Supporting Information

Synthesis of Polycyclic Heterocycles via a One-Pot *ortho*- Alkylation/Direct Heteroarylation Sequence

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General Information

The following includes general experimental procedures, specific details for representative reactions, isolation, and spectroscopic data for new compounds. All of the tandem *ortho*-alkylation/direct heteroarylation reactions were performed in capped 2.5–5 mL microwave reaction vials from Personal Chemistry. Melting points were recorded using a Fisher-Johns melting point apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were obtained using either Varian Gemini 300 MHz, Varian Mercury 300 MHz or Varian Unity 400 MHz spectrometers. ^1H spectra were referenced to tetramethylsilane (TMS, 0 ppm) or solvent carbons (DMSO, 2.53 ppm), and ^{13}C spectra were referenced to solvent carbons (77.23 ppm for CDCl_3). IR spectra were obtained using a Perkin Elmer Spectrum 1000 FT-IR spectrometer on NaCl plates. High-resolution mass spectra were obtained using a VG 70-250S (double focusing) mass spectrometer at 70 eV for electron impact ionization or a Sciex QStar operating at a spray voltage of 5500 V for electrospray ionization. Dry dichloromethane and diethyl ether were obtained from an MBraun solvent purification system, and used without further treatment. Acetonitrile was distilled under $\text{N}_{2(g)}$ over CaH_2 , and stored under $\text{N}_{2(g)}$ in a sealed Wheaton bottle over 4 Å molecular sieves. Neutral silica (Silicycle, Quebec, Canada) for flash chromatography was used as received. All reagents, metal catalysts and ligands were purchased from Sigma-Aldrich, VWR International, or Strem Chemical Company and used as received unless otherwise noted.

Abbreviations:

Et_2O : Diethyl Ether
 EtOAc : Ethyl Acetate
br: broad (IR)
w: weak (IR)

RT: Room Temperature
h: hours
s: strong (IR)
m: moderate (IR)

General Procedure

General Procedure for Domino Pd-Catalyzed *ortho*-Alkylation/Direct Heteroarylation Reaction:

In a 2.5–5 mL microwave reaction vial with a magnetic stir bar, Cs₂CO₃ (2 equiv, 0.6 mmol), Pd(OAc)₂ (10 mol%, 0.03 mmol), P(2-Furyl)₃ (20 mol%, 0.06 mmol), and norbornene (2 equiv, 0.6 mmol) were added sequentially. In a separate vial, Ar-I (1 equiv, 0.3 mmol) and 3-(bromoalkyl)heteroaryl (2 equiv, 0.6 mmol) were combined and added to the reaction vial. CH₃CN (0.1 M of Ar-I, 3 mL) was added, and the vial capped and sealed. The vial was then flushed with N_{2(g)}. The vial was then heated in an oil bath until the reaction was complete (appearance of Pd-black usually signifies completion of reaction). The vial was then removed from the oil bath, cooled, and H₂O (3 mL) added. The mixture was then washed with Et₂O (3 × 5 mL), and the combined organic extracts combined, dried with MgSO₄, filtered, and concentrated *in vacuo*. The crude product was then purified by column chromatography on silica gel to afford product.

Experimental Data

N-(3-iodo-2-methylphenyl)acetamide (**1b**)

3-iodo-2-methylaniline (500 mg, 2.14 mmol), Et_3N (569 μL , 4.28 mmol) and DMAP (26.0 mg, 0.210 mmol) were combined, and dissolved in 10 mL dry CH_2Cl_2 . Acetyl chloride (305 μL , 4.28 mmol) was then added dropwise, and the mixture stirred at RT for 40 h. The reaction was quenched by addition of 10 mL H_2O , 20 mL 5 % $\text{HCl}_{(\text{aq})}$, and diluted with 20 mL EtOAc . The layers were separated, and the aqueous phase washed with 35 mL EtOAc . The combined organic phases were washed with saturated $\text{NaHCO}_{3(\text{aq})}$, dried with Na_2SO_4 , filtered, and concentrated *in vacuo*. This yielded a solid crude product ($R_f = 0.10$ in 30 % EtOAc /hexane) which was recrystallized from EtOAc to afford **1b** as a fibrous white solid with needle-like crystals (mp = 167-169 $^\circ\text{C}$). Isolated yield: 372 mg (63 %). ^1H NMR (300 MHz, CDCl_3) δ 2.22 (s, 3 H), 2.41 (s, 3 H), 6.91 (t, $J=8.0$ Hz, 1 H), 6.97 (br s, 1 H), 7.64 (d, $J=8.2$ Hz, 1 H), 7.69 (d, $J=8.2$ Hz, 1 H); ^{13}C NMR (75 MHz, CDCl_3) δ 23.8, 24.4, 102.8, 126.8, 128.4, 136.0, 136.6, 137.4, 169.0; IR neat, ν (cm^{-1}) 710 (w), 777 (m), 861 (w), 899 (w), 1018 (w), 1289 (m), 1367 (m), 1427 (m), 1525 (m), 1565 (m), 1658 (s), 3266 (s); Elemental Anal. Calc'd for $\text{C}_9\text{H}_9\text{INO}$: C: 39.30 % (found 39.45 %), H: 3.66 % (found 3.71 %), N: 5.09 % (found 5.01 %).

