Metal-free Brønsted acid mediated synthesis of fully substituted thiophenes via chemo- and regioselective intramolecular cyclization of $\alpha,\alpha'$-bis($\beta$-oxodithioesters) at room temperature

B. Janaki Ramulu, Suvajit Koley, and Maya Shankar Singh

Department of Chemistry, Faculty of Science, Banaras Hindu University, Varanasi-221005, India.

*E-mail: mayashankarbhu@gmail.com; mssingh@bhu.ac.in; Fax: +91-542-2368127

Table of Contents

General Information..................................................................................................................2

Procedure for the Synthesis of $\alpha,\alpha'$-Bis($\beta$-oxodithioesters) 1..................................2

General Procedure for the Synthesis of Thiophenes 2.........................................................2

Characterization data of isolated compounds.........................................................................3

Procedure for transformation of compound 2b to 6 and 7..................................................8

Copies of the $^1$H and $^{13}$C-NMR Spectra of the Compounds 2a-t, 6, and 7...........10-54

ORTEP diagram of 2f.............................................................................................................22
General Information. Commercial solvents and reagents were used as received without any further purification. All reactions were performed in single-neck round-bottomed flask fitted with Teflon-coated stir bar under open atmosphere. Organic solutions were concentrated by rotary evaporation. Column chromatography was performed with 100-200 mesh silica gel. $^1$H and $^{13}$C NMR spectra were recorded on NMR spectrometer operating at 300 and 75.5 MHz, respectively. Chemical shifts ($\delta$) are given in parts per million (ppm) using the residue solvent peaks as reference relative to TMS. Data are represented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constant ($J$, Hz) and integration. Mass spectra were recorded using electrospray ionization (ESI) mass spectrometry. X-ray crystallographic analysis was performed with Xcalibur Oxford CCD diffractometer. The melting points are uncorrected.

Procedure for the Synthesis of $\alpha,\alpha'$-Bis($\beta$-oxodithioesters) 1. To a stirring solution of $\alpha$-enolic dithioesters (1.0 mmol) in DMSO (5 mL), NCS (0.5 equiv) was added at room temperature and the reaction mixture was stirred for 10 min. After completion of the reaction (monitored by TLC), water was added. The content was extracted with dichloromethane (2×10 mL). The combined extract was dried over anhydrous Na$_2$SO$_4$ and the solvent was evaporated under vacuum. The crude residue thus obtained was purified by column chromatography over silica gel using ethyl acetate/hexane (1:10) as eluent to afford the pure $\alpha,\alpha'$-bis($\beta$-oxodithioesters) 1.

General Procedure for the Synthesis of Thiophenes 2. To a stirring solution of $\alpha,\alpha'$-bis($\beta$-oxodithioesters) 1 (1.0 mmol) in 5 mL of glacial acetic acid, $p$-TSA (4 equiv) was added at room temperature and the reaction mixture was stirred for a stipulated period of time (Table 2). After completion of the reaction (monitored by TLC), quenched with water and the content was extracted with dichloromethane. The combined extract was dried over anhydrous Na$_2$SO$_4$ and the solvent was evaporated under vacuum. The crude residue thus obtained was
purified by column chromatography over silica gel using ethyl acetate/hexane (1:10) as eluent to afford the pure tetrasubstituted thiophenes 2a-t.

Characterization data of isolated compounds

2-Methylsulphonyl-3-benzoyl-4-methylthioester-5-phenyl thiophene (2a). Yield: 380 mg; 95%. Red solid; mp 138 °C; H NMR (300 MHz, CDCl3): δ 7.84 (d, J = 7.2 Hz, 2H), 7.51 (d, J = 7.5 Hz, 1H), 7.43-7.31 (m, 7H), 2.45 (s, 3H), 2.38 (s, 3H); C NMR (75 MHz, CDCl3): δ 223.7, 192.1, 143.6, 141.7, 141.4, 139.4, 137.7, 133.0, 132.3, 129.6, 128.7, 128.5, 128.1, 21.0, 20.6; HRMS (ESI): calcd for C20H17OS4 [M+H]+ 401.0162, found 401.0160.

