Substitution Reactions of Benzo[*b*]thiophen Derivatives. Part III.[1] Nitration of Benzo[*b*]thiophen-2-carboxylic Acid and its 3-Methyl Derivative

By **J. Cooper** and **R. M. Scrowston,*** Department of Chemistry, The University, Hull HU6 7RX

The nitration of benzo[*b*]thiophen-2-carboxylic acid has been re-examined under two different sets of conditions (in sulphuric acid and acetic acid at 60° and in acetic acid and acetic anhydride at 0°). A mixture of the 3-, 4-, 6-, and 7-substitution products was obtained in each case, together with a small amount of 2-nitrobenzo[*b*]thiophen formed by electrophilic displacement of the carboxy-group. Under similar conditions, the nitration of 3-methylbenzo[*b*]thiophen-2-carboxylic acid took place in all positions of the benzene ring apart from the 5-position, and the replacement of the carboxy-group by a nitro-group became a more significant process, particularly in the higher temperature reaction. Structures of new compounds were established by n.m.r. spectroscopy; that of 3-methyl-7-nitrobenzo[*b*]thiophen-2-carboxylic acid was confirmed by synthesis from 2′-chloro-3′-nitroacetophenone. 6-Acetamidobenzo[*b*]thiophen was nitrated in an attempt to obtain the 7-nitro-compound, but a large amount of the 2-nitro-isomer was also formed. Attention is drawn to unusual features in the i.r. spectra of some esters of 3-methyl-7-nitrobenzo[*b*]thiophen-2-carboxylic acid.

THE nitration of benzo[*b*]thiophen-3-carboxylic acid has been investigated rigorously by Martin-Smith and his co-workers,[2] who found that substitution took place in all four positions of the benzene ring, but not in the deactivated 2-position. When the nitration was carried out at 60° some 3-nitrobenzo[*b*]thiophen (13%) was also formed, by electrophilic replacement of the carboxy-group. The nitration of benzo[*b*]thiophen-2-carboxylic acid has been studied less thoroughly [3] and the products therefrom have not been separated and purified. Instead, the total nitration product was decarboxylated and catalytically reduced to give mixed aminobenzo[*b*]thiophens, which were then treated with Raney nickel. The resulting mixture of aminoethylbenzenes contained the *ortho*-isomer (arising from the 4-nitro-compound) and the *meta*-isomer (from the 5- and/or 7-nitro-compound), but none of the *para*-isomer (from the 6-nitro-compound). This method did not prove reliably the absence of the 3-nitro-isomer, because of the instability of the derived 3-aminobenzo[*b*]thiophen.

We have repeated the nitration of benzo[*b*]thiophen-2-carboxylic acid in sulphuric acid and acetic acid at 60° or in acetic acid and acetic anhydride at 0° and here report the separation and characterisation of the products. Each procedure gave a mixture of products which was treated with an excess of ethereal diazomethane. The resulting mixture of methyl esters was analysed quantitatively by g.l.c. (Table 1) and separated by column chromatography into the methyl ester of the starting material and five other products (A—E).

Product (A) was 2-nitrobenzo[*b*]thiophen; its i.r. spectrum lacked carbonyl absorption and its n.m.r.

[1] Part II, J. Cooper and R. M. Scrowston, *J. Chem. Soc.* (*C*), 1971, 3052.

[2] I. Brown, S. T. Reid, N. M. D. Brown, K. J. Armstrong, M. Martin-Smith, W. E. Sneader, G. C. Brophy, and S. Sternhell, *J. Chem. Soc.* (*C*), 1969, 2755.

[3] G. Van Zyl, C. J. Bredeweg, R. H. Rynbrandt, and D. C. Neckers, *Canad. J. Chem.*, 1966, **44**, 2283.

spectrum showed one uncoupled thiophen proton signal. Although (A) was obtained in only low yield (2—4%), its formation provides one of the first examples of the electrophilic replacement of a 2-substituent by a nitro-group in the benzo[*b*]thiophen series.

TABLE 1

Nitration products of benzo[*b*]thiophen-2-carboxylic acid [a]

Substituents	R_t/min	Yield (%) from procedure [b] A	B
2-CO_2Me	7·00	31	11
2-NO_2	9·24	2	4
2-CO_2Me, 3-NO_2	30·80	16	3
2-CO_2Me, 4-NO_2	57·20	21	27
2-CO_2Me, 5-NO_2 [c]	70·80		
2-CO_2Me, 6-NO_2	67·20	16	11
2-CO_2Me, 7-NO_2	74·40	12	26

[a] Analysis by g.l.c. Acidic products were converted into the methyl esters and estimated as such. [b] See Experimental section for conditions. [c] Included for comparison.