N-(3-iodo-2-methylphenyl)-4-methylbenzenesulfonamide (**9**)

3-iodo-2-methylaniline (597 mg, 2.56 mmol) and TsCl (586 mg, 3.07 mmol) were combined and dissolved in 20 mL dry pyridine. The mixture was capped and stirred for 24 h at 70 $^\circ\text{C}$. The mixture was concentrated *in vacuo*, taken up in 15 mL 10% $\text{HCl}_{(\text{aq})}$, and extracted with 3 x 20 mL Et_2O . The combined organic phases were then washed with saturated $\text{NaHCO}_{3(\text{aq})}$, then dried with MgSO_4 , filtered and concentrated *in vacuo*. The resulting crude solid was then recrystallized from EtOAc by addition of hexane to afford **9** as pale purple crystals (mp = 151–153 $^\circ\text{C}$, R_f 0.19 in 30% Et_2O /hexane). Isolated yield: 816 mg (82%). ^1H NMR (300 MHz, CDCl_3) δ 2.18 (s, 3H), 2.41 (s, 3H), 6.37 (br s, 1H), 6.82 (t, $J=8.1$ Hz, 1H), 7.21–7.26 (m, 3H), 7.59 (d, $J=8.0$ Hz, 2H), 7.67 (d, $J=8.0$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 21.6, 23.5, 102.0, 125.3, 127.2, 128.1, 129.7, 134.3, 135.5, 137.6, 144.1; IR thin film, ν (cm^{-1}) 664 (m), 710 (m), 813 (w), 916 (w), 1092 (m), 1161 (s), 1325 (m), 1395 (w), 1455 (m), 1559 (w), 3276 (br, m); HRMS (ESI) Calc'd for $\text{C}_{14}\text{H}_{15}\text{NO}_2\text{IS}$: 387.9862 ($\text{M}+\text{H}^+$), found 387.9853.

N-(3-iodo-2-methylphenyl)-*N*,4-dimethylbenzenesulfonamide (**1g**)

Compound **9** (803 mg, 2.07 mmol), MeI (258 μ L, 4.15 mmol), and K_2CO_3 (429 mg, 3.10 mmol) were combined and 25 mL acetone added. The mixture was then stirred under reflux for 6 h, and concentrated *in vacuo*. The crude product was then worked up in EtOAc/ H_2O , and the organic phase dried with $MgSO_4$, filtered and concentrated *in vacuo*. This afforded **1g** as a clear, viscous, pale orange-pink oil which slowly solidified to an off-white solid (mp = 104–106 $^{\circ}C$, R_f 0.42 in 30% Et₂O/hexane). Isolated yield: 861 mg (100%). 1H NMR (300 MHz, $CDCl_3$) δ 2.46 (s, 3H), 2.52 (s, 3H), 3.11 (s, 3H), 6.61 (dd, $J=7.9, 1.5$ Hz, 1H), 6.75 (t, $J=7.9$ Hz, 1 H), 7.31 (d, $J=7.9$ Hz, 2H), 7.56–7.61 (m, 2H), 7.78 (dd, $J=7.8, 1.3$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.6, 24.6, 39.0, 102.7, 127.2, 127.6, 128.0, 129.5, 139.3, 140.4, 142.7, 143.7; IR neat, ν (cm^{-1}) 584 (s), 659 (s), 713 (s), 794 (m), 815 (m), 883 (m), 990 (m), 1061 (m), 1089 (m), 1155 (m), 1348 (s), 1455 (s), 1557 (m), 1598 (m), 2255 (w), 2923 (m); HRMS (EI) Calc'd for $C_{18}H_{16}NO_2S$: 400.9946 (M^+), found 400.9939.

10-Methyl-9-nitro-5,6-dihydro-4*H*-benzo[6,7]cyclohepta[1,2-*b*]thiophene (**3a**)

Following the general procedure 2-iodo-6-nitrotoluene **1a** (80.0 mg, 0.300 mmol) and 3-(3-bromopropyl)thiophene **2a** (123 mg, 0.600 mmol) were reacted at 95 $^{\circ}C$ for 18 h. The crude mixture was purified by flash chromatography on silica gel (R_f 0.34 in 10% Et₂O/hexane) using 5% to 10% Et₂O/hexane to afford **3a** as a viscous yellow oil. Isolated yield: 69 mg (89 %). 1H NMR (300 MHz, $CDCl_3$) δ 2.18 (quintet, $J=6.6$ Hz, 2H), 2.43 (br s, 2H), 2.59 (s, 3H), 6.98 (d, $J=5.0$ Hz, 1H), 7.24 (d, $J=8.3$ Hz, 1H), 7.40 (d, $J=5.1$ Hz, 1H), 7.70 (d, $J=8.2$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.2, 25.1, 33.3, 34.0, 123.2, 126.0, 127.5, 128.0, 130.7, 133.1, 136.9, 142.2, 146.7, 150.2; IR neat ν (cm^{-1}) 653 (s), 833 (s), 853 (s), 989 (m), 1020 (m), 1090 (m), 1116 (m), 1156 (m), 1347 (s), 1449 (s), 1518 (s), 1592 (s), 1902 (w), 2400 (w), 2859 (s), 2933 (s), 3105 (m); HRMS (EI) Calc'd for $C_{14}H_{13}NO_2S$: 259.0667 (M^+), found 259.0666.

