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The reaction of 2-lithiobenzo[*b*]thiophenes with ketones produced 2-hydroxyalkylbenzo[*b*]thiophenes which were cyclized in thionyl chloride to give novel thieno[3,2-*b*][1]benzothiophenes. Oxidation with peroxyacetic acid gave the *S,S*-dioxides whose regiochemistry was identified from ^1H nmr model studies using substituted benzo[*b*]thiophenes and their corresponding-1,1-dioxides [1].

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Introduction.

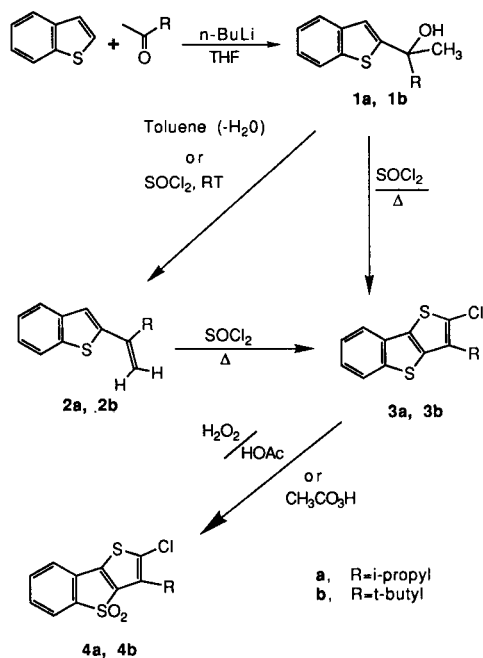
Thieno[3,2-*b*][1]benzothiophenes were prepared previously by Chapman [2]. Benzo[*b*]thiophene-3-thiol was condensed with chloroacetaldehyde diethyl acetal and chloroacetone in the presence of base, and the resulting products were cyclized with hot polyphosphoric acid. Krubsack [3] prepared benzo[*b*]thiophenes from *beta*-arylcarboxylic acids by treatment with hot thionyl chloride in the presence of a catalytic amount of pyridine in quantitative yield. We applied the latter method to a simple and convenient synthesis of new thieno[3,2-*b*][1]benzothiophenes **3** from hindered 2-thianaphthenyl carbinols **1**.

Results and Discussion.

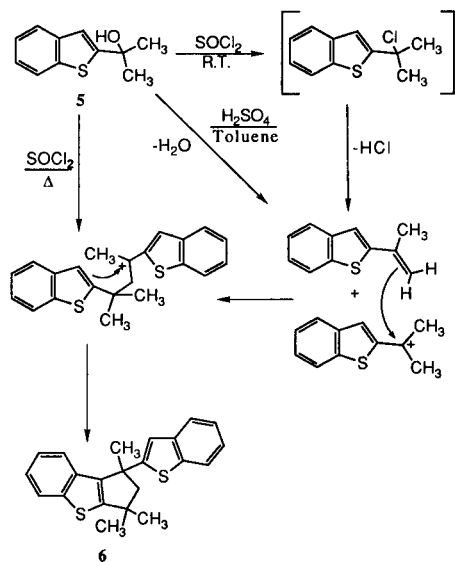
The reaction of 2-lithiobenzo[*b*]thiophene with methyl ketones gave 2-hydroxyalkylbenzo[*b*]thiophenes in good yield (**1a**, **1b**, Scheme I). Cyclization of these intermediates in hot thionyl chloride gave directly new thieno[3,2-*b*][1]benzothiophenes **3a**, **3b**. The reactions proceeded

through the olefin intermediates **2a**, **2b**, which were prepared by dehydration of **1a**, **1b** with either thionyl chloride at room temperature or by azeotroping in toluene. At reflux, thionyl chloride also converted **2a**, **2b** to **3a**, **3b** in good yields. Interestingly, under similar reaction conditions, a non-hindered 2-thianaphthenylcarbinol **5** (Scheme II) exhibited principally the olefin dimerization product **6** in low yield. Oxidation of **3a**, **3b** to the *S,S*-dioxides **4a**, **4b** (Scheme I) was effected with peroxyacetic acid.