The n.m.r. spectrum of (B) showed the absence of thiophen ring protons and of substituents in the benzenoid ring. Hydrolysis and decarboxylation gave 3-nitrobenzo[*b*]thiophen, proving conclusively that (B) was methyl 3-nitrobenzo[*b*]thiophen-2-carboxylate. This result is similar to that for the nitration of benzo[*b*]thiophen-2-carbaldehyde,[4] which gives the 2-nitro-compound (11%), but it differs markedly from that for the 3-carboxylic acid [2] or the 3-carbaldehyde,[5] in which the thiophen position adjacent to the carboxy-group resists substitution even under forcing conditions. As the 3-position is adjacent to a powerfully electron-withdrawing group, it would be expected that the activation energy for nitration in this position might be rather higher than that for substitution in the benzene ring. This might explain in part why much more of the 3-nitro-compound is formed at 60° (16%) than at 0° (3%).

The n.m.r. spectra of (C) and (E) were very similar; each showed signals due to three adjacent benzenoid protons, indicating the presence of a 4- or a 7-substituent. It is often possible to distinguish between 4- or 7-substituted benzo[*b*]thiophens in cases where the 4-substituent twists out of coplanarity with the ring as a result of *peri*-interaction with a 3-substituent (*cf.* ref. 6 and later discussion). In the present case the 4-nitro-group was not twisted significantly out of plane by the hydrogen atom in the 3-position and the chemical shifts of the aromatic protons of the two isomers were not significantly different. However, (C) was identified as the 4-nitro-isomer because the n.m.r. spectrum showed long-range coupling [6] between 3-H and 7-H (0·8 Hz) and also a large anisotropic deshielding of 3-H. Long-range coupling of this type was not observed for (E), which must therefore be methyl 7-nitrobenzo[*b*]thiophen-2-carboxylate.

Product (D) was recognised as either the 5- or the 6-nitro-isomer from the characteristic ABX splitting pattern in the n.m.r. spectrum. From the long-range coupling between 3-H and 7-H (0·6 Hz) it was possible to identify 7-H with certainty. As the coupling constants associated with this signal were too small for *ortho*-coupling, it was concluded that 6-H was absent and that (D) must be the 6-nitro-isomer. Further, an authentic specimen of methyl 5-nitrobenzo[*b*]thiophen-2-carboxylate had an i.r. spectrum different from that of (D). The isolation of the 6-nitro-isomer was surprising in view of the fact that earlier workers [3] had found no evidence for its presence in the mixture from the nitration reaction.

We next investigated the nitration of 3-methylbenzo[*b*]thiophen-2-carboxylic acid, partly to observe how the results just described are modified by the presence of the electron-releasing 3-methyl group, and partly in continuation of our study [1,7] of the substitution reactions of a range of 2,3-disubstituted benzo[*b*]thiophen derivatives. Nitration was carried out under conditions identical with those used for benzo[*b*]thiophen-2-carboxylic acid and the mixtures of products were analysed and separated as before. The results are shown in Table 2. The presence of the 3-methyl group increased

TABLE 2

Nitration products of 3-methylbenzo[*b*]thiophen-2-carboxylic acid [a]

Substituents	R_t/min	Yield (%) from procedure [b] A	B
2-CO_2Me, 3-Me	5·52	44	36
3-Me, 2-NO_2	7·72	23	13
2-CO_2Me, 3-Me, 4-NO_2	31·00	19	29
2-CO_2Me, 3-Me, 5-NO_2 [c]	44·50		
2-CO_2Me, 3-Me, 6-NO_2	45·70	6	9
2-CO_2Me, 3-Me, 7-NO_2	51·40	5	10

[a,b,c] See footnotes to Table 1.

the ease of replacement of the carboxy-group by the nitro-group to such an extent that 3-methyl-2-nitrobenzo[*b*]thiophen (identified by the lack of carbonyl absorption in the i.r. spectrum) became the major nitration product (23%) in the higher temperature reaction. As before, the n.m.r. spectra of methyl 3-methyl-4-nitrobenzo[*b*]thiophen-2-carboxylate and the 7-nitro-isomer formed a pair, with similar coupling patterns. However, these were readily distinguished because the 4-nitro-group was twisted out of coplanarity with the ring by *peri*-interaction with the 3-methyl group. Hence the proton signals for this isomer were at a higher field than for the 7-nitro-isomer, in which the nitro-group was free to exert its full mesomeric effect. The remaining product, methyl 3-methyl-6-nitrobenzo[*b*]-

[4] O. P. Shkurko and V. P. Mamaev, *Sb. Dokl. Sibirsk. Soveshch. Spektrosk.*, 3*rd*, *Krasnoyarsk*, 1966, 45 (*Chem. Abs.*, 1968, **68**, 68,250).

