# Studies in Sulphur Heterocycles. Part 6.[1] Convenient Synthesis of 5-Substituted Benzo[*b*]thiophene Derivatives and a Facile Entry to the Thieno[2,3-*g*]indole System†

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From 6,7-dihydrobenzo[*b*]thiophen-4(5*H*)-one and its 2-methyl derivative as starting materials 5-formyl, 5-acetyl, 5-carboxy, and 5-cyano-benzo[*b*]thiophene and 2-methylbenzo[*b*]thiophene, have been prepared in good to excellent yields. Benzo[*b*]thiophene-5-carbaldehyde on base catalysed condensation with ethyl azidoacetate, followed by thermal cyclisation of the resulting azidocinnamate provided a facile entry into the thieno[2,3-*g*]indole system.

Many biologically active benzo[*b*]thiophenes[2,3] are 5-substituted compounds. These are usually synthesized[3,4] by cyclising intermediates obtained by incorporating a two carbon unit into expensive *para*-substituted thiophenols. Another method is Rossi's,[6] later exploited by others,[7,8] which consists of a one-pot synthesis of methyl or ethyl 5-nitrobenzo[*b*]thiophene-2-carboxylates from 2-chloro-5-nitrobenzaldehyde and the corresponding mercaptoacetate. The nitro group serves as a precursor to other functional groups *via* reduction[9] and diazotisation.[7,8]

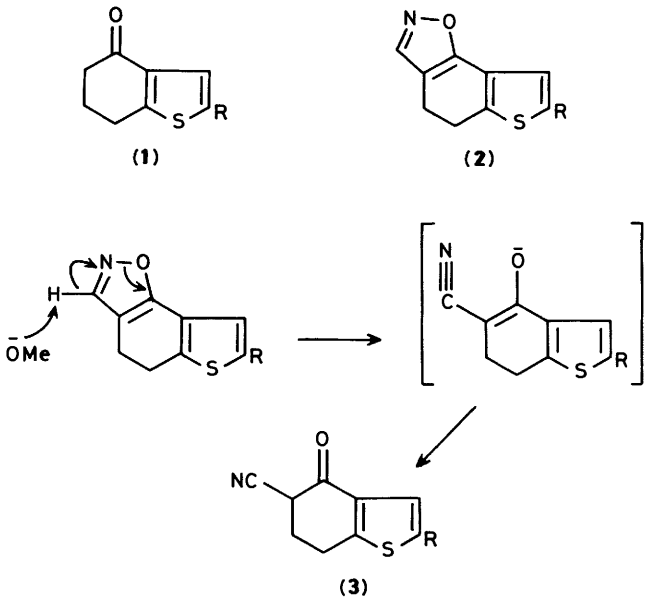
Because of its low reactivity,[10–13] direct functionalisation of the 5-position of benzo[*b*]thiophene, by electrophilic substitution, usually results in low product yields and intractable mixtures. Further bromination and formylation at this position proceed in reasonable yields only in the presence of a 4-hydroxy group,[14] whilst nitration of the same compound, affords a mixture of mono- and poly-nitro derivatives.[14]

We report syntheses of several 5-substituted benzo[*b*]thiophenes *via* simpler routes with improved overall yields; the functional groups introduced can be elaborated into side chains, associated with their biological activities. In one instance, such functionalisation helped us to provide a facile entry into the thieno[2,3-*g*]indole system, which is present in sulphur congeners of the antitumour compounds dideoxy PDE-I and PDE-II.[15]

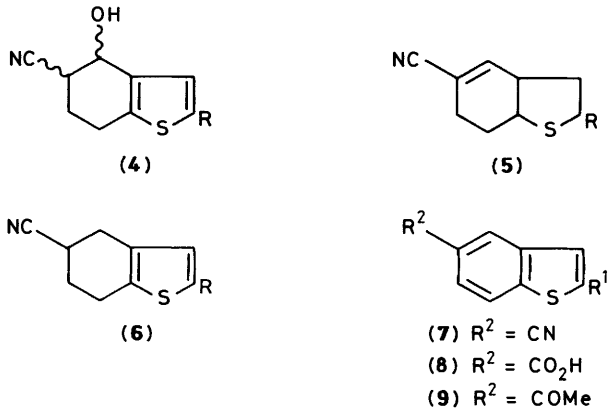
## Results and Discussion

We reported earlier, the use of 6,7-dihydrobenzo[*b*]thiophen-4(5*H*)-one (**1**; R = H) as well as its 2-methyl (**1**; R = Me) and 2-bromo (**1**; R = Br) derivatives in the synthesis of various tricyclic compounds[16,17] and also of 4-substituted benzo[*b*]-thiophenes.[1,18] The commercially available ketone (**1**; R = H) and its 2-methyl derivative (**1**; R = Me) are further exploited as starting materials for the compounds reported herein.

