Condensed Thiophen Ring Systems. Part XV.[1] Preparation and Some Reactions of 2- and 3-(Secondary amino)benzo[*b*]thiophens

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The 2-(secondary amino)benzo[*b*]thiophens (1)—(3) were obtained from 2,3-dibromobenzo[*b*]thiophen and the appropriate amine. They reacted with acetyl chloride in dry benzene to give the corresponding 3-acetyl derivatives (10)—(12). 2-Piperidinobenzo[*b*]thiophen was brominated in the 3-position and nitration with a mixture of acetic acid and fuming nitric acid gave the 3,6-dinitro-derivative (20) and tar. Successive treatment of 3-piperidinobenzo[*b*]thiophen with n-butyl-lithium and dimethylformamide gave 3-piperidinobenzo[*b*]thiophen-2-carbaldehyde, which was prepared also from 3-bromobenzo[*b*]thiophen-2-carbaldehyde and piperidine. Nitrosation of 3-piperidinobenzo[*b*]thiophen gave the 2-oxime of benzo[*b*]thiophen-2,3-dione *via* 3-hydroxy-2-nitrosobenzo[*b*]-thiophen. 2-Nitro-3-piperidino-, 3-morpholino-2-nitro-, and 3,6-dinitro-2-piperidino-benzo[*b*]thiophen were treated with trialkyl phosphites and the tosylhydrazones of 2-morpholinobenzo[*b*]thiophen-3-carbaldehyde and 3-piperidinobenzo[*b*]thiophen-2-carbaldehyde were heated in bis-(2-methoxyethyl) ether in the presence of base (Bamford–Stevens reaction), but in no case did we observe cyclisation.

FOR the work described in this paper we required 2(and 3)-(secondary amino)benzo[*b*]thiophens; this led us to study the chemistry of the amines (1)—(3) and (14).

2-Piperidinobenzo[*b*]thiophen (2) was prepared from 2-bromobenzo[*b*]thiophen and piperidine.[2] A similar attempt to prepare 3-bromo-2-piperidinobenzo[*b*]thiophen (4) from 2,3-dibromobenzo[*b*]thiophen and piperidine surprisingly gave 2-piperidinobenzo[*b*]thiophen (2) exclusively. The yield of the 2-piperidino-compound (2) obtained in this way was optimised as shown in Table 1. 2-Pyrrolidino- (1) and 2-morpholinobenzo[*b*]thiophen (3) were prepared similarly from 2,3-dibromobenzo[*b*]thiophen and the corresponding amine. It seemed likely that the amines (1)—(3) arise from 2,3-dibromobenzo[*b*]thiophen *via* the corresponding 2-(secondary amino)-3-bromobenzo[*b*]thiophen, which is protodebrominated by the excess of amine. In keeping with this suggestion, bromination of 2-piperidinobenzo-[*b*]thiophen (2) with bromine in chloroform and reaction of the resulting 3-bromo-derivative (4) with piperidine gave back starting material in high yield. Since the completion [3] of our work Reinecke *et al.*[4] have reported similar observations. Protodebromination appears to be favoured by overcrowding [5] and is probably promoted in the present case by *peri*-interaction of the large bromine atom with the 4-proton and the presence of a large substituent in the 2-position.

The signals for the 3-protons in the n.m.r. spectra of 2-aminobenzo[*b*]thiophen [6] and the amines (1)—(3) occur at surprisingly high field. This, together with the fact that 2(and 3)-piperidinobenzo[*b*]thiophen are hydrolysed readily by acid to benzo[*b*]thiophen-2(3*H*)-one and benzo[*b*]thiophen-3(2*H*)-one, respectively, suggested that the amines (1)—(3) possess enamine character. In keeping with this suggestion, each of these amines reacted with acetyl chloride in anhydrous benzene to give a high yield of the corresponding acetyl derivative [(10)—(12), respectively]. Likewise, the 2-piperidino-compound (2) gave the 3-benzoyl derivative (13) with benzoyl chloride. It failed to react, however, with benzyl chloride and ethyl chloroformate in benzene. Benzo[*b*]thiophen-2(3*H*)-one reacted with piperidine in boiling toluene in the presence of toluene-*p*-sulphonic acid to give 2-piperidinobenzo[*b*]thiophen (2), albeit in low yield. Aminothiophens also bear a marked resemblance in their physical and chemical properties to enamines.[7,8]