N-(10-methyl-5,6-dihydro-4*H*-benzo[6,7]cyclohepta[1,2-*b*]thien-9-yl)acetamide (**3b**)

Following the general procedure *N*-(3-iodo-2-methylphenyl)acetamide **1b** (82.0 mg, 0.300 mmol) and 3-(3-bromopropyl)thiophene **2a** (153 mg, 0.600 mmol) were reacted at 105 °C for 18 h. The crude mixture was purified by flash chromatography on silica gel (R_f 0.30 in 60% EtOAc/hexane) using 40% to 60% EtOAc/hexane to afford **3b** as an off-white solid (mp = 145–147 °C). Isolated yield: 62 mg (76%). ^1H NMR (400 MHz, CDCl_3) δ 1.91–2.18 (m, 5H), 2.22 (s, 3H), 2.31–2.55 (m, 6H), 6.96 (d, $J=5.0$ Hz, 1H), 6.98 (br s, 1H), 7.14 (d, $J=7.9$ Hz, 1H), 7.32 (d, $J=4.8$ Hz, 1H), 7.54 (d, $J=7.9$ Hz, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 16.0, 24.2, 25.1, 32.6, 33.9, 123.8, 124.5, 127.2, 127.8, 128.8, 134.2, 134.7, 134.8, 139.0, 141.3, 168.5; IR thin film, ν (cm^{-1}) 680 (w), 731 (m), 827 (w), 908 (w), 1108 (m), 1301 (m), 1371 (m), 1445 (m), 1472 (m), 1521 (s), 1651 (s), 2856 (s), 2928 (s), 3276 (br, s); HRMS (EI) Anal. Calc'd for $\text{C}_{16}\text{H}_{17}\text{NOS}$: 271.1031 (M^+), found 271.1029.

9-Chloro-10-methyl-5,6-dihydro-4H-benzo[6,7]cyclohepta[1,2-*b*]thiophene (**3c**)

Following the general procedure 2-chloro-6-iodotoluene **1c** (76.0 mg, 0.300 mmol) and 3-(3-bromopropyl)thiophene **2a** (123 mg, 0.600 mmol) were reacted at 95 °C for 18 h. The crude mixture was purified by flash chromatography on silica gel (R_f 0.70 in hexane) using hexane to afford **3c** as a clear, colourless oil. Isolated yield: 42 mg (57 %). ^1H NMR (400 MHz, CDCl_3) δ 2.08–2.15 (m, 2 H), 2.27–2.52 (br m, 4 H), 2.54 (s, 3 H), 6.95 (d, $J=4.8$ Hz, 1 H), 7.05 (d, $J=8.1$ Hz, 1 H), 7.25 (s, 1 H), 7.33 (d, $J=4.8$ Hz, 1 H); ^{13}C NMR (75 MHz, CDCl_3) δ 18.6, 25.0, 32.5, 33.9, 124.7, 127.5, 127.7, 128.1, 133.3, 134.0, 134.5, 135.8, 139.9, 141.4; IR thin film, ν (cm^{-1}) 682 (s), 723 (s), 764 (s), 817 (s), 834 (m), 1026 (s), 1138 (m), 1381 (m), 1446 (s), 1459 (s), 1566 (m), 1582 (m), 1749 (br, w), 1880 (br, w), 2856 (s), 2938 (s) 3065 (w), 3103 (w); HRMS (EI) Anal. Calc'd for $\text{C}_{14}\text{H}_{13}\text{ClS}$: 248.0426 (M^+), found 248.0416.

N,4-dimethyl-*N*-(10-methyl-5,6-dihydro-4H-benzo[6,7]cyclohepta[1,2-*b*]thien-8-yl)benzenesulfonamide (**3d**)

Following the general procedure *N*-(4-iodo-3-methylphenyl)-*N*,4-dimethylbenzenesulfonamide **1d** (98.0 mg, 0.249 mmol) and 3-(3-bromopropyl)thiophene **2a** (100 mg, 0.488 mmol) were reacted at 105 °C for 18 h. The crude mixture was purified by flash chromatography on silica gel (R_f 0.21 in 20% Et_2O /hexane) using 15% to 22% Et_2O /hexane. The product obtained was contaminated by ~20% of the *ortho*-alkylation/reduction product, so it was then recrystallized from

Et₂O to afford **3d** as an off-white solid (mp = 139–141 °C). Isolated yield: 55 mg (56%). ¹H NMR (400 MHz, CDCl₃) δ 2.06–2.14 (m, 2H), 2.32 (t, *J*=6.9 Hz, 2H), 2.43 (s, 6H), 2.44–2.49 (m, 2H), 3.16 (s, 3H), 6.81 (d, *J*=2.2 Hz, 1H), 6.92 (d, *J*=2.2 Hz, 1H), 6.95 (d, *J*=5.0 Hz, 1H), 7.26 (d, *J*=8.3 Hz, 2H), 7.31 (d, *J*=5.0 Hz, 1H), 7.50 (d, *J*=8.1 Hz, 2H); ¹³C NMR (75 MHz, CDCl₃) δ 21.8, 22.1, 25.4, 33.0, 34.4, 38.4, 124.6, 125.0, 127.1, 128.0, 128.2, 129.5, 133.5, 134.0, 134.4, 136.8, 140.3, 141.4, 142.3, 143.7; IR thin film, ν (cm⁻¹) 668 (s), 730 (m), 816 (w), 1021 (m), 1081 (m), 1456 (s), 1506 (s), 1558 (s), 2337 (s), 2360 (s), 2918 (s); HRMS (EI) Calc'd for C₂₂H₂₃NO₂S₂: 397.1170 (M⁺), found 397.1167.

