Condensed Thiophen Ring Systems. Part VII.[1] Stability of 3-Benzo[*b*]-thienyl-lithium [2]

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Ring-cleavage reactions of 3-benzo[*b*]thienyl-lithium (1) and its 2-methyl derivative are reported. When an ethereal solution of compound (1), prepared by treating 3-bromobenzo[*b*]thiophen with n-butyl-lithium at −70 °C, was kept for 1 h at room temperature prior to treatment of the product with dimethyl sulphate, it gave a mixture of benzo[*b*]thiophen, 3-bromo-2-methylbenzo[*b*]thiophen, *o*-(methylthio)phenylacetylene, and methyl-[*o*-(methylthio)phenyl]acetylene. A similar reaction mixture kept for 18 h at room temperature prior to methylation of the product gave a mixture of benzo[*b*]thiophen, the two acetylenes obtained before, and methyl -[*o*-(n-butylthio)-phenyl]acetylene. Methyl-[*o*-(methylthio)phenyl]acetylene was also obtained as the major product when an ethereal solution of 2-methyl-3-benzo[*b*]thienyl-lithium was similarly treated (30 min at room temperature). In contrast, when ethereal solutions of compound (1) were kept at room temperature and the products carboxylated instead of methylated, mixtures of benzo[*b*]thiophen, 3-bromobenzo[*b*]thiophen-2-carboxylic acid, and benzo[*b*]-thiophen-2-carboxylic acid were formed. A mechanism is given to account for these results. An unambiguous synthesis of *o*-(methylthio)phenylacetylene was attempted and a synthesis of methyl 3-bromobenzo[*b*]thiophen-2-carboxylate is reported. In tetrahydrofuran ring cleavage of compound (1) does not occur but the transmetallation reactions that predominate in this solvent, even at −70 °C, give rise to mixtures of products following either methylation or carboxylation.

PREVIOUSLY we have reported the synthesis [3] and several reactions [3-5] of 3-benzo[*b*]thienyl-lithium (1) [equation (1)]. More recently, Gronowitz *et al.*[6] have reported similar results. Because 3-thienyl-lithium is unstable at room temperature [7] and 3-benzo[*b*]furyl-lithium [8] is unstable at −70 °C we decided to study the relative stability of compound (1).

When an ethereal solution of 3-bromobenzo[*b*]thiophen was treated successively with n-butyl-lithium, carbon dioxide, and acid at −70 °C, it gave benzo[*b*]thiophen-3-carboxylic acid (84% yield) and a trace of 3-bromobenzo[*b*]thiophen-2-carboxylic acid (*cf.* ref. 3). Formation of the latter acid can be attributed to the occurrence of reaction (2), and was consequently avoided when the reaction was carried out with reverse addition [Table 1; no. (i)] (accidental hydrolysis during carboxylation presumably accounts for the lower yield of the 3-acid in this case). This mode of addition was used in all the following experiments.

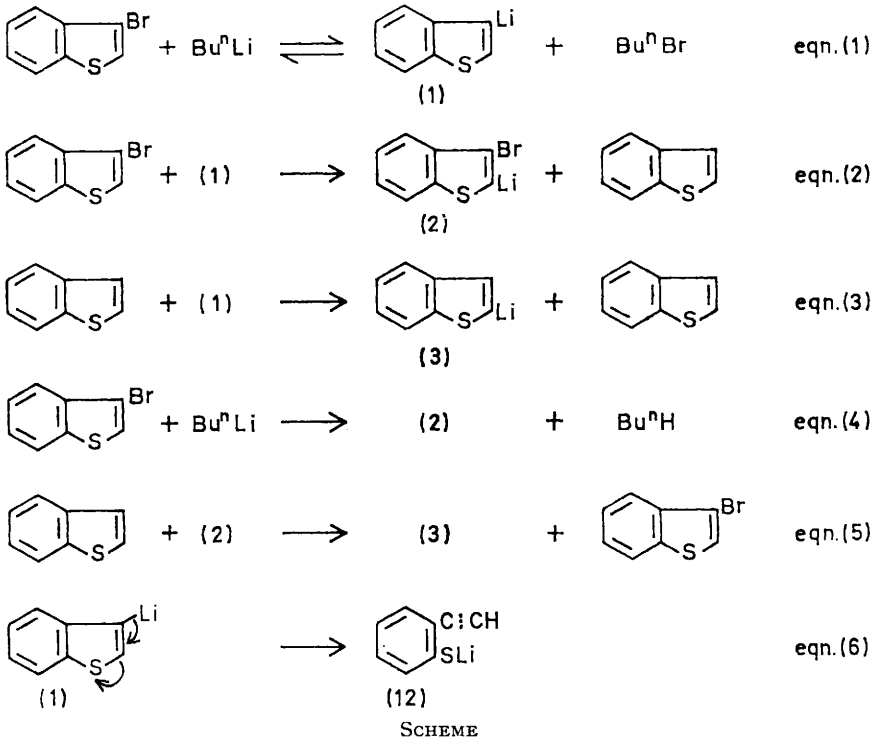
In view of the well known [9] accelerating effect of tetrahydrofuran (THF) in metal–halogen replacement reactions we decided to study the preparation and synthetic uses of compound (1) in this solvent. However, when a solution of 3-bromobenzo[*b*]thiophen in THF was added to a solution of n-butyl-lithium in THF at −70 °C and the resulting mixture was carboxylated, a mixture of 3-bromobenzo[*b*]thiophen-2-carboxylic acid, benzo[*b*]thiophen-2-carboxylic acid, and benzo[*b*]thiophen-3-carboxylic acid was obtained, together with starting material and benzo[*b*]thiophen [Table 1; nos. (iv) and (v)]. Clearly THF is an unsuitable solvent for the preparation of compound (1) as a synthetic intermediate.

