6.58; S, 14.30; MS (EI+) m/z 219 (M^+).

Synthesis of 3-*N*-(*N'*-methyl)piperazinobenzo[*b*]thiophene (5i): 3-*N*-(*N'*-methyl)piperazinobenzo[*b*]thiophene 1-oxide **4c** (360 mg, 1.45 mmol) and Dibal-H (2.45 mL, 3.62 mmol, 1.5 M in toluene) in anhydrous toluene (1.5 mL). Room temperature for 4 h. The crude product was purified by flash chromatography ($\text{CH}_2\text{Cl}_2/\text{MeOH}$: 98/2) to afford **5i** in 68% (230 mg) as a off-white solid; R_f 0.3 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$: 95/5) ; mp 66-68°C; ^1H NMR (CDCl_3 , 300 MHz) δ 2.39 (s, 3H), 2.65 (m, 4H), 3.17 (m, 4H), 6.62 (s, 1H), 7.34 (m, 2H), 7.75 (dd, 1H, J = 2.8, 6.4 Hz), 7.79 (dd, 1H, J = 2.7, 6.3 Hz); ^{13}C NMR (CDCl_3 , 75 MHz) δ 146.9, 139.4, 134.7, 124.6, 123.7, 122.0, 107.1, 55.4, 52.4, 46.3; Anal. Calcd for $\text{C}_{13}\text{H}_{16}\text{N}_2\text{S}$: C, 67.20; H, 6.94; N, 12.06; S, 13.80. Found: C, 67.13; H, 7.04; N, 11.86; S, 13.96; MS (EI+) m/z 232 (M^+).

Synthesis of 3-(*p*-cyanophenoxy)benzo[*b*]thiophene (5f): To a stirred suspension of 3-(*p*-cyanophenoxy)benzo[*b*]thiophene 1-oxide **3f** (500 mg, 1.87 mmol) and *N,N*-dimethylaniline (5.0 mL, 74.9 mmol) in xylene (5 mL) was added dropwise at 0°C under inert atmosphere the trichlorosilane (7.56 mL, 74.9 mmol). The mixture was heated at 100°C for 3 h. The resulting mixture was then cooled to 0°C, hydrolyzed with a solution of sodium hydroxide 1M and extracted with CH₂Cl₂. The combined organic layers were successively washed with a solution of hydrochloric acid 1N, a solution of hydrochloric acid 2N and water, dried over MgSO₄, filtered and solvents were removed under reduced pressure. **5f** was obtained in 75% yield (353 mg) as a green solid; *R_f* 0.3 (cyclohexane/CH₂Cl₂: 6/4) ; mp 116-118°C; ¹H NMR (CDCl₃, 300 MHz) δ 6.99 (s, 1H), 7.10 (d, 2H, *J* = 9.0 Hz), 7.39 (m, 2H), 7.55 (d, 1H, *J* = 7.5 Hz), 7.61 (d, 2H, *J* = 9.0 Hz), 7.85 (d, 1H, *J* = 7.5 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 161.6, 145.2, 138.3, 134.3, 131.7, 125.7, 124.7, 123.5, 121.0, 118.8, 117.4, 111.5, 106.4; Anal. Calcd for C₁₅H₉NOS: C, 71.69; H, 3.61; N, 5.57; S, 12.76. Found: C, 71.63; H, 3.91; N, 5.36; S, 12.73; MS (EI+) *m/z* 251 (M⁺).

General procedure for Heck-type coupling of 3-substituted benzo[*b*]thiophene: In DMF were successively added DCH-18-C-6 (1 equivalent), K₂CO₃ (3 equivalents), 3-substituted benzo[*b*]thiophene and aryl bromide (1.1 equivalents). The mixture was heated at 100°C for 5 min and Pd(OAc)₂ (5%) was added. The resulting mixture was then heated at 110°C. After cooling to room temperature, the mixture was filtered over celite which was rinsed with CH₂Cl₂. The resulting organic layer was successively washed with water and brine, dried over MgSO₄, filtered and solvents were removed under reduced pressure.