Treatment of 4,5-dihydrothieno[2,3-*g*]-1,2-benzisoxazole (**2**; R = H) and its 2-methyl derivative, with sodium methoxide in methanol readily cleaved the isoxazole ring[19] to afford the β-oxonitriles (**3**; R = H, Me) (90%); the mechanism[20] for this cleavage is shown in Scheme 1. Reduction of the carbonyl function in (**3**) with sodium borohydride in methanol resulted in the alcohols (**4**) which were dehydrated, without further purification, to afford 6,7-dihydrobenzo[*b*]thiophene-5-carbonitrile (**5**; R = H) and its 2-methyl derivative (**5**; R = Me). The double bond was reduced in both the cases with magnesium in methanol, to give the fully saturated compounds (**6**; R = H, Me). However, different methods were necessary for their aromatisation. While the aromatisation of 6,7-dihydrobenzo-[*b*]thiophene-5-carbonitrile (**5**; R = H) was best achieved *via* bromination–dehydrobromination with *N*-bromosuccinimide in boiling carbon tetrachloride under irradiation with two 200 W tungsten lamps, aromatisation of the 2-methyl derivative (**7**;




Scheme 1.

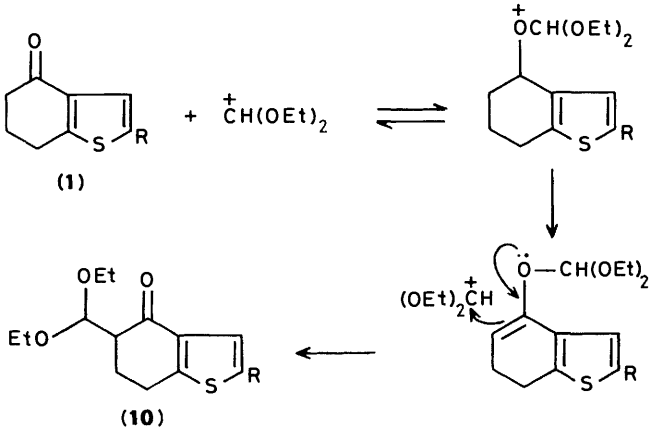



† Abstracted from the PhD thesis of S. D.

$R^1$ = Me) was accomplished only with Pd–charcoal in boiling decalin, and this was sluggishly.[21] The product was never completely freed of decalin. Use of sulphur in boiling diphenyl *ether* gave a product even more difficult to purify. Notwithstanding these problems, the 2-methyl-5-cyanobenzo-[*b*]thiophene (**7**; $R^1$ = Me) was pure enough for further reactions. Benzo[*b*]thiophene-5-carbonitrile (**7**; $R^1$ = H) was earlier prepared[22] by a longer route, involving Sandmeyer reaction of diazotised 5-aminobenzo[*b*]thiophene. The corresponding 2-methyl compound was unknown presumably owing to difficulty in preparing 5-amino-2-methylbenzo[*b*]thiophene.

The nitriles (**7**; $R^1$ = H, Me) on hydrolysis with refluxing methanolic potassium hydroxide gave the corresponding carboxylic acids (**8**; $R^1$ = H, Me) in high yield. A literature report[22] of the hydrolysis of the nitrile (**7**; $R^1$ = H) to give the acid (**8**; $R^1$ = H) mentions no yield. Other reported procedures of its synthesis, *e.g.* from the corresponding benzo[*b*]thienylmagnesium halide[23] or from oxidation of the corresponding aldehyde,[24] involve longer routes. The nitrile (**7**; $R^1$ = H), on treatment with methylmagnesium iodide and the acid treatment of the intermediate imino compound in the usual way, afforded 5-acetylbenzo[*b*]thiophene (**9**; $R^1$ = H) (80%).[22] The corresponding 2-methyl derivative (**9**; $R^1$ = Me) was synthesized from the chloride of the acid (**8**; $R^1$ = Me) and acid treatment of the intermediate.

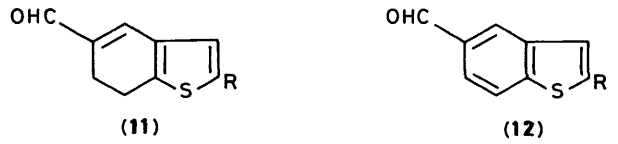
The aldehydes (**12**) were obtained by aromatising the dihydro compounds (**11**), produced in good yield when the oxo acetals (**10**) were reduced with sodium borohydride followed by acidic work up. Facile synthesis[25–27] of the oxo acetals (**10**) from the ketones (**1**; R = H, Me) by treatment with ethyl orthoformate in the presence of boron trifluoride–diethyl ether and *N*,*N*-diisopropylethylamine, apparently involves an attack by diethoxyoxonium fluoroborate, in a manner similar to the Vilsmeier reagent (Scheme 2). Enolisation and concomitant *o*-