2-Ethylsulphonyl-3-benzoyl-4-ethylthioester-5-phenylthiophene (2b). Yield: 419 mg; 98%. Red sticky solid; H NMR (300 MHz, CDCl3): δ 7.84 (d, J = 7.5 Hz, 2H), 7.51-7.33 (m, 8H), 3.04 (q, J = 7.3 Hz, 2H), 2.90 (q, J = 7.5 Hz, 2H), 1.29 (t, J = 7.5 Hz, 3H), 1.01 (t, J = 7.5 Hz, 3H); C NMR (75 MHz, CDCl3): δ 222.9, 192.3, 143.7, 143.6, 142.3, 137.7, 136.3, 133.0, 132.3, 129.8, 128.8, 128.5, 128.52, 128.2, 32.5, 31.1, 14.6, 11.4; HRMS (ESI): calcd for C22H20NaOS4 [M+Na]+ 451.0294, found 451.0326.

2-Benzylsulphonyl-3-benzoyl-4-benzylthioester-5-phenylthiophene (2c). Yield: 508 mg; 92%. Red sticky solid; H NMR (300 MHz, CDCl3): δ 7.80 (d, J = 7.2 Hz, 2H), 7.52 (d, J = 7.2 Hz, 2H), 7.40-7.19 (m, 14H), 6.97 (d, J = 4.5 Hz, 2H), 4.22 (s, 2H), 4.02 (s, 2H); C NMR (75 MHz, CDCl3): δ 221.9, 192.3, 182.0, 143.6, 142.9, 137.6, 136.3, 134.8, 134.4, 133.1, 132.1, 129.8, 129.1, 128.9, 128.8, 128.5, 128.4, 128.2, 127.5, 127.4, 43.0, 41.7. HRMS (ESI): calcd. for C32H25OS4 [M+H]+ 553.0782, found 553.0789.

2-Ethylsulphonyl-3-(3'-methylbenzoyl)-4-ethylthioester-5-(3'-methylphenyl)thiophene (2d). Yield: 434 mg; 95%. Red liquid; H NMR (300 MHz, CDCl3): δ 7.61 (s, 2H), 7.34-7.12 (m, 6H), 3.04 (q, J = 7.2 Hz, 2H), 2.90 (q, J = 7.2 Hz, 2H), (2.34, 2.33) (two singlets, 6H), 1.29 (t, J = 7.2 Hz, 3H), 1.01 (t, J = 7.3 Hz, 3H); C NMR (75 MHz, CDCl3): δ 223.0, 192.3,
143.7, 143.4, 142.4, 138.1, 137.8, 137.6, 136.1, 133.8, 132.7, 132.2, 130.1, 129.3, 129.3, 128.3, 127.2, 126.2, 125.9, 32.4, 31.0, 21.2, 14.6, 11.3. HRMS (ESI): calcd for C_{24}H_{25}O_{3}S_{4} [M+H]^+ 457.0788, found 457.0774.

2-Ethylsulphanyl-3-(3'-methoxybenzoyl)-4-ethylthioester-5-(3'-methoxyphenyl) thiophene (2e). Yield: 453 mg; 93%. Red liquid; ^1H NMR (300 MHz, CDCl$_3$): $\delta$ 7.37 (d, $J = 18.9$ Hz, 2H), 7.28-7.22 (m, 2H), 7.08-7.02 (m, 2H), 6.90 (d, $J = 8.1$ Hz, 2H), 3.83 (s, 3H), 3.77 (s, 3H), 3.06 (q, $J = 7.4$ Hz, 2H), 2.91 (q, $J = 7.4$ Hz, 2H), 1.30 (t, $J = 7.3$ Hz, 3H), 1.04 (t, $J = 7.5$ Hz, 3H); ^13C NMR (75 MHz, CDCl$_3$): $\delta$ 223.0, 192.0, 159.4, 159.4, 143.6, 142.0, 139.0, 136.4, 133.5, 129.5, 129.2, 123.2, 121.2, 120.0, 114.5, 114.0, 113.1, 55.3, 32.5, 31.1, 14.6, 11.5; HRMS (ESI): calcd for C$_{24}$H$_{25}$O$_3$S$_4$ [M+H]$^+$ 489.0686, found 489.0682.