Synthesis of 2-(*m*-benzonitrile)-3-(*p*-methoxyphenoxy)benzo[*b*]thiophene (8a): DCH-18-C-6 (373 mg, 1 mmol), K₂CO₃ (414 mg, 3 mmol), 3-(*p*-methoxyphenoxy)benzo[*b*]thiophene **5a** (256 mg, 1 mmol), 2-bromobenzonitrile (200 mg, 1.1

mmol) and Pd(OAc)₂ (11 mg, 0.05 mmol) in DMF (1 mL). 110°C for 6 h. The crude product was purified by flash chromatography (heptane/CH₂Cl₂: 7/3) to afford **5a** in 67% yield (240 mg) as a colorless oil; *R_f* 0.2 (heptane/CH₂Cl₂: 6/4) ; ¹H NMR (CDCl₃, 300 MHz) δ 3.72 (s, 3H), 6.73 (d, 2H, *J* = 9.0 Hz), 6.87 (d, 2H, *J* = 9.0 Hz), 7.38 (m, 3H), 7.56 (m, 2H), 7.65 (d, 1H, *J* = 7.9 Hz), 7.71 (d, 1H, *J* = 7.7 Hz), 7.83 (d, 1H, *J* = 7.7 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 155.0, 151.8, 143.7, 137.3, 135.6, 133.8, 132.7, 132.6, 131.7, 128.7, 125.9, 124.7, 124.0, 123.0, 122.4, 118.2, 117.0, 114.7, 113.3, 55.7; Anal. Calcd for C₂₂H₁₅NO₂S: C, 73.93; H, 4.23; N, 3.92; S, 8.97. Found: C, 73.77; H, 4.41; N, 3.86; S, 9.26; MS (EI+) *m/z* 357 (M⁺).

Synthesis of 2-(*m*-benzonitrile)-3-(*m*-dimethoxy-*p*-methoxy)benzo[*b*]thiophene (8b): DCH-18-C-6 (153 mg, 0.4 mmol), K₂CO₃ (170 mg, 1.2 mmol), 3-(*m*-dimethoxy-*p*-methoxyphenoxy)benzo[*b*]thiophene **5b** (130 mg, 0.4 mmol), 2-bromobenzonitrile (81 mg, 0.44 mmol), and Pd(OAc)₂ (5 mg, 0.02 mmol) in DMF (1 mL). 110°C for 7 h. The crude product was purified by flash chromatography (cyclohexane/EtOAc: 8/2) to afford **8b** in 51% yield (87 mg) as a colorless oil; *R_f* 0.3 (CH₂Cl₂); ¹H NMR (CDCl₃, 300 MHz) δ 3.69 (s, 6H), 3.74 (s, 3H), 6.18 (s, 2H), 7.39 (m, 3H), 7.61 (m, 3H), 7.71 (d, 1H, *J* = 7.9 Hz), 7.84 (d, 1H, *J* = 7.7 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 154.1, 153.7, 143.1, 137.3, 135.6, 133.7, 133.5, 132.7, 131.7, 128.9, 126.0, 124.9, 124.0, 123.0, 122.3, 118.2, 113.4, 94.0, 61.1, 56.2; Anal. Calcd for C₂₄H₁₉NO₄S: C, 69.05; H, 4.59; N, 3.36; S, 7.68. Found: C, 68.91; H, 4.72; N, 3.43; S, 8.08; MS (EI+) *m/z* 417 (M⁺).

Synthesis of 2-(*m*-benzonitrile)-3-phenoxybenzo[*b*]thiophene (8c): DCH-18-C-6 (261 mg, 0.7 mmol), K₂CO₃ (290 mg, 2.1 mmol), 3-phenoxybenzo[*b*]thiophene **5c** (158 mg, 0.7 mmol), 2-bromobenzonitrile (139 mg, 0.77 mmol) and Pd(OAc)₂ (9 mg, 0.04 mmol) in DMF (1 mL). 110°C for 6 h. The crude product was purified by flash chromatography (heptane/CH₂Cl₂: 6/4) to afford **8c** in 69% yield (157 mg) as a white solid; *R_f* 0.2 (heptane/CH₂Cl₂: 6/4); mp 98-100°C; ¹H NMR (CDCl₃, 300 MHz) δ 6.96 (m, 3H), 7.21 (m,

