Selectively Substituted Thiophenes and Indoles by a Tandem Palladium Catalyzed Multicomponent Reaction

Koichi Mitsudo, Praew Thansandote, Thorsten Wilhelm, Brian Mariampillai and Mark Lautens*

General. ^1H and ^{13}C NMR spectra were recorded in CDCl_3 with chemical shifts using TMS or residual chloroform as internal standard. High-resolution mass spectra were obtained at 70 eV. Unless otherwise noted, all materials were obtained from commercial suppliers and used without further purification. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were freshly distilled under nitrogen from sodium benzophenone ketyl prior to use. Acetonitrile was distilled from CaH_2 . 3-Phenyl-1-iodopropane ¹ and 3-(*tert*-butyldimethylsiloxy)-1-iodopropane, ² were prepared according to literature procedures. All reactions were performed under nitrogen.

General procedure for Sequential Alkylation/Alkenylation Reaction of 1 with Alkyl Halide and Olefins (2a). A mixture of 3-iodothiophene (42 mg, 0.2 mmol), 1-iodobutane (368 mg, 2.0 mmol), *tert*-butyl acrylate (53 mg, 0.4 mmol), $\text{Pd}(\text{OAc})_2$ (4.5 mg, 10 mol %), TFP (9.3 mg, 20 mol %), norbornene (113 mg, 1.2 mmol), and Cs_2CO_3 (326 mg, 1.0 mmol) in dry CH_3CN (2.0 mL) was stirred at 80°C for 20 h under nitrogen. After cooling to room temperature, the resulting mixture was treated with water and extracted with Et_2O (3×2 mL). The combined organic phase was dried over MgSO_4 and concentrated under reduced pressure. The residue was purified by chromatography on silica gel (hexane/ AcOEt = 20/1 – 10/1) to afford **2a** (59 mg, 91%) as pale yellow oil.

3-(2-*tert*-Butoxycarbonyl)vinyl-2,4-(butan-1-yl)thiophene (2a). ^1H NMR (300 MHz, CDCl_3): δ 7.63 (d, J = 16.2 Hz, 1H), 6.73 (s, 1H), 6.03 (d, J = 16.2 Hz, 1H), 2.89 (t, J = 7.5 Hz, 2H), 2.62 (t, J = 7.5 Hz, 2H), 1.72–1.24 (m, 8H), 1.54 (s, 9H), 0.95 (t, J = 7.5 Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 167.0, 148.1, 142.8, 136.5, 131.0, 120.2, 117.1, 80.2, 33.5, 31.5. IR (neat): 3405, 2956, 2931, 2867, 1708, 1627, 1456, 1367, 1296, 1150 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{19}\text{H}_{30}\text{O}_2\text{S}$: 322.2, found 322.4856.

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(2) Heslin, J. C.; Moody, C. J. *J. Chem. Soc., Perkin Trans. I* **1988**, 1417–1423.

2,4-Di(butan-1-yl)-3-[(2-ethoxycarbonyl)vinyl]thiophene (2b). ^1H NMR (300 MHz, CDCl_3): δ 7.72 (d, $J = 16.2$ Hz, 1H), 6.74 (s, 1H), 6.11 (d, $J = 16.2$ Hz, 1H), 4.27 (q, $J = 7.2$ Hz, 2H), 2.90 (t, $J = 7.2$ Hz, 2H), 2.63 (t, $J = 7.2$ Hz, 2H), 1.72–1.54 (m, 4H), 1.49–1.25 (m, 4H), 1.34 (t, $J = 7.2$ Hz, 3H), 0.95 (t, $J = 7.2$ Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 167.6, 148.6, 142.7, 137.5, 130.8, 118.2, 117.2, 60.3, 33.5, 31.5, 30.0, 29.1, 22.5, 22.4, 14.3, 13.9, 13.8. IR (neat): 2958, 2931, 2872, 1714, 1628, 1465, 1292, 1176, 1040 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{17}\text{H}_{26}\text{O}_2\text{S}$: 294.1654, found 294.1661.