[5] G. C. Brophy, S. Sternhell, N. M. D. Brown, I. Brown, K. J. Armstrong, and M. Martin-Smith, *J. Chem. Soc.* (*C*), 1970, 933.

[6] N. B. Chapman, D. F. Ewing, R. M. Scrowston, and R. Westwood, *J. Chem. Soc.* (*C*), 1968, 764.

[7] J. Cooper, D. F. Ewing, R. M. Scrowston, and R. Westwood, *J. Chem. Soc.* (*C*), 1970, 1949.

thiophen-2-carboxylate, could not be identified unambiguously from its n.m.r. spectrum because of a close similarity with that of the 5-nitro-isomer. However, its i.r. spectrum differed from that of authentic methyl 3-methyl-5-nitrobenzo[*b*]thiophen-2-carboxylate and its structure was confirmed by synthesis. 2-Bromo-3-methyl-6-nitrobenzo[*b*]thiophen [1] reacted with copper(I) cyanide in dimethylformamide to give the 2-carbonitrile, which was hydrolysed to the corresponding 2-carboxylic acid. The methyl ester of this was identical with the product from the nitration reaction. As in the nitration of benzo[*b*]thiophen-2-carboxylic acid, there was no g.l.c. or other evidence for the presence of any of the 5-nitro-isomer in the reaction mixture.

7-Nitrobenzo[*b*]thiophen has been prepared previously,[8,9] but only a few of its derivatives are known. We decided therefore to investigate possible routes to 7-nitro-derivatives, and to confirm the structure of methyl 3-methyl-7-nitrobenzo[*b*]thiophen-2-carboxylate by synthesis. The starting material required for these studies was the hitherto unknown 2′-chloro-3′-nitroacetophenone. In our first attempt to prepare this, we sulphonated 2′-chloroacetophenone and obtained the potassium salt of the 5′-sulphonic acid, identified by the coupling pattern in its n.m.r. spectrum. We had hoped that successive nitration and desulphonation would yield the required product, but attempted nitration even under forcing conditions gave back starting material. Next we treated the diazonium salt of 2-chloro-3-nitroaniline [10] with acetaldehyde oxime in an attempted Beech reaction,[11] but obtained only small amounts of carbonyl-containing material. 2′-Chloro-3′-nitroacetophenone was finally obtained by treatment of the acid chloride of 2-chloro-3-nitrobenzoic acid [12] with diethyl ethoxymagnesiomalonate and hydrolysis of the product with sulphuric acid. When it was treated with ethyl mercaptoacetate in the presence of sodium ethoxide, ethyl 3-methyl-7-nitrobenzo[*b*]thiophen-2-carboxylate (86%) was formed in a single step by nucleophilic replacement of the chlorine atom and spontaneous cyclisation of the product. The corresponding methyl ester was identical with that obtained from the nitration reaction. Acidic hydrolysis of the ethyl ester gave the 2-carboxylic acid, decarboxylation of which afforded 3-methyl-7-nitrobenzo[*b*]thiophen in high yield.

The i.r. spectra of some esters of 3-methyl-7-nitrobenzo[*b*]thiophen-2-carboxylic acid showed points of interest. The solid phase spectrum (KCl) of the ethyl ester showed two carbonyl peaks of approximately equal intensity at 1712 and 1684 cm^{-1}, whereas the solution spectrum ($CHCl_3$) had only one sharp peak, at 1712 cm^{-1}, indicating that the splitting was associated with the crystal structure of the compound. The methyl ester showed only one carbonyl absorption, at 1712 cm^{-1} (in KCl), which was broader than usual, suggesting that the splitting of the carbonyl band might depend on the size of the *O*-alkyl group. In support of this suggestion, the t-butyl ester absorbed at 1710 and 1684 cm^{-1} (in KCl), but the lower frequency band was now three times more intense than the 1710 cm^{-1} band. The origin of this effect is not certain, but it seems to depend on the crystal structure of the compound, on the size of the ester alkyl group, and on the presence of a 7-nitro-group. Ethyl 3-methyl-5-nitrobenzo[*b*]thiophen-2-carboxylate, for example, shows only a single C=O band at 1714 cm^{-1} (in KCl).