2-Ethylsulphanyl-3-(4'-methoxybenzoyl)-4-ethylthioester-5-(4'-methoxyphenyl) thiophene (2f). Yield: 460 mg; 94%. Yellow solid; mp 120 °C; ^1H NMR (300 MHz, CDCl$_3$): $\delta$ 7.84 (d, $J = 8.7$ Hz, 2H), 7.38 (d, $J = 8.7$ Hz, 2H), 6.89-6.84 (m, 4H), (3.849, 3.817) (two singlets, 6H, two OMe), 3.09 (q, $J = 7.5$ Hz, 2H), 2.87 (q, $J = 7.5$ Hz, 2H), 1.28 (t, $J = 7.2$ Hz, 3H), 1.07 (t, $J = 7.5$ Hz, 2H); ^13C NMR (75 MHz, CDCl$_3$): $\delta$ 223.5, 191.0, 163.6, 159.9, 144.5, 142.7, 133.9, 132.3, 130.9, 130.0, 124.8, 113.9, 113.5, 55.4, 55.2, 32.6, 31.1, 14.7, 11.5; HRMS (ESI): calcd for C$_{24}$H$_{25}$O$_3$S$_4$ [M+H]$^+$ 489.0686, found 489.0684.

2-Ethylsulphanyl-3-(3',4'-methylenedioxybenzoyl)-4-ethylthioester-5-(3',4'-methylenedioxyphenyl) thiophene (2g). Yield: 490 mg; 95%. Red liquid; ^1H NMR (300 MHz, CDCl$_3$): $\delta$ 7.40 (t, $J = 6.0$ Hz, 2H), 6.94 (t, $J = 5.2$ Hz, 2H), 6.79 (d, $J = 7.5$ Hz, 2H), (6.02, 5.98) (two singlets, 4H), 3.12 (q, $J = 7.3$ Hz, 2H), 2.88 (q, $J = 7.2$ Hz, 2H), 1.29 (t, $J = 7.2$ Hz, 3H), 1.10 (t, $J = 7.3$ Hz, 3H); ^13C NMR (75 MHz, CDCl$_3$): $\delta$ 223.1, 190.4, 152.0, 148.0, 147.9, 147.7, 144.0, 143.1, 142.3, 134.4, 132.6, 127.3, 126.0, 122.9, 109.1, 109.1, 108.8, 108.4, 107.6, 101.8, 101.3, 32.6, 31.1, 14.7, 11.5; HRMS (ESI): calcd for C$_{24}$H$_{20}$NaO$_5$S$_4$ [M+Na]$^+$ 539.0091, found, 539.0119.
2-Ethylsulphonyl-3-(4'-fluorobenzoyl)-4-ethylthioester-5-(4'-fluorophenyl) thiophene (2h). Yield: 417 mg; 90%. Red solid; mp 86 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.83 (d, $J = 5.4$ Hz, 2H), 7.38 (d, $J = 5.1$ Hz, 2H), 7.07-7.01 (m, 4H), 3.04 (q, $J = 7.0$ Hz, 2H), 2.88 (q, $J = 6.8$ Hz, 2H), 1.27 (t, $J = 7.2$ Hz, 3H), 1.02 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 222.5, 190.5, 167.3, 164.4, 163.9, 161.1, 143.5, 143.1, 141.0, 136.2, 134.0, 132.4, 132.2, 130.6, 130.5, 128.2, 115.7, 115.4, 115.1, 32.4, 31.0, 14.5, 11.4; HRMS (ESI): calcd for C$_{22}$H$_{19}$F$_2$OS$_4$ [M+H]$^+$ 465.0286, found 465.0298.

2-Ethylsulphonyl-3-(4'-chlorobenzoyl)-4-ethylthioester-5-(4'-chlorophenyl) thiophene (2i). Yield: 442 mg; 89%. Red solid; mp 82 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.78-7.67 (m, 2H), 7.29-7.24 (m, 6H), 2.99 (q, $J = 7.2$ Hz, 2H), 2.82 (q, $J = 7.3$ Hz, 2H), 1.21 (t, $J = 7.2$ Hz, 3H), 0.97 (t, $J = 7.2$ Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 222.3, 190.8, 143.7, 142.9, 140.7, 139.5, 137.0, 136.0, 134.7, 131.10, 130.6, 129.9, 129.2, 128.7, 128.5, 32.5, 31.2, 14.6, 11.4; HRMS (ESI): calcd for C$_{22}$H$_{19}$Cl$_2$OS$_4$ [M+H]$^+$ 496.9695, found 496.9698.