10-Methyl-5,6-dihydro-4*H*-benzo[6,7]cyclohepta[1,2-*b*]thiophene (**3e**)

Following the general procedure 2-iodotoluene **1e** (38.0 μL, 0.300 mmol) and 3-(3-bromopropyl)thiophene **2a** (123 mg, 0.600 mmol) were reacted at 85 °C. The crude mixture was purified by flash chromatography on silica gel (R_f 0.74 in hexane) using hexane to afford **3e** as a clear, colourless oil. Isolated yield: 12 mg (19 %). ¹H NMR (300 MHz, CDCl₃) δ 2.10–2.20 (m, 2H), 2.41 (t, *J*=6.9 Hz, 2H), 2.44–2.49 (m, 2H), 2.50 (s, 3H), 6.96 (d, *J*=5.0 Hz, 1H), 7.11–7.18 (m, 3H), 7.31 (d, *J*=5.3 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 21.8, 25.2, 32.8, 34.3, 123.9, 126.9, 127.2, 127.7, 128.7, 134.1, 134.9, 135.8, 140.9, 141.4; IR thin film, ν (cm⁻¹) 657 (s), 680 (s), 721 (m), 762 (s), 789 (m), 830 (w), 892 (w), 969 (w), 1097 (w), 1379 (w), 1444 (m), 1463 (s), 2855 (s), 2938 (s), 3062 (m); HRMS (EI) Anal. Calc'd for C₁₄H₁₄S: 214.0816 (M⁺), found 214.0821.

10-methoxy-8-nitro-5,6-dihydro-4*H*-benzo[6,7]cyclohepta[1,2-*b*]thiophene (**3f**)

Following the general procedure 2-iodo-5-nitroanisole **1f** (68.1 mg, 0.244 mmol) and 3-(3-bromopropyl)thiophene **2a** (100 mg, 0.488 mmol) were reacted at 105 °C for 18 hours. The crude mixture was purified by flash chromatography on silica gel (R_f 0.46 in 5% Et₂O/hexane) using 2.5% to 5% Et₂O/hexane to afford **3f** as a clear, viscous yellow oil, slowly solidifying to yellow, needle-like crystals (mp = 127–128 °C). Isolated yield: 35 mg (52%). ¹H NMR (400 MHz, CDCl₃) δ 2.31 (tt, *J*=7.2, 7.1 Hz, 2H), 2.56 (td, *J*=7.1, 2.7 Hz, 4H), 3.96 (s, 3H), 6.99 (d, *J*=5.0 Hz, 1H), 7.44 (d, *J*=5.0 Hz, 1H), 7.71 (d, *J*=2.4 Hz, 1H), 7.85 (d, *J*=2.2 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 26.0, 33.4, 34.9, 56.3, 104.1, 117.6, 127.1, 128.2, 130.6, 131.4, 143.0, 143.4, 156.0; IR thin film, ν (cm⁻¹) 652 (s), 688 (m), 741 (m), 772 (m), 861 (m), 1105 (s), 1268 (s), 1331 (s), 1461 (m), 1514 (s), 1582 (m), 2929 (s); HRMS (EI) Calc'd for C₁₄H₁₃NO₃S: 275.0616 (M⁺), found 275.0623. The crystallographic information file (CIF) for this compound can also be found on the

Cambridge Crystallographic Data Centre database (data_request@ccdc.cam.ac.uk) as CCDC 614852.

9-methyl-8-nitro-4,5-dihydronaphtho[1,2-*b*]thiophene (**3g**)

Following the general procedure 2-iodo-6-nitrotoluene **1a** (74.0 mg, 0.280 mmol) and 3-(2-bromoethyl)thiophene **2b** (107 mg, 0.560 mmol) were reacted at 105 °C for 12 hours. The crude mixture was purified by flash chromatography on silica gel (R_f 0.41 in 5% Et₂O/hexane) using 0% to 5% Et₂O/hexane to afford **3g** as a yellow solid (mp = 82–84 °C). Isolated yield: 40 mg (58%). ¹H NMR (400 MHz, CDCl₃) δ 2.69 (s, 3H), 2.80–2.85 (m, 2H), 2.93–2.97 (m, 2H), 7.00 (d, J =5.0 Hz, 1H), 7.20 (d, J =8.1 Hz, 1H), 7.38 (d, J =5.0 Hz, 1H), 7.50 (d, J =8.1 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 17.8, 24.1, 31.4, 121.6, 125.8, 126.3, 126.4, 126.9, 132.8, 133.7, 140.8, 141.3; IR thin film, ν (cm⁻¹) 740 (w), 835 (w), 1346 (m), 1442 (m), 1469 (s), 1530 (s), 1589 (m), 1642 (m), 2957 (s), 3452 (br, s); HRMS (EI) Calc'd for C₁₃H₁₁NO₂S: 245.0510 (M⁺), found 245.0505.

N-(9-methyl-4,5-dihydronaphtho[1,2-*b*]thien-8-yl)acetamide (**3h**)

Following the general procedure *N*-(3-iodo-2-methylphenyl)acetamide **1b** (77.0 mg, 0.280 mmol) and 3-(2-bromoethyl)thiophene **2b** (107 mg, 0.560 mmol) were reacted at 105 °C for 14 hours. The crude mixture was purified by flash chromatography on silica gel (R_f 0.30 in 60% EtOAc/hexane) using 50% to 70% EtOAc/hexane to afford **3h** as a off-white solid of scaly crystals (mp = 187–188 °C). Isolated yield: 59 mg (82%). ¹H NMR (400 MHz, CDCl₃) δ 1.88 (s, 0.7H, COCH₃ rotamer), 2.23 (s, 2.3H, COCH₃ rotamer), 2.53 (s, 2.3H, ArCH₃ rotamer), 2.59 (s, 0.7H, ArCH₃ rotamer), 2.76–2.84 (m, 2H), 2.84–2.95 (m, 2H), 6.88–7.02 (m, 2H), 7.12 (d, J =8.1 Hz, 1H), 7.24–7.35 (m, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 16.3, 23.8, 24.4, 30.8, 123.9, 124.0, 126.0, 126.6, 127.5, 132.0, 134.2, 134.3, 135.0, 139.4, 169.0; IR thin film, ν (cm⁻¹) 682 (m), 716 (m), 821 (w), 836 (w), 868 (w), 916 (w), 970 (w), 1039 (w), 1109 (m), 1275 (m), 1296 (m), 1368 (m), 1434 (m), 1471 (m), 1532 (s), 1593 (m), 1652 (s), 2358 (w), 2930 (m), 3279 (br, s); HRMS (ESI) Calc'd for C₁₅H₁₆NOS: 258.0947 (M+H⁺), found 258.0942.