In another attempt to prepare 7-nitrobenzo[*b*]thiophen derivatives, we first obtained 6-acetamidobenzo[*b*]thiophen by means of a Schmidt reaction with 6-acetylbenzo[*b*]thiophen,[7] and predicted that it should undergo nitration in the 7-position by use of an argument analogous to that applied to explain why the corresponding 5-acetamido-compound undergoes substitution predominantly in the 4-position.[13] However, a mixture containing two major products was obtained, and could be separated only by preparative t.l.c. One of the components was shown to be the expected 7-acetamido-compound, since the n.m.r. spectrum showed the presence of two *ortho*-coupled benzenoid protons and two thiophen protons. The second component was slightly impure, but the n.m.r. spectrum showed that nitration had taken place in the thiophen ring. The three benzenoid protons were assigned from their coupling patterns and it was found that 4-H and 5-H were deshielded by 0·22 and 0·10 p.p.m., respectively, relative to their positions in the spectrum of 6-acetamidobenzo[*b*]thiophen. These values are very close to the deshielding values calculated for the same protons in 3-methyl-2-nitrobenzo[*b*]thiophen [14] (0·19 and 0·13 p.p.m.), but are very different from those for 3-nitrobenzo[*b*]thiophen [0·72 and 0·19 p.p.m. (calculated from data in ref. 8)]. This suggests that the unknown nitro-compound contains a 2-nitro-group rather than a 3-nitro-group, and is therefore probably 6-acetamido-2-nitrobenzo[*b*]thiophen. No long-range coupling between H-3 and H-7 was detected.[6] The nitration of 6-acetamido-2,3-dibromobenzo[*b*]thiophen gave a single product which was too insoluble to enable a satisfactory n.m.r. spectrum to be obtained. However, the i.r. spectrum showed a peak at 840 cm^{-1} (1,2,3,4-tetrasubstituted benzene ring), consistent with the presence of a 7-nitro-group.

EXPERIMENTAL

General experimental directions have been described previously.[1,7]

Benzo[*b*]thiophen-2-carboxylic acid (86%) was prepared by the carboxylation of 2-benzo[*b*]thienyl-lithium [15] and

[8] K. J. Armstrong, M. Martin-Smith, N. M. D. Brown, G. C. Brophy, and S. Sternhell, *J. Chem. Soc.* (*C*), 1969, 1766.
[9] D. E. Boswell, J. A. Brennan, P. S. Landis, and P. G. Rodewald, *J. Heterocyclic Chem.*, 1968, **5**, 69.
[10] F. D. Gunstone and S. Horwood Tucker, *J. Appl. Chem.*, 1952, **2**, 204.
[11] W. F. Beech, *J. Chem. Soc.*, 1954, 1297.
[12] J. Kenner and W. V. Stubbings, *J. Chem. Soc.*, 1921, 593.
[13] F. G. Bordwell and H. Stange, *J. Amer. Chem. Soc.*, 1955, **77**, 5939.
[14] J. Cooper, Ph.D. Thesis, Hull, 1970.
[15] D. A. Shirley and M. D. Cameron, *J. Amer. Chem. Soc.*, 1950, **72**, 2788.

purified by precipitation from its solution in sodium carbonate; it had m.p. 238—239° (lit.,[15] 237°) (from ethanol). Prepared similarly from 3-methyl-2-benzo[*b*]thienyl-lithium,[16] 3-methylbenzo[*b*]thiophen-2-carboxylic acid (79%) had m.p. 244—245° (lit.,[16] 244·5—246°) (from ethanol).

Nitration of Benzo[b]*thiophen-2-carboxylic Acid.—Method A.* A solution of fuming nitric acid (*d* 1·5; 2·7 ml) in glacial acetic acid (10 ml) was added dropwise during 20 min to a stirred solution of the benzothiophen acid (8·9 g, 0·05 mol) in glacial acetic acid (100 ml) and concentrated sulphuric acid (10 ml). The mixture was then stirred at 60° for 3 h, and poured into water. The resulting precipitate was filtered off, dried, and treated with an excess of ethereal diazomethane.

Method B. A stirred solution of the acid (1·8 g, 0·01 mol) in acetic anhydride (15 ml) was treated dropwise at 0° with a solution of fuming nitric acid (*d* 1·5; 3 ml) in glacial acetic acid (3 ml). Stirring was continued for 30 min at 0°, then for 3 h at room temperature, and the product was isolated and treated with diazomethane as described in method A.