In an attempt to prepare the 3-nitro-derivative (5) we treated 2-piperidinobenzo[*b*]thiophen (2) with acetic acid (or acetic anhydride)–fuming nitric acid. This gave a low yield of the 3,6-dinitro-compound (20) as the only isolable product. The use of copper(II) nitrate in acetic anhydride, potassium nitrate in concentrated sulphuric acid, or a mixture of concentrated nitric and sulphuric acids gave tars, and starting material was isolated after the 2-piperidino-compound (2) had been stirred in 4N-nitric acid for 4 h at ambient temperature. Attempted nitration of 2-morpholinobenzo[*b*]thiophen (3) with acetic acid–fuming nitric acid gave only tar. An attempt to prepare 3-nitro-2-piperidinobenzo[*b*]-thiophen (5) by the reaction of 2-bromo-3-nitrobenzo-[*b*]thiophen with piperidine failed also.

Nitrosation of 3-piperidinobenzo[*b*]thiophen (14) gave the 2-oxime (22) of benzo[*b*]thiophen-2,3-dione, presumably by hydrolysis of the initially formed 2-nitroso-derivative (17) and tautomerisation [(21) ⟶ (22)]. 3-Piperidinobenzo[*b*]thiophen (14), treated successively with n-butyl-lithium, dimethylformamide, and acid, gave 3-piperidinobenzo[*b*]thiophen-2-carbaldehyde (18), which was prepared also from 3-bromobenzo[*b*]thiophen-2-carbaldehyde and piperidine. 3-Piperidinobenzo[*b*]-thiophen (14) was prepared *via* reaction of 3-bromobenzo[*b*]thiophen 1,1-dioxide with piperidine [9] and reduction [10] with lithium aluminium hydride of the

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[2] K. R. Brower and E. D. Amstutz, *J. Org. Chem.*, 1954, **19**, 411.
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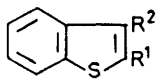
[10] G. Van Zyl, D. C. De Jongh, V. L. Heasley, and J. W. Van Dyke, *J. Org. Chem.*, 1961, **26**, 4946.

resulting 3-piperidinobenzo[*b*]thiophen 1,1-dioxide. However, Reinecke *et al.*[4] have shown that reaction of



(1) $R^1 = NC_4H_8$, $R^2 = H$

(2) $R^1 = NC_5H_{10}$, $R^2 = H$

(3) R^1 =  $R^2 = H$

(4) $R^1 = NC_5H_{10}$, $R^2 = Br$

(5) $R^1 = NC_5H_{10}$, $R^2 = NO_2$

(6) R^1 =  R^2 = CHO

(7) R^1 =  R^2 = CH:N·NHTs

(8) R^1 =  R^2 = CH:N·NH_2

(9) R^1 =  R^2 = CH:N·$[CH_2]_2$·OMe

(10) $R^1 = NC_4H_8$, R^2 = Ac

(11) $R^1 = NC_5H_{10}$, R^2 = Ac

(12) R^1 =  R^2 = Ac

(13) $R^1 = NC_5H_{10}$ R^2 = Bz

(14) R^1 = H, $R^2 = NC_5H_{10}$

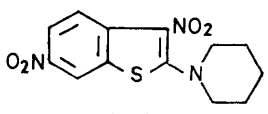
(15) $R^1 = NO_2$, $R^2 = NC_5H_{10}$

(16) $R^1 = NO_2$, R^2 = 

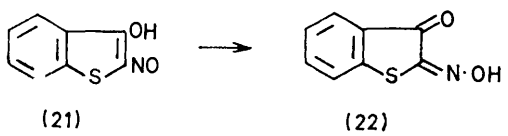
(17) R^1 = NO, $R^2 = NC_5H_{10}$

(18) R^1 = CHO, $R^2 = NC_5H_{10}$

(19) R^1 = CH:N·NHTs, $R^2 = NC_5H_{10}$



(20)



(21) (22)

pure 3-bromobenzo[*b*]thiophen with piperidine gives primarily the 3-piperidino-compound (14) and only a small amount of its 2-isomer (2), in contrast to the earlier report by Brower and Amstutz.[2]