2,4-Di(butan-1-yl)-3-[(2-methoxycarbonyl)vinyl]thiophene (2c). ^1H NMR (300 MHz, CDCl_3): δ 7.72 (d, $J = 16.2$ Hz, 1H), 6.74 (s, 1H), 6.12 (d, $J = 16.2$ Hz, 1H), 3.81 (s, 3H), 2.89 (t, $J = 7.2$ Hz, 2H), 2.63 (t, $J = 7.2$ Hz, 2H), 1.72–1.54 (m, 4H), 1.49–1.33 (m, 4H), 0.95 (t, $J = 7.5$ Hz, 6H); ^{13}C NMR (75 MHz): δ 168.0, 148.7, 142.8, 137.8, 130.8, 117.9, 117.3, 51.6, 33.5, 31.5, 30.0, 29.2, 22.5, 22.4, 13.9, 13.8. IR (neat): 2957, 2930, 1722, 1629, 1465, 1434, 1296, 1193, 1171 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{16}\text{H}_{24}\text{O}_2\text{S}$: 280.1497, found 280.1498.

2,4-Di(butan-1-yl)-3-[(2-*N,N*-dimethylaminocarbonyl)vinyl]thiophene (2d). ^1H NMR (300 MHz, CDCl_3): δ 7.69 (d, $J = 15.6$ Hz, 1H), 6.74 (s, 1H), 6.55 (d, $J = 15.6$ Hz, 1H), 3.13 (s, 3H), 3.08 (s, 3H), 2.89 (t, $J = 7.8$ Hz, 2H), 2.63 (t, $J = 7.8$ Hz, 2H), 1.72–1.55 (m, 4H), 1.48–1.33 (m, 4H), 0.94 (t, $J = 7.2$ Hz, 6H); ^{13}C NMR (100 MHz, CDCl_3): δ 167.1, 146.7, 142.5, 135.5, 131.9, 118.1, 117.1, 37.2, 35.8, 33.6, 31.6, 30.1, 29.1, 22.5, 22.4, 13.9, 13.8. IR (neat): 3406 (br), 2957, 2930, 2238, 1737, 1651, 1607, 1466, 1393, 1144 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{17}\text{H}_{27}\text{NOS}$: 293.1813, found 293.1815.

2,4-Di(butan-1-yl)-3-[(2-*N*-tert-butylaminocarbonyl)vinyl]thiophene (2e). ^1H NMR (300 MHz, CDCl_3): δ 7.62 (d, $J = 15.6$ Hz, 1H), 6.72 (s, 1H), 5.98 (d, $J = 15.6$ Hz, 1H), 5.41 (br s, 1H), 2.88 (t, $J = 7.8$ Hz, 2H), 2.61 (t, $J = 7.8$ Hz, 2H), 1.72–1.55 (m, 4H), 1.50–1.32 (m, 4H), 1.44 (s, 9H), 0.94 (t, $J = 7.2$ Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 165.7, 146.9, 142.6, 133.6, 131.3, 122.3, 116.9, 51.5, 33.5, 31.4, 30.0, 29.1, 28.9, 22.52, 22.46, 13.99, 13.87. IR (thin film): 3268, 3071, 2959, 2928, 1652, 1613, 1556, 1453, 1363, 1248, 1226 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{19}\text{H}_{31}\text{NOS}$: 321.2126, found 321.2120.

2,4-Di(butan-1-yl)-3-(3-oxopent-1-enyl)thiophene (2f). ^1H NMR (300 MHz, CDCl_3): δ 7.61 (d, $J = 16.5$ Hz, 1H), 6.76 (s, 1H), 6.45 (d, $J = 16.5$ Hz, 1H), 2.90 (t, $J = 7.8$ Hz, 2H), 2.66 (quintet, $J = 7.2$ Hz, 4H), 1.73–1.34 (m, 8H), 1.18 (t, $J = 7.2$ Hz, 3H), 0.95 (t, $J = 7.2$ Hz, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 201.2, 149.0, 142.8, 135.2, 130.9, 126.2, 117.4, 34.2, 33.5, 31.5, 30.1, 29.3, 22.5, 22.4, 13.9, 13.8, 8.3. IR (neat): 2928, 1743, 1693, 1667, 1602, 1538, 1461, 1194, 1119, 1040 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{17}\text{H}_{26}\text{OS}$: 278.1704, found 278.1702.