The yields of acids given in Table 1 were determined by g.l.c. analysis of the mixtures of esters obtained by quantitative esterification of the acidic fractions of the carboxylation products with diazomethane. Authentic samples of the methyl esters were similarly prepared in quantitative yields from the individual acids. From the acidic fraction of the product of reaction (v) (Table 1) the three acids were separated by fractional crystallisation. The yields of starting material and benzo[*b*]thiophen given in Table 1 were similarly determined by

[1] Part VI, R. P. Dickinson and B. Iddon, *J. Chem. Soc.* (*C*), 1971, 2504.
[2] Preliminary communications, R. P. Dickinson and B. Iddon, Abstracts of the Cork Mechanisms Conferences, Structure and Mechanism in Sulphur Chemistry, Cork, Sept. 29th to Oct. 3rd, 1969, paper L-8; *Internat. J. Sulphur Chem.* (*C*) *Mechanisms*, 1971, **6**, in the press; *Tetrahedron Letters*, 1970, 975.
[3] R. P. Dickinson and B. Iddon, *J. Chem. Soc.* (*C*), 1968, 2733.
[4] B. Iddon, C. K. Thadani, B. Northover, and R. G. Somerville, *Chim. Therap.*, 1970, **5**, 149.
[5] R. P. Dickinson and B. Iddon, *J. Chem. Soc.* (*C*), 1970, 1926.
[6] S. Gronowitz, J. Rehnö, and J. Sandström, *Acta Chem. Scand.*, 1970, **24**, 304.
[7] P. Moses and S. Gronowitz, *Arkiv Kemi*, 1962, **18**, 119.
[8] H. Gilman and S. S. Melstrom, *J. Amer. Chem. Soc.*, 1948, **70**, 1655.
[9] H. J. S. Winkler and H. Winkler, *J. Amer. Chem. Soc.*, 1966, **88**, 964.

g.l.c. analysis of the neutral fractions of the products of the carboxylation reactions.

We have also studied the effect of temperature on the stability of compound (1). When an ethereal solution was prepared at −70 °C and allowed to warm to room temperature prior to carboxylation [Table 1; no. (ii)], it gave only small amounts of the acids; the major product was benzo[*b*]thiophen. A similar result [Table 1; no. (iii)] was obtained when the reaction was carried out entirely at room temperature. There was a difference between the amounts of benzo[*b*]thiophen formed in reactions (ii) and (iii) (Table 1) and in reactions (i), (iv), and (v); the reason for this difference will become apparent later. We concluded at the time, however, that considerable accidental hydrolysis of any lithium compounds present in the reaction mixtures may have occurred and that, consequently, carbon dioxide is unsuitable as a quenching reagent for a quantitative study of these reactions. Previously we believed that the behaviour of compound (1) in ether [3] and in THF paralleled the reported [7] behaviour of 3-thienyl-lithium in ether and that reactions (1)—(3) were predominantly responsible for the formation of the mixtures of acids. We decided therefore to attempt to determine the extent to which these reactions may occur by examining the ratios of the products, and particularly the amounts of benzo[*b*]thiophen formed. This required a method whereby the lithium compounds (1), (2), and (3) could be quantitatively converted into volatile derivatives suitable for analysis by g.l.c. We found that 3-benzo[*b*]thienyl-lithium (1) [Table 2; no. (i)] (*cf.* ref. 3), 2-benzo[*b*]thienyl-lithium (3),[10] and 3-bromo-2-benzo[*b*]thienyl-lithium (2) [11] each react with a *twofold* excess of dimethyl sulphate (methylation) to



SCHEME

TABLE 1

Products of carboxylation reactions

Reaction no.	Solvent	Temp. (°C)	Time (min)	Yields (%) of products [a,b] (A) [c]	(B) [c]	(C) [d]	(D) [d]	(E) [d]
(i)	Ether	−70	30	6	20	71		
(ii)	Ether	−70 } [e] 20 }	30 } [e] 60 }	5	70	1	10	4
(iii)	Ether	20	30	10	67		15	6
(iv)	THF	−70	5	5	6	58	8	12
(v)	THF	−70	30	6	12	37	13	26

[a] Starting material (A) 3-bromobenzo[*b*]thiophen (4·26 g, 10 mmol). [b] Products: (B) benzo[*b*]thiophen; (C) benzo[*b*]thiophen-3-carboxylic acid; (D) 3-bromobenzo[*b*]thiophen-2-carboxylic acid; (E) benzo[*b*]thiophen-2-carboxylic acid. [c] Neutral fractions analysed by g.l.c. on column B at 180 °C (flow rate 25 ml N_2 min^{-1}). [d] Acidic fractions converted into mixtures of methyl esters which were analysed on column A at 190 °C (flow rate 25 ml N_2 min^{-1}). [e] 30 min at −70 °C then 60 min at 20 °C.

[10] D. A. Shirley and J. C. Goan, *J. Organometallic Chem.*, 1964, **2**, 304; D. A. Shirley and M. J. Danzig, *J. Amer. Chem. Soc.*, 1952, **74**, 2935.

[11] W. Ried and H. Bender, *Chem. Ber.*, 1955, **88**, 34; 1956, **89**, 1574.

give a quantitative yield of the corresponding methyl derivative. This reagent was considered therefore to be suitable for quenching and was used to quench a series of reactions (Table 2) carried out under various conditions in both ether and THF. It had the added advantage that it allowed us to analyse the products directly by g.l.c. The assumption that any lithium compounds present in the reaction mixtures prior to quenching react so rapidly with dimethyl sulphate that no interconversion between them occurs is probably justified.[12]

Surprisingly, however, a mixture of benzo[*b*]thiophen, 3-bromo-2-methylbenzo[*b*]thiophen, *o*-(methylthio)-phenylacetylene (4), and methyl-[*o*-(methylthio)phenyl]-acetylene (5) was obtained when an ethereal solution of (1) was prepared at −70 °C, allowed to warm to room temperature during 1 h, and then methylated [Table 2; no. (ii)]. Similar results were obtained when reactions were carried out entirely at room temperature [Table 2; nos. (iii) and (iv)]. After stirring an ethereal solution of (1) at room temperature for 18 h prior to methylation of the product [Table 2; no. (v)], in addition to benzo-[*b*]thiophen and the acetylenes (4) and (5), we also obtained methyl-[*o*-(n-butylthio)phenyl]acetylene (6). In order to confirm that these acetylenes were derived from the lithium compound (1), we prepared an ethereal solution of compound (1) at −70 °C as before, methylated a portion of the mixture at −70 °C, and allowed the remainder to warm to room temperature during 1 h prior to methylation. The former treatment [Table 2; no. (vi*a*)] gave 3-methylbenzo[*b*]thiophen as the only methylated product and no acetylenes could be detected in the product by g.l.c. or i.r. analysis [*cf.* no. (i)] (the benzo[*b*]thiophen present in the product in this case is considered to have arisen by accidental hydrolysis during the removal by pipette of the methylation sample), whilst the latter treatment [Table 2; no. (vi*b*)] gave the same products as reaction (ii) (Table 2) in almost equal amounts.