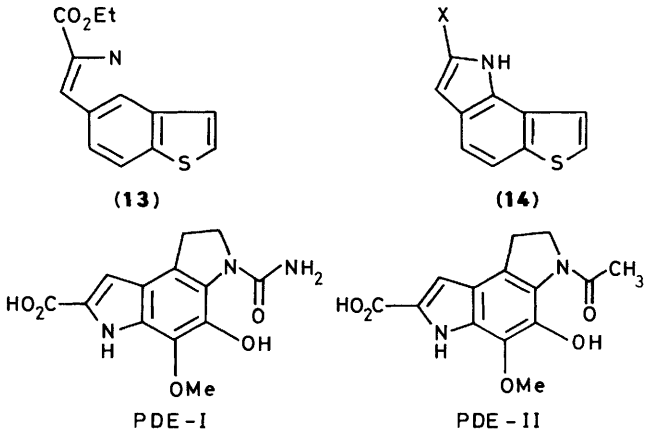

Scheme 2.

alkylation, followed by deprotonation by the base leads to an enol ether which finally affords the oxo acetal through electrophilic addition of diethoxycarbonium ion to the double bond. Aromitisation of (**11**; R = H) was accomplished with *N*-bromosuccinimide; a small amount of allylic oxidation product was also obtained. The use of *N*-bromosuccinimide being precluded with the 2-methyl compound (**11**; R = Me), aromatisation of the latter was achieved with sulphur in boiling diphenyl ether, in a moderate yield and involving repeated chromatography to remove traces of diphenyl ether. The aldehyde (**12**; R = H) was earlier obtained[24] by Sommelet reaction on the 5-halogenomethyl compound.

The aldehyde (**12**; R = H) was conveniently used to prepare the thieno[2,3-*g*]indole system, which has importance in view




of its presence in sulphur congeners of the antitumour compounds dideoxy PDE-I and PDE-II. Base catalysed condensation[28] of the aldehyde with ethyl azidoacetate provided the azidocinnamate (**13**), the n.m.r. spectrum of which revealed the presence of only one geometrical isomer. Thermolysis of the azidocinnamate (**13**) in boiling xylene afforded ethyl thieno[2,3-*g*]indole-2-carboxylate (**14**; X = $CO_2Et$) (78%). Hydrolysis of the ethoxycarbonyl function followed by decarboxylation was only achieved after prolonged refluxing with potassium hydroxide in ethanol to give the thieno[2,3-*g*]indole (**14**; X = H).




## Experimental

M.p.s were recorded in open capillaries and are uncorrected. Product purities were routinely checked by t.l.c. using silica gel 60 $HF_{254}$ (E. Merck). Light petroleum, unless otherwise stated, refers to the fraction of b.p. 60—80 °C. I.r. spectra were recorded on a Perkin-Elmer 298 spectrometer. $^1H$ N.m.r. spectra were recorded at 100 and 200 MHz on FX-100 and Varian XL-200 instruments in deuteriochloroform (unless otherwise stated) with tetramethylsilane as internal standard. U.v. absorption spectra were measured in 95% ethanol solution on a Hitachi Model 200-20 spectrophotometer; ε expressed in $dm^3\ mol^{-1}\ cm^{-1}$. P. P. Bhattacharyya and B. Pathak carried out the C,H,N analyses.

*5-Cyano-6,7-dihydrobenzo*[b]*thiophen-4(5H)-one* (**3**; R = H).—To an ice-cold stirred solution of the isoxazole derivative (**2**; R = H) (5.3 g, 30 mmol) in dry THF (15 ml) was added dropwise during 30 min, a cold solution of sodium methoxide prepared from Na (1.5 g, 60 mmol) and dry methanol (40 ml) under a nitrogen atmosphere. The reaction mixture was magnetically stirred for 2 h with cooling and then cold 5% aqueous potassium hydroxide (50 ml) was added to it. After dilution with water to make up a total volume of 700 ml, the neutral part was removed by extraction with ether. The alkaline part was acidified with dilute hydrochloric acid to liberate the desired β-oxo nitrile, which was then extracted into ether. The organic phase was washed with saturated brine, dried ($Na_2SO_4$), evaporated, and the residue recrystallised from a mixture of ether–light petroleum (b.p. 40—60 °C) to give white needles (4.7 g, 90%), m.p. 76—77 °C (Found: C, 60.7; H, 4.15; N, 7.8. $C_9H_7NOS$ requires C, 61.0; H, 4.0; N, 7.8%); $\nu_{max.}$ 1 695 (C=O) and 2 220 $cm^{-1}$ (C=N); δ 2.48—2.72 (m, 2 H, 7-$CH_2$),

3.06—3.40 (m, 3 H, 6-$CH_2$ and 5-H), 7.01 (d, 1 H, 2-H, *J* 6 Hz), and 7.47 (d, 1 H, 3-H, *J* 6 Hz).

