Substitution Reactions of Benzo[*b*]thiophen Derivatives. Part VII.[1] Reactions of 4-Hydroxybenzo[*b*]thiophen, its 3-Methyl Derivative, and Related Compounds

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Electrophilic substitution reactions of 4-hydroxybenzo[*b*]thiophen and its 3-methyl derivative are described. Formylation under modified Gattermann conditions and bromination with *N*-bromosuccinimide gave the 5-substituted product in each case, whereas treatment with bromine in carbon tetrachloride gave the corresponding 5,7-dibromo-compound. Nitration in acetic acid gave a mixture of the 5-nitro-, the 7-nitro-, and the 5,7-dinitro-compounds, of which the 5-nitro-compound was the major component in each case. Claisen rearrangement of 4-allyloxybenzo[*b*]thiophen and its 3-methyl derivative gave the appropriate 5-allyl-4-hydroxy-compound. Fries rearrangement of 4-acetoxybenzo[*b*]thiophen with aluminium chloride in boiling benzene gave a mixture of 7-acetyl-4-hydroxybenzo[*b*]thiophen (90%) and its 2,3-dihydro-derivative (7%). Similar treatment of 4-acetoxy-3-methylbenzo[*b*]thiophen gave a mixture of 7-acetyl-4-hydroxy-3-methylbenzo[*b*]thiophen (21%) and the 2-acetyl isomer (68%). Bromination of 4-methylsulphonyloxybenzo[*b*]thiophen in acetic acid gave a mixture of 3-bromo- (60%) and 5-bromo-4-methylsulphonyloxybenzo[*b*]thiophen (20%) and the corresponding 5,7-dibromo-compound (6%), together with two unidentified products. 3-Bromomethyl-4-methylsulphonyloxybenzo[*b*]thiophen, obtained by treatment of the corresponding 3-methyl compound with *N*-bromosuccinimide, was used as a key intermediate in the synthesis of 2-(4-hydroxy-3-benzo[*b*]thienyl)ethylamine, the sulphur analogue of 4-hydroxytryptamine.

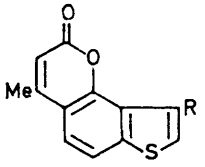
PREVIOUSLY we have described[1] some electrophilic substitution reactions of 4-methoxybenzo[*b*]thiophen and its 3-methyl derivative. Our studies[2] which led to the synthesis of the sulphur analogue of psilocin included an investigation of the electrophilic substitution of 4-hydroxybenzo[*b*]thiophen and its 3-methyl derivative, the results of which we now report. Campaigne and his co-workers[3] showed that treatment of 4-hydroxybenzo[*b*]thiophen with *N*-bromosuccinimide gave the 5-bromo-compound (88%), but that conventional bromination and nitration procedures gave intractable mixtures. We found that attempted monosubstitution with bromine in carbon tetrachloride gave a mixture of the 5,7-dibromo-compound and starting material, but that the use of bromine (2 mol. equiv.) readily gave 5,7-dibromo-4-hydroxybenzo[*b*]thiophen (89%). We confirmed that the 5-bromo-compound was obtained easily by treatment of 4-hydroxybenzo[*b*]thiophen with *N*-bromosuccinimide. Nitration of 4-hydroxybenzo[*b*]thiophen with nitric acid in acetic acid at −5° gave a mixture of the 5-nitro- (70%), 7-nitro- (25%), and 5,7-dinitro-compounds (5%).

Bromination of 4-hydroxy-3-methylbenzo[*b*]thiophen gave results similar to those just described; nitration gave a mixture of the 5-nitro- (80%), 7-nitro- (2%), and 5,7-dinitro-derivatives (16%). 4-Hydroxy-3-methyl-7-nitrobenzo[*b*]thiophen was identified by comparison with authentic material, obtained by demethylation of the corresponding 4-methoxy-compound.[1] There was no evidence for the formation of any 2-substituted products in either the bromination or the nitration reaction, indicating that the activation of the 2-position by the 3-methyl group is not sufficient to counterbalance the activation of the benzenoid ring by the phenolic hydroxy-group. The results just described are analogous to those reported recently[4] for 7-hydroxy-3-methylbenzo[*b*]thiophen, for which the positions *ortho* and *para* to the hydroxy-group were the most reactive.