2H), 7.38 (m, 3H), 7.56 (m, 2H), 7.66 (d, 1H, $J = 7.7$ Hz), 7.71 (d, 1H, $J = 7.7$ Hz), 7.85 (d, 1H, $J = 7.7$ Hz); ^{13}C NMR (CDCl_3 , 75 MHz) δ 157.8, 143.0, 137.3, 135.4, 133.8, 132.7, 132.6, 131.7, 129.6, 128.7, 126.0, 124.8, 123.0, 122.6, 122.3, 118.1, 116.0, 113.3; Anal. Calcd for $\text{C}_{21}\text{H}_{13}\text{NOS}$: C, 77.04; H, 4.00; N, 4.28; S, 9.79. Found: C, 76.03; H, 3.93; N 4.28; S, 10.26; MS (EI+) m/z 327 (M^+).

Synthesis of 3-phenoxy-2-phenylbenzo[*b*]thiophene (9c): DCH-18-C-6 (280 mg, 0.75 mmol), K_2CO_3 (310 mg, 2.25 mmol), 3-phenoxybenzo[*b*]thiophene **5c** (170 mg, 0.75 mmol), bromobenzene (90 μL , 0.83 mmol)) and $\text{Pd}(\text{OAc})_2$ (9 mg, 0.04 mmol) in DMF (1 mL). 110°C for 8 h. The crude product was purified by flash chromatography (heptane) to afford **9c** in 73 % yield (167 mg) as a white solid; R_f 0.7 (CH_2Cl_2 /heptane: 5/5); mp 98-100°C; ^1H NMR (CDCl_3 , 300 MHz) δ 7.03 (m, 3H), 7.35 (m, 8H), 7.81 (m, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 157.9, 140.6, 135.9, 134.2, 132.2, 129.9, 129.8, 128.9, 128.2, 127.9, 125.3, 124.6, 112.9, 122.4, 121.8, 115.8; Anal. Calcd for $\text{C}_{20}\text{H}_{14}\text{OS}$: C, 79.44; H, 4.67; S, 10.60. Found: C, 78.84; H, 4.71; S, 10.84; MS (EI+) m/z 302 (M^+).

Synthesis of 2-(*p*-anisyl)-3-phenoxybenzo[*b*]thiophene (10c): DCH-18-C-6 (261 mg, 0.70 mmol), K_2CO_3 (290 mg, 2.1 mmol), 3-phenoxybenzo[*b*]thiophene **5c** (158 mg, 0.70 mmol), *p*-bromoanisole (100 μL , 0.77 mmol) and $\text{Pd}(\text{OAc})_2$ (8 mg, 0.035 mmol) in DMF (1 mL). 110°C for 9 h. The crude product was purified by flash chromatography (heptane/ CH_2Cl_2 : 9/1) to afford **10c** in 70 % yield (165 mg) as a white solid; R_f 0.6 (heptane/ CH_2Cl_2 : 5/5); mp 140-142°C; ^1H NMR (CDCl_3 , 300 MHz) δ 3.81 (s, 3H), 6.92 (d, 2H, $J = 8.9$ Hz), 7.02 (m, 3H), 7.30 (m, 4H), 7.42 (d, 1H, $J = 7.9$ Hz), 7.75 (d, 2H, $J = 8.9$ Hz), 7.85 (d, 1H, $J = 7.7$ Hz); ^{13}C NMR (CDCl_3 , 75 MHz) δ 159.6, 157.9, 138.5, 135.4, 134.3, 129.8, 129.7, 129.2, 124.9, 124.8, 124.5, 122.8, 122.3, 121.4, 115.7, 114.4, 55.4; Anal. Calcd for $\text{C}_{21}\text{H}_{16}\text{O}_2\text{S}$: C, 75.88; H, 4.85; S, 9.65. Found: C, 75.44; H, 4.96; S, 9.73; MS (EI+) m/z 332 (M^+).