2-n-Propylsulphonyl-3-(3'-bromobenzoyl)-4-n-propythioester-5-(3'-bromophenyl) thiophene (2j). Yield: 534 mg; 87%. Red liquid; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.82 (s, 1H), 7.67-7.36 (m, 3H), 7.29-7.09 (m, 4H), 2.95 (t, $J = 7.0$ Hz, 2H), 2.79 (t, $J = 7.0$ Hz, 2H), 1.61-1.54 (m, 2H), 1.38-1.31 (m, 2H), 0.89 (t, $J = 3.6$ Hz, 3H), 0.75 (t, $J = 3.6$ Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 222.1, 190.4, 144.1, 141.9, 139.3, 139.1, 135.7, 134.0, 132.3, 131.5, 129.9, 129.7, 128.2, 127.3, 122.4, 40.1, 38.8, 22.6, 20.1, 13.3, 13.0; HRMS (ESI): calcd for C$_{24}$H$_{23}$Br$_2$OS$_4$ [M+H]$^+$ 612.8998, found 612.9003.

2-Ethylsulphonyl-3-(4'-phenylbenzoyl)-4-ethylthioester-5-biphenyl thiophene (2k). Yield: 528 mg; 91%. Red solid, mp 172 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.93 (d, $J = 8.1$ Hz, 2H), 7.64-7.32 (m, 16H), 3.09 (q, $J = 7.4$ Hz, 2H), 2.93 (q, $J = 7.4$ Hz, 2H), 1.32 (t, $J = 7.3$ Hz, 3H), 1.04 (t, $J = 7.3$ Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 223.0, 191.8, 145.8, 144.0, 143.7, 141.3, 140.1, 139.9, 136.5, 131.3, 130.4, 129.2, 128.8, 128.85, 128.1, 127.6, 127.2,
127.1, 126.9, 126.92, 32.6, 31.2, 14.7, 11.5; HRMS (ESI): calcd for C$_{34}$H$_{28}$NaOS$_{4}$ [M+Na]$^+$ 603.0920, found 603.0927.

2-Ethylsulphonyl-3-(1'-naphthoyl)-4-ethylthioester-5-(1'-napthyl) thiophene (2l).

Yield: 301 mg; 57%. Red liquid; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.75 (s, 1H), 7.87-7.74 (m, 6H), 7.55-7.40 (m, 7H), 2.97 (q, $J$ = 7.3 Hz, 2H), 2.97 (q, $J$ = 7.3 Hz, 2H), 2.43 (q, $J$ = 7.0 Hz, 2H), 1.31 (t, $J$ = 7.3 Hz, 3H), 0.35 (t, $J$ = 4.2 Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 221.2, 192.1, 146.4, 142.4, 141.8, 135.3, 135.1, 133.1, 132.6, 132.4, 130.8, 129.2, 129.1, 127.9, 127.8, 126.4, 126.2, 126.0, 125.7, 124.7, 123.9, 31.4, 30.5, 14.3, 10.9; HRMS (ESI): calcd for C$_{30}$H$_{25}$OS$_{4}$ [M+H]$^+$ 529.0788, found 529.0787.

2-Ethylsulphonyl-3-(2'-naphthoyl)-4-n-butylthioester-5-(2'-napthyl) thiophene (2m).

Yield: 485 mg; 92%. Red sticky solid; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.19 (s, 1H), 7.91 (d, $J$ = 10.5 Hz, 1H), 7.76-7.67 (m, 6H), 7.45-7.34 (m, 6H), 2.82-2.72 (m, 4H), 1.19 (t, $J$ = 7.2 Hz, 3H), 0.68 (t, $J$ = 7.4 Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 223.0, 191.9, 143.9, 143.4, 141.8, 137.5, 135.4, 135.0, 132.9, 132.2, 132.1, 129.7, 129.6, 128.3, 128.1, 128.0, 128.0, 127.6, 126.6, 126.5, 126.4, 32.4, 30.9, 14.6, 11.2; HRMS (ESI): calcd for C$_{30}$H$_{25}$OS$_{4}$ [M+H]$^+$ 529.0788, found 529.0799.

2-n-Butylsulphonyl-3-(2'-naphthoyl)-4-n-butylthioester-5-(2'-napthyl) thiophene (2n).