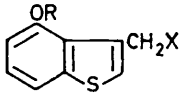
We next formylated 4-hydroxybenzo[*b*]thiophen by a modified Gattermann procedure[5] and obtained almost exclusively the 5-formyl derivative, whereas similar formylation of the 3-methyl derivative gave the 5-formyl product (68%) and tarry material; there was no evidence for substitution in the 7-position (*cf.* formylation of 7-hydroxy-3-methylbenzo[*b*]thiophen[4]). von Pech-

[1] Part VI, K. Clarke, R. M. Scrowston, and T. M. Sutton, *J.C.S. Perkin I*, 1973, 623.
[2] N. B. Chapman, R. M. Scrowston, and T. M. Sutton, *J.C.S. Perkin I*, 1972, 3011.
[3] E. Campaigne, A. Dinner, and M. Haseman, *J. Heterocyclic Chem.*, 1971, **8**, 755.
[4] N. B. Chapman, K. Clarke, and A. Manolis, *J.C.S. Perkin I*, 1972, 2593.
[5] R. Adams and I. Levine, *J. Amer. Chem. Soc.*, 1923, **45**, 2373.

mann reaction [6] of 4-hydroxybenzo[*b*]thiophen with ethyl acetoacetate in methanolic hydrogen chloride gave 4-methylthieno[2,3-*h*][1]benzopyran-2-one (1); the 4,9-dimethyl derivative (2) was obtained similarly from 4-hydroxy-3-methylbenzo[*b*]thiophen.



(1) R = H
(2) R = Me



(3) R = SO_2Me, X = Br
(4) R = SO_2Me, X = CN
(5) R = H, X = CN
(6) R = H, X = $CH_2{\cdot}NH_2$

We carried out the Claisen rearrangement of 4-allyloxybenzo[*b*]thiophen and its 3-methyl derivative, and observed the expected migration of the allyl group into the 5-position in each case. Lechartier [7] has claimed that 4-acetoxybenzo[*b*]thiophen undergoes the Fries rearrangement when treated with aluminium chloride at 90° in the absence of a solvent, to give 7-acetyl-4-hydroxybenzo[*b*]thiophen (1·27%) and a compound (3·2%) that claimed by Lechartier.[7] The same product was obtained by demethylating 7-acetyl-4-methoxybenzo[*b*]thiophen.[1] A minor product (7%) from the rearrangement reaction was identified spectroscopically as 7-acetyl-2,3-dihydro-4-hydroxybenzo[*b*]thiophen. Its proportion in the mixture increased with increasing reaction time; after 24 h it was obtained almost quantitatively. The scope and mechanism of this unusual reaction are being investigated further. Fries rearrangement of 4-acetoxy-3-methylbenzo[*b*]thiophen gave a mixture of 2-acetyl-4-hydroxy-3-methylbenzo[*b*]thiophen (68%) and the corresponding 7-acetyl isomer (21%). Previous workers have shown that, whereas Fries rearrangement of 5-acetoxybenzo[*b*]thiophen [9] gives the 4-acetyl compound, both 5-acetoxy- [10] and 7-acetoxy-3-methylbenzo[*b*]thiophen [4] rearrange to give mainly the 2-acetyl derivative.

The structures of all new compounds, except where stated otherwise, were determined by n.m.r. spectroscopy, using the methods described previously.[1] Relevant details of the spectra are shown in the Table. The structures of 4-hydroxybenzo[*b*]thiophen derivatives containing a 5-bromo-, 5-nitro-, or 5-formyl substituent were confirmed by observing intramolecular hydrogen bonding in their i.r. spectra (*cf.* ref. 11).

N.m.r. spectral data for substituted 4-hydroxybenzo[*b*]thiophen derivatives [a]

