Studies in sulfur heterocycles. Part 14.[1] Application of heteroatom directed *ortho*-metallation in functionalisation of benzo[*b*]thiophene derivatives

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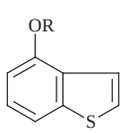
Heteroatom directed *ortho*-metallation of 2-*tert*-butyldimethylsilyl-4-methoxybenzo[*b*]thiophene and 2-*tert*-butyldimethylsilyl-4-carbamoyloxybenzo[*b*]thiophene has been followed by quenching with electrophiles. Anionic *ortho*-Fries rearrangement has been carried out on 4-carbamoyloxybenzo[*b*]-thiophene. The rearranged product has been used as the starting material in the synthesis of a novel linearly fused thienoisochromene.

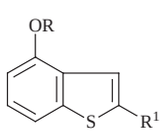
Heteroatom directed *ortho*-metallation,[2] in spite of its wide use in regioselective introduction of functional groups in aromatic and heteroaromatic compounds, has so far been sparsely used in benzo[*b*]thiophene chemistry.[1,3,4] Further to our reports[1,5–7] on the expedient synthesis of 4-, 5-, 6- and 7-substituted benzo-[*b*]thiophene and their use in various annelation reactions, we report herein application of 'directed metallation' in regio-selective functionalisation of benzo[*b*]thiophene and the synthesis of a novel linearly fused thienobenzopyranone, as a continuation of our earlier endeavour in this area.[1–4]

Results and discussion

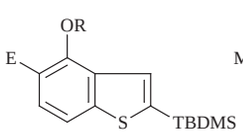
The substrates used were 4-methoxy- **1** and 4-*N*,*N*-diethyl-carbamoyloxy-benzo[*b*]thiophene **2**. Of the two functional groups, *viz.* methoxy and *O*-carbamoyl, the latter occupies a higher position in the hierarchy of the directing groups due to a greater magnitude of directing power.[2] Under standard directed metallation conditions (Bu^{t}Li–TMEDA–THF, −78 °C) both



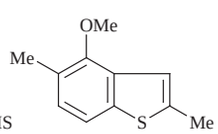
1, R = Me
2, R = $CONEt_2$



3, R = R^1 = Me
4, R = $CONEt_2$, R^1 = Me
5, R = Me, R^1 = TBDMS
6, R = $CONEt_2$, R^1 = TBDMS



7, R = Me, E = Me
8, R = Me, E = CHO
9, R = Me, E = $CONEt_2$
10, R = Me, E = $SnBu_3$
11, R = $CONEt_2$, E = Me
12, R = $CONEt_2$, E = CHO
13, R = $CONEt_2$, E = $SnBu_3$



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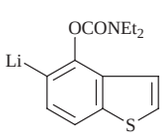
1 and **2** were exclusively deprotonated in the 2-position. Quenching the lithio derivatives with methyl iodide afforded **3** and **4**, respectively. Deprotonation of the position α to the ring sulfur in preference to the position *ortho* to the directing groups in **1** and **2**, is not entirely surprising in view of a previous report by Doadt and Snieckus on directed metallation of thiophene derivatives.[8] The silyl protected species **5** and **6** obtained by quenching the lithio derivatives with *tert*-butyldimethylchlorosilane smoothly deprotonated in the positions *ortho* to the directing groups under the same experimental conditions. The silyl protected deprotonated species were quenched with a number of representative electrophiles *viz.* methyl iodide, *N*,*N*-dimethylformamide, *N*,*N*-diethylcarbamoyl chloride and tributyltin chloride affording the compounds **7**–**13**. The ^{1}H NMR spectrum of **10** showed signals with appropriate chemical shifts but the compound could not be obtained in a sufficiently pure form to have correct elemental analysis even after repeated column chromatography. Not surprisingly the methoxy group showed reduced directing power and to ensure the generation of a sufficient quantity of the anion, the reaction mixture was refluxed for one hour before quenching with methyl iodide. After usual work-up, a mixture of the starting material and 2,5-dimethyl-4-methoxybenzo[*b*]thiophene **14** was obtained, which were separated by preparative thin layer chromatography. Desilylation in the 2-position has apparently occurred in the presence of a strong base under refluxing conditions. Similar desilylation induced by *tert*-butyllithium in partially hydrogenated benzo[*b*]thiophene was earlier observed.[4a]