Previously we have reported the synthesis of benzothieno[3,2-*b*]indoles,[11] benzothienopyrroles,[12] and benzothienopyrazoles [13] by reaction with a trialkyl phosphite of a 2- or 3-nitrobenzo[*b*]thiophen substituted in the adjacent position with a suitable side-chain. Attempts to prepare benzothienoimidazoles by reaction of the amines (15) and (16) (see Experimental section) with hot triethyl or trimethyl phosphite [14-16] gave back starting materials, the remainder of the product being tar. Failure of these amines to cyclise is probably not due to instability of the benzothienoimidazole ring system under the reaction conditions, since the 2-methyl derivative (23) is produced when 2,3-diacetamidobenzo[*b*]thiophen is heated at 290—310 °C.[17] The amines (15) and (16) may be unstable in hot trialkyl phosphites, but failure to cyclise is most likely due to *peri*-interaction between the 4-proton of the benzo[*b*]-thiophen ring and the α-methylene protons of the piperidine or morpholine ring, which prevents an intermediate, such as a nitrene, from adopting a suitable conformation for cyclisation. Inspection of molecular models indicates that such interactions are significant. A similar proposal has been made [11] to account for the failure of 2-nitro-3-phenylbenzo[*b*]thiophen to cyclise in hot triethyl phosphite. In contrast, 3-nitro-2-phenylbenzo[*b*]thiophen yields 10*H*-[1]benzothieno[3,2-*b*]indole under these conditions. We were not able to test the present case experimentally because the isomeric amine (5) was unavailable. However, compounds with the general formula (24) are cyclised to the corresponding nitrobenzimidazoles by trialkyl phosphites; *i.e.* the trialkyl phosphite preferentially attacks the nitro-group *ortho* to the amino-substituent.[14] Under these conditions the 3,6-dinitro-compound (20) gave only tar.

With iron(II) oxalate [18] at 225 °C, or at higher temperatures, 2-nitro-3-piperidinobenzo[*b*]thiophen (15) gave starting material and tar. The use of titanium(II) chloride [19] was similarly unsuccessful.

We also prepared the *p*-tolylsulphonylhydrazones (7) and (19) of the aldehydes (6) and (18) and treated these with sodium methoxide in hot bis-(2-methoxyethyl) ether (Bamford–Stevens reaction [20]) in attempts to prepare the corresponding benzothienoindolines by analogy with previous work.[21-23] The *p*-tolylsulphonylhydrazone (7) gave mainly tar from which a product was

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[12] K. E. Chippendale, B. Iddon, and H. Suschitzky, *J.C.S. Perkin I*, 1973, 125.
[13] K. E. Chippendale, B. Iddon, and H. Suschitzky, *J.C.S. Perkin I*, 1973, 129.
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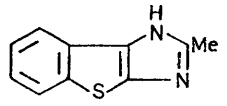
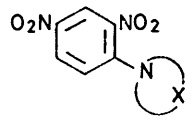
isolated with the molecular formula $C_{16}H_{20}N_2O_2S$ (mass spectrometry and elemental analysis). A prominent feature in the mass spectrum of this compound is the loss of C_3H_7O (*m/e* 59·0497) to give a fragment ion at *m/e* 245·0749 ($C_{13}H_{13}N_2OS$). A metastable peak at *m/e* 197·6 accompanied this fragmentation. These data,



(23)



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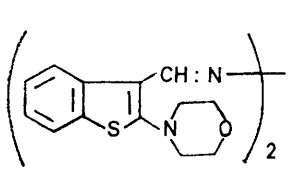

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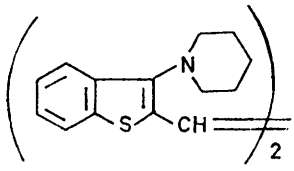

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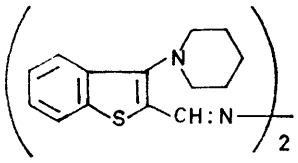

(27)

together with the n.m.r. spectrum, allowed us to propose the tentative structure (9) for this compound. Various unsuccessful attempts were made [3] to confirm this assignment. Compound (9) arises presumably by interaction of an intermediate with the solvent. Thermolysis of the *p*-tolylsulphonylhydrazone (7) in anisole gave only tar. The azine (25) appeared to be a likely precursor. Therefore, we prepared this compound by reaction of 2-morpholinobenzo[*b*]thiophen-3-carbaldehyde (6) with hydrazine and treated it with sodium methoxide in hot bis-(2-methoxyethyl) ether. This only gave back starting material. An attempt to prepare 3-diazomethyl-2-morpholinobenzo[*b*]thiophen by reaction of the *p*-tolylsulphonylhydrazone (7) with sodium methoxide in pyridine (Farnum's [24] modification of the Bamford–Stevens [20] reaction) gave only a small amount of starting material. Oxidation of the hydrazone (8) of the aldehyde (6) with yellow mercury(II) oxide in ether at 0 °C or under reflux [22] failed to give the diazomethane derivative also; the azine (25) (see before) was obtained instead.