TABLE 2

Products of methylation reactions

Reaction no.	Solvent	Temp. (°C)	Time (min)	Mole % composition of products [a,b,c] (A)	(B)	(C)	(D)	(E)	(4)	(5)	(6)
(i)	Ether	−70	30	2			98				
(ii)	Ether	−70	30 } [d]		48			9	1	42	
		20	60 }								
(iii)	Ether	20	5	30	33			10	1	26	
(iv)	Ether	20	30	20	30			9	5	36	
(v)	Ether	−70	30 }		54				1	25	20
		20	1080 }								
(vi*a*)	Ether	−70	30 } [e]	15	28		57				
(vi*b*)		20	60 }		48			5	4	43	
(vii)	THF	−70	30		13	14	59	14			

[a] Starting material (A) 3-bromobenzo[*b*]thiophen (2·13 g, 10 mmol), except in reaction (v) where the scale was doubled (20 mmol). [b] Products analysed on column B at 180 °C (flow rate 25 ml N_2 min^{-1}). [c] Products: (B) benzo[*b*]thiophen; (C) 2-methylbenzo[*b*]-thiophen; (D) 3-methylbenzo[*b*]thiophen; (E) 3-bromo-2-methylbenzo[*b*]thiophen. [d] Stirred at −70 °C for 30 min, then at 20 °C for the given time. [e] Approximately half of the reaction mixture was methylated at −70 °C; the remainder was allowed to warm to room temperature and stirred for 60 min before methylation.

The presence of the acetylenes in the products of reactions (ii)—(vi) (Table 2) was first indicated by an i.r. absorption at about 2230 cm^{-1}; the presence of the terminal acetylene (4) in some of the products was also suggested by an absorption at 3290 cm^{-1}. The products of the methylation reactions given in Table 2 were identified by comparison of their g.l.c. retention times on two different columns with those of authentic samples. Benzo[*b*]thiophen and the acetylene (5) were isolated from the product of reaction (v) (Table 2) by column chromatography. We [13] have previously reported an alternative synthesis of compound (6) *via* a ring-cleavage reaction of 2-methyl-3-benzo[*b*]thienyl-lithium. By stirring a similar reaction mixture for 30 min at room temperature prior to methylation we were able to synthesise the acetylene (5). An unambiguous synthesis of the terminal acetylene (4) was also attempted. Thus, reduction of *o*-(methylthio)benzoyl chloride with lithium hydro-tri-t-butoxyaluminate gave *o*-(methylthio)benzaldehyde, which was condensed with malonic acid in the presence of base to give *o*-(methylthio)cinnamic acid (11). An alternative synthesis of compound (11) has been reported [14] since the completion of our work. The ethyl ester of compound (11) was treated successively with bromine and ethanolic potassium hydroxide, to give a small amount of an unidentified compound [not (7)], polymer, and an impure neutral compound (A). Polymer formation and decarboxylation are known side-reactions in the preparation of phenylpropiolic acids by this route.[15] The i.r. and n.m.r. spectra of compound (A) were consistent with those expected for the terminal acetylene (4), but the n.m.r. spectrum indicated the presence of an aromatic impurity. The mass spectrum of compound (A) showed a low intensity peak at *m/e* 148 corresponding to the parent molecular ion of (4) and a base peak at *m/e* 133 corresponding to loss of methyl. Low intensity peaks at higher *m/e* ratios confirmed the presence of a

[12] *E.g.*, N. Gjös and S. Gronowitz, *Arkiv Kemi*, 1969, **30**, 225.
[13] R. P. Dickinson and B. Iddon, *J. Chem. Soc.* (*C*), 1971, 182.
[14] A. Ruwet and M. Renson, *Bull. Soc. chim. belges*, 1970, **79**, 61.
[15] T. L. Jacobs, *Org. Reactions*, 1949, **5**, 1.

higher molecular weight impurity. G.l.c. analysis of compound (A) established the presence of two components, but the major one, which was eluted first, had a retention time corresponding to that of the terminal acetylene shown to be present in trace amounts in the methylation products (Table 2). Despite the fact that several attempts to purify compound (A) have failed, we feel that the evidence presented here confirms that the terminal acetylene present in the methylation products has structure (4).

Although reactions (1)—(3) in the Scheme would account for the products of the carboxylation reactions (Table 1), they do not account for the products of the methylation reactions (Table 2). We conclude therefore that the lithium compound (1) is unstable in ether at temperatures much in excess of −70 °C and undergoes a ring-cleavage reaction (6) (Scheme) leading directly to the formation of the acetylene (12), which is metallated by compound (1) to give the acetylene (8) and benzo[*b*]thiophen (this accounts for some of the benzo[*b*]thiophen present in the methylation products—see later). Following methylation, the lithium compounds (8) and (12) give the acetylenes (5) and (4), respectively. The acetylene (6) presumably arises by alkylation of compound (8) at the sulphur atom by the n-butyl bromide liberated by reaction (1) (*cf.* refs. 16 and 17) prior to methylation. The small amount of 3-bromo-2-methylbenzo[*b*]thiophen which is also formed is considered to arise from the lithium compound (2) formed by reaction (2) (this reaction accounts for the remainder of the benzo[*b*]thiophen formed in the methylation reactions).