Anionic Fries rearrangement of *ortho*-deprotonated *O*-carbamates into salicylamides and the use of the rearranged product in regioselective polysubstitution and in annelation reactions, developed by Sibi and Snieckus,[9] was also attempted on **2**. The lithio derivative **15** obtained at −78 °C was allowed to



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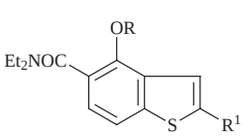

16, R = R^1 = H
17, R = Me, R^1 = H
18, R = R^1 = Me
19, R = Me, R^1 = TBDMS

attain room temperature and was left stirring for 12 h. The resulting salicylamide **16** was converted into its methyl ether **17**. It is conjectured that alkyllithium deprotonates both the 2- and 5-positions, but in the absence of a quenching agent, the thermodynamically stable species[2] **15** predominates and undergoes rearrangement.

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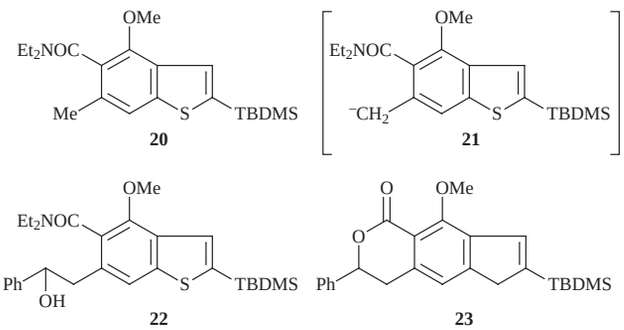
Compound **17** deprotonated (Bu′Li–TMEDA–THF, −78 °C) in the 2-position and the anion quenched with methyl iodide and *tert*-butyldimethylchlorosilane to afford **18** and **19** respectively, corroborating the above conjecture. Directed metallation of the silyl protected compound **19** followed by quenching with methyl iodide afforded **20** and the methyl group in the latter was used as a 'handle' for annelating an oxygenated ring. The anion generated by treating **20** with lithium diisopropylamide reacted with benzaldehyde and the resulting secondary alcohol **22** smoothly cyclised with alkali to afford the novel linearly fused thienoisochromene **23**.



Experimental

Melting points (uncorrected) were recorded in open capillaries on a hot stage apparatus. IR spectra were recorded on a Perkin-Elmer 298 Spectrometer, for solids in potassium bromide discs and for liquids by placing a thin layer of the sample between two potassium bromide discs. ^{1}H NMR spectra were recorded in $CDCl_3$ solutions unless otherwise stated, on Varian EM-360, JEOL FX-100 and Bruker DPX-300 spectrometer. Chemical shifts (δ) are expressed in ppm using tetramethylsilane as internal standard. Coupling constant (J) values are given in Hz.

Commercially available solvents were distilled prior to use. Light petroleum (bp 60–80 °C) was used. Tetrahydrofuran was dried by the benzophenone ketyl method.

N,*N*,*N*′,*N*′-Tetramethylethylenediamine (TMEDA) and *N*,*N*-dimethylformamide were freshly distilled over calcium hydride prior to use. All lithiation reactions were carried out in an argon atmosphere. Anhydrous sodium sulfate was used as drying agent.

4-Hydroxybenzo[*b*]thiophene was synthesized according to literature[11] procedure.