The *p*-tolylsulphonylhydrazone (19) reacted with sodium methoxide in hot bis-(2-methoxyethyl) ether to give a complex mixture of products from which the ethylene derivative (26) (36% yield) was isolated. An attempt to prepare the intermediate aryldiazomethane by Farnum's [24] modification of the Bamford–Stevens [20] reaction also gave a complex mixture from which we isolated a compound with the molecular formula $C_{28}H_{30}N_4S_2$ [M^+ 486·1908 (4%)]. Prominent features of the mass spectrum of this compound were fragment ion peaks at *m/e* 243·0954 ($C_{14}H_{15}N_2S$; 50%) and 228·0847 ($C_{14}H_{14}NS$; base peak), which suggests that the compound is the azine (27). Ethylene derivatives and azines are common by-products in these reactions and arise *via* interaction of the intermediate carbene with its aryldiazomethane precursor.[22]

EXPERIMENTAL

Most of the spectroscopic instruments used were described in Part XIII.[25] Accurate mass measurements were made with an A.E.I. MS902S instrument at 70 eV.

Light petroleum refers to the fraction of b.p. 60—80 °C unless stated otherwise.

3-Piperidinobenzo[*b*]thiophen (67%), m.p. 64—66 °C (from ethanol) (lit.,[10] 64—65 °C), 2-morpholinobenzo[*b*]-thiophen-3-carbaldehyde (77%), m.p. 109—111 °C (from light petroleum) (lit.,[26] 109—111 °C), 3-bromo-2-nitrobenzo[*b*]thiophen (25%), m.p. 161—163 °C (from ethanol) (lit.,[27] 162—163 °C), 2-bromo-3-nitrobenzo[*b*]thiophen (15%), m.p. 47—49 °C (distilled) (lit.,[28] oil), 2-nitro-3-piperidinobenzo[*b*]thiophen (83%), m.p. 118—120 °C (from ethanol) (lit.,[29] 119—121 °C), 3-morpholino-2-nitrobenzo-[*b*]thiophen (65%), m.p. 168—170 °C (from ethanol) (lit.,[10] 168—169 °C), 3-bromobenzo[*b*]thiophen-2-carbaldehyde (65%), m.p. 122—123 °C (from light petroleum) (lit.,[30] 118—118·5 °C), and benzo[*b*]thiophen-2(3*H*)-one (73%), m.p. 43—45 °C [from light petroleum (b.p. 40—60 °C)] (lit.,[31] 43—44 °C), were prepared by literature procedures.

TABLE 1

Reaction of 2,3-dibromobenzo[*b*]thiophen (A) with piperidine (B)

Ratio A : B	Temp. (±5 °C)	Starting material (%)	2-Piperidinobenzo[*b*]thiophen (%)
1 : 1	175	85	9
1 : 2	175	Trace	46
1 : 3	175	Trace	57
1 : 4	175	Trace	74
1 : 2	185	Trace	42
1 : 2	210	0	11

2-Piperidinobenzo[b]*thiophen*. The optimum conditions (see Table 1) were as follows. A mixture of 2,3-dibromobenzo[*b*]thiophen [30] (9·0 g, 31·25 mmol) and piperidine (10·6 g, 125 mmol) was heated in a Carius tube at 175 ± 5 °C for 24 h. The contents were cooled and poured into water. Extraction with chloroform gave a product which was chromatographed on alumina. Light petroleum eluted 2-piperidinobenzo[*b*]thiophen (4·9 g, 72%), m.p. 96—98 °C

[24] D. G. Farnum, *J. Org. Chem.*, 1963, **28**, 870.
[25] Part XIII, B. Iddon, H. Suschitzky, D. S. Taylor, and M. W. Pickering, *J.C.S. Perkin I*, 1974, 575.
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[29] H. D. Hartough and S. L. Meisel, in ' Compounds with Condensed Thiophene Rings,' ed. A. Weissberger, Interscience, New York, 1954, Table II-7, p. 52.
[30] W. Ried and H. Bender, *Chem. Ber.*, 1955, **88**, 34.
[31] R. P. Dickinson and B. Iddon, *J. Chem. Soc.* (*C*), 1970, 1926.

