Condensed Thiophen Ring Systems. Part III.[1] A New Synthesis of Benzo[*b*]thiophen-2(3*H*)- and -3(2*H*)-ones and Some Reactions of Benzo[*b*]thiophen-2(3*H*)-one with Dimethyl Sulphate in the Presence of Base

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Benzo[*b*]thiophen-2(3*H*)-one (thio-oxindole) (72% overall yield) was prepared by treating 2,4,6-tri-(2-benzo[*b*]-thienyl)cyclotriboroxane with hydrogen peroxide. The boroxane was obtained when 2-benzo[*b*]thienyl-lithium was treated successively with n-butylborate and acid. 3-Methylbenzo[*b*]thiophen-2(3*H*)-one and benzo[*b*]-thiophen-3(2*H*)-one (thioindoxyl) were prepared similarly. The reactions of benzo[*b*]thiophen-2(3*H*)-one with dimethyl sulphate in the presence of base in various solvents were studied. Successive treatment of this compound with sodium hydride and dimethyl sulphate in hexamethylphosphoramide gave 2-methoxybenzo[*b*]thiophen (90% yield).

THE methods used previously [2] to prepare benzo[*b*]thiophen-2(3*H*-)one (thio-oxindole) (Ia) either give low yields or involve several stages. We now report a simple two-stage synthesis of (Ia) which utilises commercially available benzo[*b*]thiophen as the starting material. The method is a general one and can be used to prepare other benzo[*b*]thiophen-2(3*H*)- and -3(2*H*)-ones.

Treatment of 2-benzo[*b*]thienyl-lithium with n-butyl borate followed by hydrolysis of the product with acid gave 2,4,6-tri-(2-benzo[*b*]thienyl)cyclotriboroxane (II) (95%). This product arises by dehydration of the intermediate boronic acid (III) during work up; such dehydrations of boronic acids to cyclotriboroxanes are known [3] to occur readily. A patent [4] claims the preparation of (III) by this method but the reported m.p. of the product indicates that it was probably the cyclotriboroxane (II). When the cyclotriboroxane (II) was treated with hydrogen peroxide, it gave a 76% yield of benzo[*b*]thiophen-2(3*H*)-one (Ia). The previously unknown 3-methylbenzo[*b*]thiophen-2(3*H*)-one (Ib) (64·5%) and benzo[*b*]thiophen-3(2*H*)-one (thioindoxyl) were prepared similarly. In the latter case a 92% yield of the cyclotriboroxane was obtained, but treatment of this with hydrogen peroxide gave thioindoxyl (51%) together with a deep red solid, which was probably thioindigo. We [5] have prepared thioindoxyl (23% yield) previously by treating 3-benzo[*b*]thienyl-lithium with oxygen.

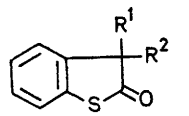
It has been shown [2] that thio-oxindole exists exclusively as the keto-form, (Ia), both in the solid state and in solution. The n.m.r. (in CCl_4) and i.r. (solid film and KBr disc) spectra [6] of the sample prepared by us showed no evidence for the presence of the enol form.

Since we required a sample of 2-methoxybenzo[*b*]thiophen (IVa), which was unknown at the outset of our work, we decided to study the methylation reactions of thio-oxindole (Ia). *O*-Alkylation of ambident anions such as (V) is favoured in polar aprotic solvents. Consequently, when (Ia) was treated successively with sodium hydride and dimethyl sulphate in hexamethylphosphoramide,[7] it gave (IVa) as the major product (90 mole %). The n.m.r. spectrum [6] of the crude product after starting material had been removed by treatment with sodium hydroxide suggested that it contained *ca.* 5—10 mole % of 2-methoxy-3-methylbenzo[*b*]thiophen (IVb) together with a trace of (Ib). These products may arise by initial *C*-alkylation of (Ia) to give (Ib) followed by *O*-alkylation. However, an attempt to prepare (IVb) by a method similar to the one used recently by Matsuki and Adachi [8] to prepare 2-methoxybenzo[*b*]thiophen (IVa) was unsuccessful.