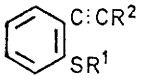
The fact that the amount of benzo[*b*]thiophen formed after methylation is always approximately equal to the amounts of compound (5) and 3-bromo-2-methylbenzo[*b*]thiophen [or of compounds (5) and (6) and 3-bromo-2-methylbenzo[*b*]thiophen] formed suggests that, after the initial metal–halogen replacement reaction (1), reactions (2) and (6) occur concurrently, with the latter predominating, and are followed by metallation of the acetylene (12) to give the dilithio-compound (8). Direct metallation of 3-bromobenzo[*b*]thiophen by the n-butyllithium to give compound (2) [equation (4)] (*cf.* ref. 7) cannot occur to any significant extent, otherwise the product ratios given in Table 2 would be different. The possibility that reaction (3) occurs is excluded by the fact that no 2-methylbenzo[*b*]thiophen is formed. The absence of 2-methylbenzo[*b*]thiophen in the products also excludes reaction (5). This reaction is unlikely to occur in any case because 3-bromo-2-benzo[*b*]thienyllithium is more stable than 2-benzo[*b*]thienyl-lithium. Gilman and Melstrom [8] have suggested, however, that a reaction analogous to (5) accounts for the formation of benzo[*b*]furan-2-carboxylic acid following the successive treatment of 3-bromobenzo[*b*]furan with n-butyl-lithium, carbon dioxide, and acid. However, when compound (2) was treated successively with benzo[*b*]thiophen, carbon dioxide, and acid in ether [11] at room temperature, or in THF at −70 °C, it gave 3-bromobenzo[*b*]thiophen-2-carboxylic acid as the only acidic product (by g.l.c. analysis of the esterified product).

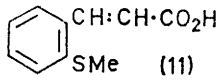
Ring-cleavage reactions analogous to (6) (Scheme) had been reported prior to our work for 3,4-dilithio-2,5-diphenylthiophen,[18–20] 3-benzo[*b*]furyl-lithium,[8] the pyranyl-lithium compound (13),[21] and 3-benzo[*b*]furylmagnesium bromide [22] and its 2-phenyl derivative.[23] Since our work was completed [2] ring-cleavage reactions have been reported for 2,4-dibromo-3-thieno[2,3-*b*]-thienyl-lithium,[24] 2,5-dimethylselenophen-3-yl-lithium,[16,25] the oxazoline derivative (14),[26] and several other five-membered heteroaromatic compounds with more than one hetero-atom in the ring undergoing cleavage.[17] Previously we [2] suggested that the unidentified 'unsaturated aliphatic products' which Moses and Gronowitz [7] isolated when an ethereal solution of 3-thienyl-lithium was kept at room temperature for 24 h were acetylenes formed by a ring-cleavage reaction analogous to (6) (Scheme). Recently Gronowitz and Frejd [25] and Jakobsen [27] have reported that 2,5-dimethyl-3-thienyl-lithium and 2-methyl-3-thienyl-lithium respectively, undergo ring-cleavage reactions to give acetylenes.

Several ring-cleavage reactions alternative to (6) (Scheme) have also been considered by us and discounted because none of them adequately accounts for all the experimental facts. Direct nucleophilic attack of n-butyl-lithium at the sulphur atom of 3-bromobenzo[*b*]thiophen with expulsion of bromide ion (15) (*cf.* ref. 17) and the alternative reaction (16) involving attack by the lone-pair electrons of the ring sulphur atom of compound (1) on the n-butyl bromide generated by reaction (1) are unlikely to occur because the acetylene (6) is formed only after long reaction times (Table 2). These mechanisms would require its immediate formation. In addition, we have established that reaction (1) occurs to completion before ring cleavage. The former mechanism (15) would require this reaction to be completely reversed, since 3-methylbenzo[*b*]thiophen is not formed in the methylation reactions following ring cleavage. Jakobsen [27] has suggested that 2-methyl-3-thienyl-lithium undergoes a ring-cleavage reaction analogous to (16). The alternative mechanism (17) (*cf.* ref. 16) is also unlikely to occur because any scheme incorporating this process does not account for

[16] S. Gronowitz and T. Frejd, *Acta Chem. Scand.*, 1969, **23**, 2540.
[17] R. G. Micetich, *Canad. J. Chem.*, 1970, **48**, 2006, and references cited therein.
[18] G. Wittig and M. Rings, *Annalen*, 1968, **719**, 127.
[19] M. Rings, Dissertation, University of Heidelberg, 1966.
[20] R. W. Hoffmann, 'Dehydrobenzene and Cycloalkynes,' Academic Press, New York, 1967, pp. 290—291.
[21] R. Paul and S. Tchelitcheff, *Bull. Soc. chim. France*, 1952, 808.
[22] T. Reichstein and J. Baud, *Helv. Chim. Acta*, 1937, **20**, 892.
[23] A. S. Angeloni and M. Tramontini, *Boll. sci. Fac. Chim. ind. Bologna*, 1963, **21**, 243.
[24] A. Bugge, *Acta Chem. Scand.*, 1969, **23**, 2704.
[25] S. Gronowitz and T. Frejd, *Acta Chem. Scand.* 1970, **24**, 2656.
[26] A. I. Meyers and E. W. Collington, *J. Amer. Chem. Soc.*, 1970, **92**, 6677.
[27] H. J. Jakobsen, *Acta Chem. Scand.*, 1970, **24**, 2663.