Each mixture of products was analysed quantitatively by g.l.c., to give the results shown in Table 1.

The product (8·5 g) from method A was chromatographed on silica gel. Elution with light petroleum–chloroform (95 : 5) gave, in the following order: 2-nitrobenzo[*b*]thiophen (80 mg), which crystallised from light petroleum as pale yellow needles, m.p. 113—115° (lit.,[9] 115—117°) (Found: *M*, 179. Calc. for $C_8H_5NO_2S$: *M*, 179), $\nu_{max.}$ 1516 and 1350 (NO_2) cm^{-1}, R_t 9·24 min, identical with authentic material; methyl benzo[*b*]thiophen-2-carboxylate (2·0 g) as needles, m.p. 71—72° (lit.,[17] 72—73°) (from ethanol), $\nu_{max.}$ 1716 (C=O) cm^{-1}, R_t 7·00 min, identical with an authentic sample; *methyl* 3-*nitrobenzo*[b]*thiophen-2-carboxylate* (0·8 g), which formed pale yellow needles, m.p. 104—105° (from ethanol) (Found: C, 50·9; H, 3·0; N, 5·65%; *M*, 237. $C_{10}H_7NO_4S$ requires C, 50·65; H, 2·95; N, 5·9%; *M*, 237), $\nu_{max.}$ 1723 (C=O), 1535, and 1338 (NO_2) cm^{-1}, R_t 30·80 min; *methyl* 4-*nitrobenzo*[b]*thiophen-2-carboxylate* (1·0 g) as silvery-yellow plates, m.p. 147—149° (from ethanol) (Found: C, 50·8; H, 3·0; N, 6·0%; *M*, 237), $\nu_{max.}$ 1718 (C=O), 1530, and 1350 (NO_2) cm^{-1}, δ 8·82 (s, 3-H), 8·37 (dd, 5-H), 7·59 (dd, 6-H), and 8·17 (dd, 7-H) p.p.m. ($J_{5,6}$ 8·0, $J_{5,7}$ 1·2, and $J_{6,7}$ 8·0 Hz),* R_t 57·20 min. Successive hydrolysis and decarboxylation gave 4-nitrobenzo[*b*]thiophen, m.p. 80—82° (lit.,[8] 83—84°), the i.r. spectrum of which was identical with that recorded;[9] *methyl* 6-*nitrobenzo*[b]*thiophen-2-carboxylate* (0·8 g), which crystallised from ethyl acetate as pale yellow needles, m.p. 204—205° (Found: C, 50·5; H, 2·8; N, 6·0%; *M*, 237), $\nu_{max.}$ 1719 (C=O), 1530, and 1345 (NO_2) cm^{-1}, δ 8·13 (s, 3-H), 8·00 (dd, 4-H), 8·25 (dd, 5-H), and 8·81 (dd, 7-H) p.p.m. ($J_{4,5}$ 9·0, $J_{4,7}$ 0·6, and $J_{5,7}$ 2·1 Hz), R_t 67·20 min; *methyl* 7-*nitrobenzo*[b]*thiophen-2-carboxylate* (0·65 g) as pale yellow needles, m.p. 170—171° (from ethanol) (Found: C, 50·7; H, 3·1; N, 6·0%; *M*, 237), $\nu_{max.}$ 1725 (C=O), 1532, and 1332 (NO_2) cm^{-1}, δ 8·16 (s, 3-H), 8·21 (dd, 4-H), 7·60 (dd, 5-H), and 8·50 (dd, 6-H) p.p.m. ($J_{4,5}$ 7·8, $J_{4,6}$ 1·2, and $J_{5,6}$ 7·6 Hz), R_t 74·40 min.

3-*Nitrobenzo*[b]*thiophen-2-carboxylic Acid.*—Prepared (85%) by hydrolysis of the methyl ester already described with a mixture of sulphuric acid and acetic acid, this formed *needles*, m.p. 231—233° (from butan-2-one) (Found: C, 48·4; H, 2·2; N, 6·4. $C_9H_5NO_4S$ requires C, 48·45; H, 2·25; N, 6·3%), $\nu_{max.}$ 1665 (C=O) cm^{-1}.

Decarboxylation of the acid with copper bronze and quinoline (*cf.* ref. 8) gave 3-nitrobenzo[*b*]thiophen (82%), m.p. 79—80° (lit.,[8] 80—80·5°).