5-*Cyano*-2-*methyl*-6,7-*dihydrobenzo*[b]*thiophen*-4(5H)-*one* (**3**; R = Me).—This compound was prepared from the corresponding isoxazole derivative (**2**; R = Me) (1.6 g, 8.3 mmol) in THF and sodium methoxide [Na (0.42 g, 16.6 mmol) and dry MeOH (15 ml)] in a manner similar to that previously described. It was purified by column chromatography over silica gel (ether–light petroleum) (1.35 g, 84%), and had m.p. 75 °C (Found: C, 63.05; H, 4.9; N, 7.45. $C_{10}H_9ONS$ requires C, 62.82; H, 4.75; N, 7.33%); $\nu_{max.}$ 1 695 (C=O) and 2 220 $cm^{-1}$ (C≡N); δ 2.34—3.48 (m, 2 H, 7-$CH_2$), 3.01—3.45 (m, 3 H, 6-$CH_2$ and 5-H), and 7.45 (d, 1 H, 3-H, *J* 6 Hz).

4-*Hydroxy*-6,7-*dihydrobenzo*[b]*thiophene*-5-*carbonitrile* (**4**; R = H).—5-Cyano-6,7-dihydrobenzo[*b*]thiophen-4(5*H*)-one (**3**; R = H) (4.53 g, 25 mmol) was dissolved in twice distilled methanol (100 ml) with stirring and cooling. To the cooled mixture finely powdered sodium borohydride (1.02 g, 25 mmol) was added in small portions, while the temperature was maintained at 0—5 °C. The reaction mixture was kept at room temperature for 16 h after which crushed ice was added and the whole acidified carefully with hydrochloric acid. The mixture was then extracted with ether, the extract washed with saturated brine, dried ($Na_2SO_4$), and evaporated to provide the crude reduction product (4.39 g, 96%); $\nu_{max.}$ 2 200 (C=N) and 3 400 $cm^{-1}$ (OH); δ 2.24—2.44 (m, 2 H, 7-$CH_2$), 2.70—3.22 (m, 3 H, 6-$CH_2$ and 5-H), 7.15 (d, 1 H, 2-H, *J* 6 Hz), and 7.61 (d, 1 H, 3-H, *J* 6 Hz).

4-*Hydroxy*-2-*methyl*-6,7-*dihydrobenzo*[b]*thiophene*-5-*carbonitrile* (**4**; R = Me).—Reduction of 5-cyano-2-methyl-6,7-dihydrobenzo[*b*]thiophen-4(5*H*)-one (**3**; R = Me) (0.830 g, 5 mmol) with sodium borohydride (200 mg, 5 mmol) in the usual manner gave a yellow gum (610 mg, 76%); $\nu_{max.}$ 2 200 (C≡N) and 3 400 $cm^{-1}$ (OH); δ 2.10—2.40 (m, 2 H, 6-$CH_2$), 2.46 (s, 3 H, 2-$CH_3$), 2.64—3.14 (m, 3 H, 5-H and 7-$CH_2$), 4.90 (br s, 1 H, OH), and 6.72 (br s, 1 H, 3-H).

6,7-*Dihydrobenzo*[b]*thiophene*-5-*carbonitrile* (**5**; R = H).—To the crude sodium borohydride reduction product (**4**; R = H) (4.36 g, 24 mmol) dissolved in dry benzene (125 ml) in a flask fitted with a condenser and a Dean-Stark water separator was added a catalytic amount (200 mg) of toluene-*p*-sulphonic acid. The reaction mixture was refluxed under an atmosphere of nitrogen for 8 h, allowed to cool to room temperature, and washed with 5% aqueous sodium hydrogen carbonate and saturated brine, dried ($Na_2SO_4$), and evaporated to give an oil which was purified by column chromatography over silica gel [ether–light petroleum (1:9) as eluant] and recrystallised from ether–light petroleum (b.p. 40—60 °C) to give (**5**) (3.33 g, 85%), m.p. 56—57 °C (Found: C, 67.3; H, 4.5; N, 9.0. $C_9H_7NS$ requires C, 67.08; H, 4.34; N, 8.69%); $\nu_{max.}$ 2 180 $cm^{-1}$ (C≡N); δ 2.62 (t, 1 H, 6-$CH_2$, *J* 8 Hz), 2.98 (t, 2 H, 7-$CH_2$, *J* 8 Hz), 6.92 (d, 1 H, 2-H, *J* 6 Hz), 7.11 (d, 1 H, 2-H or 3 H, *J* 6 Hz), and 7.18 (s, 1 H, 4-H); $\lambda_{max.}$ 237.8 (ε 19 647.532), 245 (19 627.391), and 314 nm (10 120.845).