Scheme I. Synthesis of Thieno[3,2-*b*][1]benzothiophenes



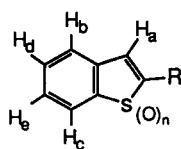
Scheme II. Olefin dimerization of unhindered carbinol



The regiochemistry of oxidation products **4a**, **4b** was identified from ^1H nmr model studies using simple benzo[*b*]thiophenes [4] and their 1,1-dioxide *eg.* **7/8** (Table 1). The ^1H nmr spectrum indicated that oxidation of the ring sulfur of **7** produced a distinctive upfield shift (~ 0.4 ppm) of the H_b ring proton. Surprisingly, protons in the H_a and H_c ring positions remained unchanged, while H_d and H_e ring protons exhibited a slight shift downfield. Similar spectral behavior for 5-substituted-benzo[*b*]thiophenes and their dioxides was observed by Chapman (1968) [5]. Thus, the benzenoid (2H, 2H) pattern of **7** shifted characteristically to a (1H, 2H, 1H) pattern upon oxidation to **8**,

and these results are consistent with the observations of Chapman [2] for thieno[3,2-*b*]benzothiophenes.

Table 1. Benzenoid ^1H NMR Chemical Shifts (ppm/ CDCl_3)



	$\underline{H_a}$	$\underline{H_b}$	$\underline{H_c}$	$\underline{H_d}$	$\underline{H_e}$
7 R=Cl n=0	7.1	7.7	7.6	7.3	7.3
8 R=Cl n=2	7.1	7.3	7.7	7.6	7.5
3a	—	7.8	7.7	7.4	7.4
4a	—	7.3	7.7	7.5	7.4
3b	—	7.8	7.7	7.3	7.3
4b	—	7.4	7.8	7.5	7.5

Similarly, the (2H, 2H) spectral pattern of **3a**, **3b** shifted to a (1H, 2H, 1H) pattern upon oxidation to **4a**, **4b**, respectively, which confirmed that the sulfur atom adjacent to the benzenoid ring was oxidized.

Conclusion.

Apart from the limiting olefin dimerization reaction (Scheme II), the formation of thieno[3,2-*b*]benzothiophenes from the action of hot thionyl chloride on 2-hydroxyalkylbenzo[*b*]thiophenes is a novel route permitting acquisition of a variety of substitution products.

EXPERIMENTAL

The ^1H nmr spectra were obtained on either an IBM NR-80 or Bruker 250 MHz spectrometer, and chemical shifts are reported in ppm relative to tetramethylsilane in deuteriochloroform solvent. Melting points ($^{\circ}\text{C}$) were determined on a Thomas-Hoover melting point apparatus and are uncorrected. Compounds **7** and **8** were reported previously [6]. All reagents were commercially available.

2-(3-Methyl-2-hydroxy-2-butyl)benzo[*b*]thiophene (**1a**).

To 5.0 g (37 mmoles) of thianaphthene in 50 ml of tetrahydrofuran (THF) at $0-5^{\circ}$ was added 15.4 ml of 2.2 *M* *n*-butyllithium (37 mmoles) in hexane. The mixture was allowed to come to room temperature and stirred one hour. To the mixture at $0-5^{\circ}$ was added 3.5 g (41 mmoles) of 3-methyl-2-butanone in 5 ml of THF dropwise. After the addition, the reaction was stirred for 12 hours at room temperature, and 2 ml of 95% ethanol was added. The volatiles were evaporated under vacuum, and the resulting oil was purified by column chromatography on silica gel with ethyl acetate/hexane (1:4) to give **1a**, 4.8 g (59%), oil; ^1H nmr: 7.7 (m, 2H), 7.3 (m, 2H), 7.1 (s, 1H), 2.1 (m, 2H), 1.7 (s, 3H), 1.0 (d, $J = 7.7$ Hz, 3H), 0.9 (d, $J = 7.7$ Hz, 3H); ms: 220 (6.6), 203 (100), 177 (58.9), 147 (26.8), 87 (34.4).