Substituents	2-H	3-H	5-H	6-H	7-H	OH	3-Me	$J_{2,3}$	$J_{5,6}$	$J_{6,7}$	$J_{2,6}$	$J_{2,Me}$	Other data
5-Br [b]	7·42	7·42		7·65	7·65	3·45							
5,7-Br_2	7·42 (d)	7·55 (d)		7·47		5·80		5·95			0·5		
5-NO_2	7·42 (d)	7·72 (d)		8·02 (d)	7·42 (d)	11·51		5·5		7·95	0·4		$J_{3,7}$ 0·7
7-NO_2	7·65 (d)	7·75 (d)	7·03 (d)	8·31 (d)		8·80		5·95	8·35		0·5		
5,7-$(NO_2)_2$ [b]	7·35 (d)	7·55 (d)		7·75		8·95		6·4			0·5		
5-CHO	7·55 (d)	7·61 (d)		7·82 (d)	7·01 (d)	12·40		5·95		7·95	0·4		10·05 (CHO), $J_{3,7}$ 0·7
5-Allyl	7·23 (d)	7·35 (d)		6·95 (d)	7·35 (d)	5·45br		5·85		8·05	0·5		$J_{3,7}$ 0·7
7-Ac [b]	7·51 (d)	7·65 (d)	6·85 (d)	8·05 (d)		3·4br		5·75	7·85		0·5		2·60 (Ac)
4-OAc	7·32 (d)	7·43 (d)	7·05 (dd)	7·15 (dd)	7·69 (dd)			5·9	8·1	8·0	0·5		2·35 (OAc), $J_{5,7}$ 1·9, $J_{3,7}$ 0·7
3-Br	7·22		6·85 (dd)	7·28 (dd)	7·45 (dd)	7·10			7·85	7·95	0·4		$J_{5,7}$ 1·8
3-Me	6·82		6·55 (dd)	7·12 (dd)	7·35 (dd)	5·15	2·60		7·55	8·0	0·5	0·75	$J_{5,7}$ 1·8
5-Br,3-Me [c]	6·78			7·46 (d)	7·18 (d)	5·62	2·35			7·8	0·5	0·8	
5,7-Br_2,3-Me	6·91			7·42		5·75	2·52				0·5	0·8	
5-NO_2,3-Me	7·01			7·92 (d)	7·28 (d)	11·92	2·65			8·05	0·5	0·8	
5,7-$(NO_2)_2$,3-Me	7·68			8·55		11·59	2·39				0·5	0·7	
7-NO_2,3-Me	7·35		6·91 (d)	8·31 (d)		8·65	2·65		8·05		0·5	0·7	
5-CHO,3-Me [c]	6·35			6·92 (d)	6·55 (d)	12·69	2·51			8·15	0·4	0·8	9·28 (CHO)
5-Allyl,3-Me	6·85			7·02 (d)	7·35 (d)	5·45	2·65			8·1	0·5	0·8	
4-OAc,3-Me	6·98		6·91 (dd)	7·22 (t)	7·55 (dd)		2·40		8·0	8·0	0·5	0·8	2·25 (OAc), $J_{5,7}$ 1·95
2-Ac,3-Me			6·92 (dd)	7·32 (t)	7·45 (dd)	3·40	2·85		7·85	7·85			2·60 (Ac), $J_{5,7}$ 1·85
7-Ac,3-Me [b]	7·22		6·85 (d)	8·05 (d)		3·38	2·58		8·25		0·5	0·7	2·50 (Ac)

[a] Spectra were determined at 100 MHz for 10% w/v solutions in deuteriochloroform unless stated otherwise. Chemical shifts are given as δ values (p.p.m. downfield from tetramethylsilane); coupling constants (J) are in Hz; for simplicity, long-range couplings have been omitted when describing the multiplicity of a signal. [b] In $(CD_3)_2SO$. [c] In C_6D_6.

which he described first [7] as the 5-acetyl derivative, and later [8] as the 2-acetyl derivative. We treated 4-acetoxybenzo[*b*]thiophen with aluminium chloride in boiling benzene for 4 h and obtained 7-acetyl-4-hydroxybenzo[*b*]thiophen (90%), with m.p. 254—256°,* similar to

We noted previously [2] that the bromination of 4-methylsulphonyloxybenzo[*b*]thiophen in acetic acid gives a complex mixture of products. It is convenient to discuss this reaction further here because we treated the total mixture (five components) with sodium and ethanol,

* Campaigne *et al.*[3] give m.p. 115—116° for this compound, prepared by hydrolysis of 7-acetyl-4-benzoyloxybenzo[*b*]thiophen.

[6] S. Sethna and R. Phadke, *Org. Reactions*, 1953, **7**, 1.
[7] J.-P. Lechartier, Thesis, University of Paris, 1964.
[8] M.-L. Desvoye, P. Demerseman, J.-P. Lechartier, C. Pène, A. Cheutin, and R. Royer, *Bull. Soc. chim. France*, 1965, 1473.
[9] A. Mustafa, S. M. A. D. Zayed, and A. Emran, *Annalen*, 1967, **704**, 176.
[10] P. M. Chakrabarti N. B. Chapman, and K. Clarke, *J. Chem. Soc.* (*C*), 1969, 1.
[11] R. G. Simard, I. Hasegawa, W. Bandaruk and C. E. Headington, *Analyt. Chem.*, 1951, **23**, 1384.

and separated and identified three of the resulting bromohydroxybenzo[*b*]thiophens. These were 3-bromo- (60%), 5-bromo- (20%), and 5,7-dibromo-4-hydroxybenzo[*b*]thiophen (6%). We could not separate the remaining two components [4 and 6% (g.l.c.)].

Finally, treatment of 3-methyl-4-methylsulphonyloxybenzo[*b*]thiophen with *N*-bromosuccinimide gave the corresponding 3-bromomethyl compound (3). This provided a convenient intermediate for the preparation of 2-(4-hydroxy-3-benzo[*b*]thienyl)ethylamine (6), the sulphur analogue of 4-hydroxytryptamine, which we had tried [2] unsuccessfully to obtain by demethylation of the corresponding 4-methoxy-compound. The bromomethyl compound (3) reacted with sodium cyanide in aqueous acetone to give the nitrile (4), treatment of which with sodium in ethanol gave 4-hydroxy-3-benzo[*b*]thienylacetonitrile (5). This was reduced slowly by diborane to give the hydroxy-amine (6).