2,4-Bis[3-(tert-butyldimethylsiloxy)propyl]-3-[(2-ethoxycarbonyl)vinyl]thiophene (2g). ^1H NMR (300 MHz, CDCl_3): δ 7.70 (d, $J = 16.5$ Hz, 1H), 6.77 (s, 1H), 6.15 (d, $J = 16.5$ Hz, 1H), 4.25 (q, $J = 7.2$ Hz, 2H), 3.68 (tm, $J = 4.3$ Hz, 4H), 2.98 (t, $J = 7.2$ Hz, 2H), 2.70 (t, $J = 7.2$ Hz, 2H), 1.95–1.78 (m, 4H), 1.33 (t, $J = 7.2$ Hz, 3H), 0.90 (s, 18H), 0.06 (s, 12H); ^{13}C NMR (100 MHz, CDCl_3): δ 167.4, 147.8, 142.1, 137.2, 131.1, 118.8, 117.5, 62.4, 61.9, 60.2, 34.2, 32.3, 26.6, 25.92, 25.91, 25.8, 18.29, 18.27, 14.3, –5.35, –5.37. IR (neat): 2956, 2929, 2857, 1716, 1629, 1472, 1256, 1175, 1103 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{26}\text{H}_{47}\text{O}_4\text{SSi}_2$ [$\text{M} - \text{CH}_3$] $^+$: 511.2734, found 511.2726.

2,4-Bis(3-phenylpropyl)-3-[(2-ethoxycarbonyl)vinyl]thiophene (2h). ^1H NMR (300 MHz, CDCl_3): δ 7.68 (d, $J = 16.2$ Hz, 1H), 7.34–7.12 (m, 10H), 6.77 (s, 1H), 6.06 (d, $J = 16.2$ Hz, 1H), 4.27 (q, $J = 7.2$ Hz, 2H), 2.94 (t, $J = 7.5$ Hz, 2H), 2.75–2.60 (m, 6H), 2.08–1.88 (m, 4H), 1.35 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (75 MHz): δ 167.4, 147.8, 142.2, 142.0, 141.5, 137.3, 131.2, 128.40, 128.36, 128.27, 125.9, 125.8, 118.8, 117.7, 60.4, 35.6, 35.4, 32.9, 31.0, 29.9, 29.0, 14.4. IR (neat): 3027, 2937, 2860, 2252, 1735, 1711, 1627, 1496, 1454, 1366, 1290, 1264, 1174, 1032 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{27}\text{H}_{30}\text{O}_2\text{S}$: 418.1966, found 418.1963.

3-(2-tert-Butoxycarbonyl)vinyl-2,4-bis(3-chloropropyl)thiophene (2i). ^1H NMR (300 MHz, CDCl_3): δ 7.60 (d, $J = 16.2$ Hz, 1H), 6.83 (s, 1H), 6.06 (d, $J = 16.2$ Hz, 1H), 3.59 (t, $J = 6.3$ Hz, 2H), 3.57 (t, $J = 6.3$ Hz, 2H), 3.08 (t, $J = 7.5$ Hz, 2H), 2.82 (t, $J = 7.5$ Hz, 2H), 2.23–1.99 (m, 4H), 1.54 (s, 9H); ^{13}C NMR (75 MHz): δ 145.5, 140.7, 135.8, 131.6, 121.3, 118.6, 80.6, 44.2, 43.8, 33.7, 31.9, 28.2, 27.1, 26.3. IR (neat): 2958, 1704, 1628, 1455, 1392, 1367, 1299, 1152 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{17}\text{H}_{24}\text{Cl}_2\text{O}_2\text{S}$: 362.0874, found 362.0876.

2-(butan-1-yl)-3-[(2-tert-butylcarbonyl)vinyl]benzo[*b*]thiophene (6). ^1H NMR (300 MHz, CDCl_3): δ 7.97 (d, $J = 7.8$ Hz, 1H), 7.87 (d, $J = 16.2$ Hz, 1H), 7.78 (d, $J = 7.8$ Hz, 1H), 7.41 (td, $J = 7.8$, 1.2 Hz, 1H), 7.32 (td, $J = 7.8$, 1.2 Hz, 1H), 6.41 (d, $J = 16.2$ Hz, 1H), 3.03 (t, $J = 7.8$ Hz, 2H), 1.74 (quintet, $J = 7.5$ Hz, 2H), 1.57 (s, 9H), 1.45 (sextet, $J = 7.5$ Hz, 2H), 0.97 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 166.9, 150.0, 138.3, 138.0, 135.4, 126.6, 124.7, 124.1, 122.31, 122.29, 120.85, 80.5, 33.5, 29.0, 28.3, 22.4, 13.8. IR (neat): 2960, 2931, 1708, 1627, 1460, 1367, 1293, 1256, 1151 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{19}\text{H}_{24}\text{O}_2\text{S}$: 316.1497, found 316.1489.