Yield: 550 mg; 94%. Red sticky solid; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.29 (s, 1H), 8.01-7.74 (m, 8H), 7.56-7.44 (m, 5H), 2.91-2.83 (m, 4H), 1.64-1.54 (m, 2H), 1.42-1.25 (m, 2H), 1.06-0.79 (m, 7H), 0.56 (t, $J$ = 7.6 Hz, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 223.0, 191.8, 143.9, 143.4, 141.8, 137.5, 135.4, 135.0, 132.9, 132.8, 132.1, 129.8, 129.5, 128.3, 128.0, 127.9, 127.6, 126.5, 126.4, 126.2, 124.6, 38.0, 36.4, 31.2, 28.4, 21.6, 21.4, 13.3, 13.18; HRMS (ESI): calcd for C$_{34}$H$_{33}$OS$_{4}$ [M+H]$^+$ 585.1408, found 585.1417.

2-Ethylsulphonyl-3-(2'-thienoyl)-4-ethylthioester-5-(2'-thiophene) thiophene (2o).

Yield: 427 mg; 97%. Red sticky solid; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.67 (d, $J$ = 4.2 Hz,
1H), 7.55 (d, J = 3.6 Hz, 1H), 7.33 (d, J = 4.5 Hz, 1H), 7.18 (d, J = 3.6 Hz, 1H), 7.06-6.98 (m, 2H), 3.16 (q, J = 7.3 Hz, 2H), 2.92 (q, J = 7.2 Hz, 2H), 1.31 (t, J = 7.3 Hz, 3H), 1.14 (t, J = 7.3 Hz, 3H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 222.4, 183.8, 144.5, 143.3, 142.9, 135.6, 134.9, 132.9, 127.9, 127.4, 32.7, 31.3, 14.7, 11.4; HRMS (ESI): calcd for C\(_{18}\)H\(_{17}\)O\(_3\)S\(_6\) [M+H]\(^{+}\) 440.9598, found 440.9615.

**2-Ethylsulphonyl-3-(2′-furoyl)-4-ethylthioester-5-(2′-furan) thiophene (2p).** Yield: 387 mg; 95%. Red sticky solid; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.52 (s, 1H), 7.34 (d, J = 0.9 Hz, 1H), 7.01 (d, J = 3.0 Hz, 1H), 6.46-6.43 (m, 2H), 6.34-6.33 (m, 1H), 3.17 (q, J = 7.3 Hz, 2H), 2.84 (q, J = 7.3 Hz, 2H), 1.23-1.11 (m, 6H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 223.2, 178.5, 152.8, 147.4, 147.3, 145.8, 142.8, 142.7, 142.1, 136.5, 131.2, 120.9, 112.3, 111.9, 109.4, 32.7, 31.2, 14.6, 11.7; HRMS (ESI): calcd for C\(_{18}\)H\(_{17}\)OS\(_6\) [M+H]\(^{+}\) 409.0055, found 409.0069.

**2-n-Pentanesulphonyl-3-(2′-furoyl)-4-n-pentanethioester-5-(2′-furan) thiophene (2q).** Yield: 472 mg; 96%. Red sticky solid; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.51 (s, 1H), 7.33 (s, 1H), 7.01 (d, J = 3.0 Hz, 1H), (6.45, 6.33) (t&d, J = 3.9 Hz, J = 1.5 Hz, 3H), 3.17 (q, J = 7.2 Hz, 2H), 2.81 (t, J = 7.3 Hz, 2H), 1.56-1.46 (m, 4H), 1.22 (br, 8H), 0.79 (br, 6H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 223.3, 178.4, 152.8, 147.3, 145.8, 142.7, 142.1, 136.5, 131.2, 120.9, 112.3, 111.9, 109.4, 32.7, 31.2, 14.6, 11.7; HRMS (ESI): calcd for C\(_{24}\)H\(_{29}\)O\(_3\)S\(_4\) [M+H]\(^{+}\) 493.0999, found 493.1016.