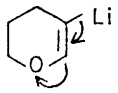
all the observed products, particularly the large amounts of benzo[*b*]thiophen formed. This process too would require reaction (1) to be completely reversed. The absence of 3-methylbenzo[*b*]thiophen in the methylation products (Table 2) also excludes a dimethyl sulphate-





(11)

(4) $R^1 = Me$, $R^2 = H$
(5) $R^1 = R^2 = Me$
(6) $R^1 = Bu^n$, $R^2 = Me$
(7) $R^1 = Me$, $R^2 = CO_2H$
(8) $R^1 = R^2 = Li$
(9) $R^1 = H$, $R^2 = CO_2H$
(10) $R^1 = R^2 = H$



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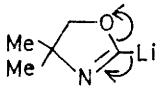

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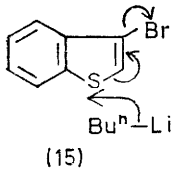

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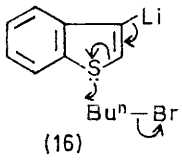
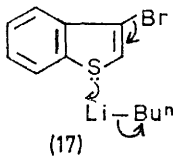
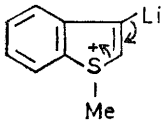


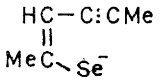
(16)



(17)



(18)

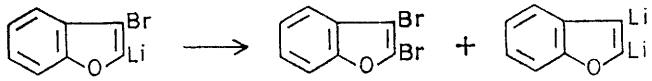


(19)

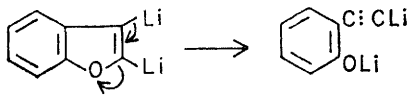
promoted ring-cleavage reaction (18) (*cf.* ref. 28). 3-Bromo-2-benzo[*b*]furyl-lithium is reported to disproportionate at 90 °C to give 2,3-dibromobenzo[*b*]furan and 2,3-dilithiobenzo[*b*]furan [equation (7)].[20,29] The latter is unstable under these conditions and undergoes a ring-cleavage reaction [equation (8)]. However, 2,3-dilithiobenzo[*b*]thiophen is stable at room temperature [11] and we could not detect any 2,3-dibromobenzo[*b*]thiophen in our products [*cf.* equation (7)]. Nevertheless, we prepared an ethereal solution of compound (2), kept it overnight at room temperature, and then methylated the product. G.l.c. analysis showed that this gave only 3-bromo-2-methylbenzo[*b*]thiophen. The stability of compound (2) under our reaction conditions also excludes 2,3-dehydrobenzo[*b*]thiophen (*cf.* ref. 18) as an intermediate. The possibility that 2-benzo[*b*]thienyl-lithium (3) is formed by reaction (3) and undergoes a ring-cleavage reaction seems unlikely because 2-methylbenzo[*b*]thiophen was not present in our methylation products (Table 2). However, an ethereal solution of compound (3) was kept at room temperature overnight and the product was methylated. This gave only 2-methylbenzo[*b*]thiophen. It is noteworthy that Gilman and Melstrom [8] detected *o*-hydroxyphenylacetylene in the product arising from successive treatment of 2-bromobenzo[*b*]furan with n-butyl-lithium and acid.

In order to establish conclusively that the products which arise following carboxylation (Table 1) and methylation (Table 2) arise from the same intermediate, namely (1), we treated an ethereal solution of 3-bromobenzo[*b*]thiophen with n-butyl-lithium at room temperature, stirred the mixture at this temperature for 30 min, then carboxylated a portion of the product and methylated the remainder. The product of the carboxylation reaction was identical with that of reaction (ii) (Table 1) whilst the product of the methylation reaction was identical to that of reaction (ii) (Table 2).

Following carboxylation of the ring-cleavage products we believe that the lithium compounds (8) and (12) give *o*-mercaptophenylpropiolic acid (9) and *o*-mercaptophenylacetylene (10), respectively. Compounds (9) and (10) then cyclise to give benzo[*b*]thiophen-2-carboxylic acid and benzo[*b*]thiophen. We suggest that the phenylpropiolic acid (9) also undergoes decarboxylation to give compound (10), which cyclises to give a further quantity of benzo[*b*]thiophen. The formation of benzo[*b*]thiophen in this way together with its formation as a product of reaction (2) (Scheme) and from the metallation of compound (12) to give the dilithio-derivative (8) accounts for the considerable amounts (up to 70% yield) of it present in the carboxylation products (Table 1). These conclusions also explain why benzo[*b*]thiophen-2-carboxylic acid is formed following carboxylation of the ring-cleavage products whereas no 2-methylbenzo[*b*]thiophen is formed following their methylation. Acetylenes were not detected in the products of the carboxylation reactions.



eqn. (7)



eqn. (8)

Conclusive evidence that compound (10) cyclises to benzo[*b*]thiophen was obtained when we prepared an ethereal solution of compound (1) at room temperature, stirred it at this temperature for 30 min, and then methylated a portion of the product and hydrolysed the remainder with acid. Methylation gave a product identical to that of reaction (ii) (Table 2), whereas hydrolysis gave only starting material and

[28] W. E. Parham and P. L. Stright, *J. Amer. Chem. Soc.*, 1956, **78**, 4783.
[29] G. Kolb, Dissertation, University of Heidelberg, 1959.

benzo[*b*]thiophen. In the i.r. spectrum of the product of the hydrolysis reaction there was a weak absorption at 3290 cm^{-1} which may be due to traces of a disulphide (see later).

Gronowitz and Frejd [25] obtained an equimolar mixture of iodobenzene and 2,5-dimethylselenophen by successively treating an ethereal solution of 3-iodo-2,5-dimethylselenophen with phenyl-lithium, carbon dioxide, and acid at room temperature. Ring-opening of 2,5-dimethylselenophen-3-yl-lithium to give the selenolate ion (19) followed by ring closure of (19) by a type of Michael addition was proposed to explain this result. Earlier they [16] had obtained evidence for the formation of (19) by adding copper(II) chloride to a reaction mixture obtained from ethereal 3-iodo-2,5-dimethylselenophen and ethyl-lithium. This gave the corresponding diselenide. We believe that a radical mechanism is not excluded for the ring-closure reactions reported by us and those discovered independently by Gronowitz *et al.*[16,25] Thiophenols undergo exothermic radical additions with phenylacetylene,[30] and the cyclisations of *o*-mercaptophenylacetylenes reported in this paper may occur by a similar though intramolecular mechanism. If this is the case, traces of disulphides should also be formed. However, we have been able to detect a compound which may be a disulphide in only one reaction (see preceding paragraph). Selenols readily form radicals. Thus, a radical ring-closure mechanism would account for the apparent ease of cyclisation of the selenolate ion (19), the relative ease of cyclisation of thiolate ions reported in this paper, and the reported [8,22,23] failures of *o*-hydroxyphenylacetylenes to cyclise under similar conditions. Indoles, benzo[*b*]thiophens, and benzo[*b*]furans [5,6] have been synthesised recently *via* the *in situ* formation of *o*-amino-, *o*-mercapto-, and *o*-hydroxy-phenylacetylenes in the presence of copper salts.[31–33] However, these reactions proceed *via* an intermediate copper complex.[31]