2-*Methyl*-6,7-*dihydrobenzo*[b]*thiophene*-5-*carbonitrile* (**5**; R = Me).—The desired compound was synthesized from (**4**; R = Me) (600 mg, 3 mmol) by treatment with toluene-*p*-sulphonic acid (200 mg) in benzene (25 ml). The crude material was purified by column chromatography over silica gel (eluted with light petroleum) to give a clear glass (430 mg, 79%) (Found: C, 68.3; H, 4.95; N, 8.35. $C_{10}H_9NS$ requires C, 68.57; H, 5.14; N, 8.00%); $\nu_{max.}$ 2 170 $cm^{-1}$ (C≡N); δ 2.36 (s, 3 H, 2-$CH_3$), 2.52—2.68 (m, 2 H, 6-$CH_2$), 2.82—2.98 (m, 2 H, 7-$CH_2$), 6.66 (br s, 1 H, 3-H), and 7.06 (s, 1 H, 4-H).

4,5,6,7-*Tetrahydrobenzo*[b]*thiophene*-5-*carbonitrile* (**6**; R = H).—Mg turnings (1.114 g, 40 equiv.) were added to (**5**; R = H) (250 mg, 1.5 mmol) in methanol (15 ml) to give after 10 min an exothermic reaction which was moderated by external cooling. After the mixture had been stirred for 1 h at 0 °C and 5 h at 25 °C, HCl (6M, 25 ml) was cautiously added and kept at 0 °C for further 1 h. The mixture was extracted with ether and the extract washed with brine, dried ($Na_2SO_4$), and evaporated to afford a yellow oil. Chromatography of this over silica gel (eluant, ether–light petroleum, 1:4) gave compound (**6**; R = H) (192 mg, 76%), m.p. 58 °C (Found: C, 66.1; H, 5.65; N, 8.5. $C_9H_9NS$ requires C, 66.20; H, 5.50; N, 8.60%); $\nu_{max.}$ 2 220 $cm^{-1}$ (C≡N); δ 2.00—2.40 (m, 2 H, 6-$CH_2$), 2.80—3.18 (m, 5 H, 4-$CH_2$, 5-H and 7-$CH_2$), 6.81 (d, 1 H, 2-H or 3-H, *J* 6 Hz), and 7.12 (d, 1 H, 2-H or 3-H, *J* 6 Hz).

*Benzo*[b]*thiophene*-5-*carbonitrile* (**7**; $R^1$ = H).—Freshly crystallised *N*-bromosuccinimide (0.178 g, 1 mmol) was added portionwise to a boiling solution of 6,7-dihydrobenzo-[*b*]thiophene-5-carbonitrile (0.16 g, 1 mmol) and dibenzoyl peroxide (catalytic amount) in dry carbon tetrachloride (15 ml) under a flow of nitrogen while the mixture was irradiated with two 200 W lamps. After a period of 30 min the reaction mixture was cooled, filtered, and evaporated, and the crude residue was recrystallised from ether–light petroleum (b.p. 40—60 °C); the product had m.p. 63 °C (Found: C, 68.0; H, 3.2; N, 8.7. Calc. for $C_9H_5NS$: C, 67.90; H, 3.10; N, 8.8%); $\nu_{max.}$ 2 180 $cm^{-1}$ (C≡N); δ 7.43 (d, 1 H, 2-H or 3-H, *J* 6 Hz), 7.58 (dd, 1 H, 6-H, $J_{6,7}$ 9 Hz, $J_{4,6}$ 2 Hz), 7.64 (d, 1 H, 2-H or 3-H, *J* 6 Hz), 7.99 (d, 1 H, 7-H, *J* 9 Hz), and 8.17 (d, 1 H, 4-H, *J* 2 Hz); $\lambda_{max.}$ 211.2 (ε 22 954.545), 240.1 (85 378.787), and 265 nm (6 515.15).

2-*Methylbenzo*[b]*thiophene*-5-*carbonitrile* (**7**; $R^1$ = Me).—The compound (**5**; R = Me) (1 g, 5 mmol) was refluxed in decalin in the presence of catalytic amount of Pd/C for 10 h. After cooling, the reaction mixture was filtered, the residue washed with ether, and the combined filtrates were evaporated. The crude product remaining was chromatographed over silica gel (light petroleum as eluant) to give the desired compound (**7**; $R^1$ = Me) which contained traces of decalin; $\nu_{max.}$ 2 220 $cm^{-1}$ (C≡N); δ 7.05 (br s, 1 H, 3-H), 7.51 (dd, 1 H, 6-H, $J_{6,7}$ 9 Hz, $J_{4,6}$ 2 Hz), 7.84 (d, 1 H, 7-H, *J* 9 Hz), and 7.96 (d, 1 H, 4-H, *J* 2 Hz).