Anal. Calcd. for $\text{C}_{13}\text{H}_{16}\text{OS}$: C, 70.87; H, 7.32; S, 14.55. Found: C, 70.59; H, 7.55; S, 14.36.

2-(3,3-Dimethyl-2-hydroxy-2-butyl)benzo[*b*]thiophene (**1b**).

Similarly, this compound was obtained from thianaphthenyl lithium and 3,3-dimethyl-2-butanone in 50 ml of tetrahydrofuran (THF) at $0-5^{\circ}$, mp $60-63^{\circ}$; ^1H nmr: 7.8 (m, 2H), 7.3 (m, 2H), 7.2 (s, 1H), 2.0 (s, 1H), 1.7 (s, 3H), 1.1 (s, 9H); ms: 234 (15.1), 177 (100), 134 (7.1), 88 (12.7), 43 (95.2).

Anal. Calcd. for $\text{C}_{14}\text{H}_{18}\text{OS}$: C, 71.75; H, 7.74. Found: C, 71.98; H, 7.68.

2-(2-Hydroxy-2-propyl)benzo[*b*]thiophene (**5**).

Similarly, this compound was obtained from thianaphthenyl lithium and acetone in 50 ml of tetrahydrofuran (THF) at $0-5^{\circ}$, mp $54-55^{\circ}$; ^1H nmr: 7.8 (d, $J = 6.9$ Hz, 1H), 7.7 (d, $J = 6.9$ Hz, 1H), 7.3 (m, 2H), 7.2 (s, 1H), 2.1 (s, 1H), 1.7 (s, 6H).

Anal. Calcd. for $\text{C}_{11}\text{H}_{12}\text{OS}$: C, 68.71; H, 6.29. Found: C, 68.65; H, 6.29.

2-(3-Methyl-1-buten-2-yl)benzo[*b*]thiophene (**2a**).

A. To 20 ml of toluene was added 1.6 g (7 mmoles) of **1a** and the mixture was heated under a Dean Stark trap for 24 hours. The volatiles were removed under vacuum, and the resulting oil was purified by column chromatography on silica gel with pentane to give **2a**, 1.1 g (78%), oil; ^1H nmr: 7.7 (m, 2H), 7.3 (m, 3H), 5.5 (s, 1H), 5.1 (s, 1H), 2.9 (m, 1H), 1.2 (d, $J = 6.8$ Hz, 6H); ms: 202 (57), 187 (33.3), 174 (21.5), 159 (43.3), 134 (33.6), 115 (100).

Anal. Calcd. for $\text{C}_{13}\text{H}_{14}\text{S}$: C, 77.18; H, 6.97. Found: C, 76.96; H, 6.91.

B. To 20 ml of stirred thionyl chloride was added 1.6 g (7 mmoles) of **1a**, and the mixture was stirred at room temperature for 1 hour. Excess thionyl chloride was evaporated under vacuum. The resulting oil was dissolved in ethyl acetate and washed with saturated sodium bicarbonate solution, dried over anhydrous sodium sulfate, and evaporated under vacuum to give **2a**, 1.2 g (83%), oil, whose spectral characteristics was identical to the product of procedure A above.

2-(3,3-Dimethyl-1-buten-2-yl)benzo[*b*]thiophene (**2b**).

Similarly, this compound was obtained from **1b**, oil; ^1H nmr: 7.7 (m, 2H), 7.3 (m, 2H), 7.1 (s, 1H), 6.3 (s, 1H), 6.2 (s, 1H), 1.2 (s, 9H); ms: 216 (80.9), 201 (24.9), 174 (11.3), 159 (100), 147 (16.4), 115 (67.3).

Anal. Calcd. for $\text{C}_{14}\text{H}_{16}\text{S}$: C, 77.73; H, 7.40. Found: C, 77.25; H, 7.65.

2-Chloro-3-(1,1-dimethylethyl)thieno[3,2-*b*]benzothiophene (**3b**).