4-Methoxybenzo[*b*]thiophene 1

Potassium carbonate (0.92 g, 6.67 mmol) was added to a solution of 4-hydroxybenzo[*b*]thiophene (1 g, 6.67 mmol) in dry acetone (50 ml). After refluxing for 3 h, the reaction mixture was cooled to 0 °C and methyl iodide (1.14 g, 8.0 mmol) in dry acetone (10 ml) was added dropwise at that temperature under magnetic stirring. After stirring for 2 h at 0 °C and for 10 h at room temperature, the solid was filtered, the solvent removed under reduced pressure and the residue poured into crushed ice. After extraction with diethyl ether, the organic layer was washed with water and dried. Removal of solvent afforded **1** as a colourless oily liquid (1.06 g, 97%) which was purified by short path distillation. Bp 80 °C/0.05 mmHg, lit.[10] bp 141 °C/17 mmHg; $\delta_H(CCl_4)$ 7.42–7.06 (m, 4H, H-2, H-3, H-6 and H-7), 6.63 (dd, 1H, H-5, J 2 and 6), 3.95 (s, 3H, OCH_3).

4-(*N*,*N*-Diethylcarbamoyloxy)benzo[*b*]thiophene 2

This compound was synthesized similarly using *N*,*N*-diethylcarbamoyl chloride. The compound was purified by column chromatography [ethyl acetate–light petroleum (1:9) as eluent] to obtain **2** as a colourless viscous liquid (1.4 g, 82%) (Found: C, 62.24; H, 6.37; N, 5.72. $C_{13}H_{15}NO_2S$ requires C, 62.62; H, 6.06; N, 5.61%); ν_{max}/cm^{-1} 1700 ($OCONEt_2$); $\delta_H(CCl_4)$ 7.7–6.8 (m, 4H, H-2, H-3, H-6 and H-7), 6.35–6.15 (dd, 1H, H-5, J 2 and 8), 3.66–3.2 (q, 4H, CH_2–CH_3), 1.54–1.10 (t, 6H, CH_2–CH_3).

General procedure for metallation and reaction with electrophiles

tert-Butyllithium (1.5 M, 1.2 equiv.) was slowly added by syringe to a well stirred mixture of tetrahydrofuran (20 ml) and TMEDA (1.2 equiv.) at −78 °C. When a yellow colour developed (in approximately 30 min), the substrate (1 equiv.) was added similarly at that temperature. The reaction mixture was stirred for 30 min at a temperature between −20 and −10 °C when $OCONEt_2$ or $CONEt_2$ were the directing groups and for 4 h at room temperature for methoxy derivatives. After cooling the reaction mixture again to −78 °C, the electrophile (1 equiv.) was slowly added by syringe and kept for 10–15 min with the cooling bath in place, followed by stirring at room temperature for 12 h. Work-up consisted of neutralising the reaction mixture with saturated ammonium chloride solution (25 ml) and water (100 ml), diethyl ether extraction (3 × 25 ml), washing the organic layer with water and drying. Evaporation of the solvent afforded the crude material.

2-Methyl-4-methoxybenzo[*b*]thiophene 3. The crude product was purified by column chromatography [ethyl acetate–light petroleum (1:19) as eluent] to obtain **3** as a viscous liquid. Yield 73% (Found: C, 67.46; H, 5.59. $C_{10}H_{10}OS$ requires C, 67.38; H, 5.65%); $\delta_H(CCl_4)$ 7.46–6.95 (m, 3H, H-3, H-6 and H-7), 6.56 (dd, 1H, H-5, J 2 and 8), 3.86 (s, 3H, OCH_3), 2.53 (s, 3H, 2-CH_3).