EXPERIMENTAL

Light petroleum had b.p. 60—80°. Molecular weights of compounds containing bromine refer to the ^{79}Br isotope. Other general experimental directions are given in Part VI [1] and preceding papers.

4-Hydroxy-3-methylbenzo[*b*]thiophen was prepared as already described.[2]

Monobromination Reactions.—*N*-Bromosuccinimide (1·08 g) was added in portions to a boiling solution of 4-hydroxybenzo[*b*]thiophen (1 g) and benzoyl peroxide (20 mg) in dry carbon tetrachloride (40 ml). The mixture was stirred under reflux for 0·75 h, then cooled and filtered. Evaporation of the filtrate gave 5-bromo-4-hydroxybenzo[*b*]thiophen as white needles (1·43 g, 94%), m.p. 132—133° (from light petroleum)(charcoal) (lit.,[3] 129—130°), $\nu_{max.}$ (CCl_4) 3515 cm^{-1} (sharp, unaltered by dilution) (OH).

5-Bromo-4-hydroxy-3-methylbenzo[*b*]thiophen (94%) was obtained similarly and formed white *needles*, m.p. 131—132° (from n-pentane, followed by sublimation at 120° and 0·2 mmHg) (Found: C, 44·5; H, 2·85; Br, 32·85; S, 13·4%; *M*, 242. C_9H_7BrOS requires C, 44·45; H, 2·9; Br, 32·85; S, 13·2%; *M*, 242), $\nu_{max.}$ (CCl_4) 3510 cm^{-1} (OH).

Dibromination Reactions.—A solution of bromine (2·16 g, 0·0134 mol) in dry carbon tetrachloride (10 ml) was added dropwise to a stirred solution of 4-hydroxybenzo[*b*]thiophen (1 g, 0·0067 mol) in dry carbon tetrachloride (60 ml) at 0°. The resulting solution was stirred at 0° for 15 min, diluted with chloroform (40 ml), washed with aqueous sodium hydrogen carbonate, and dried (Na_2SO_4). Evaporation gave 5,7-*dibromo-4-hydroxybenzo*[b]*thiophen* (1·82 g, 89%) as white needles, m.p. 108—110° (from light petroleum) (charcoal) (Found: C, 31·2; H, 1·3; Br, 51·85%; *M*, 306. $C_8H_4Br_2OS$ requires C, 31·2; H, 1·3; Br, 51·9%; *M*, 306), $\nu_{max.}$ (CCl_4) 3515 cm^{-1} (OH).

Prepared similarly, except that stirring was continued at 0° for 5 h, 5,7-dibromo-4-hydroxy-3-methylbenzo[*b*]thiophen (94%) formed white *needles*, m.p. 134° (from light petroleum, followed by sublimation at 125° and 0·1 mmHg) (Found: C, 33·35; H, 1·8; Br, 49·4; S, 9·7%; *M*, 320. $C_9H_6Br_2OS$ requires C, 33·55; H, 1·85; Br, 49·65; S, 9·95%; *M*, 320), $\nu_{max.}$ (CCl_4) 3510 cm^{-1} (OH).

Nitration of 4-*Hydroxybenzo*[b]*thiophen.*—A solution of concentrated nitric acid (0·84 g) in glacial acetic acid (10 ml) was added dropwise to a stirred solution of 4-hydroxybenzo[*b*]thiophen (2 g) in glacial acetic acid (50 ml) at −5°. The resulting solution was poured into water and the precipitate (2·58 g) was collected and steam distilled. The *5-nitro-compound* (1·8 g, 70%) separated from the cooled aqueous distillate and formed pale yellow needles, m.p. 143—144° (from ethanol) (Found: C, 49·6; H, 2·8; N, 7·3; S, 16·4%; *M*, 195. $C_8H_5NO_3S$ requires C, 49·2; H, 2·6; N, 7·2; S, 16·4%; *M*, 195), $\nu_{max.}$ (CCl_4) 3170 cm^{-1} (OH). The material which was not steam volatile was resolved by preparative t.l.c. in chloroform–ethanol (95 : 5) into the 7-nitro-compound (0·65 g, 25%), R_F 0·53, m.p. 228—230° (yellow needles from ethanol) (lit.,[3] 192—193·5°) (Found: C, 49·4; H, 2·55; N, 7·3; S, 16·4%; *M*, 195), $\nu_{max.}$ (KCl) *ca.* 3350br cm^{-1} (OH), and the *5,7-dinitro-compound* (0·13 g, 5%), R_F 0·15, m.p. 310—312° (deep yellow needles from ethanol) (Found: C, 40·1; H, 1·65; N, 11·7; S, 13·3%; *M*, 240. $C_8H_4N_2O_5S$ requires C, 40·0; H, 1·65; N, 11·65; S, 13·35%; *M*, 240).