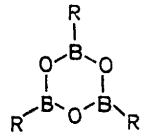
3-Methoxybenzo[*b*]thiophen has been prepared by methylation of thioindoxyl by dimethyl sulphate in alkaline solution.[9] A similar attempt by Hawthorne

[1] Part II, B. Iddon, C. K. Thadani, B. Northover, and R. G. Sommerville, *Chim. Therap.*, 1970, **5**, 149.
[2] B. Iddon and R. M. Scrowston, *Adv. Heterocyclic Chem.*, 1970, **11**, 296.
[3] W. Gerrard, 'The Organic Chemistry of Boron,' Academic Press, London, 1961, p. 68.
[4] J. Yates and R. S. Airs, B.P. 814,647/1959 (*Chem. Abs.*, 1960, **54**, 8851).
[5] R. P. Dickinson and B. Iddon, *J. Chem. Soc.* (*C*), 1968, 2733.
[6] R. P. Dickinson, Ph.D. Thesis, University of Salford, 1969.
[7] H. Normant, *Angew. Chem. Internat. Edn.*, 1967, **6**, 1046.
[8] Y. Matsuki and Y. Adachi, *J. Chem. Soc. Japan*, 1968, **89**, 192 (*Chem. Abs.*, 1968, **69**, 67,165).
[9] P. Friedländer, *Annalen*, 1907, **351**, 390.

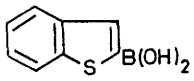
and Porter [10] to prepare 2-methoxybenzo[*b*]thiophen (IVa) gave only *o*-(methylthio)phenylacetic acid (VIb); Brower and Amstutz [11] obtained the parent acid (VIa) when they treated (Ia) successively with hot sodium



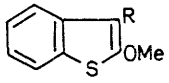
(I) a; R^1 = R^2 = H
b; R^1 = Me, R^2 = H



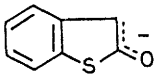
(II) R = 2-benzo[*b*]thienyl



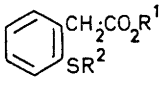
(III)



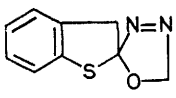
(IV) a; R = H
b; R = Me



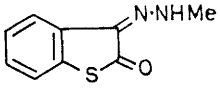
(V)



(VI) a; R^1 = R^2 = H
b; R^1 = H, R^2 = Me
c; R^1 = R^2 = Me



(VII)



(VIII)

hydroxide and acid We prepared methyl *o*-(methylthio)phenyl acetate (VIc) (see later) similarly by treating (Ia) successively with 2 equiv. of hot sodium hydroxide and dimethyl sulphate.

We have also studied the reactions of (Ia) with dimethyl sulphate in methanol in the presence of sodium methoxide and in 50% aqueous acetone in the presence of sodium hydroxide. In the former case ring-opening occurred predominantly to give (VIc); in the latter case a complex mixture of compounds was obtained which was not investigated fully. The n.m.r. spectrum [6] of the mixture showed that it contained considerable amounts of the *O*- and *C*-alkylated products (IVa) and (Ib), respectively.

There are conflicting reports concerning the reaction of (Ia) with diazomethane. Hawthorne and Porter [10] have reported the formation of the spiro-oxadiazoline (VII); more recently, Schmiechen [12] has reported the formation of (VIII).

[10] D. G. Hawthorne and Q. N. Porter, *Austral. J. Chem.*, 1966, **19**, 1751.
[11] K. R. Brower and E. D. Amstutz, *J. Org. Chem.*, 1954, **19**, 411.

EXPERIMENTAL

N.m.r. spectra were recorded by using a Varian A60 spectrometer; tetramethylsilane was used as an internal standard and the recorded signals are singlets unless otherwise stated. Molecular weights were determined by mass spectrometry by using an A.E.I. MS 12 instrument.

Benzo[*b*]thiophen and n-butyl-lithium were available commercially: the latter was purchased as a 20% (w/w) solution in hexane. Reactions with n-butyl-lithium were carried out under dry nitrogen and the solvents and reagents used were dried by standard procedures.

2,4,6-*Tri*-(2-*benzo*[b]*thienyl*)*cyclotriboroxane*.— n-Butyl-lithium (300 mmoles) in hexane (135 ml.) was added dropwise at 0° to a stirred solution of benzo[*b*]thiophen (40·2 g., 300 mmoles) in ether (450 ml.) and the resulting mixture was stirred at room temperature for 1 hr. n-Butyl borate (82·8 g., 360 mmoles) in ether (100 ml.) was then added during 10 min. to the cooled (0°) mixture and stirring was continued at room temperature for 1 hr. Following the addition of 2N-hydrochloric acid, the organic layer was separated and the aqueous layer was extracted with ether. The combined organic layer and ethereal extracts were extracted with 2N-sodium hydroxide, the combined alkaline extracts were acidified with concentrated hydrochloric acid, and the *product* (45·5 g., 95%) was extracted with ether; m.p. *ca.* 250° (from benzene) (lit.,[4] 259—260°) (see Discussion section) (Found: C, 60·1; H, 3·45%; *M*, 480. $C_{24}H_{15}B_3O_3S_3$ requires C, 60·1; H, 3·15%; *M*, 480).