2-Methyl-4-(*N*,*N*-diethylcarbamoyloxy)benzo[*b*]thiophene 4. Column chromatography [ethyl acetate–light petroleum (1:9) as eluent] afforded **4** as a viscous liquid. Yield 88%; ν_{max}/cm^{-1} 1700 ($OCONEt_2$) (Found: C, 63.57; H, 6.67; N, 4.99. $C_{14}H_{17}NO_2S$ requires C, 63.85; H, 6.5; N, 5.32%); $\delta_H(CCl_4)$ 7.56–6.99 (m, 3H, H-3, H-6 and H-7), 6.39–6.23 (dd, 1H, H-5, J 2 and 8), 3.52–3.19 (q, 4H, CH_2CH_3), 2.42 (s, 3H, 2-CH_3), 1.29–1.06 (t, 6H, CH_2CH_3).

2-*tert*-Butyldimethylsilyl-4-methoxybenzo[*b*]thiophene 5. The solid left after removal of the solvent was crystallised from light petroleum. Yield 74%; mp 75–76 °C (Found: C, 64.81; H, 7.86. $C_{15}H_{22}OSiS$ requires C, 64.69; H, 7.96%); δ_H 7.64 (s, 1H, H-3), 7.47 (d, 1H, H-7, J 8.1), 7.25 (dd, 1H, H-6, J 7.8 and 8.1), 6.72 (d, 1H, H-5, J 7.8), 3.96 (s, 3H, OCH_3), 0.96 [s, 9H, $Si(CH_3)_2C(CH_3)_3$], 0.35 [s, 6H, $Si(CH_3)_2C(CH_3)_3$].

2-*tert*-Butyldimethylsilyl-4-(*N*,*N*-diethylcarbamoyloxy)benzo[*b*]thiophene 6. Purified by column chromatography [ethyl acetate–light petroleum (1:9) as eluent] and short path distillation to obtain **6** as a low melting solid. Yield 70%; bp 80 °C/0.01 mmHg; ν_{max}/cm^{-1} 1700 ($OCONEt_2$) (Found: C, 62.61; H, 7.84; N, 3.75. $C_{19}H_{29}NO_2SSi$ requires C, 62.76; H, 8.03; N, 3.85%); δ_H 7.70 (d, 1H, H-7, J 8.1), 7.39 (s, 1H, H-3), 7.30 (dd, 1H, H-6, J 7.5 and 8.1), 7.14 (d, 1H, H-5, J 7.5), 3.57 (q, 2H, CH_2CH_3), 3.44 (q, 2H, CH_2CH_3), 1.36 (t, 3H, CH_2CH_3), 1.24 (t, 3H, CH_2CH_3), 0.97 [s, 9H, $Si(CH_3)_2C(CH_3)_3$], 0.36 [s, 6H, $Si(CH_3)_2C(CH_3)_3$].

2-*tert*-Butyldimethylsilyl-4-methoxy-5-methylbenzo[*b*]thiophene 7. Purified by preparative thin layer chromatography to obtain **7** as a viscous liquid. Yield 30% (Found: C, 65.98; H, 8.42. $C_{16}H_{24}OSSi$ requires C, 65.69; H, 8.27%); $\delta_H(CCl_4)$ 7.75–6.80 (m, 3H, H-3, H-6 and H-7), 4.03 (s, 3H, OCH_3), 2.22 (s, 3H, 5-CH_3), 1.00 [s, 9H, $Si(CH_3)_2C(CH_3)_3$], 0.36 [s, 6H, $Si(CH_3)_2C(CH_3)_3$].

2-*tert*-Butyldimethylsilyl-4-methoxybenzo[*b*]thiophene-5-carbaldehyde 8. Purified by column chromatography [ethyl acetate–light petroleum (1:9) as eluent] to obtain **8** as a light yellow solid. Yield 41%; mp 80–82 °C; ν_{max}/cm^{-1} 1680 (CHO) (Found: C, 63.05; H, 7.62. $C_{16}H_{22}O_2SSi$ requires C, 62.70; H, 7.23%); $\delta_H(CCl_4)$ 9.92 (s, 1H, CHO), 7.82–7.6 (m, 3H, H-3, H-6 and H-7), 4.07 (s, 3H, OCH_3), 1.00 [s, 9H, $Si(CH_3)_2C(CH_3)_3$], 0.36 [s, 6H, $Si(CH_3)_2C(CH_3)_3$].