When a solution of compound (1) in THF was treated with dimethyl sulphate at −70 °C [Table 2; no. (vii)], it gave a mixture of benzo[*b*]thiophen, 2- and 3-methylbenzo[*b*]thiophen, and 3-bromo-2-methylbenzo[*b*]thiophen; acetylenes could not be detected in the product. Thus, the product of reaction (vii) (Table 2) is comparable to the products of the carboxylation reactions (iv) and (v) (Table 1). We believe therefore that the greater solvating power of THF allows the transmetallation reactions (2) and (3) (Scheme) to occur in preference to the ring-cleavage reaction (6). Support for this suggestion is provided by the fact that, after carboxylation of the product, less benzo[*b*]thiophen-3-carboxylic acid and correspondingly more benzo[*b*]thiophen, benzo[*b*]thiophen-2-carboxylic acid, and 3-bromobenzo[*b*]thiophen-2-carboxylic acid are formed with increasing time of reaction [Table 1; nos. (iv) and (v)]. The benzo[*b*]thiophen formed in these reactions arises from reactions (2) and (3). Thus, the amount of benzo[*b*]thiophen formed after carboxylation is approximately equal to the amount of the 2-acid formed [Table 1; nos. (iv) and (v)] and, after methylation, to the amount of the 2-methyl derivative formed [Table 2; no. (vii)].

2-Methyl-,[13] 2-methylthio-,[13] and 2-phenyl-3-benzo[*b*]thienyl-lithium [34] and their derivatives also undergo ring-cleavage reactions and provide useful starting materials for the synthesis of substituted phenylacetylenes.

EXPERIMENTAL

I.r. spectra were recorded with a Perkin-Elmer 257 spectrometer, mass spectra with an A.E.I. MS12 instrument, and n.m.r. spectra with a Varian A60 spectrometer (tetramethylsilane as internal standard). G.l.c. analysis was carried out with a Pye 104 Chromatograph fitted with a flame-ionisation detector and 5 ft. × 5·0 mm columns of either 10% polyethylene glycol adipate on Celite (column A) or 10% Apiezon L on Embacel (column B). In quantitative g.l.c. work the percentage compositions of the mixtures (Tables 1 and 2) were calculated from the corrected peak areas measured gravimetrically. The peak areas could not be corrected for the terminal acetylene (4) because a pure reference sample was not available.

Dimethyl sulphate was freshly distilled. The other experimental precautions which were taken have been reported previously.[3,34]

3-Bromo-2-methylbenzo[*b*]thiophen (100%), m.p. 40—42° (lit.,[35] 42—42·5°) was prepared by treating 3-bromo-2-benzo[*b*]thienyl-lithium [11] with 2 equiv. of dimethyl sulphate, and 2-[36] and 3-methylbenzo[*b*]thiophen [3] were similarly prepared (100% yields) by literature procedures.

Methyl 3-Bromobenzo[b]*thiophen-2-carboxylate*.—An excess of ethereal diazomethane was added to a solution of 3-bromobenzo[*b*]thiophen-2-carboxylic acid [11] (1·0 g) in ether (250 ml) at 0 °C and the mixture was kept overnight at room temperature. It was then washed successively with dilute aqueous sodium hydrogen carbonate and water, and dried ($MgSO_4$). Distillation gave the *product* (100%), m.p. 70—71·5° [from light petroleum (b.p. 40—60°)] (Found: C, 44·6; H, 2·7. $C_{10}H_7BrO_2S$ requires C, 44·3; H, 2·6%).

The following compounds were similarly prepared: methyl benzo[*b*]thiophen-2-carboxylate (100%), b.p. 186—188° at 20 mmHg, m.p. 70—73° [from light petroleum (b.p. 40—60°)] (lit.,[37] b.p. 171° at 14 mmHg, m.p. 72—73°); and methyl benzo[*b*]thiophen-3-carboxylate (100%), b.p. 181—183° at 20 mmHg (lit.,[38] 165—166° at 17 mmHg).

[30] E. P. Kohler and H. Potter, *J. Amer. Chem. Soc.*, 1935, **57**, 1316; L. I. Smith and H. R. Davis, *J. Org. Chem.*, 1950, **15**, 824; W. E. Truce, H. G. Klein, and R. B. Kruse, *J. Amer. Chem. Soc.*, 1961, **83**, 4636.
[31] C. E. Castro, R. Havlin, V. K. Honwad, A. Malte, and S. Mojé, *J. Amer. Chem. Soc.*, 1969, **91**, 6464.
[32] A. M. Malte and C. E. Castro, *J. Amer. Chem. Soc.*, 1967, **89**, 6770.
[33] C. E. Castro, E. J. Gaughan, and D. C. Owsley, *J. Org. Chem.*, 1966, **31**, 4071.
[34] R. P. Dickinson and B. Iddon, *J. Chem. Soc.* (*C*), 1970, 2592.
[35] D. A. Shirley, M. J. Danzig, and F. C. Canter, *J. Amer. Chem. Soc.*, 1953, **75**, 3278.
[36] E. N. Karaulova, D. Sh. Meĭlanova, and D. G. Gal'pern, *Doklady Akad. Nauk S.S.S.R.*, 1958, **123**, 99 (*Chem. Abs.*, 1959, **53**, 5229).
[37] R. Weissgerber and O. Kruber, *Ber.*, 1920, **53***B*, 1551.
[38] G. Komppa and S. Weckman, *J. prakt. Chem.*, 1933, **138**, 109.