Nitration of 4-*Hydroxy*-3-*methylbenzo*[b]*thiophen.*—Use of the conditions already described gave a mixture of products, of which the *5-nitro-compound* was steam volatile. It formed deep yellow needles (80%), m.p. 120° (from ethanol, followed by sublimation at 90° and 0·3 mmHg) (Found: C, 51·6; H, 3·2; N, 6·55; S, 15·15%; *M*, 209. $C_9H_7NO_3S$ requires C, 51·65; H, 3·35; N, 6·7; S, 15·3%; *M*, 209), $\nu_{max.}$ (CCl_4) 3170 cm^{-1} (OH). The material remaining after steam distillation was shaken with benzene (3 × 20 ml) and the extracts were dried and evaporated. The residue contained two components in the ratio 9 : 1 (t.l.c.); these were separated by preparative t.l.c. in benzene–ethanol (9 : 1). The *5,7-dinitro-compound* (16%), R_F 0·12, crystallised from ethanol as bronze needles, m.p. 189—191° (Found: C, 42·55; H, 2·05; N, 11·3; S, 12·4%; *M*, 254. $C_9H_6N_2O_5S$ requires C, 42·5; H, 2·35; N, 11·05; S, 12·6%; *M*, 254). The *7-nitro-compound* (2%), R_F 0·38, had m.p. 198—200° (yellow needles from ethanol) (Found: C, 51·6; H, 3·25; N, 6·55; S, 15·45%; *M*, 209), $\nu_{max.}$ (KCl) 3420 cm^{-1} (OH).

Demethylation of 4-*Methoxy*-3-*methyl*-7-*nitrobenzo*[b]*thiophen.*—A mixture of 4-methoxy-3-methyl-7-nitrobenzo[*b*]thiophen [1] (0·5 g) and pyridine hydrochloride (1 g) was kept at 220° for 10 min. 4-Hydroxy-3-methyl-7-nitrobenzo[*b*]thiophen (0·45 g, 95%), m.p. 198—200°, was isolated in the usual way (*cf.* ref. 2) and was identical with the product already described.

Formylation Reactions.—A rapid stream of dry hydrogen chloride was passed during 2·5 h into a vigorously stirred, cooled (ice–salt) mixture of 4-hydroxybenzo[*b*]thiophen (1 g), anhydrous zinc cyanide (4·5 g), and dry ether (30 ml). The rate of flow of hydrogen chloride was then decreased while the mixture was allowed to attain room temperature. The ether was decanted off and the heavy oil which had separated was boiled under reflux for 15 min with 10% hydrochloric acid (15 ml). The mixture was diluted with water and extracted with chloroform, to yield an orange solid which, on steam distillation, gave 4-*hydroxybenzo*[b]-*thiophen-5-carbaldehyde* (1·14 g, 96%) as needles, m.p. 201·5—203° (from light petroleum) (charcoal) (Found: C, 60·7; H, 3·4; S, 17·95%; *M*, 178. $C_9H_6O_2S$ requires C, 60·65; H, 3·45; S, 18·0%; *M*, 178), $\nu_{max.}$ 1640 cm^{-1} (H-bonded C=O).

4-Hydroxy-3-methylbenzo[*b*]thiophen-5-carbaldehyde (68%) was prepared similarly, except that the reaction mixture was hydrolysed and immediately steam distilled.

It formed pale yellow *needles*, m.p. 91—92° (from ethanol) (Found: C, 62·25; H, 4·25; S, 16·65%; *M*, 192. $C_{10}H_8O_2S$ requires C, 62·45; H, 4·2; S, 16·7%; *M*, 192), $\nu_{max.}$ 1640 cm^{-1} (H-bonded C=O).