Methyl 5-*Nitrobenzo*[b]*thiophen-2-carboxylate.*—This was prepared by the action of ethereal diazomethane on the corresponding acid.[13] It crystallised from ethyl acetate as yellow *needles* (92%), m.p. 219—221° (Found: C, 50·4; H, 2·9; N, 6·0%; *M*, 237), $\nu_{max.}$ 1720 (C=O) cm^{-1}, δ 8·19 (s, 3-H), 8·77 (dd, 4-H), 8·30 (dd, 6-H), and 8·00 (dd, 7-H) p.p.m. ($J_{4,6}$ 2·1, $J_{4,7}$ 0·7, and $J_{6,7}$ 9·0 Hz), R_t 70·80 min.

Nitration of 3-*Methylbenzo*[b]*thiophen-2-carboxylic Acid.*—Use of conditions described for benzo[*b*]thiophen-2-carboxylic acid (methods A and B) gave semi-solid products which were treated with ethereal diazomethane as before. The resulting mixtures had the compositions shown in Table 2 (g.l.c.).

The mixture (9·1 g) obtained by method A was separated chromatographically as before. The following products were obtained, in order of elution: 3-methyl-2-nitrobenzo[*b*]thiophen (1·4 g) as pale yellow needles (from ethanol), m.p. 148—149° (lit.,[16] 148—149°), $\nu_{max.}$ 1530 and 1340 (NO_2) cm^{-1}, R_t 7·72 min, identical with an authentic material; *methyl* 3-*methylbenzo*[b]*thiophen-2-carboxylate* (3·1 g), which formed needles, m.p. 103—104° (from ethanol) (Found: C, 64·2; H, 5·0%; *M*, 206. $C_{11}H_{10}O_2S$ requires C, 64·05; H, 4·9%; *M*, 206), $\nu_{max.}$ 1712 (C=O) cm^{-1}, R_t 5·52 min, identical with authentic material prepared (92%) by treatment of 3-methylbenzo[*b*]thiophen-2-carboxylic acid with diazomethane; *methyl* 3-*methyl*-4-*nitrobenzo*[b]*thiophen-2-carboxylate* (0·95 g), which crystallised from ethanol as yellow needles, m.p. 112—113° (Found: C, 52·65; H, 3·6; N, 5·55%; *M*, 251. $C_{11}H_9NO_4S$ requires C, 52·6; H, 3·6; N, 5·55%; *M*, 251), $\nu_{max.}$ 1723 (C=O), 1520, and 1360 (NO_2) cm^{-1}, δ 7·62 (dd, 5-H), 7·49 (dd, 6-H), 7·98 (dd, 7-H), and 2·65 (s, Me) p.p.m. ($J_{5,6}$ 7·9, $J_{5,7}$ 1·3, and $J_{6,7}$ 8·1 Hz), R_t 31·00 min; *methyl* 3-*methyl*-6-*nitrobenzo*[b]*thiophen-2-carboxylate* (0·4 g) as yellow needles, m.p. 202—203° (from ethanol) (Found: C, 52·3; H, 3·4; N, 5·7%; *M*, 251), $\nu_{max.}$ 1720 (C=O), 1540, and 1346 (NO_2) cm^{-1}, δ 7·95 (dd, 4-H), 8·27 (dd, 5-H), 8·75 (dd, 7-H), and 2·81 (s, Me) p.p.m. ($J_{4,5}$ 9·0, $J_{4,7}$ 0·5, and $J_{5,7}$ 1·8 Hz), R_t 45·70 min; *methyl* 3-*methyl*-7-*nitrobenzo*[b]*thiophen-2-carboxylate* (0·2 g), which gave yellow-grey needles, m.p. 201—202° (Found: C, 52·4; H, 3·4; N, 5·8%; *M*, 251), $\nu_{max.}$ 1715 (C=O), 1515, and 1325 (NO_2) cm^{-1}, δ 8·18 (dd, 4-H), 7·61 (dd, 5-H), 8·52 (dd, 6-H), and 2·81 (s, Me) p.p.m. ($J_{4,5}$ 7·9, $J_{4,6}$ 1·4, and $J_{5,6}$ 7·7 Hz), R_t 45·70 min.