[from light petroleum (b.p. 40—60 °C)] (lit.,[2] 97—99 °C), τ ($CDCl_3$) 2·25—3·00 (m, aromatic), 6·60—6·85 (m, α-CH_2), 8·13—8·43 (m, β- and γ-CH_2), and 3·82 (s, 3-H), identical (mixed m.p. and i.r.) with a sample prepared by the literature procedure.[2]

2-Pyrrolidinobenzo[b]*thiophen* (21%), m.p. 86—88 °C [from light petroleum (b.p. 40—60 °C)], τ ($CDCl_3$) 2·25—3·00 (m, aromatic), 6·50—6·75 (m, α-CH_2), 7·83—8·10 (m, β-CH_2), and 4·11 (s, 3-H) (Found: C, 70·7; H, 6·4; N, 6·9%; *M*, 203. $C_{12}H_{13}NS$ requires C, 70·9; H, 6·45; N, 6·9%; *M*, 203), and *2-morpholinobenzo*[b]*thiophen* (39%), m.p. 170—172 °C (from ethanol) (lit.,[9] m.p. not given), τ ($CDCl_3$) 2·25—3·00 (m, aromatic), 6·04—6·28 (m, CH_2), 6·70—6·80 (m, CH_2), and 3·76 (s, 3-H) (Found: C, 65·6; H, 5·9; N, 6·5%; *M*, 219. $C_{12}H_{13}NOS$ requires C, 65·7; H, 6·0; N, 6·4%; *M*, 219), were prepared similarly. In benzo[*b*]thiophen (0·8 g, 83%), identical (m.p. and i.r.) with an authentic sample.

Nitration of 2-Piperidinobenzo[b]*thiophen.*—A mixture of fuming nitric acid (2·5 ml) and acetic acid (2·5 ml) was added dropwise to a mixture of 2-piperidinobenzo[*b*]thiophen (2·5 g, 11·6 mmol) and acetic acid (25 ml) at 0 °C. The resulting mixture was stirred at 0 °C for 2 h and then poured into water. The product was extracted with chloroform; the combined extracts were washed successively with aqueous 10% sodium hydrogen carbonate and water, and dried ($MgSO_4$). Distillation under reduced pressure and extraction of the residue with hot benzene gave 3,6-*dinitro-2-piperidinobenzo*[b]*thiophen* (0·4 g, 11%), m.p. 184—186 °C (decomp.) (from benzene), τ (C_6D_6) 1·64 (m, 4-H), 2·01 (m, 5- and 7-H), and 7·15—7·38 (m, α-CH_2) and 8·78—9·00 (m, β- and γ-CH_2) (compound not very

TABLE 2

Data for 3-acyl-2-dialkylaminobenzo[*b*]thiophens (10)—(13)

Compd.	Yield (%)	M.p. or b.p. (°C) [mmHg]	ν_{max} (cm^{-1}) (C:O) [a]	Chemical shifts (τ) [b] 4-H	Me	Aromatic	Amine ring	Found (%) C	H	N	Formula	Required (%) C	H	N
(10)	82	215 [2·0]	1635	2·18 (m)	7·57 (s)	2·40—3·00 (m)	6·56—6·85 (m) and 7·92—8·20 (m)	68·2	6·2		$C_{14}H_{15}NOS$	68·5	6·2	
(11)	87	63—65 [c]	1660	1·61 (m)	7·32 (s)	2·20—2·80 (m)	6·68—6·96 (m) and 8·09—8·45 (m)	69·7	6·6	5·4	$C_{15}H_{17}NOS$	69·45	6·6	5·4
(12)	88	138—140 [d]	1670	1·65 (m)	7·30 (s)	2·15—2·75 (m)	5·97—6·23 (m) and 6·66—6·92 (m)	63·5	5·7	5·5	$C_{14}H_{15}NO_2S$	64·35	5·8	5·4
(13)	68	125—127 [d]	1630	2·10 (m)		2·20—2·75 (m)	6·80—7·04 (m) and 8·62—8·85 (m)	74·3	5·9	4·3	$C_{20}H_{19}NOS$	74·7	6·0	4·4

[a] The liquid run as a film and the solids as Nujol mulls. [b] In $CDCl_3$ except compound (10) (in CCl_4); for the 4-H multiplets (m) the figure given is for the approximate centre of the signal. [c] From light petroleum (b.p. 40—60 °C). [d] From methanol.

the case of the morpholino-compound the reaction time was increased to 48 h.