**2-Ethylsulphonyl-3-cyclopropanecarbonyl-4-ethylthioester-5-cyclopropane thiophene (2r).** Yield: 338 mg; 95%. Yellow liquid; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 2.97-2.86 (m, 4H), 2.32-2.18 (m, 2H), 1.39-1.27 (m, 10H), 1.09-1.03 (m, 4H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 199.3, 197.1, 144.47, 139.11, 138.50, 112.3, 32.7, 32.0, 22.9, 21.8, 14.3, 14.2, 13.16, 13.12; HRMS (ESI): calcd for C\(_{16}\)H\(_{21}\)OS\(_4\) [M+H]\(^{+}\) 357.0475, found 357.0464.
2(1'-Butenylsulphanyl)-3-(3'-bromobenzoyl)-4-(1'-butenylthioester)-5-(3'-bromophenyl) thiophene (2s). Yield: 587 mg; 92%. Red sticky solid; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.90 (s, 1H), 7.74 (d, $J = 7.2$ Hz, 1H), 7.65 (d, $J = 8.1$ Hz, 1H), 7.58 (s, 1H), 7.51 (d, $J = 7.8$ Hz, 1H), 7.46-7.18 (m, 3H), 5.79-5.56 (m, 2H), 5.09-4.94 (m, 4H), 3.11 (t, $J = 7.3$ Hz, 2H), 2.96 (t, $J = 7.5$ Hz, 2H), 2.41 (q, $J = 6.8$ Hz, 2H), 2.17 (q, $J = 6.7$ Hz, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 221.7, 190.3, 144.1, 142.5, 140.1, 139.3, 138.4, 135.9, 135.3, 134.0, 132.4, 131.6, 130.0, 129.8, 128.3, 127.4, 122.5, 122.5, 116.8, 116.6, 37.5, 36.1, 33.3, 30.6, 29.6 (grease); HRMS (ESI): calcd for C$_{26}$H$_{23}$Br$_2$O$_4$ [M+H]$^+$ 638.8978, found 638.8981.

2(1'-pentenylphanyl)-3-(2'-naphthoyl)-4-(1'-pentenylthioester)-5-(2'-napthyl) thiophene (2t). Yield: 548 mg; 90%. Red sticky solid; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.20 (s, 1H), 7.92 (d, $J = 7.2$ Hz, 2H), 7.82-7.89 (m, 6H), 7.47-7.40 (m, 5H), 5.61-5.62 (m, 1H), 5.35-5.29 (m, 1H), 4.90-4.82 (m, 2H), 4.73-4.61 (m, 2H), 3.84 (t, $J = 7.3$ Hz, 3H), 2.01 (d, $J = 6.9$ Hz, 2H), 1.67-1.60 (m, 4H), 1.17-1.10 (m, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 222.9, 192.0, 143.9, 143.8, 142.6, 137.2, 137.0, 136.9, 136.8, 135.6, 135.1, 133.1, 132.9, 132.3, 132.2, 132.1, 129.8, 129.6, 128.4, 128.2, 128.0, 127.7, 126.7, 126.7, 126.6, 126.3, 124.7, 115.4, 115.2, 37.8, 36.1, 32.4, 32.3, 28.4, 25.6; HRMS (ESI): calcd for C$_{36}$H$_{33}$O$_4$ [M+H]$^+$ 609.1414, found 609.1417.

**Procedure for transformation of compound 2b to 6 and 7.** To a stirring solution of 2-ethylsulphanyl-3-benzoyl-4-ethylthioester-5-phenyl thiophene 2b (1 mmol) in EtOH (5 mL), allylamine (1.2 equiv.) was added at 80 °C and the reaction mixture was stirred for 12 hrs. After completion of the reaction (monitored by TLC), water was added. The content was extracted with dichloromethane (2×10 mL). The combined extract was dried over anhydrous Na$_2$SO$_4$ and the solvent was evaporated under vacuum. The crude residue thus obtained was purified by column chromatography over silica gel using ethylacetate/hexane (3:10) as eluent.
to afford the pure 2-ethylsulphonyl-3-benzoyle -4-n-allylthamide-5-phenyl thiophene 6. After isolated compound 6 we treated reaction with I₂ (1 equiv.) in DCM at room temperature the reaction was completed within minute (monitored on TLC), water was added. The content was extracted with dichloromethane (2×10 mL). The combined extract was dried over anhydrous Na₂SO₄ and the solvent was evaporated under vacuum. The crude residue thus obtained was purified by column chromatography over silica gel using ethylacetate/hexane (2:10) as eluent to afford the pure 2-ethylsulphonyl-3-benzoyle-4-(5′-iodomethyl-4′,5′-dihydrothiazole)-5-phenyl thiophene 7.