Identification of 3-*Methyl*-6-*nitrobenzo*[b]*thiophen-2-carboxylic Acid.*—(*a*) Treatment of 3-methyl-5-nitrobenzo[*b*]thiophen-2-carboxylic acid [18] with an excess of ethereal diazomethane gave the *methyl ester* (95%) as yellow plates (from ethanol), m.p. 187—188° (Found: C, 52·3; H, 3·5; N, 5·8%; *M*, 251), $\nu_{max.}$ 1713 (C=O), 1536, and 1344 (NO_2) cm^{-1}, R_t 44·50 min. It was not identical with the methyl ester of the product from the nitration reaction.

(*b*) A stirred mixture of 2-bromo-3-methyl-6-nitrobenzo[*b*]thiophen [1] (0·8 g), copper(I) cyanide (0·35 g), and dimethylformamide (10 ml) was heated under reflux for 5 h, then poured into water. Extraction with benzene gave a

* Details of long-range couplings are omitted in all cases in order to simplify the presentation.

[16] D. A. Shirley, M. J. Danzig, and F. C. Canter, *J. Amer. Chem. Soc.*, 1953, **75**, 3278.

[17] R. Weissgerber and O. Kruber, *Ber.*, 1920, **53**, 1551.

[18] N. B. Chapman, K. Clarke, and S. N. Sawhney, *J. Chem. Soc.* (*C*), 1968, 518.

yellow solid, m.p. 205—208°, $\nu_{max.}$ 2220 (C≡N), 1530, 1340 (NO_2), and 1690 (C=O impurity) cm^{-1}.

The crude product (0·5 g) was heated under reflux for 1 h with an excess of aqueous ethanolic sodium hydroxide. Dilution and acidification of the resulting solution gave a precipitate, crystallisation of which from acetic acid gave 3-methyl-6-nitrobenzo[*b*]thiophen-2-carboxylic acid as yellow *needles* (0·25 g), m.p. 300—302° (Found: C, 50·4; H, 2·8; N, 6·1. $C_{10}H_7NO_4S$ requires C, 50·6; H, 2·95; N, 5·9%), $\nu_{max.}$ 1695 (C=O), 1536, and 1344 (NO_2) cm^{-1}. The methyl ester was identical with that of the product from the nitration reaction.

Potassium 2′-Chloroacetophenone-5′-sulphonate.—A mixture formed by the dropwise addition of *o*-chloroacetophenone (5·2 g, 0·033 mol) to warm (50°) oleum (20% SO_3) (20 ml) was kept for 4 h at 120°, then cooled and poured on ice (100 g). Potassium nitrate (5 g) was added and the solution was kept for 48 h at 0°. The resulting pale yellow precipitate formed almost colourless needles (8·5 g) (from water), $\nu_{max.}$ 1704 (C=O) cm^{-1}, δ 8·07 (dd, 3-H), 8·32 (dd, 4-H), and 8·63 (dd, 6-H) p.p.m. ($J_{3,4}$ 8·5, $J_{3,6}$ 0·5, and $J_{4,6}$ 2·3 Hz). Satisfactory analytical data could not be obtained.

The product was recovered unchanged after treatment for 4 h at 130° with potassium nitrate and oleum (10% SO_3).

2-Chloro-3-nitrobenzoyl Chloride.—2-Chloro-3-nitrobenzoic acid (78%), prepared by the oxidation of 2-chloro-3-nitrotoluene with nitric acid,[12] formed white needles, m.p. 179—180° (lit.,[12] 181°) (from xylene), $\nu_{max.}$ 1702 (C=O) cm^{-1}. When heated with an excess of thionyl chloride it gave the acid chloride (85%) as *needles*, m.p. 57—58° (from light petroleum) (Found: C, 38·5; H, 1·45; N, 6·4. $C_7H_3Cl_2NO_3$ requires C, 38·2; H, 1·35; N, 6·35%), $\nu_{max.}$ 1795 and 1765 (C=O) cm^{-1}.

2′-Chloro-3′-nitroacetophenone.—A solution of the acid chloride just described (8·8 g) in dry ether (30 ml) was treated with a solution of diethyl ethoxymagnesiomalonate [19] [from diethyl malonate (7·05 g) and magnesium (1·1 g)] in ether (30 ml). The mixture was stirred and heated under reflux for 1·5 h, cooled, washed with dilute sulphuric acid, then with water, dried, and evaporated. The residual oil was heated under reflux for 6 h with a mixture of acetic acid (12 ml), concentrated sulphuric acid (1·5 ml), and water (8 ml). The solution was cooled and made alkaline with 2N-sodium hydroxide, then extracted with ether. The product (6 g, 75%) was obtained as *needles*, m.p. 39—40° (from light petroleum) (Found: C, 48·3; H, 3·3; N, 7·3. $C_8H_6ClNO_3$ requires C, 48·15; H, 3·05; N, 7·0%), $\nu_{max.}$ 1710 (C=O) cm^{-1}, δ 2·67 (s, Me) p.p.m.