Acylation of the 2-(Secondary amino)benzo[b]*thiophens* (1)—(3).—*General procedure.* A mixture of the amine (1·0 equiv.), acetyl or benzoyl chloride (1·1 equiv.), and anhydrous benzene (10% w/v) was heated under reflux for 24 h. It was then cooled and an excess of triethylamine was added. The mixture was filtered and evaporated to dryness under reduced pressure, and the residue was chromatographed on alumina. Ether–light petroleum (1 : 1) eluted the product (see Table 2 for details).

Bromination of 2-Piperidinobenzo[b]*thiophen.*—A solution of bromine (1·85 g, 11·6 mmol) in chloroform (20 ml) was added dropwise during 30 min to a stirred solution of 2-piperidinobenzo[*b*]thiophen (2·5 g, 11·6 mmol) in chloroform (25 ml) at 0 °C and the mixture was stirred at 0 °C for a further 1 h. The precipitate was filtered off and stirred with aqueous 10% sodium hydrogen carbonate (50 ml) for 1 h. Extraction with ether gave unstable 3-bromo-2-piperidinobenzo[*b*]thiophen (1·6 g, 47%), m.p. 71—73 °C (decomp.) (lit.,[4] 76—77 °C), τ ($CDCl_3$) 2·20—2·70 (m, aromatic), 6·72—6·94 (m, α-CH_2), and 8·10—8·45 (m, β- and γ-CH_2); *methanesulphonate salt*, m.p. 142—144 °C (from ether–ethanol) (Found: C, 43·2; H, 4·5; N, 3·8. $C_{14}H_{18}BrNO_3S_2$ requires C, 42·85; H, 4·6; N, 3·6%).

Debromination of 3-Bromo-2-piperidinobenzo[b]*thiophen.*—A mixture of the bromo-amine (1·3 g, 4·4 mmol) and piperidine (0·75 g, 8·8 mmol) was heated in a Carius tube at 175 ± 5 °C for 24 h. Work-up as before gave 2-piperidinobenzo[*b*]thiophen (0·8 g, 83%), identical (m.p. and i.r.) with an authentic sample.

Nitration of 2-Piperidinobenzo[b]*thiophen.*—A mixture of fuming nitric acid (2·5 ml) and acetic acid (2·5 ml) was added dropwise to a mixture of 2-piperidinobenzo[*b*]thiophen (2·5 g, 11·6 mmol) and acetic acid (25 ml) at 0 °C. The resulting mixture was stirred at 0 °C for 2 h and then poured into water. The product was extracted with chloroform; the combined extracts were washed successively with aqueous 10% sodium hydrogen carbonate and water, and dried ($MgSO_4$). Distillation under reduced pressure and extraction of the residue with hot benzene gave 3,6-*dinitro-2-piperidinobenzo*[b]*thiophen* (0·4 g, 11%), m.p. 184—186 °C (decomp.) (from benzene), τ (C_6D_6) 1·64 (m, 4-H), 2·01 (m, 5- and 7-H), and 7·15—7·38 (m, α-CH_2) and 8·78—9·00 (m, β- and γ-CH_2) (compound not very soluble, therefore difficult to measure coupling constants) (Found: C, 51·1; H, 4·2; N, 13·4%; *M*, 307. $C_{13}H_{13}N_3O_4S$ requires C, 50·8; H, 4·3; N, 13·7%; *M*, 307). When acetic anhydride was used in place of the acetic acid the yield of the 3,6-dinitro-compound was 12%.

Nitrosation of 3-Piperidinobenzo[b]*thiophen.*—A solution of sodium nitrite (1·02 g, 14·8 mmol) in water (2·3 ml) was added dropwise to a stirred solution of 3-piperidinobenzo[*b*]thiophen (3·0 g, 13·8 mmol) in 5N-hydrochloric acid (12 ml) at 0 °C at such a rate that the temperature did not rise above 2 °C. The mixture was stirred for a further 45 min at 0 °C and then made alkaline with 2N-sodium hydroxide. The precipitate (1·8 g, 73%) was filtered off and recrystallised from benzene, to give benzo[*b*]thiophen-2,3-dione 2-oxime, m.p. 173—177 °C (decomp.) [lit.,[32] 172 °C (decomp.)], $\nu_{max.}$ (Nujol) 3250br (OH) and 1685 cm^{-1} (C:O).