***N*,*N*-Diethyl-2-*tert*-butyldimethylsilyl-4-methoxybenzo[*b*]-thiophene-5-carboxamide 9.** Purified by column chromatography [ethyl acetate–light petroleum (1:9) as eluent] to obtain **9** as a viscous liquid. Yield 52%; bp 95 °C/0.02 mmHg; ν_{max}/cm^{-1} 1630 (CONEt$_2$) (Found: C, 63.94; H, 8.04; N, 3.81. $C_{20}H_{31}NO_2SSi$ requires C, 63.61; H, 8.28; N, 3.71%); δ_H 7.63 (d, 1H, H-7, *J* 8.4), 7.59 (s, 1H, H-3), 7.18 (d, 1H, H-6, *J* 8.4), 4.02 (s, 3H, OCH_3), 3.64 (q, 2H, CH_2CH$_3$), 3.16 (q, 2H, CH_2CH$_3$), 1.30 (t, 3H, CH$_2$CH_3), 1.04 (t, 3H, CH$_2$CH_3), 0.98 [s, 9H, Si(CH$_3$)$_2$-C(CH_3)$_3$], 0.37 [s, 6H, Si(CH_3)$_2$C(CH$_3$)$_3$].

2-*tert*-Butyldimethylsilyl-4-(*N*,*N*-diethylcarbamoyloxy)-5-methylbenzo[*b*]thiophene 11. Purified by column chromatography [ethyl acetate–light petroleum (1:9) as eluent] to obtain **11** as a colourless liquid. Yield 58%; bp 60 °C/0.01 mmHg; ν_{max}/cm^{-1} 1700 (OCONEt$_2$) (Found: C, 63.81; H, 8.05; N, 3.80. $C_{20}H_{31}NO_2SSi$ requires C, 63.62; H, 8.28; N, 3.71%); δ_H 7.62 (d, 1H, H-7, *J* 8.4), 7.39 (s, 1H, H-3), 7.17 (d, 1H, H-6, *J* 8.4), 3.57 (q, 2H, CH_2CH$_3$), 3.44 (q, 2H, CH_2CH$_3$), 2.37 (s, 3H, 5-CH_3), 1.35 (t, 3H, CH$_2$CH_3), 1.25 (t, 3H, CH$_2$CH_3), 0.97 [s, 9H, Si(CH$_3$)$_2$C(CH_3)$_3$], 0.36 [s, 6H, Si(CH_3)$_2$C(CH$_3$)$_3$].

2-*tert*-Butyldimethylsilyl-4-(*N*,*N*-diethylcarbamoyloxy)benzo-[*b*]thiophene-5-carbaldehyde 12. Purified by column chromatography [ethyl acetate–light petroleum (1:9) as eluent] to obtain **12** as a colourless viscous liquid. Yield 65%; bp 80 °C/0.02 mmHg; ν_{max}/cm^{-1} 1680 (C*H*O), 1700 (OCONEt$_2$) (Found: C, 61.05; H, 7.26; N, 3.73. $C_{20}H_{29}NO_3SSi$ requires C, 61.34; H, 7.46; N, 3.57%); δ_H 9.96 (s, 1H, C*H*O), 7.47 (d, 1H, H-7, *J* 6), 7.41 (d, 1H, H-6, *J* 6), 7.26 (s, 1H, H-3), 3.86 (q, 2H, CH_2CH$_3$), 3.48 (q, 2H, CH_2CH$_3$), 1.33 (t, 3H, CH$_2$CH_3), 1.29 (t, 3H, CH$_2$CH_3), 0.97 [s, 9H, Si(CH$_3$)$_2$C(CH_3)$_3$], 0.36 [s, 6H, Si(CH_3)$_2$-C(CH$_3$)$_3$].