8-chloro-9-methyl-4,5-dihydronaphtho[1,2-*b*]thiophene (**3i**)

Following the general procedure 2-chloro-6-iodotoluene **1c** (76.0 mg, 0.300 mmol) and 3-(2-bromoethyl)thiophene **2b** (115 mg, 0.600 mmol) were reacted at 105 °C for 14 hours. The crude mixture was purified by flash chromatography on silica gel (R_f 0.46 in hexane) using hexane to afford **3i** as a clear, viscous oil. Isolated yield: 54 mg (77%). ^1H NMR (400 MHz, CDCl_3) δ 2.73 (s, 3H), 2.76–2.81 (m, 2 H), 2.83–2.89 (m, 2H), 6.97 (d, $J=5.0$ Hz, 1H), 7.03 (d, $J=7.9$ Hz, 1H), 7.18 (d, $J=7.9$ Hz, 1H), 7.30 (d, $J=5.3$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 18.8, 24.6, 30.9, 124.5, 126.7, 126.9, 127.2, 130.5, 133.1, 133.9, 134.2, 135.5, 140.0; IR thin film, ν (cm^{-1}) 635 (m), 653 (m), 684 (m), 717 (m), 764 (m), 808 (m), 854 (w), 912 (w), 1017 (s), 1033 (m), 1088 (w), 1142 (w), 1432 (m), 1459 (s), 1567 (w), 1582 (w), 2362 (w), 2947 (s); HRMS (EI) Calc'd for $\text{C}_{13}\text{H}_{11}\text{ClS}$: 237.0270 (M^+), found 234.0273.

N,4-dimethyl-*N*-(9-methyl-4,5-dihydronaphtho[1,2-*b*]thien-8-yl)benzenesulfonamide (**3j**)

Following the general procedure *N*-(3-iodo-2-methylphenyl)-*N*,4-dimethylbenzenesulfonamide **1g** (120 mg, 0.300 mmol) and 3-(2-bromoethyl)thiophene **2b** (115 mg, 0.600 mmol) were reacted at 105 °C for 15 hours. The crude mixture was purified by flash chromatography on silica gel (R_f 0.32 in 30% Et_2O /hexane) using 20% to 30% Et_2O /hexane to afford **3j** as a powdery, white solid (mp = 166–167 °C). Isolated yield: 76 mg (66%). ^1H NMR (400 MHz, CDCl_3) δ 2.45 (s, 3H), 2.67 (s, 3H), 2.74–2.84 (m, 2H), 2.85–2.93 (m, 2H), 3.15 (s, 3H), 6.46 (d, $J=7.9$ Hz, 1H), 6.95–6.98 (m, 2H), 7.31 (d, $J=7.9$ Hz, 2H), 7.31 (d, $J=5.0$ Hz, 1H), 7.63 (d, $J=8.3$ Hz, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 17.1, 21.6, 24.3, 30.9, 39.2, 104.8, 124.4, 124.8, 125.9, 126.5, 128.0, 129.4, 132.8, 133.6, 134.3, 135.3, 136.7, 139.3, 139.6, 143.4; IR thin film, ν (cm^{-1}) 620 (s), 677 (s), 730 (m), 815 (m), 847 (m), 881 (m), 919 (m), 1043 (m), 1089 (m), 1155 (s), 1170 (m), 1346 (s), 1470 (m), 1597 (w), 2938 (m); HRMS (ESI) Calc'd for $\text{C}_{21}\text{H}_{22}\text{NO}_2\text{S}_2$: 384.1086 ($\text{M}+\text{H}^+$), found 384.1100.

methyl 9-methyl-4,5-dihydronaphtho[1,2-*b*]thiophene-8-carboxylate (**3k**)

Following the general procedure methyl 3-iodo-2-methylbenzoate **1h** (83.0 mg, 0.300 mmol) and 3-(2-bromoethyl)thiophene **2a** (115 mg, 0.600 mmol) were reacted at 95 °C for 14 hours. The crude mixture was purified by flash chromatography on silica gel (R_f 0.38 in 5% Et_2O /hexane) using 2.5% to 5% Et_2O /hexane to afford **3k** as a viscous yellow oil. Isolated yield: 55 mg (71%). ^1H NMR (300 MHz, CDCl_3) δ 2.77–2.83 (m, 2H), 2.81 (s, 3H), 2.89–2.95 (m, 2H), 3.90 (s, 3H), 6.97 (d, $J=5.3$ Hz, 1H), 7.14 (d, $J=7.9$ Hz, 1H), 7.31 (d, $J=5.0$ Hz, 1H), 7.53 (d, $J=7.9$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 19.5, 24.3,

31.6, 52.3, 124.7, 125.8, 126.8, 127.9, 132.8, 133.3, 139.9, 140.6, 169.5; IR thin film, ν (cm^{-1}) 415 (s), 651 (m), 685 (w), 720 (m), 751 (m), 776 (w), 818 (w), 913 (w), 1062 (m), 1200 (m), 1236 (m), 1282 (m), 1435 (m), 1721 (s), 2947 (m), 3420 (br, m); HRMS (EI) Calc'd for $\text{C}_{15}\text{H}_{14}\text{O}_2\text{S}$: 258.0714 (M^+), found 258.0714.