(3,4-Dihydro-2H-dibenzothiophen-1-ylidene)-acetic acid ethyl ester (7): Pd(OAc)₂ (4.5 mg, 0.02 mmol, 0.1 equiv), PPh₃ (10.5 mg, 0.04 mg, 0.2 equiv), 3-iodobenzothiophene (52.0 mg, 0.2 mmol, 1 equiv), Cs₂CO₃ (325 mg, 1.0 mmol, 5 equiv), norbornene (113 mg, 1.2 mmol, 6 equiv) and 6-Bromo-hex-2-enoic acid ethyl ester (88.4 mg, 0.4 mmol, 2 equiv), were dissolved in 2 mL dry acetonitrile under nitrogen. The reaction mixture was heated to 180°C in the microwave for 5 min. The mixture was cooled to room temperature, diluted with pentane, hydrolyzed with water and extracted with pentane or ether. After drying with MgSO₄, the crude product was purified by chromatography (silica, hexane/EtOAc 95:5) to afford **7** (30 .0 mg, 55%): ¹H NMR (300 MHz, CDCl₃): δ 8.10 (d, *J*=8.1 Hz, 1H), 7.78 (d, *J*=7.8 Hz, 1H), 7.43-7.29 (m, 2H), 6.51 (s, 1H), 4.23 (q, *J*=7.2 Hz, 2H), 3.26 (t, *J*= 8.6 Hz, 2H), 3.00 (t, *J*=6.3 Hz, 2H), 2.05 (quintet, *J*=6.3 Hz, 2H), 1.34 (t, *J*=6.9 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 167.5, 151.2, 147.7, 138.5, 136.5, 129.2, 124.9, 124.1, 122.9, 122.6, 112.3, 59.8, 27.5, 26.6, 23.8, 14.4; IR (neat): 2253, 1700, 1458, 1153, 909, 737 cm⁻¹; HRMS (EI) *m/z* calcd for C₁₆H₁₆O₂S: 272.0871, found 272.0871.

Halogen–magnesium Exchange Reaction of 2,3-Diiodothiophene (8). To a solution of 2,3-diiodothiophene (168 mg, 0.5 mmol) in THF (2.0 mL) was added a solution of EtMgCl (2.0 M, 0.55 mmol) at 0 °C. The mixture was warmed to room temperature and stirred for 30 min. Thereafter, iodobenzene (144 mg, 0.60 mmol) and Pd(PPh₃)₄ were added to the mixture, followed by heating at 60 °C for 5 h. The resulting mixture was quenched with H₂O and was extracted with Et₂O (3 × 5 mL). The combined organic layer was dried over MgSO₄ and subsequent silica gel chromatography (hexane/EtOAc = 5/1) afforded 3-iodo-2-phenylthiophene (**8**, 115 mg, 80%). ¹H NMR (300 MHz, CDCl₃): δ 7.62–7.57 (m, 2H), 7.46–7.34 (m, 3H), 7.27 (d, *J* = 5.4 Hz, 1H), 7.13 (d, *J* = 5.4 Hz, 1H); ¹³C NMR (75 MHz): δ 142.4, 136.5, 134.2, 129.4, 128.40, 128.35, 126.7, 78.1. IR (neat): 3104, 1598, 1482, 1444, 1336, 1137, 1074, 1031 cm⁻¹. HRMS (EI) *m/z* calcd for C₁₀H₇SI: 285.9313, found 285.9319.

4-(butan-1-yl)-3-[(2-ethoxycarbonyl)vinyl]-2-phenylthiophene (9). ^1H NMR (300 MHz, CDCl_3): δ 7.70 (d, $J = 16.5$ Hz, 1H), 7.44–7.32 (m, 5H), 6.96 (s, 1H), 6.09 (d, $J = 16.5$ Hz, 1H), 4.20 (q, $J = 7.5$ Hz, 2H), 2.72 (t, $J = 7.5$ Hz, 2H), 1.68 (quintet, $J = 7.5$ Hz, 2H), 1.45 (sextet, $J = 7.5$ Hz, 2H), 1.28 (t, $J = 7.5$ Hz, 3H), 0.98 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 167.4, 146.5, 143.1, 138.2, 134.1, 131.2, 129.7, 128.7, 128.2, 120.2, 119.3, 60.3, 31.5, 30.2, 22.5, 14.3, 14.0. IR (neat): 2958, 2928, 2867, 1712, 1628, 1454, 1303, 1259, 1165 cm^{-1} . HRMS (EI) m/z calcd for $\text{C}_{19}\text{H}_{23}\text{O}_2\text{S}$ [$\text{M} + \text{H}$]: 314.1413, found 1426.