2-*tert*-Butyldimethylsilyl-4-(*N*,*N*-diethylcarbamoyloxy)-5-tributylstannylbenzo[*b*]thiophene 13. Purified by column chromatography [ethyl acetate–light petroleum (1:19) as eluent] to obtain **13** as a dense colourless liquid. Yield 62%; bp 70 °C/0.02 mmHg; ν_{max}/cm^{-1} 1700 (OCONEt$_2$) (Found: C, 56.46; H, 8.01; N, 1.79. $C_{31}H_{55}NO_2SSiSn$ requires C, 57.05; H, 8.49; N, 2.14%); δ_H 7.70 (d, 1H, H-7, *J* 8.4), 7.36 (s, 1H, H-3), 7.12 (d, 1H, H-6, *J* 8.4), 3.56 (q, 2H, CH_2CH$_3$), 3.45 (q, 2H, CH_2CH$_3$), 1.62 (t, 3H, CH$_2$CH_3), 1.56 (t, 3H, CH$_2$CH_3), 1.41–0.87 [m, 27H, Sn(C$_4H_9$)$_3$], 0.97 [s, 9H, Si(CH$_3$)$_2$C(CH_3)$_3$], 0.36 [s, 6H, Si(CH_3)$_2$-C(CH$_3$)$_3$].

2,5-Dimethyl-4-methoxybenzo[*b*]thiophene 14. The reaction mixture obtained after addition of methyl iodide was allowed to attain room temperature followed by refluxing for 4 h at 80 °C (bath temperature). Usual work-up afforded **14** as a low melting solid which was purified by preparative TLC [ethyl acetate–light petroleum (1:19) as eluent]. Yield 66% (Found: C, 68.50; H, 6.51. $C_{11}H_{12}OS$ requires C, 68.70; H, 6.29%); δ_H(CCl$_4$) 7.21–6.54 (m, 3H, H-3, H-6 and H-7), 3.90 (s, 3H, OCH_3), 2.48 (s, 3H, 2-CH_3), 2.22 (s, 3H, 5-CH_3).

5-(*N*,*N*-Diethylcarbamoyl)-4-hydroxybenzo[*b*]thiophene 16
To a well stirred solution of tetrahydrofuran (50 ml) and TMEDA (1.2 equiv.), 1.5 M *tert*-butyllithium (1.2 equiv.) was slowly added by syringe at −78 °C and kept for 30 min when a yellow colour developed, followed by a solution of **2** (0.25 g, 1 mmol) in tetrahydrofuran (10 ml). The reaction mixture was stirred for 12 h after attaining room temperature. Ammonium chloride work-up afforded **16** as a light brown gummy liquid which was sufficiently pure for methylation. Yield (0.2 g, 80%); ν_{max}/cm^{-1} 1645 (CONEt$_2$), 3360 (br, OH); δ_H 7.79–7.16 (m, 4H, H-2, H-3, H-6 and H-7), 3.66–3.39 (q, 4H, CH_2CH$_3$), 1.46–1.23 (t, 6H, CH$_2$CH_3).

***N*,*N*-Diethyl-4-methoxybenzo[*b*]thiophene-5-carboxamide 17**
Anhydrous potassium carbonate (0.11 g, 0.8 mmol) and **16** (0.2 g, 0.8 mmol) in dry acetone (15 ml) were refluxed for 3 h. Then the reaction mixture was cooled to 0 °C and methyl iodide (0.14 g, 0.96 mmol) in dry acetone (10 ml) was added at that temperature under magnetic stirring. The stirring was continued for 2 h at 0 °C and for 10 h at room temperature. After usual work-up **17** was obtained as a dense colourless liquid which was purified by column chromatography [ethyl acetate–light petroleum (3:17) as eluent]. Yield 0.19 g (90%); bp 80 °C/0.02 mmHg; ν_{max}/cm^{-1} 1635 (CONEt$_2$) (Found: C, 63.53; H, 6.63; N, 5.69. $C_{14}H_{17}NO_2S$ requires C, 63.85; H, 6.51; N, 5.31%); δ_H(CCl$_4$) 7.79–7.20 (m, 4H, H-2, H-3, H-6 and H-7), 3.96 (s, 3H, OCH_3), 3.69–3.26 (q, 4H, CH_2CH$_3$), 1.43–1.10 (t, 6H, CH$_2$CH_3).