4-*Methylthieno*[2,3-h][1]*benzopyran-2-one* (1).—A cooled (ice–salt) solution of 4-hydroxybenzo[*b*]thiophen (4 g) and ethyl acetoacetate (3·47 g) in dry methanol (15 ml) was saturated with dry hydrogen chloride, then set aside overnight at 0°. More hydrogen chloride was added during 1 min, then the mixture was kept at 0° for a further 2 h. The precipitate was collected and crystallised from methanol, to give the *pyrone* (1) (4·35 g, 89%) as glistening needles, m.p. 185—187° (Found: C, 66·8; H, 3·9; S, 14·75%; *M*, 216. $C_{12}H_8O_2S$ requires C, 66·65; H, 3·7; S, 14·8%; *M*, 216), $\nu_{max.}$ 1720 cm^{-1} (C=O), δ 2·53 (d, Me), 6·26 (q, 3-H), 7·45 (dd, 5-H), 7·72 (dd, 6-H), and 7·75 (dd, 9-H) ($J_{5.6}$ 8·1, $J_{8.9}$ 5·95, $J_{3.Me}$ 0·8, $J_{6.9}$ 0·75, and $J_{5.8}$ 0·45 Hz).

Prepared similarly, the 4,9-*dimethyl compound* (2) (87%) formed platelets, m.p. 168—170° (from methanol) (Found: C, 67·55; H, 4·45; S, 13·65%; *M*, 230. $C_{13}H_{10}O_2S$ requires C, 67·8; H, 4·4; S, 13·9%; *M*, 230), $\nu_{max.}$ 1710 cm^{-1} (C=O), δ 2·48 (d, 4-Me), 2·78 (d, 9-Me), 6·27 (q, 3-H), 7·06 (m, 8-H), 7·44 (dd, 5-H), and 7·67 (d, 6-H) ($J_{5.6}$ 8·25, $J_{3.Me}$ 0·9, $J_{8.Me}$ 0·8, and $J_{5.8}$ 0·5 Hz).

4-*Allyloxybenzo*[b]*thiophen*.—A stirred mixture of 4-hydroxybenzo[*b*]thiophen (1 g), allyl bromide (1·5 ml), anhydrous potassium carbonate (3 g), and butanone (40 ml) was heated under reflux for 3·5 h, then cooled and filtered. Evaporation of the filtrate gave the *allyl ether* (1·2 g, 95%) as an oil, b.p. 94—96° at 0·3 mmHg (Found: C, 69·5; H, 5·25; S, 16·85%; *M*, 190. $C_{11}H_{10}OS$ requires C, 69·45; H, 5·3; S, 16·85%; *M*, 190).

4-Allyloxy-3-methylbenzo[*b*]thiophen (81%) was obtained similarly (heating time 4·5 h) as white *needles*, m.p. 34—35° [from light petroleum (b.p. 40—60°)], b.p. 88—90° at 0·1 mmHg (Found: C, 70·25; H, 5·9; S, 15·7%; *M*, 204. $C_{12}H_{12}OS$ requires C, 70·55; H, 5·9; S, 15·7%; *M*, 204).

Claisen Rearrangements.—A solution of 4-allyloxybenzo[*b*]thiophen (0·5 g) in freshly distilled *NN*-dimethylaniline (20 ml) was heated under reflux for 3·5 h, then cooled and added to ice-cold 10% hydrochloric acid (30 ml). Extraction with benzene and isolation of phenolic material with alkali in the usual way afforded 5-*allyl*-4-*hydroxybenzo*[b]*thiophen* (0·45 g, 90%) as an oil, b.p. 100—101° at 0·1 mmHg (Found: C, 69·5; H, 5·3; S, 16·85%; *M*, 190. $C_{11}H_{10}OS$ requires C, 69·45; H, 5·3; S, 16·85%; *M*, 190), $\nu_{max.}$ 3500 cm^{-1} (OH).

Similar treatment of 4-allyloxy-3-methylbenzo[*b*]thiophen for 4 h gave 5-*allyl*-4-*hydroxy*-3-*methylbenzo*[b]*thiophen* (81%) as an oil, b.p. 111—113° at 0·4 mmHg (Found: C, 70·4; H, 6·05; S, 15·7%; *M*, 204. $C_{12}H_{12}OS$ requires C, 70·55; H, 5·9; S, 15·7%; *M*, 204).

4-*Acetoxybenzo*[b]*thiophen*.—A solution of 4-hydroxybenzo[*b*]thiophen (1 g) in acetic anhydride (5 ml) and acetic acid (2 ml) was heated under reflux for 15 min, then poured into ice–water. Sodium hydrogen carbonate was added and the product was filtered off. Crystallisation from light petroleum (b.p. 40—60°) gave needles (1·2 g, 94%), m.p. 38·5—40° (lit.,[7] b.p. 166° at 16 mmHg), $\nu_{max.}$ 1760 cm^{-1} (C=O).

4-Hydroxy-3-methylbenzo[*b*]thiophen was acetylated similarly to give the 4-*acetoxy-compound* (91%), which was obtained by ether extraction as an oil, b.p. 110—112° at 0·25 mmHg (Found: C, 64·3; H, 5·1; S, 15·5%; *M*, 206. $C_{11}H_{10}O_2S$ requires C, 64·05; H, 4·9; S, 15·55%; *M*, 206), $\nu_{max.}$ (film) 1735 cm^{-1} (C=O).