*Benzo*[b]*thiophene*-5-*carboxylic Acid* (**8**; $R^1$ = H).—Compound (**6**; R = H) (0.47 g, 2.3 mmol) was hydrolysed by refluxing with methanolic KOH (20%, 20 ml) for 24 h. After removal of the neutral part with ether the aqueous phase was acidified with dilute HCl and the crude acid was extracted with ether. Further purification afforded a white solid which was recrystallised from ethyl acetate–benzene (355 mg, 88%), m.p. 208—210 °C (lit.,[22] 211—212 °C) (Found: C, 60.9; H, 3.5. Calc. for $C_9H_6O_2S$: C, 60.70; H, 3.40%); $\nu_{max.}$ 1 700 (C=O) and 3 140 $cm^{-1}$ (OH); δ 7.92 (d, 1 H, 3-H, *J* 6 Hz), 8.19 (d, 1 H, 2-H, *J* 6 Hz), 8.25 (dd, 1 H, 6-H, $J_{6,7}$ 9 Hz, $J_{4,6}$ 2 Hz), 8.41 (d, 1 H, 7-H, *J* 9 Hz), and 8.88 (d, 1 H, 4-H, *J* 2 Hz); $\lambda_{max.}$ 213 (ε 13 267.326) and 241.8 nm (50 693.069).

2-*Methylbenzo*[b]*thiophene*-5-*carboxylic Acid* (**8**; $R^1$ = Me).—Crude material (620 mg; containing traces of decalin), obtained from aromatisation of compound (**5**; R = Me) was hydrolysed by heating under reflux for 24 h with a solution of methanolic KOH (20%; 10 ml). Work-up gave the crude product which was recrystallised from ethyl acetate–benzene to provide a white crystalline solid (560 mg, 82%), m.p. 205—206 °C (Found: C, 62.55; H, 4.2. $C_{10}H_8O_2S$ requires C, 62.50; H, 4.20%); $\nu_{max.}$ 1 700 (C=O) and 3 150 $cm^{-1}$ (OH); δ 2.44 (s, 3 H, 2-$CH_3$), 7.68 (br s, 1 H, 3-H), 7.76 (dd, 1 H, 6-H, $J_{6,7}$ 9 Hz, $J_{4,6}$ 2 Hz), 8.00 (d, 1 H, 7-H, *J* 9 Hz), and 8.28 (d, 1 H, 4-H, *J* 2 Hz).

**Table.**

| Compd. | Yield (%) | $\nu_{max.}$/cm$^{-1}$ | $\delta_H$ | $\lambda_{max.}$/nm | Found C,H,N (%) (requires) |
|---|---|---|---|---|---|
| (**11**; R = H) | 83 | 1 660 (C=O) | 2.73 (t, 2 H, 6-$CH_2$), 2.89 (t, 2 H, 7-$CH_2$), 7.03 (d, 1 H, 2-H or 3-H, *J* 6 Hz), 7.15 (d, 1 H, 2-H or 3-H, *J* 6 Hz), 7.27 (s, 1 H, 4-H), 9.6 (s, 1 H, CHO) | 245 (ε 13 047.445), 252 (13 540.145), 332 (8 394.160) | Found: C, 66.0; H, 4.6. Calc. (C, 65.85; H, 4.88) |
| (**11**; R = Me) | 84 | 1 660 (C=O) | 2.46 (s, 3 H, 2-$CH_3$), 2.71 (t, 2 H, 6-$CH_2$), 2.94 (t, 2 H, 7-$CH_2$), 6.74 (s, 1 H, 3-H), 7.35 (s, 1 H, 4-H), 9.61 (s, 1 H, CHO) | 202.8 (ε 6 132.315), 246.2 (6 386.768) | Found: C, 67.65; H, 5.85. (C, 67.4; H, 5.6) |

*5-Acetylbenzo*[b]*thiophene* (**9**; $R^1$ = H).—The carboxylic acid (**8**; R = H) (640 mg, 4 mmol) in dry benzene (5 ml) was added in one portion to methylmagnesium iodide (4 molar excess) suspended in dry benzene (10 ml) after removal of ether. The mixture was refluxed for 6 h after which it was acidified and refluxed for further 6 h. The crude product obtained upon work-up was chromatographed over neutral alumina (eluant, benzene–petroleum, 1:4) and recrystallised from ether–light petroleum (b.p. 40—60 °C); m.p. 63 °C (lit.,[22] 63—65 °C) (Found: C, 68.0; H, 4.65. Calc. for $C_{10}H_8OS$: C, 68.20; H, 4.60%); $\nu_{max.}$ 1 680 cm$^{-1}$ (C=O); δ 2.69 (s, 3 H, Ac), 7.48 (d, 1 H, 2-H or 3 H, *J* 6 Hz), 7.57 (d, 1 H, 2-H or 3-H, *J* 6 Hz), 7.98 (br s, 2 H, 6-H and 7-H), and 8.47 (br s, 1 H, 4-H); $\lambda_{max.}$ 242.14 (ε 56 947.162).