To 15 ml of stirred thionyl chloride was added 1.2 g (5.5 mmoles) of **1b**, and the mixture was heated at reflux for 1 hour. The excess thionyl chloride was removed under vacuum. The resulting oil was dissolved in ethyl acetate, washed with saturated sodium bicarbonate solution, dried over anhydrous sodium sulfate, and the volatiles removed under vacuum to give **3b**, 0.8 g (53%), oil; ¹H nmr: 7.8 (d, J = 8.7 Hz, 1H), 7.7 (d, J = 8.7 Hz, 1H), 7.3 (m, 2H), 1.7 (s, 9H); ms: 280 (62.7), 265 (76.6), 230 (100), 197 (40.5), 77 (68.3).

Anal. Calcd. for C₁₄H₁₃ClS₂: C, 59.88; H, 4.67. Found: C, 60.09; H, 4.77.

2-Chloro-3-(1-methylethyl)thieno[3,2-*b*][1]benzothiophene (**3a**).

Similarly, this compound was obtained from thionyl chloride and **1a**, (33%), oil; ¹H nmr: 7.8 (d, J = 7.7 Hz, 1H), 7.7 (d, J = 7.7 Hz, 1H), 7.4 (m, 2H), 3.4 (m, 1H), 1.4 (d, J = 6.0 Hz, 6H); ms: 266 (99.5), 251 (97.3), 216 (100), 171 (15.9).

Anal. Calcd. for C₁₃H₁₁ClS₂: C, 58.52; H, 4.16. Found: C, 58.60; H, 4.24.

2-Chloro-3-(1-methylethyl)thieno[3,2-*b*][1]benzothiophene 4,4-Dioxide (**4a**).

To 10 ml of acetic acid containing 0.6 g (2 mmoles) of **3a** was added 2.0 g (10 mmoles) of 40% peroxyacetic acid. The mixture was heated on a steam bath with occasional shaking for 2 hours, poured into ice water, filtered, and recrystallized from 95% ethanol to give **4a**, 0.21 g (33%), mp 152-154°; ¹H nmr: 7.7 (d, J = 8.6 Hz, 1H), 7.4 (m, 2H), 7.3 (d, J = 8.6 Hz, 1H), 3.3 (m, 1H), 1.4 (d, J = 7.3 Hz, 6H).

Anal. Calcd. for C₁₃H₁₁ClO₂S₂: C, 52.25; H, 3.70. Found: C, 52.52; H, 3.37.

2-Chloro-3-(1,1-dimethylethyl)thieno[3,2-*b*][1]benzothiophene 4,4-Dioxide (**4b**).

Similarly, this compound was obtained from **3b**, (53%), mp

91-92°; ¹H nmr: 7.8 (d, J = 8.6 Hz, 1H), 7.4 (m, 3H), 1.7 (s, 9H).

Anal. Calcd. for C₁₄H₁₃ClO₂S₂: C, 53.75; H, 4.19. Found: C, 53.69; H, 4.29.

Dimerization of Compound **5**.

To 10 ml of thionyl chloride at -5 to 0° was added 0.5 g (3 mmoles) of **5**. The mixture was allowed to come to room temperature and stirred for 1 hour. Excess thionyl chloride was removed under vacuum, and the resulting oil was dissolved in ethyl acetate, washed with water, and with dilute aqueous sodium bicarbonate. The mixture was dried over sodium sulfate, and volatiles were removed under vacuum. The resulting oil was purified by column chromatography on silica gel with pentane to give **6**, 0.3 g (33%), mp 125-127°; ¹H nmr: 7.7 (m, 2H), 7.4 (m, 2H), 7.1 (m, 4H), 6.9 (s, 1H), 2.8 (d, J = 12.7 Hz, 1H), 2.5 (d, J = 12.7 Hz, 1H), 1.9 (s, 3H), 1.4 (s, 3H), 1.3 (s, 3H).

Anal. Calcd. for C₂₂H₂₀S₂: C, 75.82; H, 5.78. Found: C, 75.60; H, 5.84.

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REFERENCES AND NOTES

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