Fries Rearrangements.—A mixture of 4-acetoxybenzo[*b*]thiophen (0·5 g, 0·0026 mol) and aluminium chloride (0·8 g, 0·006 mol) in dry benzene (15 ml) was stirred under reflux for 4 h, then cooled and treated with 10% hydrochloric acid (10 ml). Ether extraction, followed by extraction of phenolic material with aqueous 5% sodium hydroxide gave a solid mixture of two components (t.l.c.), which was separated by preparative t.l.c. in chloroform. 7-Acetyl-4-hydroxybenzo[*b*]thiophen (0·45 g, 90%), R_F 0·16, crystallised from ethanol as white needles, m.p. 254—256° (lit.,[7] 260°; lit.,[3] 115—116°) (Found: C, 62·25; H, 4·3%; *M*, 192. Calc. for $C_{10}H_8O_2S$: C, 62·5; H, 4·2%; *M*, 192), $\nu_{max.}$ 1635 cm^{-1} (C=O). 7-*Acetyl*-2,3-*dihydro*-4-*hydroxybenzo*[b]-*thiophen* (30 mg, 7%), R_F 0·84, formed pale yellow needles, m.p. 79—81° (from light petroleum) (Found: C, 61·55; H, 5·2; S, 16·45%; *M*, 194·03847. $C_{10}H_{10}O_2S$ requires C, 61·8; H, 5·2; S, 16·5%; *M*, 194·04007), $\nu_{max.}$ 1635 cm^{-1} (C=O), $\lambda_{max.}$ (EtOH) 255 (ε 14,200), 292 (13,800), and 330 nm (6950) (*i.e.* spectrum different from that [12] of a normal benzo[*b*]thiophen derivative), δ 3·2—3·5 (4H, m, 2- and 3-CH_2). When the heating with aluminium chloride was continued for a further 20 h, the dihydro-compound became the major product (95%).

Treatment of 4-acetoxy-3-methylbenzo[*b*]thiophen with aluminium chloride in boiling benzene for 2 h gave a mixture which was separated as before. 2-*Acetyl*-4-*hydroxy*-3-*methylbenzo*[b]*thiophen* (68%), R_F 0·68, formed pale yellow needles, m.p. 127—128° (from light petroleum) (Found: C, 63·95; H, 4·85; S, 15·5%; *M*, 206. $C_{11}H_{10}O_2S$ requires C, 64·05; H, 4·9; S, 15·55%; *M*, 206), $\nu_{max.}$ 1650 cm^{-1} (C=O). 7-*Acetyl*-4-*hydroxy*-3-*methylbenzo*[b]*thiophen* (21%), R_F 0·32, formed white needles, m.p. 232—234° (from light petroleum) (Found: C, 64·4; H, 5·05; S, 15·65%; *M*, 206), $\nu_{max.}$ 1635 cm^{-1} (C=O).

Authentic samples of 7-acetyl-4-hydroxybenzo[*b*]thiophen and of 2- and 7-acetyl-4-hydroxy-3-methylbenzo[*b*]thiophen were obtained in >90% yield by demethylation of the corresponding 4-methoxy-compounds [1] with pyridine hydrochloride (*cf.* ref. 2). They were identical with the products from the rearrangement reactions.

Bromination of 4-*Methylsulphonyloxybenzo*[b]*thiophen*.—4-Methylsulphonyloxybenzo[*b*]thiophen (1 g) was treated in the usual way with bromine (0·71 g) in acetic acid at room temperature for 8 h. A solution of the viscous red product (1·3 g) in dry ethanol (5 ml) was stirred under reflux for 0·5 h with a solution of sodium (0·2 g) in dry ethanol (20 ml). The cooled suspension was filtered, and the filtrate was acidified with hydrochloric acid and shaken with ether. Evaporation of the washed ($NaHCO_3$ and water) and dried ethereal extracts gave a pale orange solid (0·85 g), which contained five components (g.l.c.) in the proportions indicated in the text. This was steam distilled, and the steam volatile material was separated by preparative t.l.c. in benzene–light petroleum (85 : 15) into 5-bromo-4-hydroxybenzo[*b*]thiophen (0·17 g), m.p. 133° after sublimation at 120° and 0·2 mmHg, and 5,7-dibromo-4-hydroxybenzo[*b*]thiophen (51 mg), m.p. 109—110° after sublimation at 90° and 0·2 mmHg. These bromo-compounds were identical with those described earlier. The non-volatile residue from the steam distillation was crystallised from light petroleum (b.p. 40—60°), and then sublimed at 90° and 0·1 mmHg, to

[12] B. Iddon and R. M. Scrowston, *Adv. Heterocyclic Chem.*, 1970, **11**, 177.

give 3-bromo-4-hydroxybenzo[*b*]thiophen (0·51 g), m.p. 102—103° (lit.,[3] 102—104°). The mother liquors from the crystallisation contained two components (4 and 6% of the original mixture), which we could not separate.