***N*,*N*-Diethyl-2-methyl-4-methoxybenzo[*b*]thiophene-5-carboxamide 18**
Synthesized from **17** following the general procedure using methyl iodide as electrophile. The crude material was purified by column chromatography [ethyl acetate–light petroleum (15:85) as eluent]. Yield 88%; bp 80 °C/0.02 mmHg; ν_{max}/cm^{-1} 1635 (CONEt$_2$) (Found: C, 64.63; H, 7.02; N, 4.93. $C_{15}H_{19}NO_2S$ requires C, 64.95; H, 6.90; N, 5.05%); δ_H(CCl$_4$) 7.56–6.80 (m, 3H, H-3, H-6 and H-7), 4.03 (s, 3H, OCH_3), 3.60–3.23 (q, 4H, CH_2CH$_3$), 2.5 (s, 3H, 2-CH_3), 1.39–1.09 (t, 6H, CH$_2$CH_3).

***N*,*N*-Diethyl-2-*tert*-butyldimethylsilyl-4-methoxybenzo[*b*]thiophene-5-carboxamide 19**
Synthesized from **17** following the general procedure using *tert*-butyldimethylsilyl chloride (TBDMSCl) as electrophile. The crude material was purified by column chromatography [ethyl acetate–light petroleum (1:9) as eluent] to obtain **19** as a colourless viscous liquid. Yield 58%; bp 95 °C/0.02 mmHg; ν_{max}/cm^{-1} 1630 (CONEt$_2$) (Found: C, 63.94; H, 8.04; N, 3.81. $C_{20}H_{31}NO_2SSi$ requires C, 63.61; H, 8.28; N, 3.71%); δ_H 7.63 (d, 1H, H-7, *J* 8.4), 7.59 (s, 1H, H-3), 7.18 (d, 1H, H-6, *J* 8.4), 4.02 (s, 3H, OCH_3), 3.64 (q, 2H, CH_2CH$_3$), 3.16 (q, 2H, CH_2CH$_3$), 1.30 (t, 3H, CH$_2$CH_3), 1.04 (t, 3H, CH$_2$CH_3), 0.98 [s, 9H, Si(CH$_3$)$_2$C(CH_3)$_3$], 0.37 [s, 6H, Si(CH_3)$_2$C(CH$_3$)$_3$].

***N*,*N*-Diethyl-2-*tert*-butyldimethylsilyl-4-methoxy-6-methylbenzo[*b*]thiophene-5-carboxamide 20**
Synthesized from **19** following the general procedure using methyl iodide as electrophile. The crude material was purified by column chromatography [ethyl acetate–light petroleum (1:9) as eluent] to obtain **20** as a low melting solid. Yield 65%; ν_{max}/cm^{-1} 1630 (CONEt$_2$) (Found: C, 64.85; H, 8.57; N, 3.50. $C_{21}H_{33}NO_2SSi$ requires C, 64.40; H, 8.49; N, 3.57%); δ_H 7.52 (s, 1H, H-7), 7.47 (s, 1H, H-3), 4.01 (s, 3H, OCH_3), 3.64 (q, 2H, CH_2CH$_3$), 3.16 (q, 2H, CH_2CH$_3$), 2.37 (s, 3H, 6-CH_3), 1.31 (t, 3H, CH$_2$CH_3), 1.04 (t, 3H, CH$_2$CH_3), 0.98 [s, 9H, Si(CH$_3$)$_2$-C(CH_3)$_3$], 0.38 [s, 6H, Si(CH_3)$_2$C(CH$_3$)$_3$].