Synthesis of 2-(*m*-benzonitrile)-3-(*p*-fluorophenoxy)benzo[*b*]thiophene (8d): DCH-18-C-6 (373 mg, 1 mmol), K₂CO₃ (414 mg, 3 mmol), 3-(*p*-fluorophenoxy)benzo[*b*]thiophene **5d** (244 mg, 1 mmol), 2-bromobenzonitrile (200 mg, 1.1 mmol), and Pd(OAc)₂ (11 mg, 0.05 mmol) in DMF (1 mL). 110°C for 8 h. The crude product was purified by flash chromatography (heptane/CH₂Cl₂: 7/3) to afford **8d** in 67% yield (230 mg) as a colorless oil; *R*_f 0.3 (heptane/CH₂Cl₂: 6/4); ¹H NMR (CDCl₃, 300 MHz) δ 6.87 (m, 4H), 7.38 (m, 3H), 7.57 (m, 3H), 7.71 (d, 1H, *J* = 7.9 Hz), 7.85 (d, 1H, *J* = 8.1 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 153.8, 145.2, 143.2, 137.4, 135.4, 133.8, 132.7, 132.5, 131.7, 128.9, 126.1, 124.9, 124.4, 123.1, 122.2, 121.6, 118.1, 117.2, 117.1, 116.3, 116.0, 113.4; Anal. Calcd for C₂₁H₁₂FNOS: C, 73.03; H, 3.50; N, 4.06; S, 9.28; F, 5.50. Found: C, 73.29; H, 3.64; N, 4.01; S, 9.30; F, 5.13; MS (EI+) *m/z* 345 (M⁺).

Synthesis of 2-(*m*-benzonitrile)-3-(*p*-chlorophenoxy)benzo[*b*]thiophene (8e): DCH-18-C-6 (149 mg, 0.4 mmol), K₂CO₃ (166 mg, 1.2 mmol), 3-(*p*-chlorophenoxy)benzo[*b*]thiophene **5e** (100 mg, 0.4 mmol), 2-bromobenzonitrile (81 mg, 0.44 mmol) and Pd(OAc)₂ (5 mg, 0.02 mmol) in DMF (1 mL). 110°C for 9 h. The crude product was purified by flash chromatography (heptane/ CH₂Cl₂: 6/4) to afford **8e** in 60% yield (82 mg) as a colorless oil; *R*_f 0.2 (heptane/CH₂Cl₂: 6/4); ¹H NMR (CDCl₃, 300 MHz) δ 6.85 (d, 2H, *J* = 8.9 Hz), 7.15 (d, 2H, *J* = 8.9 Hz), 7.39 (m, 3H), 7.57 (m, 3H), 7.73 (d, 1H *J* = 7.9 Hz), 7.86 (d, 1H, *J* = 8.1 Hz); Anal. Calcd for C₂₁H₁₂ClNOS: C, 69.71; H, 3.34; N, 3.87; S, 8.86. Found: C, 69.20; H, 3.59; N, 3.79; S, 8.01; MS (EI+) *m/z* 361 (M⁺).

Synthesis of 2-(*m*-benzonitrile)-3-(*p*-cyanophenoxy)benzo[*b*]thiophene (8f): DCH-18-C-6 (443 mg, 1.2 mmol), K₂CO₃ (493 mg, 3.6 mmol), 3-(*p*-cyanophenoxy)benzo[*b*]thiophene **5f** (300 mg, 1.2 mmol), 2-bromobenzonitrile (242 mg, 1.32 mmol) and Pd(OAc)₂ (14 mg, 0.06 mmol) in DMF (1.5 mL). 110°C for 5 h. The crude product was purified by flash chromatography (cyclohexane/EtOAc: 9/1) to afford **8f** in 73% yield (306 mg) as a white

solid; R_f 0.4 (cyclohexane/EtOAc: 8/2); mp 128-130°C; ^1H NMR (CDCl_3 , 300 MHz) δ 6.98 (d, 2H, $J = 9.1$ Hz), 7.43 (m, 6H), 7.60 (d, 2H, $J = 4.0$ Hz), 7.73 (d, 1H, $J = 7.7$ Hz), 7.88 (d, 1H, $J = 7.7$ Hz); ^{13}C NMR (CDCl_3 , 75 MHz) δ 160.8, 141.4, 137.3, 134.6, 134.2, 133.9, 132.8, 131.9, 131.5, 129.2, 126.4, 125.5, 125.2, 123.2, 121.7, 118.7, 117.8, 116.6, 113.2, 106.2; Anal. Calcd for $\text{C}_{22}\text{H}_{12}\text{N}_2\text{OS}$: C, 74.98; H, 3.43; N, 7.95; S, 9.10. Found: C, 74.78; H, 3.51; N, 7.91; S, 9.10; MS (EI+) m/z 352 (M^+).