Ethyl 3-Methyl-7-nitrobenzo[b]*thiophen-2-carboxylate.*—2′-50·6; H, 2·95; N, 5·9%), $\nu_{max.}$ 1692 and 1660 (C=O) cm^{-1}. The methyl ester was identical with one of the products from the nitration reaction.

Decarboxylation of the acid with copper bronze and quinoline (*cf.* ref. 18) gave the *product* (88%) as yellow needles, m.p. 120—121° (Found: C, 56·2; H, 3·4; N, 7·1%; *M*, 193. $C_9H_7NO_2S$ requires C, 55·95; H, 3·65; N, 7·25%; *M*, 193), $\nu_{max.}$ 1510 and 1347 (NO_2) cm^{-1}, δ 2·48 (s, Me), 7·28 (s, 2-H), 8·01 (dd, 4-H), 7·53 (dd, 5-H), and 8·39 (dd, 6-H) p.p.m. ($J_{4,5}$ 8·1, $J_{4,6}$ 1·4, and $J_{5,6}$ 8·0 Hz).

t-Butyl 3-Methyl-7-nitrobenzo[b]*thiophen-2-carboxylate.*—Toluene-*p*-sulphonyl chloride (0·5 g) and t-butyl alcohol (0·1 g) were added successively to a cooled (10°) solution of 3-methyl-7-nitrobenzo[*b*]thiophen-2-carboxylic acid (0·3 g) in pyridine (6 ml). The mixture was stirred for 6 h at 10°, then poured into water. The resulting precipitate was filtered off and extracted with portions of boiling chloroform, in which starting material was insoluble. Evaporation of the extract gave yellow *needles* (0·15 g, 40%), m.p. 155—156° (Found: C, 57·45; H, 4·9; N, 4·8%; *M*, 293. $C_{14}H_{15}NO_4S$ requires C, 57·3; H, 5·15; N, 4·8%; *M*, 293), $\nu_{max.}$ 1710, 1684 (C=O), 1510, and 1323 (NO_2) cm^{-1}.

6-Acetamidobenzo[b]*thiophen.*—Sodium azide (0·5 g) was added during 1 h to a stirred solution (70°) of 6-acetylbenzo[*b*]thiophen [7] (0·5 g) in glacial acetic acid (5 ml) and concentrated sulphuric acid (2 ml). The mixture was kept at 80° for 3 h, cooled, poured into saturated aqueous sodium acetate, and set aside at 0° overnight. The product was filtered off and crystallised from ethanol, to give *needles* (0·36 g, 70%), m.p. 117—119° (Found: C, 62·5; H, 4·7. $C_{10}H_9NOS$ requires C, 62·8; H, 4·75%), $\nu_{max.}$ 3295 (NH) and 1663 (C=O) cm^{-1}.

Nitration of 6-Acetamidobenzo[b]*thiophen.*—Concentrated nitric acid (0·2 ml) was added to a stirred solution of the acetamido-compound (0·15 g) in glacial acetic acid (5 ml). Stirring was continued for 6 h, then the mixture was poured into water. The yellow product was filtered off and separated by preparative t.l.c. [in light petroleum–benzene (1 : 1)] into two components. 6-Acetamido-7-nitrobenzo[*b*]thiophen (higher R_F value) formed yellow *needles* (79 mg, 43%), m.p. 180—181° (from ethanol) (Found: C, 51·2; H, 3·45. $C_{10}H_8N_2O_3S$ requires C, 50·85; H, 3·4%), $\nu_{max.}$ 3328 (NH) and 1704 (C=O) cm^{-1}, δ [$(CD_3)_2CO$] 2·32 (s, Me), 7·58 (d, 2-H), 7·78 (d, 3-H), 8·26 (d, 4-H), and 8·71 (d, 5-H) p.p.m. ($J_{2,3}$ 5·5 and $J_{4,5}$ 8·6 Hz).

The slightly impure second component (*ca.* 35%) was probably 6-acetamido-2-nitrobenzo[*b*]thiophen, m.p. 200—204°, $\nu_{max.}$ 3310 (NH) and 1670 (C=O) cm^{-1}.

Nitration of 6-Acetamido-2,3-dibromobenzo[b]*thiophen.*—