General procedure for double ortho-alkylation/C-H coupling to produce 2,4-disubstituted thiophenes. $\text{Pd}(\text{OAc})_2$ (5.3 mg, 0.0238 mmol, 0.1 equiv), PPh_3 (12.5 mg, 0.0476 mmol, 0.238 equiv) and molecular sieves (powder, 4 Å, 50 mg) were dissolved in absolute acetonitrile (0.6 mL) under nitrogen and stirred for 15 min. In a 10 mL round bottom flask fused with a condenser was added 3-iodothiophene (0.238 mmol, 1 equiv), Cs_2CO_3 (387 mg, 1.19 mmol, 5 equiv), norbornene (135 mg, 1.428 mmol, 6 equiv) the alkyl halide (2.38 mmol, 10 equiv), 0.1 mL DMPU and 0.6 mL acetonitrile. The mixture was heated to 80°C, followed by addition of the catalyst mixture. Isopropylboronic acid (31.4 mg, 0.357 mmol, 1.5 equiv) dissolved in 1.0 mL acetonitrile was then added at a rate of 0.08 mL/h via syringe pump. After the 24 h addition terminated, the mixture was allowed to stir for another 24 hours at 80°C. The mixture was then cooled to room temperature and filtered through celite. The crude product was purified by chromatography (silica, hexane/EtOAc = 10/1 – 1/2).

2,4-di(4-propylethoxycarbonyl)thiophene (10a). ^1H NMR (300 MHz, CDCl_3): δ 6.72 (s, 1H), 6.63 (s, 1H), 4.13 (dd, $J = 7.2$ Hz & 2.7 Hz, 4H); 2.81 (t, $J = 7.5$ Hz, 2H), 2.59 (t, $J = 7.5$ Hz, 2H); 2.36 (t, $J = 7.5$ Hz, 2H), 2.32 (t, $J = 7.5$ Hz, 2H), 2.03–1.90 (m, 4H). ^{13}C NMR (75 MHz, CDCl_3): δ 173.5, 144.5, 141.7, 126.0, 118.5, 66.1, 60.5, 60.5, 34.0, 30.0, 29.6, 27.0, 25.8, 15.5, 14.5; IR (neat): 1729, 1446, 1375, 1187, 1027, 909, 735 cm^{-1} ; HRMS (ESI) m/z calcd for $[\text{C}_{16}\text{H}_{24}\text{O}_4\text{SH}]^+$:

313.1474, found 313.1468.

2,4-di(3-propyloxiranyl)thiophene (10b). ^1H NMR (300 MHz, CDCl_3): δ 6.71 (s, 1H), 6.63 (s, 1H), 2.96-2.85 (m, 2H), 2.83 (t, $J = 7.5$ Hz, 2H), 2.77-2.73 (m, 2H), 2.61 (t, $J = 7.5$ Hz, 2H), 2.49-2.45 (m, 2H), 1.84-1.76 (m, 4H), 1.62-1.57 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3): δ 142.3, 129.8, 118.0, 66.1, 60.6, 52.4, 52.2, 47.2, 32.0, 30.0, 21.3, 15.5, 14.3; IR (neat): 1718, 1653, 909, 734 cm^{-1} ; HRMS (ESI) m/z calcd for $[\text{C}_{14}\text{H}_{20}\text{O}_2\text{SNa}]^+$: 275.1082, found 275.1076.

2,4-di[2-(1,3-dioxolanyl)]thiophene (10c). ^1H NMR (300 MHz, CDCl_3): δ 6.73 (s, 1H), 6.67 (s, 1H), 4.93-4.87 (m, 2H), 3.99-3.97 (m, 4H), 3.89-3.84 (m, 4H), 2.91 (t, $J = 7.5$ Hz, 2H), 2.68 (t, $J = 8.1$ Hz, 2H), 2.06-1.92 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3): δ 144.4, 141.5, 125.6, 117.8, 103.8, 103.5, 65.0, 64.9, 35.6, 34.5, 24.9, 24.5; IR (neat): 1718, 1395, 1139, 1034, 910, 734 cm^{-1} ; HRMS (EI) m/z calcd for $\text{C}_{14}\text{H}_{20}\text{O}_4\text{S} [\text{M}^+]$: 284.1082, found 284.1082.