methyl (2E)-3-(1-benzothiien-3-yl)acrylate (**10**)

Benzothiophene-3-carbaldehyde (10.0 g, 61.6 mmol) was added to a solution of methyl (triphenyl-phosphoranylidene)acetate (30.9 g, 92.5 mmol) in 150 mL CH_2Cl_2 . The mixture was stirred overnight and was quenched with 100 mL H_2O , and the layers separated. The aqueous phase was then washed with 3 x 50 mL CH_2Cl_2 , and the combined organic phases dried with MgSO_4 , filtered, and concentrated *in vacuo*. The crude product was purified by flash chromatography on silica gel (R_f 0.38 in 10 % Et_2O /hexane) using 2% to 12 % Et_2O /hexane to afford **10** as a clear, pale yellow oil, slowly solidifying to a waxy, pale yellow solid (mp = 40–41 $^\circ\text{C}$). Isolated yield: 9.63 g (72 %). ^1H NMR (300 MHz, CDCl_3) δ 3.84 (s, 3H), 6.54 (d, $J=15.9$ Hz, 1H), 7.41 (td, $J=7.1$, 0.5 Hz, 1H), 7.47 (td, $J=7.1$, 1.1 Hz, 1H), 7.77 (s, 1H), 7.88 (ddd, $J=8.0$, 0.8, 0.5 Hz 1H), 7.98 (d, $J=16.2$ Hz, 1H), 8.02–8.04 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 51.9, 118.3, 122.1, 123.1, 125.0, 125.1, 128.2, 131.6, 136.6, 137.2, 140.5, 167.6; IR neat, ν (cm^{-1}) 737 (s), 761 (s), 861 (m), 974 (s), 1171 (s), 1284 (s), 1629 (s), 1718 (s), 2947 (m), 3090 (m); Elemental Anal. Calc'd for $\text{C}_{12}\text{H}_{10}\text{O}_2\text{S}$: C: 66.03 % (found 66.07 %), H: 4.62 % (found 4.66 %).

methyl 3-(1-benzothiien-3-yl)propanoate (**11**)

Compound **10** (10.93 g, 50.1 mmol) was dissolved in 250 mL EtOAc , and 10 % Pd/C (1.0 g) was added. The mixture was shaken under 40 psig $\text{H}_{2(\text{g})}$ in a Parr Hydrogenator for 6 hours. The mixture was then filtered through a pad of celite, rinsed with EtOAc , and concentrated, yielding **11** as a clear, colourless oil. Isolated yield: 10.63 g (96 %); under the same reaction conditions on a ~ 1 mmol scale, a quantitative yield was obtained. ^1H NMR (300 MHz, CDCl_3) δ 2.74 (t, $J=7.8$ Hz, 2H), 3.17 (t, $J=7.6$ Hz, 2H), 3.67 (s, 3H), 7.10 (s, 1H), 7.29–7.39 (m, 2H), 7.71–7.75 (m, 1H), 7.81–7.85 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 23.8, 33.6, 51.7, 121.5, 121.7, 122.9, 124.0, 124.3, 134.9, 138.6, 140.5,

173.2; IR neat, ν (cm⁻¹) 734 (m), 762 (m), 1160 (m), 1196 (m), 1437 (m), 1459 (m), 1734 (s), 2949 (m), 3447 (br, w); HRMS (EI) Calc'd for C₁₂H₁₂O₂S: 220.0558 (M⁺), found 220.0555.

3-(1-benzothien-3-yl)propan-1-ol (**12**)

LiAlH₄ (2.07 g, 154 mmol) was suspended in 60 mL THF at room temperature. To this was added **11** (8.00 g, 36.3 mmol) in 180 mL THF *via* cannula. The mixture was stirred for 2 h, and was quenched by addition of 2 mL H₂O, then 2 mL 5 N NaOH, followed by 5 mL H₂O, and stirred overnight. The mixture was then filtered through a pad of celite, and concentrated *in vacuo*. The mixture was overweight, and was thus taken up in EtOAc and washed with 10% HCl_(aq), followed by a wash with sat. NaHCO_{3(aq)}, then dried with MgSO₄, filtered, and concentrated *in vacuo*. The crude mixture was then purified by flash chromatography on silica gel (R_f 0.15 in 30% Et₂O/hexane) using 20% to 60% EtOAc/hexane to yield **12** as a clear, pale yellow oil. Isolated yield: 5.80 g (83%). ¹H NMR (400 MHz, CDCl₃) δ 1.65 (br s, 1H), 1.96–2.03 (m, 2H), 2.93 (td, *J*=7.6, 0.8 Hz, 2H), 3.71 (t, *J*=6.3 Hz, 2H), 7.09 (s, 1H), 7.30–7.39 (m, 2H), 7.75 (dd, *J*=7.1, 1.4 Hz, 1H), 7.84 (dd, *J*=7.0, 1.3 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 24.8, 32.0, 62.3, 121.3, 121.7, 123.0, 123.9, 124.3, 136.3, 139.0, 140.5; IR neat, ν (cm⁻¹) 733 (s), 761 (s), 831 (m), 852 (m), 918 (m), 1020 (s), 1057 (s), 1157 (m), 1256 (m), 1427(s), 1458 (s), 1785 (w), 1904 (w), 1942 (w), 2874 (s), 1939 (s), 3333 (br, s); HRMS (EI) Anal. Calc'd for C₁₁H₁₂OS: 192.0609 (M⁺), found 192.0608.