Synthesis of 2-(*m*-benzonitrile)-3-piperidinobenzo[*b*]thiophene (8g): DCH-18-C-6 (335 mg, 0.9 mmol), K_2CO_3 (373 mg, 2.7 mmol), 3-piperidinobenzo[*b*]thiophene **5g** (196 mg, 0.90 mmol), 2-bromobenzonitrile (182 mg, 0.99 mmol) and $\text{Pd}(\text{OAc})_2$ (10 mg, 0.045 mmol) in DMF (1 mL). 110 °C for 3 h. The crude product was purified by flash chromatography (heptane/ CH_2Cl_2 : 8/2) to afford **8g** in 80% yield (230 mg) as a yellow solid; R_f 0.2 (heptane/ CH_2Cl_2 : 5/5); mp 106-108°C; ^1H NMR (CDCl_3 , 300 MHz) δ 1.56 (m, 6H), 3.03 (m, 4H), 7.38 (m, 2H), 7.55 (m, 3H), 7.79 (m, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 144.3, 139.5, 138.3, 137.2, 133.0, 132.6, 132.1, 128.5, 125.1, 124.2, 123.0, 122.7, 122.5, 118.2, 114.8, 52.9, 27.1, 24.4; Anal. Calcd for $\text{C}_{20}\text{H}_{18}\text{N}_2\text{S}$: C, 75.44; H, 5.70; N, 8.80; S, 10.07. Found: C, 75.52; H, 5.43; N, 8.58; S, 10.47; MS (EI+) m/z 318 (M^+).

Synthesis of 2-phenyl-3-piperidinobenzo[*b*]thiophene (9g): DCH-18-C-6 (335 mg, 0.9 mmol), K_2CO_3 (373mg, 2.7 mmol), 3-piperidinobenzo[*b*]thiophene **5g** (196 mg, 0.9 mmol), bromobenzene (100 μL , 0.99 mmol). and $\text{Pd}(\text{OAc})_2$ (10 mg, 0.045 mmol) in DMF (1mL). 110°C for 7 h. The crude product was purified by flash chromatography (heptane) to afford **9g** in 63% yield (165 mg) as a off-white solid; R_f 0.7 (heptane/ CH_2Cl_2 : 5/5); mp 70-72°C; ^1H NMR (CDCl_3 , 300 MHz) δ 1.64 (m, 6H), 3.07 (m, 4H), 7.39 (m, 5H), 7.59 (dd, 2H, $J = 1.5$, 8.1 Hz), 7.76 (dd, 1H, $J = 1.5$, 7.5 Hz), 7.83 (dd, 1H, $J = 1.3$, 7.9 Hz); ^{13}C NMR (CDCl_3 , 75 MHz) δ 141.8, 138.4, 137.6, 135.1, 130.3, 129.9, 128.1, 127.9, 124.4, 124.0, 122.7, 122.6,

53.1, 27.2, 24.6; Anal. Calcd for C₁₉H₁₉NS: C, 77.77; H, 6.53; N, 4.77; S, 10.93. Found: C, 77.79; H, 6.55; N, 4.77; S, 10.88; MS (EI+) *m/z* 293 (M⁺).