2,4-di(3-propyl-N-phthalimidyl)thiophene (10d). ^1H NMR (300 MHz, CDCl_3): δ 7.85-7.80 (m, 4H), 7.72-7.68 (m, 4H), 6.71 (s, 1H), 6.65 (s, 1H), 3.74 (q, $J = 6.9$ Hz, 4H), 2.79 (t, $J = 6.9$ Hz, 2H), 2.58 (t, $J = 7.5$ Hz, 2H), 2.07-1.94 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3): δ 168.3, 143.9, 140.9, 133.9, 132.1, 125.6, 123.2, 123.1, 118.2, 37.7, 37.5, 30.1, 29.7, 28.7, 27.8, 27.5; IR (neat): 1771, 1710, 1653, 1398, 1370, 911, 733 cm^{-1} ; HRMS (ESI) m/z calcd for $[\text{C}_{26}\text{H}_{22}\text{N}_2\text{O}_4\text{SH}]^+$: 459.1379, found 459.1373.

2,4-di(3-propylcyano)thiophene (10e). ^1H NMR (300 MHz, CDCl_3): δ 6.82 (s, 1H), 6.67 (s, 1H), 2.96 (t, $J = 5.4$ Hz, 2H), 2.73 (t, $J = 5.7$ Hz, 2H), 2.38 (t, $J = 5.4$ Hz, 2H), 2.34 (t, $J = 5.4$ Hz, 2H), 2.05-1.92 (m, 4H); ^{13}C NMR (75 MHz, CDCl_3): δ 142.9, 139.9, 126.1, 119.7, 119.3, 119.1, 29.0, 28.7, 27.1, 26.0, 16.5, 16.3; IR (neat): 2253, 908, 735 cm^{-1} ; HRMS (EI) m/z calcd for $\text{C}_{12}\text{H}_{14}\text{N}_2\text{S}$ [M^+]: 218.0878, found 218.0878.

General procedure for C-H functionalization of the tri-substituted thiophenes (11b). A mixture of 3-(2-*tert*-Butoxycarbonyl)vinyl-2,4-di(butan-1-yl) thiophene (40 mg, 0.12 mmol), 4-iodonitrobenzene (15.4 mg, 0.062 mmol), $\text{Pd}(\text{OAc})_2$ (1.5 mg, 5 mol %), tetrabutylammonium bromide (21.4 mg, 0.16 mmol), and K_2CO_3 (21.4 mg, 0.062 mmol) in a 9:1 mixture of $\text{CH}_3\text{CN}:\text{H}_2\text{O}$ (0.6 mL) was stirred at 80 $^\circ\text{C}$ for 24 h in a sealed tube flushed with argon. After cooling to room temperature, the resulting mixture was filtered through celite. The residue was purified by chromatography on silica gel (hexane/AcOEt = 20/1 – 10/1) to afford **11b** (18.6 mg, 68%) as a yellow oil.

2,4-di(4-ethylbutanoate)-5-(4-nitrophenyl)thiophene (11a). ^1H NMR (300 MHz, CDCl_3): δ 8.25 (d, $J = 8.7$ Hz, 2H), 7.56 (d, $J = 8.7$ Hz, 2H), 6.74 (s, 1H), 4.16 (q, $J = 7.5$ Hz, 2H), 4.09 (q, $J = 6.9$ Hz, 2H), 2.86 (t, $J = 7.5$ Hz, 2H), 2.68 (t, $J = 7.5$ Hz, 2H), 2.40 (t, 7.5 Hz, 2H), 2.30 (t, $J = 7.5$ Hz, 2H), 2.07-1.88 (m, 4H), 1.30-1.20 (m, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 173.1, 146.5, 145.2, 139.2, 133.6, 129.4, 127.8, 123.9, 60.4, 33.7, 33.4, 29.3, 28.3, 26.6, 25.8, 14.2; IR (neat): 1726, 1517, 1345, 910, 732 cm^{-1} ; HRMS (ESI) m/z calcd for $[\text{C}_{22}\text{H}_{27}\text{NO}_6\text{SNa}]^+$: 456.1457, found 456.1451.

3-(2-*tert*-Butoxycarbonyl)vinyl-2,4-di(butan-1-yl)-5-(4-nitrophenyl)thiophene (11b). ^1H NMR (300 MHz, CDCl_3): δ 8.27 (d, $J = 12.0$ Hz, 2H), 7.60 (d, $J = 21.6$ Hz, 1H), 7.55 (d, $J = 11.6$ Hz, 2H), 6.06 (d, $J = 21.6$ Hz, 1H), 2.96 – 2.90 (m, 2H), 2.69 – 2.64 (m, 2H), 1.77 – 1.67 (m, 2H), 1.55 (s, 9H), 1.50 – 1.43 (m, 2H), 1.35 – 1.26 (m, 2H), 0.96 (t, $J = 9.6$ Hz, 3H), 0.87 (t, $J = 9.6$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 166.5, 147.8, 142.1, 141.6, 140.2, 136.6, 132.7, 132.4, 129.8, 129.3, 123.9, 122.2, 80.6, 33.4, 32.7, 29.7, 29.2, 28.2, 27.9, 27.5, 22.6, 22.5, 22.4, 13.8, 13.7; IR (neat): 2958, 2930, 2872, 1700, 1594, 1517, 1346, 1154, 907, 734 cm^{-1} ; HRMS (EI) m/z calcd for $\text{C}_{25}\text{H}_{33}\text{NO}_4\text{S}$ [M^+]: 443.213, found 443.2130.