Methyl-[o-(*methylthio*)*phenyl*]*acetylene*.—(*a*) A solution of 3-bromo-2-methylbenzo[*b*]thiophen (4·54 g, 20 mmol) in ether (10 ml) was added during 5 min to a stirred solution of n-butyl-lithium (20 mmol) in ether (50 ml) at −70 °C, and the mixture was stirred at −70 °C for 30 min. The cooling bath was removed and the mixture was allowed to to warm to room temperature during 30 min. Dimethyl sulphate (5·04 g, 40 mmol) was added dropwise during 5 min, and the mixture was stirred at room temperature for 30 min. An excess of ethanolic sodium ethoxide was added and the mixture was stirred for a further 30 min. It was then poured into water; separation of the ethereal layer and evaporation of the solvent gave an oil (3·35 g), which was shown by g.l.c. analysis (column B at 170 °C) to be a mixture of 3-bromo-2-methylbenzo[*b*]thiophen (5 mole %), 2-methylbenzo[*b*]thiophen (12 mole %), and *methyl*-[o-(*methylthio*)*phenyl*]*acetylene* (83 mole %). The product was chromatographed on silica; light petroleum (b.p. 40—60°) eluted starting material and 2-methylbenzo-[*b*]thiophen, and carbon tetrachloride eluted the acetylene, b.p. 159—160° at 28 mmHg, $\nu_{max.}$ (film) 2205, 2230, and 2255 cm^{-1} (C⋮C); τ (CCl_4) 7·90 (Me), 7·62 (SMe), and 2·60—3·20 (m, aromatic) (Found: C, 74·1; H, 5·9%; *M* 162. $C_{10}H_{10}S$ requires C, 74·0; H, 6·2%; *M* 162).

(*b*) The product of reaction (5) (Table 2) was chromatographed on silica; light petroleum (b.p. 40—60°) eluted benzo[*b*]thiophen and carbon tetrachloride eluted a mixture of the three acetylenes followed by pure methyl-[*o*-(methylthio)phenyl]acetylene, identical with the sample prepared as described in (*a*).

o-(*Methylthio*)*benzaldehyde*.—A solution of lithium hydrotri-t-butoxyaluminate (10·24 g, 40 mmol) in bis-(2-methoxyethyl) ether (40 ml) was added during 1 h to a stirred suspension of *o*-(methylthio)benzoyl chloride [39] (7·46 g, 40 mmol) in the same solvent (40 ml) at −70 °C, and the resulting mixture was stirred at −70 °C for a further 15 min. The cooling bath was removed and the mixture was allowed to warm to room temperature during 1 h. An excess of 2N-hydrochloric acid was added, the product was extracted with ether, and the combined extracts were washed successively with 2N-sodium hydroxide and water, and dried ($MgSO_4$). Distillation gave *o*-(methylthio)-benzaldehyde (1·48 g, 24%), b.p. 109—110° at 1 mmHg (lit.,[40] 89—91° at 0·4 mmHg), $\nu_{max.}$ (film) 1680 cm^{-1} (C=O). A viscous residue remained in the distillation flask. On treatment with 4N-hydrochloric acid the sodium hydroxide washings gave *o*-(methylthio)benzoic acid (2·50 g, 37%), m.p. 166—168° (from benzene) (lit.,[40] 169—171°).

o-(*Methylthio*)*cinnamic Acid*.—A mixture of *o*-(methylthio)benzaldehyde (3·80 g, 25 mmol), malonic acid (5·20 g, 50 mmol), anhydrous pyridine (12·5 ml), and piperidine (10 drops) was heated on a steam-bath for 2 h. The resulting solution was cooled and poured on a mixture of crushed ice and concentrated hydrochloric acid. The precipitate was filtered off, washed with water, and dried. The product (3·49 g, 72%) had m.p. 180—181° (from benzene) (lit.,[14] 179°), $\nu_{max.}$ (Nujol) 1665 cm^{-1} (C=O) (Found: C, 61·8; H, 5·1; S, 16·2. Calc. for $C_{10}H_{10}O_2S$: C, 61·8; H, 5·2; S, 16·5%).

Ethyl o-(*Methylthio*)*cinnamate*.—A suspension of the acid (3·40 g) in ethanol (34 ml) was saturated with dry hydrogen chloride and the resulting mixture was heated under reflux for 18 h. It was then cooled and poured into water. Extraction with ether gave the *ester* (3·35 g, 86%), m.p. 59—61° [from light petroleum (b.p. 40—60°)], $\nu_{max.}$ (Nujol) 1710 cm^{-1} (C=O) (Found: C, 64·7; H, 6·6. $C_{12}H_{14}O_2S$ requires C, 64·8; H, 6·35%).

Ethyl 1,2-*Dibromo*-2-(o-*methylthiophenyl*)*propionate*.—A solution of bromine (2·0 g, 12·5 mmol) in carbon tetrachloride (2·5 ml) was added during 15 min to a stirred solution of ethyl *o*-(methylthio)cinnamate (2·77 g, 12·5 mmol) in carbon tetrachloride (12·5 ml) at 0 °C, and the resulting mixture was stirred at 0 °C for a further 1 h. It was then decanted from a small amount of tar, and evaporation of the solvent gave the *product* (2·80 g, 59%), m.p. 90—91° [from light petroleum (b.p. 40—60°)], $\nu_{max.}$ (Nujol) 1725 cm^{-1} (C=O) (Found: C, 37·8; H, 3·7. $C_{12}H_{14}Br_2O_2S$ requires C, 37·7; H, 3·7%).

Methyl-[o-(*methylthio*)*phenyl*]*acetylene*.—A mixture of ethyl 1,2-dibromo-2-(*o*-methylthiophenyl)propionate (2·29 g, 6 mmol), potassium hydroxide (1·52 g, 27 mmol), and ethanol (7·2 ml) was heated under reflux for 4 h. The resulting mixture was cooled and filtered, and the filtrate was neutralised with 2N-hydrochloric acid to give a precipitate. This was filtered off, combined with the residue from the filtration, and dissolved in water. The second filtrate was evaporated, the residue was shaken with ether, and the ethereal extract (see later) was extracted with 2N-sodium hydroxide. The combined alkaline extracts and aqueous solution was cooled in ice and acidified by the dropwise addition of concentrated hydrochloric acid. The precipitate was filtered off, washed with water, dried (P_2O_5), and extracted several times with boiling carbon tetrachloride. A large amount of insoluble polymeric material remained after repeated extraction. The combined carbon tetrachloride extracts were evaporated until crystallisation commenced, and the crystals (0·13 g) were filtered off and dried, m.p. 125—127° (decomp.), $\nu_{max.}$ ($CHCl_3$) 1680 cm^{-1} (C=O).