3-*Methyl*-4-*methylsulphonyloxybenzo*[b]*thiophen*.— Methane sulphonyl chloride (15 ml) was added dropwise during 20 min to an ice-cold, stirred solution of 4-hydroxy-3-methylbenzo[*b*]thiophen (2 g) in dry pyridine (100 ml), then the mixture was stirred for 1 h at 0° and poured into ice-cold water. The precipitate was filtered off, washed with 10% hydrochloric acid and water, and crystallised from light petroleum, to give feathery *needles* (2·5 g, 85%), m.p. 73—75° (Found: C, 49·95; H, 4·1; S, 26·35%; *M*, 242. $C_{10}H_{10}O_3S_2$ requires C, 49·55; H, 4·15; S, 26·45%; *M*, 242), δ 2·63 (d, 3-Me) and 3·22 (s, SMe) ($J_{2.Me}$ 0·7 Hz).

3-*Bromomethyl*-4-*methylsulphonyloxybenzo*[b]*thiophen* (3).—3-Methyl-4-methylsulphonyloxybenzo[*b*]thiophen (1·1 g) reacted with *N*-bromosuccinimide (0·74 g) in the usual way (*cf.* ref. 2) to give *prisms* (1·35 g, 95%), m.p. 78—80° (from *n*-pentane) (charcoal) (Found: C, 37·25; H, 2·8; Br, 24·85%; *M*, 320. $C_{10}H_9BrO_3S_2$ requires C, 37·4; H, 2·8; Br, 24·9%; *M*, 320), δ 3·31 (s, SMe) and 4·88br (CH_2Br).

4-*Methylsulphonyloxy*-3-*benzo*[b]*thienylacetonitrile* (4).—A solution of the foregoing bromomethyl compound (2 g) in acetone (10 ml) was added dropwise during 15 min to a stirred mixture of sodium cyanide (0·35 g), acetone (60 ml), and water (8 ml). The mixture was stirred under reflux for 20 h, then cooled and poured into water. Crystallisation of the precipitate from light petroleum gave white *needles* (0·95 g, 63%), m.p. 115—116° (Found: C, 49·6; H, 3·3; N, 5·25%; *M*, 267. $C_{11}H_9NO_3S_2$ requires C, 49·4; H, 3·4; N, 5·25%; *M*, 267), $\nu_{max.}$ 2250 cm^{-1} (C≡N), δ 3·95br (CH_2·CN).

4-*Hydroxy*-3-*benzo*[b]*thienylacetonitrile* (5).—A solution of the nitrile (4) (1·6 g) and sodium (0·28 g) in dry ethanol (25 ml) was boiled under reflux for 15 min. The mixture was cooled and filtered, and the filtrate was acidified and shaken with ether. Phenolic material was extracted from the ethereal solution with aqueous sodium hydroxide in the usual way and formed *needles* (0·95 g, 84%), m.p. 225—227° (from light petroleum) (Found: C, 63·65; H, 3·8; N, 7·55%; *M*, 189. $C_{10}H_7NOS$ requires C, 63·45; H, 3·7; N, 7·4%; *M*, 189), $\nu_{max.}$ 3260br (OH) and 2270 (C≡N) cm^{-1}, δ [$(CD_3)_2SO$] 3·95br (OH) and 4·27 (d, CH_2·CN).

2-(4-*Hydroxy*-3-*benzo*[b]*thienyl*)*ethylamine* (6).—A solution of the nitrile (5) (0·45 g) in dry tetrahydrofuran (20 ml) was added dropwise during 15 min to a stirred solution of diborane [prepared in the usual way from sodium borohydride (2·52 g) and boron trifluoride–ether (3·2 g)] in tetrahydrofuran (100 ml) at 0° under nitrogen. The mixture was then stirred under reflux for 48 h, cooled, and treated dropwise with dry ethanol (3 ml). Passage of hydrogen chloride into the resulting solution gave the amine (6) *hydrochloride* (0·35 g, 68%) as white needles, m.p. 302—304° [Found: C, 52·15; H, 5·3; Cl, 15·6; N, 6·0%; *M* (free base), 193. $C_{10}H_{12}ClNOS$ requires C, 52·25; H, 5·25; Cl, 15·45; N, 6·1%; *M* (free base), 193].

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