Synthesis of 2-(*p*-anisyl)-3-piperidinobenzo[*b*]thiophene (10g): DCH-18-C-6 (298 mg, 0.8 mmol), K₂CO₃ (331 mg, 2.4 mmol), 3-piperidinobenzo[*b*]thiophene **5g** (174 mg, 0.8mmol), *p*-bromoanisole (110 μ L, 0.88 mmol) and Pd(OAc)₂ (9 mg, 0.04 mmol) in DMF (1mL). 110°C for 4 h. The crude product was purified by flash chromatography (heptane/CH₂Cl₂: 5/5) to afford **10g** in 75% yield (196 mg) as a white solid; *R_f* 0.6 (heptane/CH₂Cl₂: 5/5); mp 110-112°C; ¹H NMR (CDCl₃, 300 MHz) δ 1.65 (m, 6H), 3.07 (m, 4H), 6.97 (d, 2H, *J* = 8.9 Hz), 7.37 (ddd, 1H, *J* = 1.4, 7.4 Hz), 7.39 (ddd, 1H, *J* = 1.4, 7.5 Hz), 7.54 (d, 2H, *J* = 8.9 Hz), 7.75 (dd, 1H, *J* = 0.8, 7.0 Hz), 7.82 (dd, 1H, *J* = 0.9, 7.0 Hz); ¹³C NMR (CDCl₃, 75 MHz) δ 159.4, 141.3, 138.5, 137.3, 131.4, 130.1, 127.3, 124.2, 123.9, 122.6, 122.4, 113.5, 55.4, 53.0, 27.2, 24.6; Anal. Calcd for C₂₀H₂₁NOS: C, 74.27; H, 6.54; N, 4.33; S, 9.91. Found: C, 74.29; H, 6.58; N, 4.31; S, 9.88; MS (EI+) *m/z* 323 (M⁺).

Synthesis of 2-(*m*-benzonitrile)-3-*N*-morpholinobenzo[*b*]thiophene (8h): DCH-18-C-6 (223 mg, 0.6mmol), K₂CO₃ (249 mg, 1.8 mmol), 3-morpholinobenzo[*b*]thiophene **5h** (132 mg, 0.6 mmol), 2-bromobenzonitrile (121 mg, 0.66 mmol) and Pd(OAc)₂ (7 mg, 0.03 mmol) in DMF (1 mL). 110°C for 9h. The crude product was purified by flash chromatography (heptane/EtOAc: 9/1) to afford **8h** in 65% yield (137 mg) as a white solid; *R_f* 0.2 (heptane/EtOAc: 8/2); mp 170-172°C; ¹H NMR (CDCl₃, 300 MHz) δ 3.09 (m, 4H), 3.74 (m, 4H), 7.61 (m, 8H); ¹³C NMR (CDCl₃, 75 MHz) δ 142.6, 138.7, 138.3, 136.6, 133.2, 132.5, 132.4, 128.9, 125.4, 125.3, 124.4, 122.9, 122.7, 118.1, 114.8, 67.9, 51.9; Anal. Calcd for C₁₉H₁₆N₂OS: C, 71.22; H, 5.03; N, 8.74; S, 10.01. Found: C, 71.21; H, 4.70; N, 9.08; S, 9.39; MS (EI+) *m/z* 320 (M⁺).

Synthesis of 2-(*m*-benzonitrile)-3-*N*-(*N*'-methyl)piperazinobenzo[*b*]thiophene (8i): DCH-18-C-6 (224 mg, 0.6 mmol), K₂CO₃ (249 mg, 1.8 mmol), 3-*N*-(*N*'-

methyl)piperazinobenzo[*b*]thiophene **5i** (140 mg, 0.6 mmol), 2-bromobenzonitrile (121 mg, 0.66 mmol) and Pd(OAc)₂ (7 mg, 0.03 mmol) in DMF (1 mL). 110°C for 9h. The crude product was purified by flash chromatography (CH₂Cl₂/MeOH: 98/2) to afford **8i** in 52% yield (105 mg) as an off-white solid ; *R_f* 0.4 (CH₂Cl₂/MeOH: 95/5); mp 144-146°C; ¹H NMR (CDCl₃, 300 MHz) δ 2.30 (s, 3H), 2.47 (m, 4H), 3.10 (dd, 4H, *J* = 4.7, 4.7 Hz), 7.38 (m, 2H), 7.54 (m, 3H), 7.77 (m, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 143.0, 138.9, 138.2, 136.8, 133.1, 132.5, 132.3, 128.8, 125.2, 124.4, 124.3, 122.7, 118.1, 114.8, 56.0, 51.4, 46.4; Anal. Calcd for C₂₀H₁₉N₃S: C, 72.04; H, 5.74; N, 12.60; S, 9.62. Found: C, 72.15; H, 5.92; N, 12.19; S, 9.73; MS (EI+) *m/z* 333 (M⁺).

References

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^1H and ^{13}C NMR spectra of compounds 2, 3c, 4a, 5c, 5g, 6, 7, 8c, 9c, 10c, 8g, 9g and 10g