2,4,6-*Tri*-(3-*methyl*-2-*benzo*[b]*thienyl*)*cyclotriboroxane* (80%), m.p. 294—296° (from benzene) (Found: C, 61·75; H, 4·2%; *M*, 522. $C_{27}H_{21}B_3O_3S_3$ requires C, 62·1; H, 4·1%; *M*, 522) was prepared similarly from 3-methylbenzo[*b*]thiophen.[5]

2,4,6-*Tri*-(3-*benzo*[b]*thienyl*)*cyclotriboroxane*.—A solution of n-butyl borate (8·28 g., 36 mmoles) in ether (10 ml.) was added dropwise at −70° to a stirred suspension of 3-benzo[*b*]thienyl-lithium [5] (30 mmoles) in ether (75 ml.) and the mixture was stirred at −70° for 4 hr. It was then allowed to warm slowly to −5°, stirred at −5° for 15 min., and worked up as already described to give the *product* (4·4 g., 92%), m.p. 229—231° (from benzene) (Found: C, 59·9; H, 3·3%; *M*, 480. $C_{24}H_{15}B_3O_3S_3$ requires C, 60·1; H, 3·15%; *M*, 480).

Benzo[b]*thiophen*-2(3H)-*one*.— 2,4,6-Tri-(2-benzo[*b*]-thienyl)cyclotriboroxane (18·7 g., 39 mmoles) was added with stirring to 30% (w/v) hydrogen peroxide (20 ml.) at such a rate that the temperature of the mixture did not exceed 50°. The mixture was then heated to 70° with stirring for 15 min., cooled, and diluted with water; extraction of the product with chloroform gave benzo[*b*]thiophen-2(3*H*)-one (13·3 g., 76%), m.p. 43—44° [from light petroleum (b.p. 40—60°)] (lit.,[13] 43—45°), $\nu_{max.}$ (KBr) 1710 cm.$^{-1}$ (C=O), τ (CCl_4) 6·21 (CH_2) and 2·70—2·90 (aromatic).

3-*Methylbenzo*[b]*thiophen*-2(3H)-*one* (64·5%), b.p. 152—153°/22 mm., $\nu_{max.}$ 1705s cm.$^{-1}$ (C=O), τ (neat liquid) 8·63 (d, *J* 7·5 Hz, Me), 6·37 (q, CH), and 2·80—3·00 (aromatic) (Found: C, 66·2; H, 4·9. C_9H_8OS requires C, 65·8; H, 4·9%), and benzo[*b*]thiophen-3(2*H*)-one (51%), m.p. 63—64° [from light petroleum (b.p. 40—60°)] (lit.,[5] 61—63°) were prepared similarly.

Reaction of Benzo[b]*thiophen*-2(3H)-*one with Dimethyl Sulphate*.—(a) *In hexamethylphosphoramide*. A cold (0°)

[12] R. Schmiechen, *Tetrahedron Letters*, 1969, 4995.
[13] G. W. Stacy, F. W. Villaescusa, and T. E. Wollner, *J. Org. Chem.*, 1965, **30**, 4074.

solution of benzo[*b*]thiophen-2(3*H*)-one (15·0 g., 100 mmoles) in hexamethylphosphoramide (50 ml.) was added to a stirred suspension of sodium hydride (2·40 g., 100 mmoles) in hexamethylphosphoramide (50 ml.) at 0° at such a rate that the evolution of hydrogen was not too vigorous, and the resulting mixture was stirred at 0° for a further 30 min. Dimethyl sulphate (12·60 g., 100 mmoles) was then added and the mixture was heated on a steam-bath for 2 hr. 4N-Sodium hydroxide (25 ml.) was added and the mixture was heated for a further 15 min., cooled, and diluted with water. Extraction of the product with ether gave an oil (7·51 g.), b.p. 152—158°/18 mm., which was shown by n.m.r. analysis to contain *ca.* 90 mole % of 2-methoxybenzo[*b*]-thiophen (90% yield). Crystallisation of the distillate from methanol gave 2-methoxybenzo[*b*]thiophen, m.p. 41—42° (lit.,[8] 41—42°), τ (CCl_4) 6·24 (OMe), 3·86 (H-3), 2·80—3·10 (H-5 and H-6), and 2·45—2·75 (H-4 and H-7).