3-Piperidinobenzo[b]*thiophen-2-carbaldehyde.*—(a) *From 3-piperidinobenzo*[b]*thiophen.* A solution of n-butyl-lithium (4·6 mmol) in hexane (1·4 ml) was added to a stirred solution of 3-piperidinobenzo[*b*]thiophen (1·0 g, 4·6 mmol) in anhydrous ether (25 ml) at 0 °C under nitrogen and the resulting mixture was stirred at 0 °C for 1 h. Dimethylformamide (0·34 g, 4·6 mmol) was then added and the mixture was stirred at 0 °C for a further 1 h. An excess of 2N-hydrochloric acid was added and the organic and

[32] Ref. 29, Table II-16, p. 98; V. G. Zhiryakov and P. I. Abramenko, *Zhur. Vsesoyuz. Khim. obshch.*, 1970, **15**, 587 (*Chem. Abs.*, 1971, **74**, 13,040).

aqueous layers were separated. The aqueous layer was washed with ether and the organic layer and ethereal extracts were combined and dried ($MgSO_4$). Distillation under reduced pressure gave 3-*piperidinobenzo*[b]*thiophen*-2-*carbaldehyde* (0·4 g, 35%), m.p. 107—108 °C (from ethanol), $\nu_{max.}$ (Nujol) 1630 cm^{-1} (C:O), τ (CCl_4) −0·30 (s, CHO), 2·20—2·90 (m, aromatic), 6·30—6·60 (m, α-CH_2), and 8·00—8·25 (m, β- and γ-CH_2) (Found: C, 68·5; H, 6·4; N, 5·7. $C_{14}H_{15}NOS$ requires C, 68·5; H, 6·2; N, 5·7%); *thiosemicarbazone*, m.p. 208—209 °C (from ethanol) (Found: C, 56·6; H, 5·7; N, 17·3. $C_{15}H_{18}N_4S_2$ requires C, 56·6; H, 5·7; N, 17·6%).

(b) *From* 3-*bromobenzo*[b]*thiophen*-2-*carbaldehyde*. A stirred mixture of 3-bromobenzo[*b*]thiophen-2-carbaldehyde (15·0 g, 62·2 mmol), piperidine (5·3 g, 62·2 mmol), sodium hydrogen carbonate (5·2 g, 62·2 mmol), and ethanol (600 ml) was heated under reflux for 20 h. It was then filtered and the ethanol was distilled off under reduced pressure, to give a residue which was dissolved in carbon tetrachloride. This solution was washed with water and dried ($MgSO_4$), the solvent was distilled off, and the residue was chromatographed on silica. Carbon tetrachloride eluted starting material, and chloroform eluted the product (7·5 g, 50%), identical (m.p., i.r., and n.m.r.) with the sample prepared as described in (a).

3-*Piperidinobenzo*[b]*thiophen*-2-*carbaldehyde* p-*Tolylsulphonylhydrazone*.—A solution of *p*-tolylsulphonylhydrazine (0·74 g, 4·0 mmol) in ethanol (5 ml) containing 4 drops of glacial acetic acid was added to a solution of 3-piperidinobenzo[*b*]thiophen-2-carbaldehyde (1·0 g, 4·0 mmol) in ethanol (25 ml) and the resulting mixture was heated under reflux for 30 min. The resulting solution was cooled to 0 °C and the *product* (1·0 g, 60%) was filtered off; m.p. 192—193 °C (from ethanol), $\nu_{max.}$ (Nujol) 3160s cm^{-1} (NH) (Found: C, 60·7; H, 5·5; N, 10·3. $C_{21}H_{23}N_3O_2S_2$ requires C, 61·1; H, 5·6; N, 10·2%).

2-*Morpholinobenzo*[b]*thiophen*-3-*carbaldehyde* p-*tolylsulphonylhydrazone* (91%) was prepared similarly; m.p. 210—211 °C (from acetic acid), $\nu_{max.}$ (Nujol) 3200s cm^{-1} (NH) (Found: C, 57·5; H, 5·1; N, 10·0%; *M*, 415. $C_{20}H_{21}N_3O_3S_2$ requires C, 57·8; H, 5·1; N, 10·1%; *M*, 415).

2-*Morpholinobenzo*[b]*thiophen*-3-*carbaldehyde hydrazone* (84%), prepared in the usual way, had m.p. 122—123 °C (from ethanol), τ ($CDCl_3$) 1·47br (s, exchangeable, NH_2), 1·80 (s, CH), 2·15—2·80 (m, aromatic), 6·05—6·25 (m, CH_2), and 6·87—7·10 (m, CH_2), $\nu_{max.}$ (Nujol) 3350w and 3200w cm^{-1} (NH_2) (Found: C, 60·0; H, 5·9; N, 16·0%; *M*, 261. $C_{13}H_{15}N_3OS$ requires C, 59·8; H, 5·8; N, 16·1%; *M*, 261).