3-(2-*tert*-Butoxycarbonyl)vinyl-2,4-di(butan-1-yl)-5-(4-methoxyphenyl)thiophene (11c). ^1H NMR (300 MHz, CDCl_3): δ 7.25 (d, $J = 8.7$ Hz, 2H), 6.83 (d, $J = 8.7$ Hz, 2H), 6.76 (s, 1H), 6.41 (s, 1H), 3.81 (s, 3H), 2.41 – 2.58 (m, 1H), 2.13 – 2.24 (m, 1H), 1.38 – 1.54 (m, 4H), 1.28 (s, 9H), 0.79 – 0.83 (m, 6H); ^{13}C NMR (75 MHz, CDCl_3): δ 165.7, 160.6, 148.6, 142.0, 140.6, 135.7, 131.7, 128.6, 119.5, 116.3, 114.1, 113.8, 79.7, 55.3, 33.3, 31.3, 29.7, 29.0, 28.4, 28.0, 27.8, 22.5, 22.4, 13.9, 13.8; IR (neat): 2930, 2958, 2862, 2253, 1710, 1684, 1600, 1509, 1253, 1145, 909, 735 cm^{-1} ; HRMS (EI) m/z calcd for $\text{C}_{25}\text{H}_{36}\text{O}_3\text{S}$ [M^+]: 428.238, found 428.2385.

3-Iodo-1-(toluene-4-sulfonyl)-1H-indole: To a solution of indole (2g, 17.07 mmol) and KOH (2.39g, 42.7 mmol) in DMF (30 mL) was added a solution of I_2 (4.39g, 17.28 mmol) in DMF (30 mL) dropwise over 10 minutes. The reaction was stirred for a further 30 minutes before addition of KOH (2.39g, 42.7 mmol) and tosyl chloride (6.85g, 35.9 mmol). The reaction was stirred for 8 hours,

diluted with water and extracted with Et₂O. The combined organic phase was washed with water and saturated sodium chloride and dried over anhydrous MgSO₄. The organic phase was then concentrated under reduced pressure and recrystallized from hexane and Et₂O to afford (**#**) (2.78g, 55 %) as a white crystalline solid: ¹H NMR (400 MHz, CDCl₃) δ 7.95 (d, *J*=9.0Hz, 1H), 7.77 (d, *J*=8.4Hz, 2H), 7.70 (s, 1H), 7.40-7.27 (m, 3H), 7.23 (d, *J*=8.1Hz, 2H), 2.35 (s, 3H); ¹³C-NMR (100 MHz, CDCl₃) δ 145.5, 135.1, 134.5, 132.6, 130.2, 129.9, 127.1, 125.8, 124.1, 122.1, 113.5, 67.0, 21.8; δ IR (film) 3136, 3050, 2983, 1596, 1492, 1442, 1374, 1306, 1264, 1174, 1188, 1126, 1109, 1090, 1023, 1014, 923, 894, 812, 732, 704, 657cm⁻¹; HRMS (ESI) *m/z* calcd for [C₁₅H₁₂NO₂NaS]⁺: 419.9525, found 419.9513; M.p. 131-133 °C.