*5-Acetyl-2-methylbenzo*[b]*thiophene* (**9**; $R^1$ = Me).—Dry ethanol (5 ml) and $CCl_4$ (1 ml) were added to Mg turnings (14.9 mg, 0.56 mmol) and the stirred mixture was warmed slightly to initiate the reaction. After several minutes, dry ether (8 ml) was added cautiously followed by freshly distilled diethyl malonate (0.099 mg, 0.56 mmol). After the mixture had been refluxed for 3 h, 2-methylbenzo[*b*]thiophene-5-carbonyl chloride (prepared in the usual manner) (118 mg, 0.56 mmol) in dry ether (10 ml) was added dropwise over 30 min. After a further period under reflux (90 min) dilute $H_2SO_4$ (10 ml) was added. The aqueous layer was extracted with ether and the extract was washed with water, dried ($Na_2SO_4$), and evaporated. The crude product so obtained was refluxed with a mixture of glacial acetic acid (8 ml), concentrated $H_2SO_4$ (1.5 ml), and water (5.5 ml) for 6 h after which the ice-cold reaction mixture was made alkaline with 20% aqueous NaOH and extracted with ether. The extract was washed with water, dried ($Na_2SO_4$), and evaporated to afford the title compound (**9**; $R^1$ = Me) which was crystallised from ether–light petroleum (b.p. 40—60 °C) (0.076 g, 77%), m.p. 78 °C (Found: C, 69.45; H, 5.3. $C_{11}H_{10}OS$ requires C, 69.70; H, 5.60%); $\nu_{max.}$ 1 680 cm$^{-1}$ (C=O); δ 2.60 (s, 3 H, 2-$CH_3$), 2.64 (s, 3 H, Ac), 7.06 (br s, 1 H, 3-H), 7.77 (dd, 1 H, 6-H, $J_{6,7}$ 9 Hz, $J_{4,6}$ 2 Hz), 7.89 (d, 1 H, *J* 9 Hz), and 8.04 (d, 1 H, 4-H, *J* 2 Hz); $\lambda_{max.}$ 247.2 nm (ε 38 888.88).

*6,7-Dihydrobenzo*[b]*thiophene-5-carbaldehyde* (**11**; R = H, Me): *General Procedure.*—To freshly distilled triethyl orthoformate (0.04 mol) kept under nitrogen at −30 °C was added a solution of freshly distilled boron trifluoride–diethyl ether (0.05 mol) in a minimum quantity of dry dichloromethane. After being stirred for 15 min at 0 °C, the reaction mixture was cooled to −78 °C and the following added, dropwise and sequentially: the ketone (**1**; R = H, Me) (20 mmol) in a minimum amount of dry dichloromethane and di-isopropylethylamine (60 mmol)—the latter over a period of 10 min. After being stirred for 2 h at −10 °C to −20 °C, the resulting mixture was poured rapidly into saturated aqueous sodium hydrogen carbonate (50 ml). More dichloromethane was added and the reaction mixture stirred at 28 °C for 20 min. The organic phase was washed with cold dilute sulphuric acid and water, dried, and evaporated, to give the crude ketoacetal, which was reduced with sodium borohydride (3.5 molar excess) in absolute ethanol at room temperature for 12 h. Acidic work-up (stirring with ice-cold HCl for 3 h) followed by washing of the organic phase with brine and drying gave, on evaporation of solvent, the crude product; this was passed through a short column of silica gel (eluant light petroleum). Physical and analytical data for the dihydro aldehydes (**11**; R = H, Me) were as shown in the Table.

*Benzo*[b]*thiophene-5-carbaldehyde* (**12**; R = H).—6,7-Dihydrobenzo[*b*]thiophene-5-carbaldehyde (**11**; R = H) (0.164 g, 10 mmol) was aromatised with *N*-bromosuccinimide and the crude product was chromatographed over silica gel (eluant ether–light petroleum, 1:10). The product was recrystallised from ether–light petroleum (120 mg, 74%); m.p. 58 °C (lit.,[24] 57 °C) (Found: C, 66.8; H, 3.6. Calc. for $C_9H_6OS$: C, 66.66; H, 3.70%); $\nu_{max.}$ 1 675 cm$^{-1}$ (C=O); δ 7.46 (d, 1 H, 2-H or 3-H, *J* 6 Hz), 7.57 (d, 1 H, 2-H or 3-H, *J* 6 Hz), 7.88 (dd, 1 H, 6-H, $J_{6,7}$ 9 Hz, $J_{4,6}$ 2 Hz), 7.95 (d, 1 H, 7-H, *J* 9 Hz), 8.32 (d, 1 H, 4-H, *J* 2 Hz), and 10.20 (s, 1 H, CHO); $\lambda_{max.}$ 243.6 nm (ε 39 807.69).