2-*Morpholinobenzo*[b]*thiophen*-3-*carbaldehyde Azine* (25).—(*a*) A mixture of 2-morpholinobenzo[*b*]thiophen-3-carbaldehyde hydrazone (0·75 g, 2·9 mmol), yellow mercury(II) oxide (2·5 g, 11·5 mmol), anhydrous sodium sulphate (2·5 g, 17·6 mmol), ethanolic potassium hydroxide (10 drops of a saturated solution), and anhydrous ether (20 ml) was heated under reflux for 3 h. It was then cooled and filtered. Extraction of the filtrate with chloroform gave the *product* (0·51 g, 73%), m.p. 256—258 °C (from anisole) (Found: C, 63·9; H, 5·4; N, 11·2%; *M*, 490. $C_{26}H_{26}N_4O_2S_2$ requires C, 63·65; H, 5·3; N, 11·4%; *M*, 490).

A 70% yield of the azine was obtained when this reaction was repeated at 0 °C.

(*b*) A mixture of 2-morpholinobenzo[*b*]thiophen-3-carbaldehyde (1·0 g, 4·00 mmol), hydrazine hydrate (0·11 g, 2·19 mmol), and 4N-acetic acid (1 drop) in ethanol (10 ml) was heated for 1 h at 70 °C. The mixture was then cooled to give a precipitate of the azine (0·87 g, 90%), identical (m.p. and i.r.) with the sample prepared as described in (*a*).

Decomposition of 2-*Morpholinobenzo*[b]*thiophen*-3-*carbaldehyde* p-*Tolylsulphonylhydrazone*.—A solution of the tosylhydrazone (1·5 g, 3·72 mmol) in bis-(2-methoxyethyl) ether (10 ml) was added to a solution of sodium methoxide (0·6 g, 11·1 mmol) in the same solvent (30 ml) heated under reflux, and the resulting mixture was heated under reflux for a further 15 min. The solvent was distilled off under reduced pressure and the residue was chromatographed on alumina. Ether eluted a product (0·35 g) to which we assign the tentative structure (9). It had m.p. 148—150 °C (from ethanol), τ ($CDCl_3$) 2·05—2·71 (4H, m, aromatic), 6·05 (m, NCH_2, CH_2O, and OCH_3), and 6·64 (m) and 6·96 (m, morpholine ring) (Found: C, 63·6; H, 6·7; N, 9·2%; *M*, 304·1266. $C_{16}H_{20}N_2O_2S$ requires C, 63·1; H, 6·6; N, 9·2%; *M*, 304·1246); for mass spectrum see Discussion section.

Decomposition of 3-piperidinobenzo[*b*]thiophen-2-carbaldehyde *p*-tolylsulphonylhydrazone (0·5 g, 1·2 mmol), carried out in a similar manner, gave a product which was chromatographed on silica. Light petroleum–ether (3 : 1) eluted 1,2-*bis*-(3-*piperidinobenzo*[b]*thiophen*-2-*yl*)*ethylene* (26) (0·1 g, 36%), m.p. 201—203 °C (from light petroleum–benzene), τ (CCl_4) 2·20—2·90 (m, aromatic), 5·38 (d, *J* 3·0 Hz, CH), 6·65 (m, α-CH_2), and 8·25 (m, β- and γ-CH_2) (Found: C, 73·0; H, 6·5; N, 5·3. $C_{28}H_{30}N_2S_2$ requires C, 73·3; H, 6·6; N, 6·1%).

Attempted Synthesis of 2-*Diazomethyl*-3-*piperidinobenzo*[b]*thiophen*.—A mixture of 3-piperidinobenzo[*b*]thiophen-2-carbaldehyde *p*-tolylsulphonylhydrazone (2·0 g, 4·8 mmol) and sodium methoxide (0·5 g, 9·3 mmol) in pyridine (20 ml) was stirred at 60 °C for 15 min and then poured into cold (0 °C) water (200 ml). Extraction with chloroform gave a residue which was chromatographed on alumina. Light petroleum–ether (5 : 1) eluted a compound (0·1 g), m.p. 258—259 °C, whose mass spectrum (see Discussion section) suggested that it may be the azine (27). Elution with more polar solvents gave intractable mixtures.

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