***N*,*N*-Diethyl-2-*tert*-butyldimethylsilyl-4-methoxy-6-(2-hydroxyphenethyl)benzo[*b*]thiophene-5-carboxamide 22**
To a well stirred solution of distilled diisopropylamine (0.042 ml, 0.3 mmol) in tetrahydrofuran (20 ml) 1.5 M *n*-butyllithium (0.2 ml, 0.3 mmol) was slowly added by syringe at −78 °C. The reaction mixture was then allowed to reach 0 °C and kept for 45 min at that temperature when a yellow colour developed. After cooling to −78 °C a solution of **21** (0.06 g, 0.15 mmol) in tetrahydrofuran (5 ml) was slowly added by syringe. The temperature was then allowed to rise to 0 °C and lowered again to −40 °C and kept at that temperature for 1 h. Benzaldehyde (0.03 ml, 0.15 mmol) was slowly added to the reaction mixture after it was cooled at −78 °C and the reaction mixture was stirred for 2 h at 0 °C and for 8 h at room temperature. The mixture was extracted with chloroform (3 × 25 ml) after pouring into ice–water and the organic layer after washing with water (2 × 30 ml) and with brine (2 × 30 ml), was dried and evaporated to afford a viscous liquid which was purified by flash chromatography [ethyl acetate–light petroleum (1:1) as eluent] to afford **22** as a dense colourless liquid. Yield 72%; ν_{max}/cm^{-1} 1630 (CONEt$_2$), 3460 (br, OH) (Found: C, 67.36; H, 7.79; N, 2.63. $C_{28}H_{39}NO_3SSi$ requires C, 67.56; H, 7.90; N, 2.81%);

δ_H 7.70 (s, 1H, H-7′), 7.55 (s, 1H, H-3′), 7.35 (s, 5H, C_6H_5), 4.59 (dd, 1H, H-1), 4.37 (s, 1H, O*H*), 3.98 (s, 3H, OCH_3), 3.78 (q, 2H, H-2), 3.51 (q, 2H, CH_2CH_3), 3.24 (q, 2H, CH_2CH_3), 1.34 (t, 3H, CH_2CH_3), 1.28 (t, 3H, CH_2CH_3), 1.02 [s, 9H, $Si(CH_3)_2C(CH_3)_3$], 0.37 [s, 6H, $Si(CH_3)_2C(CH_3)_3$].

7-Phenyl-2-*tert*-butyldimethylsilyl-4-methoxythieno[2,3-*g*]isochromen-5-one 23

A solution of **21** (0.03 g, 0.06 mmol) in ethanol (5 ml) was refluxed for 18 h with 50% aqueous sodium hydroxide (5 ml). The material left after evaporation of the solvent was acidified with dilute hydrochloric acid at 0 °C. The reaction mixture was then extracted with ethyl acetate (3 × 10 ml), the organic layer washed with water (3 × 10 ml) and brine (2 × 10 ml), was dried and evaporated to give a brown solid which was purified by column chromatography eluting with ethyl acetate–light petroleum (1:9), whereby **23** was obtained as a white solid which was crystallised from ether–light petroleum. Yield 45%; mp 115–117 °C; ν_{max}/cm^{-1} 1740 ($CONEt_2$) (Found: C, 67.60; H, 6.51. $C_{24}H_{28}O_3SSi$ requires C, 67.88; H, 6.64%); δ_H 7.51 (s, 1H, H-9), 7.38 (s, 1H, H-3), 7.20 (s, 5H, C_6H_5), 4.96 (dd, 1H, H-7), 4.28 (s, 3H, OCH_3), 3.78 (q, 2H, H-8), 1.02 [s, 9H, $Si(CH_3)_2C(CH_3)_3$], 0.37 [s, 6H, $Si(CH_3)_2C(CH_3)_3$].

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