*2-Methylbenzo*[b]*thiophene-5-carbaldehyde* (**12**; R = Me).—Compound (**11**; R = Me) (0.166 g, 1 mmol) was aromatised with sulphur (60 mg) in boiling diphenyl ether (5 ml) under a constant slow stream of nitrogen for 1 h. The crude product (with solvent) was chromatographed (× 3) over silica gel. The bulk of the diphenyl ether was eluted with light petroleum and the aldehyde was finally eluted with dichloromethane–light petroleum (2:1) as a light yellow solid which was recrystallised from the same solvent mixture, it had m.p. 140 °C (Found: C, 68.0; H, 4.3. $C_{10}H_8OS$ requires C, 68.18; H, 4.54%); $\nu_{max.}$ 1 670 cm$^{-1}$ (C=O); δ 2.58 (s, 3 H, $-CH_3$), 7.10 (br s, 1 H, 3-H), 7.86 (dd, 1 H, 6-H, $J_{6,7}$ 9 Hz, $J_{4,6}$ 2 Hz), and 10.02 (s, 1 H, CHO); $\lambda_{max.}$ 248.4 nm (ε 34 281.65).

*Ethyl 2-Azido-3-(5-benzo*[b]*thienyl)propenoate* (**13**).—Care was taken to protect the following reaction from light at all times. A mixture of compound (**11**; R = H) (900 mg, 5.5 mmol) and ethyl azidoacetate (2.83 g, 22 mmol) was added to a solution of sodium ethoxide (22 mmol) in ethanol at −15 °C. The mixture was stirred at this temperature for 2 h and then left overnight. It was then poured into aqueous ammonium chloride and extracted with ether. The combined ether extracts were washed with saturated aqueous sodium metabisulphite and water, dried ($Na_2SO_4$), evaporated, and the residue chromatographed over silica gel (eluant 3% ethyl acetate–light petroleum) (800 mg, 54%); $\nu_{max.}$ 2 120, 2 100, and 1 700 cm$^{-1}$; δ 1.6 (t, 3 H, $CO_2CH_2CH_3$, *J* 7 Hz), 4.4 (q, 2 H, $CO_2CH_2CH_3$, *J* 7 Hz), 7.4 (d, 1 H, 2-H or 3-H, *J* 6 Hz), 7.54 (d, 1 H, 2-H or 3-H, *J* 6 Hz), 7.66 (dd, 1 H, 6-H, $J_{6,7}$ 9 Hz, $J_{4,6}$ 2 Hz), 7.96 (d, 1 H, 7-H, *J* 9 Hz), 8.40 (d, 1 H, 4-H, *J* 2 Hz), and 10.30 (s, 1 H, C*H*=).

*Ethyl Thieno*[2,3-g]*indole-2-carboxylate* (**14**; X = $CO_2Et$).—Ethyl 2-azido-3-(5-benzo[*b*]thienyl)propenoate (**13**) (750 mg, 2.7 mmol) was dissolved in xylene (10 ml) and the mixture refluxed for 45 min. It was then evaporated and the crude product chromatographed (eluant 3% ethyl acetate–light petroleum), and recrystallised from ether–light petroleum (b.p. 40—60 °C) to give brownish white needles (520 mg, 78%), m.p. 156 °C (Found: C, 63.7; H, 4.8; N, 5.85. $C_{13}H_{11}NO_2S$ requires C, 63.67; H, 4.48; N, 5.71%); $\nu_{max.}$ 1 686 (C=O) and 3 345 $cm^{-1}$ (NH); δ 1.44 (t, 3 H, $CO_2CH_2CH_3$, *J* 7 Hz), 4.46 (q, 2 H, $CO_2CH_2CH_3$, *J* 7 Hz), 7.35 (d, 1 H, 8-H, *J* 6 Hz), 7.55 (d, 1 H, 5-H, *J* 9 Hz), 7.60 (d, 1 H, 7-H, *J* 6 Hz), 7.62 (s, 1 H, 3-H), 7.64 (d, 1 H, 6-H, *J* 9 Hz), and 9.48 (br s, 1 H, NH).

*Thieno*[2,3-g]*indole* (**14**; X = H).—Compound (**14**; X = $CO_2Et$) (0.4 g, 1.6 mmol) was added to an ethanolic solution of KOH (15%, 10 ml) and the mixture refluxed for 16 h under nitrogen. The mixture was allowed to cool and the neutral part was removed with ether; the aqueous layer was then acidified with HCl. The crude residue obtained after work-up was chromatographed over silica gel with ether–light petroleum (1:9) as eluant to give a low melting white solid (227 mg, 81%) (Found: C, 69.1; H, 4.0; N, 8.05. $C_{10}H_7NS$ requires C, 69.36; H, 4.04; N, 8.09%); $\nu_{max.}$ 3 410 (NH), 1 595 (C=C), and 1 485 $cm^{-1}$ (C–S); δ 7.02 (m, 1 H, 2 H), 7.23 (d, 1 H, 8-H, *J* 6 Hz), 7.30 (d, 1 H, 5-H, *J* 9 Hz), 7.41 (d, 1 H, 7-H, *J* 6 Hz), 7.52 (d, 1 H, 6-H, *J* 9 Hz), 7.54—7.58 (m, 1 H, 2-H), and 9.44 (br s, 1 H, NH).

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