The ethereal extract was washed with water, dried ($MgSO_4$), and evaporated to leave an oil (0·31 g), b.p. 130° at 24 mmHg (Kugelrohr apparatus), $\nu_{max.}$ (film) 3290 cm^{-1} (⋮CH), τ (CCl_4) 7·65 (assigned to SMe) and 6·65 (assigned to ⋮CH) (ratio 3 : 1), and 2·10—3·10 (m, aromatic). The mass spectrum of the oil showed peaks at *m/e* 148 and 133, but several low intensity peaks were also present at higher *m/e* ratios (see Discussion section). G.l.c. analysis (columns A and B at 180 °C) of the oil showed the presence of two components: the major component (eluted first) had retention times corresponding to those of the terminal acetylene (4).

Reactions of 3-*Benzo*[b]*thienyl-lithium*.—(a) *In ether*. (i) Solutions of 3-bromobenzo[*b*]thiophen (4·26 g, 20 mmol) [some reactions (see Tables 1 and 2) were carried out on half this scale] in ether (5 ml) were added during 5 min to stirred solutions of n-butyl-lithium (20 mmol) in ether (50 ml). The conditions for each reaction are given in Tables 1 and 2. The resulting mixtures were then either methylated or carboxylated by the procedures reported previously.[3]

In the methylation reactions a twofold excess of dimethyl sulphate (5·04 g, 40 mmol) was used and the products (Table 2) were identified by comparison of their g.l.c. retention times on columns A (at 150 °C) and B (at

[39] B. Eistert, W. Schade, and H. Selzer, *Chem. Ber.*, 1964, **97**, 1470.

[40] R. J. Crawford and C. Woo, *Canad. J. Chem.*, 1965, **43**, 3178.

185 °C) with those of authentic samples. Methyl-[*o*-(methylthio)phenyl]acetylene was isolated from the product of reaction (v) (Table 2) as described before.

Following carboxylation of the products, an excess of 2N-hydrochloric acid was added to the mixture, the ethereal layer was separated, and the aqueous layer was extracted with ether. Extraction of the combined ethereal layer and extracts with 2N-sodium hydroxide and acidification of the combined alkaline extracts with concentrated hydrochloric acid gave the acidic fraction. This was quantitatively esterified with diazomethane as described before and the product was analysed (see Table 1) by g.l.c. on column A at 190 °C. The ethereal layer was dried ($MgSO_4$); evaporation of the solvent gave the neutral fraction which was analysed (see Table 1) by g.l.c. on columns A (at 150 °C) and B (at 185 °C).

(ii) Reaction (iv) (Table 2) was repeated but, before the product was methylated, a portion (about half) of the reaction mixture was removed (by pipette) and treated with carbon dioxide as described previously.[3] Esterification and analysis of the product as described before showed that it was of a similar composition to the product of reaction (ii) (Table 1). Methylation of the remainder of the product and work-up in the usual manner gave a product of similar composition to the products of reactions (ii) and (iv) (Table 2).

(iii) Reaction (iv) (Table 2) was repeated but only a portion (about half) of the resulting mixture was methylated. This gave similar products. The remainder of the mixture was treated with an excess of 2N-hydrochloric acid and worked up in the usual manner to give a mixture (analysed by g.l.c. on column B at 185 °C) of 3-bromobenzo[*b*]thiophen (starting material) (22 mole %) and benzo[*b*]thiophen (78 mole %). The i.r. spectrum of the product showed a weak intensity absorption at 3330 cm^{-1} (see Discussion section).

(b) *In THF.* The reactions in this solvent were carried out exactly as described in (a) and the products (Tables 1 and 2) were similarly analysed.

The acidic product (3·25 g) of reaction (v) (Table 1) had m.p. 180—225°. The crude product was extracted several times with hot benzene and the residue was recrystallised three times from ethanol to give 3-bromobenzo[*b*]thiophen-2-carboxylic acid, m.p. 277—278° (lit.,[11] 274—275°). Light petroleum (b.p. 60—80°) was added to the hot benzene extract until crystallisation commenced and the solution was then cooled. The precipitate was filtered off and recrystallised twice from benzene; it was identical with an authentic sample of benzo[*b*]thiophen-2-carboxylic acid, m.p. 236—237° (lit.,[41] 237°). Evaporation of the filtrate and recrystallisation of the residue twice from benzene gave benzo[*b*]thiophen-3-carboxylic acid, m.p. 173—176° (lit.,[3] 173—175°).

Stability of 3-Bromo-2-benzo[b]*thienyl-lithium.*—(*a*) A solution of benzo[*b*]thiophen (1·34 g, 10 mmol) in ether (5 ml) was added to a stirred suspension of 3-bromo-2-benzo[*b*]thienyl-lithium [11] (10 mmol) in ether (50 ml) at room temperature, and the resulting mixture was stirred at room temperature for 30 min. It was then poured on a mixture of crushed solid carbon dioxide and ether. The usual work-up procedure gave only 3-bromobenzo[*b*]thiophen-2-carboxylic acid (1·64 g, 92%), m.p. 271—273° (from ethanol). Prior to recrystallisation of the crude acid a portion of it was esterified with diazomethane and analysed as described before. This showed the absence of benzo[*b*]thiophen-2-carboxylic acid in the product.

(*b*) A similar ' reaction ' to the one described in (*a*) was carried out in THF at −70 °C with a similar result.

(*c*) A suspension of the lithium compound (10 mmol) in ether (30 ml) was stirred for 18 h at room temperature and the resulting mixture was treated with dimethyl sulphate (2·52 g, 20 mmol). Work-up in the usual manner gave a product (2·20 g), m.p. 39—41°, which was shown by i.r. and g.l.c. (column A at 180 °C) analysis to be 3-bromo-2-methylbenzo[*b*]thiophen containing a trace of 2,3-dibromobenzo[*b*]thiophen (starting material).

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