(b) *In methanol.* To a stirred solution of sodium (0·69 g., 0·30 g. atoms) in methanol (15 ml.) at 0° was added a cold (0°) solution of benzo[*b*]thiophen-2(3*H*)-one (4·50 g., 30 mmoles) in methanol (15 ml.), and the resulting mixture was stirred at 0° for a further 5 min. Dimethyl sulphate (3·78 g., 30 mmoles) was added dropwise and the mixture was then heated under reflux for 2 hr. after which its volume was reduced by one half by distillation *in vacuo*. Following dilution of the residue with water, extraction of the product with ether gave an oil (4·69 g.), $\nu_{max.}$ (film) 1700—1730 $cm.^{-1}$ (thiolactone and ester C=O). N.m.r. and g.l.c. (10% polyethylene glycol adipate on Celite at 185° and 10% Apiezon L on Embacel at 170°) analysis of the product showed it to be a mixture of approximately equal amounts of methyl *o*-(methylthio)phenyl acetate (see later) and starting material, together with traces of other compounds.

(c) *In aqueous acetone.* A cold (0°) solution of benzo[*b*]-thiophen-2(3*H*)-one (4·50 g., 30 mmoles) in acetone (15 ml.) was added to a stirred solution of sodium hydroxide (1·20 g., 30 mmoles) in water (15 ml.) at 0° and the resulting mixture was stirred at 0° for 15 min. Dimethyl sulphate (3·78 g., 30 mmoles) was added; the mixture was heated under reflux for 2 hr., then cooled, diluted with water, and worked up as described in (b) to give an oil (4·25 g.), $\nu_{max.}$ (film) 1700 $cm.^{-1}$ (C=O). N.m.r. analysis showed this to be predominantly a mixture of 2-methoxybenzo[*b*]thiophen, τ ($CDCl_3$) 3·87 (H-3) and 6·33 (OMe), and 3-methylbenzo-[*b*]thiophen-2(3*H*)-one, τ ($CDCl_3$) 6·89 (d, *J* 7·5 Hz, Me) and 6·37 (q, CH): a number of other signals could not be assigned with certainty. We were unable to effect a satisfactory separation of this mixture by chromatography.

Reaction of the Product of Alkaline Hydrolysis of Benzo[b]-*thiophen*-2(3H)-*one with Dimethyl Sulphate.*—A solution of benzo[*b*]thiophen-2(3*H*)-one (1·50 g., 10 mmoles) and sodium hydroxide (0·80 g., 20 mmoles) in water (10 ml.) was heated on a steam-bath for 1 hr. Dimethyl sulphate (2·52 g., 20 mmoles) was added and the mixture was heated on the steam-bath for a further 2 hr. It was then cooled and the product was extracted with ether. The extracts were combined, washed successively with dilute aqueous sodium hydrogen carbonate and water, and dried ($MgSO_4$). Distillation gave methyl *o*-(methylthio)phenyl acetate (1·01 g., 51·5%), b.p. 152—153°/12 mm. (lit.,[14] b.p. 99—100°/0·75 mm.), $\nu_{max.}$ (film) 1730 $cm.^{-1}$ (C=O), τ (CCl_4) 7·63 (SMe), 6·38 (CO_2Me), 6·29 (CH_2), and 2·55—3·00 (aromatic) (Found: C, 61·3; H, 6·35. Calc. for $C_{10}H_{12}O_2S$: C, 61·2; H, 6·2%). Addition of 2N-hydrochloric acid to the sodium hydrogen carbonate washings gave *o*-(methylthio)phenyl-acetic acid (0·54 g., 30%), m.p. 127·5—128·5° (from carbon tetrachloride) (lit.,[10,14] m.p. 127° and 127—129°), $\nu_{max.}$ (Nujol) 1710 $cm.^{-1}$ (C=O), τ ($CDCl_3$) 7·55 (SMe), 6·15 (CH_2), and 2·60—2·85 (aromatic) (Found: C, 59·3; H, 5·55. Calc. for $C_9H_{10}O_2S$: C, 59·3; H, 5·5%).

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[14] J. Casanova, N. D. Werner, and H. Kiefer, *J. Amer. Chem. Soc.*, 1967, **89**, 2411.