2-Ethylsulphonyl-3-benzoyle-4-N-allylthioamide-5-phenyl thiophene (6). Yield: 87 mg; 92%. White solid, mp 125 °C; ¹H NMR (300 MHz, CDCl₃): δ 7.91 (d, J = 7.5 Hz, 2H), 7.58-7.37 (m, 8H), 7.25 (br, 1H, NH), 5.61-5.48 (m, 1H), 5.04-4.92 (m, 2H), 4.08 (t, J = 5.2 Hz, 2H), 2.84 (q, J = 7.3 Hz, 2H), 1.26 (t, J = 7.3 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 192.9, 192.4, 144.6, 140.8, 137.9, 135.6, 133.1, 131.7, 130.0, 128.9, 128.3, 128.2, 127.9, 118.5, 48.1, 32.5, 14.6; HRMS (ESI): calcd for C₂₃H₂₂NOS₃ [M+H]⁺ 424.0858, found 424.0862.

2-Ethylsulphonyl-3-benzoyle-4-(5′-iodomethyl-4′,5′-dihydrothiazole)-5-phenyl thiophene (7). Yield: 87 mg; 92%. Colourless liquid; ¹H NMR (300 MHz, CDCl₃): δ 7.77 (d, J = 7.5 Hz, 2H), 7.49 (d, J = 6.9 Hz, 1H), 7.41 (t, J = 6.6 Hz, 7H), (4.09, 4.03) (two singlets, 1H), 3.79-3.72 (m, 1H), 3.64-3.56 (m, 1H), 2.92 (q, J = 7.2 Hz, 2H), 2.68-2.63 (m, 1H), 2.24-2.17 (m, 1H), 1.28 (t, J = 7.2 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 191.6, 159.8, 146.3, 143.9, 137.5, 136.4, 132.7, 131.4, 130.3, 129.3, 129.0, 128.9, 128.2, 68.3, 52.3, 32.4, 14.4, 8.8; HRMS (ESI): calcd for C₂₃H₂₁INOS₃ [M+H]⁺ 549.9829, found 549.9824.
$^1$H NMR spectrum of 2a
$^{13}$C NMR spectrum of 2a
$^1$H NMR spectrum of 2b
$^{13}$C NMR spectrum of 2b
$^1$H NMR spectrum of 2c
$^{13}$C NMR spectrum of 2c
$^1$H NMR spectrum of 2d
$^{13}$C NMR spectrum of 2d
$^1$H NMR spectrum of 2e
$^{13}$C NMR spectrum of 2e
$^1$H NMR spectrum of 2f
$^{13}$C NMR spectrum of 2f
ORTEP diagram of 2f: (ellipsoid contour probability level is 50%)
$^1$H NMR spectrum of 2g
$^{13}$C NMR spectrum of 2g
$^1$H NMR spectrum of 2h
\textsuperscript{13}C NMR spectrum of 2h
$^1$H NMR spectrum of 2i
$^{13}$C NMR spectrum of 2i
$^1$H NMR spectrum of 2j
$^{13}$C NMR spectrum of 2j
$^1$H NMR spectrum of 2k
$^{13}$C NMR spectrum of 2k
$^1$H NMR spectrum of 21
$^{13}$C NMR spectrum of 2l
$^1$H NMR spectrum of 2m
$^{13}$C NMR spectrum of 2m
$^1$H NMR spectrum of 2n
$^{13}$C NMR spectrum of 2n
$^1$H NMR spectrum of 2o
$^{13}$C NMR spectrum of 2o
$^1$H NMR spectrum of 2p
$^{13}$C NMR spectrum of 2p
$^1$H NMR spectrum of 2q
$^{13}$C NMR spectrum of 2q
$^1$H NMR spectrum of 2r
$^{13}$C NMR spectrum of 2r
$^1$H NMR spectrum of 2s
$^{13}$C NMR spectrum of 2s
$^1$H NMR spectrum of 2t
$^{13}$C NMR spectrum of 2t
$^1$H NMR spectrum of 6
$^{13}$C NMR spectrum of 6
$^1$H NMR spectrum of 7
$^{13}\text{C}$ NMR spectrum of 7