3-(3-bromopropyl)-1-benzothiophene (**4**)

PPh₃ (6.01 g, 22.9 mmol) was dissolved in 150 mL CH₂Cl₂, and Br₂ (3.66 g, 22.9 mmol) in 100 mL CH₂Cl₂ was added *via* cannula, and stirred for 5 minutes. To this mixture was added **12** (4.00 g, 20.8 mmol) in 150 mL CH₂Cl₂ *via* cannula, and the mixture stirred for 6 hours. The reaction was quenched by addition of 200 mL H₂O, and the layers separated. The aqueous phase was then washed with 2 x 100 mL CH₂Cl₂, and the combined organic phases dried with MgSO₄, filtered, and concentrated *in vacuo*. The crude product mixture was triturated with hexane, and the hexane phase was loaded onto a 2 cm pad of silica gel (in a Buchner funnel) and hexane passed through until all product eluted (R_f 0.79 in 10 %

Et₂O/hexane), affording **4** as a clear oil. Isolated yield: 4.42 g (83 %). ¹H NMR (400 MHz, CDCl₃) δ 2.25–2.32 (m, 2H), 3.04 (td, *J*=7.2, 0.9 Hz, 2H), 3.46 (t, *J*=6.5 Hz, 2H), 7.15 (s, 1H), 7.33–7.41 (m, 2H), 7.75–7.78 (m, 1H), 7.85–7.88 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 26.9, 32.1, 33.5, 121.8, 122.1, 123.1, 124.1, 124.5, 135.0, 138.9, 140.7; IR neat, ν (cm⁻¹) 733 (s), 761 (s), 856 (m), 1243 (m), 1427 (s), 1458 (m), 1904 (w), 1942 (w), 2938 (m), 2958 (m), 3066 (m); HRMS (EI) Anal. Calc'd for C₁₁H₁₁BrS: 253.9765 (M⁺), found 253.9767.

1-Methyl-2-nitro-6,7-dihydro-5*H*-benzo[*b*]benzo[3,4]cyclohepta[1,2-*d*]thiophene (**5a**)

Following the general procedure 2-iodo-6-nitrotoluene **1a** (79.0 mg, 0.300 mmol) and 3-(3-bromopropyl)-1-benzothiophene **4** (153 mg, 0.600 mmol) were reacted at 95 °C for 20 hours. The crude mixture was purified by flash chromatography on silica gel (*R*_f 0.49 in 5 % Et₂O/hexane) using 0% to 5 % Et₂O/hexane to afford **5a** as a clear yellow oil, slowly crystallizing to a yellow solid (mp = 162–164 °C). Isolated yield: 72 mg (77 %). ¹H NMR (300 MHz, CDCl₃) δ 2.20–2.60 (m, 5H), 2.64 (s, 3H), 2.95–3.18 (br s, 1H), 7.29 (d, *J*=8.2 Hz, 1H), 7.36–7.47 (m, 2H), 7.77 (d, *J*=8.5 Hz, 1H), 7.80 (dd, *J*=7.0, 1.5 Hz, 1H), 7.88–7.92 (m, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 18.1, 22.2, 33.1, 33.3, 121.7, 122.5, 123.7, 124.2, 124.8, 127.4, 131.2, 133.5, 136.4, 136.8, 138.0, 140.7, 146.7, 150.1; IR thin film, ν (cm⁻¹) 734 (s), 759 (s), 1085 (m), 1347 (s), 1433 (s), 1448 (s), 1520 (s), 1592 (s), 1785 (w), 1904 (w), 2860 (s), 2944 (s), 3059 (m); HRMS (EI) Anal. Calc'd for C₁₈H₁₅NO₂S: 309.0823 (M⁺), found 309.0818.

N-(1-methyl-6,7-dihydro-5*H*-benzo[*b*]benzo[3,4]cyclohepta[1,2-*d*]thien-2-yl)acetamide (**5b**)

Following the general procedure *N*-(3-iodo-2-methylphenyl)acetamide **1b** (82.0 mg, 0.300 mmol) and 3-(3-bromopropyl)-1-benzothiophene **4** (153 mg, 0.600 mmol) were reacted at 105 °C for 24 h. The crude mixture was purified by flash chromatography on silica gel (*R*_f 0.29 in 60% EtOAc/hexane) using 50% to 60% EtOAc/hexane to afford an impure product. The crude product was then recrystallized from hot Et₂O to afford **5b** as a powdery, off-white solid (mp = 213–216 °C). Isolated yield: 59 mg (61 %). ¹H NMR (400 MHz, CDCl₃) δ 1.92–2.32 (m, 3H), 2.23 (s, 3H), 2.34–3.17 (m, 3H), 2.42 (s, 3H), 7.02 (br s, 1H), 7.18 (d, *J*=7.9 Hz, 1H), 7.34 (t, *J*=7.4 Hz, 1H), 7.40 (t, *J*=7.4 Hz, 1H), 7.61 (d, *J*=7.9 Hz, 1H), 7.78 (d, *J*=7.9 Hz, 1H), 7.86 (d, *J*=7.9 Hz, 1H); ¹³C NMR (125

MHz, CDCl₃) δ 16.4, 22.5, 24.4, 32.8, 33.7, 105.0, 121.7, 122.6, 124.2, 124.4, 124.6, 127.5, 129.3, 134.6, 135.1, 135.5, 135.8, 138.7, 139.3, 140.8, 168.7; IR thin film, ν (cm⁻¹) 730 (s), 755 (m), 825 (w), 908 (m), 1015 (w), 1108 (w), 1300 (m), 1369 (m), 1435 (m), 1520 (s), 1652 (s), 2856 (s), 2932 (s), 3263 (br, s); HRMS (EI) Calc'd for C₂₀H₁₉NOS: 321.1187 (M⁺), found 321.1190.