3-[2-Butyl-1-(toluene-4-sulfonyl)-1H-indol-3-yl]-acrylic acid tert-butyl ester (13**):** To a vial equipped with a magnetic stir bar was added Pd(OAc)₂ (4.5mg, 10 mol %), PPh₃ (11.5mg, 22 mol %), Cs₂CO₃ (195mg, 0.6mmol), norbornene (114mg, 1.2mmol) and (**#**) (80mg, 0.2 mmol). The vial was sealed with a septum and flushed with argon, dry DME (2 mL), *tert*-butylacrylate (175μL, 1.2 mmol) and iodobutane (138 μL, 1.2mmol) were then added and argon was bubbled through the vial for 5 minutes before all inlets/outlets were removed. The vial was then placed in an oil bath preheated to 90°C and stirred for 16 hours. The reaction was then cooled, diluted with water and extracted with dichloromethane. The combined organic phases were dried over MgSO₄ and concentrated under reduced pressure. The crude product was purified by column chromatography (Hexane/Et₂O = 9/1) to afford **13** (73.2 mg, 81%) as a white crystalline solid. ¹H NMR (400 MHz, CDCl₃) δ 8.26-8.21 (m, 1H), 7.80-7.76 (m, 1H), 7.73 (d, *J*=16.0Hz, 1H), 7.60 (d, *J*=8.4Hz, 2H), 7.35-7.27 (m, 1H), 7.17 (d, *J*=8.0Hz, 2H), 6.44 (d, *J*=16.2 Hz, 1H), 3.15 (dd, *J*=7.8Hz, *J*=7.8Hz, 2H), 2.33 (s, 3H), 1.70 (quintet, *J*=7.6Hz, 2H), 1.54 (s, 9H), 1.43 (sextet, *J*=7.6Hz, 2H), 0.95 (t, *J*=7.3Hz, 3H); ¹³C-NMR (100 MHz, CDCl₃) δ 166.7, 145.0, 144.7, 136.8, 135.9, 134.4, 129.9, 127.7, 126.2, 124.6, 124.2, 120.2, 120.0, 116.2, 115.2, 80.4, 33.3, 28.2, 26.3, 22.6, 21.5, 13.7; δ IR (film) 3052, 2959, 2929, 2871, 1700, 1628, 1597, 1541, 1493, 1474, 1450, 1421, 1391, 1367, 1282, 1264, 1219, 1151, 1120, 1087, 1037, 1005, 975, 936, 911, 895, 852, 811, 747, 704, 668, 657cm⁻¹; HRMS (ESI) *m/z* calcd for [C₂₆H₃₁NO₄NaS]⁺: 476.1866, found 476.1872; M.p. 137-138°C.

3-(2-*tert*-Butoxycarbonyl)vinyl-2,4-di(butan-1-yl)thiophene (2a)

2,4-Di(butan-1-yl)-3-[(2-ethoxycarbonyl)vinyl]thiophene (2b)

2,4-Di(butan-1-yl)-3-[(2-methoxycarbonyl)vinyl]thiophene (2c)

2,4-Di(butan-1-yl)-3-[(2-*N,N*-dimethylaminocarbonyl)vinyl]thiophene (2d)

2,4-Di(butan-1-yl)-3-[(2-*N*-*tert*-butylaminocarbonyl)vinyl]thiophene (2e)

2,4-Di(butan-1-yl)-3-(3-oxopent-1-enyl)thiophene (2f)

2,4-Bis[(3-*tert*-butyldimethylsiloxy)propyl]-3-[(2-ethoxycarbonyl)vinyl]thiophene (2g)

2,4-Bis(3-phenylpropyl)-3-[(2-ethoxycarbonyl)vinyl]thiophene (2h)

3-(2-*tert*-Butoxycarbonyl)vinyl-2,4-bis(3-chloropropyl)thiophene (2i)

2-(butan-1-yl)-3-[(2-*tert*-butylcarbonyl)vinyl]benzo[*b*]thiophene (6)

(3,4-Dihydro-2H-dibenzothiophen-1-ylidene)-acetic acid ethyl ester (7)

3-Iodo-2-phenylthiophene (8)

4-(Butan-1-yl)-3-[(2-ethoxycarbonyl)vinyl]-2-phenylthiophene (9)

2,4-di(4-propylethoxycarbonyl)thiophene (10a)

2,4-di(3-propyloxiranyl)thiophene (10b)

2,4-di[2-(1,3-dioxolanyl)]thiophene (10c)

2,4-di(3-propyl-N-phthalimidyl)thiophene (10d)

2,4-di(3-propylcyano)thiophene (10e)

2,4-di(4-ethylbutanoate)-5-(4-nitrophenyl)thiophene (11a)

3-(2-*tert*-Butoxycarbonyl)vinyl-2,4-di(butan-1-yl)-5-(4-nitrophenyl)thiophene (11b)

3-(2-*tert*-Butoxycarbonyl)vinyl-2,4-di(butan-1-yl)-5-(4-methoxyphenyl)thiophene (11c)

3-Iodo-1-(toluene-4-sulfonyl)-1H-indole (12)

3-[2-Butyl-1-(toluene-4-sulfonyl)-1H-indol-3-yl]-acrylic acid tert-butyl ester (13)