2-chloro-1-methyl-6,7-dihydro-5*H*-benzo[*b*]benzo[3,4]cyclohepta[1,2-*d*]thiophene (**5c**)

Following the general procedure 2-chloro-6-iodotoluene **1c** (76.0 mg, 0.300 mmol) and 3-(3-bromopropyl)-1-benzothiophene **4** (153 mg, 0.600 mmol) were reacted at 95 °C for 18 h. The crude mixture was purified by flash chromatography on silica gel (R_f 0.32 in hexane) using hexane to afford **5c** as a clear viscous oil, slowly solidifying to a powdery white solid (mp = 123–125 °C). Isolated yield: 40 mg (45 %). ¹H NMR (300 MHz, CDCl₃) δ 2.15–2.55 (m, 5H), 2.58 (s, 3H), 3.02 (br s, 1H), 7.09 (d, *J*=7.9 Hz, 1H), 7.32 (d, *J*=8.2 Hz, 1H), 7.32–7.44 (m, 2H), 7.78 (dd, *J*=7.5, 1.9 Hz, 1H), 7.88 (dt, *J*=7.9, 1.0 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 18.7, 22.3, 32.6, 33.4, 121.5, 122.4, 124.0, 124.3, 127.6, 128.7, 133.5, 134.5, 135.1, 135.6, 135.9, 138.3, 140.0, 140.5; IR thin film, ν (cm⁻¹) 636 (s), 668 (s), 730 (m), 816 (w), 1021 (m), 1081 (m), 1456 (m), 1539 (m), 1558 (s), 2337 (s), 2918 (s); HRMS (EI) Calc'd for C₁₈H₁₅ClS: 298.0583 (M⁺), found 298.0586.

10-methyl-9-nitro-5,6-dihydro-4*H*-benzo[6,7]cyclohepta[1,2-*b*]furan (**7a**)

Using the general procedure, 5-nitro-2-iodotoluene **1a** (68.0 mg, 0.260 mmol) and 3-(3-bromopropyl)furan **6** (100 mg, 0.530 mmol) were reacted at 105 °C. The crude product was purified by column chromatography on silica gel (R_f = 0.54 in 5 % Et₂O/hexane) using 1 % Et₂O/hexane to afford **7a** as a clear yellow oil. Isolated yield: 34 mg (54 %). ¹H NMR (400 MHz, CDCl₃) δ 2.07–2.14 (m, 2 H), 2.54 (s, 3 H), 2.62–2.67 (m, 4 H), 6.40 (d, *J*=1.8 Hz, 1 H), 7.13 (d, *J*=8.3 Hz, 1 H), 7.50 (d, *J*=1.8 Hz, 1 H), 7.61 (d, *J*=8.3 Hz, 1 H); ¹³C NMR (100 MHz, CDCl₃) δ 17.8, 23.8, 29.9, 34.0, 113.1, 122.4, 125.2, 127.1, 130.8, 132.8, 142.0, 146.7 (2 C); IR neat, ν (cm⁻¹) 681 (m), 758 (s), 823 (m), 894 (s), 967 (w), 1060 (m), 1086 (m), 1161 (m), 1187 (m), 1236 (w), 1348 (s), 1519 (s), 2865 (m), 2941 (s); HRMS (EI) Anal. Calc'd for C₁₄H₁₃NO₃: 243.0895 (M⁺), found 243.0901.

9-chloro-10-methyl-5,6-dihydro-4*H*-benzo[6,7]cyclohepta[1,2-*b*]furan (**7b**)

Following the general procedure 2-chloro-6-iodotoluene **1c** (76.0 mg, 0.300 mmol) and 3-(3-bromopropyl)furan **6** (113 mg, 0.600 mmol) were reacted at 105 °C for 20 hours. The crude mixture was purified by flash chromatography on silica gel (R_f 0.61 in hexane) using hexane to afford **7b** as a clear, viscous oil. Isolated yield: 37 mg (53%). ^1H NMR (300 MHz, CDCl_3) δ 2.01–2.11 (m, 2H), 2.51 (s, 3H), 2.53–2.56 (m, 2H), 2.58 (q, $J=7.5$ Hz, 2H), 6.37 (d, $J=1.8$ Hz, 1H), 6.97 (d, $J=8.0$ Hz, 1H), 7.20 (d, $J=8.2$ Hz, 1H), 7.45 (d, $J=1.8$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 18.6, 23.9, 30.6, 33.8, 113.3, 124.2, 127.7, 128.0, 132.3, 133.7, 134.4, 140.8, 141.5, 148.1; IR thin film, ν (cm^{-1}) 501 (s), 690 (w), 739 (m), 770 (m), 807 (m), 889 (m), 909 (w), 965 (w), 1037 (m), 1085 (m), 1464 (m), 1802 (w), 2936 (m); HRMS (EI) Calc'd for $\text{C}_{14}\text{H}_{13}\text{ClO}$: 232.0655 (M^+), found 232.0652.

Representative Spectra (in numerical order)

Compound **1b**

Compound **1g**

Compound **2a** (for purity)

See: Moustrou, C.; Samat, A.; Guglielmetti, R.; Dubest, R.; Garnier, F. *Helv. Chim. Acta* **1995**, 78, 1887–1893.

Compound **2b** (for purity)

Compound 3a

Compound 3b

Compound 3c

Compound 3d

Compound 3e

Compound 3f

Compound 3g

Compound 3h

Compound **3i**

Compound 3j

Compound 3k

Compound 4

Compound **5a**

Compound 5b

Compound 5c

Compound **6** – for purity

Compound **7a**

Compound 7b

Compound 9

Compound 10

Compound 11

Compound 12