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SYNTHESIS OF DERIVATIVES OF CYCLOBUTENO[*c*]THIOPHEN AND ATTEMPTS TO SYNTHESISE THIOPHEN ANALOGUES OF BIPHENYLENE

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Abstract—Starting from 2,5-dichlorothiophen many new 3,4-disubstituted thiophens have been made including the dialdehyde. Treatment of this with phosphorus pentabromide could be made to give 2,5-dichloro-3-dibromomethylthiophen-4-aldehyde, 2,5-dichloro- or 2-bromo-5-chloro-3,4-bisdibromomethylthiophen. the latter two compounds reacted with sodium iodide to give the corresponding *cis*- and *trans*-3,4-dibromo cyclobuteno[*c*]thiophen derivatives (**18-21**). Reaction of *trans*-3,4-dibromo-2,5-dichlorocyclobuteno[*c*]thiophen with N-bromosuccinimide resulted in fission of the 4-membered ring regenerating 2,5-dichloro-3,4-bisdibromomethylthiophen.

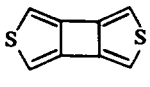
When 2,5-dichloro-3,4-di-iodothiophen was treated with butyl-lithium followed by dimethylsulphate it gave 2,5-dichloro-3,4-dimethylthiophen together with a low yield of a red compound which is considered to be a dichloro dimethyl derivative (**11**) of bisthiophenindigo.

Several unsuccessful approaches to the synthesis of dithiophen analogues of biphenylene are outlined. These included heating various 3,4-di-iodothiophens and 4,4'-di-iodo-3,3'-bithienyls with copper as well as the flash vacuum pyrolysis of the latter compounds, of thiophen-3,4-dicarboxylic anhydrides and of 2,5-dichloro-3-iodothiophen-4-carboxylic acid.

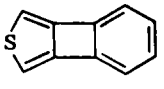
There are four possible isomers for a dithia-analogue of biphenylene in which each benzene ring has been replaced by a thiophen ring. The most stable isomer will almost certainly be the one represented by structure **1** since this has the least cyclobutadienoid character in the 4-membered ring. During the last few years we have attempted to synthesise this compound by methods described below. Wynberg *et al.* have also worked in this field, so far without success.[1] More recently the synthesis of 2-thianorbiphenylene (**2**) by Garratt and Vollhardt[2] by the reaction of benzocyclobutenedione with a sulphur-containing Wittig reagent prompted us to attempt the synthesis of the appropriate thiophen analogue (**3**) of benzocyclobutenedione in the hope of using this for the synthesis of compound **1** and other heterocyclic analogues of biphenylene.

Synthesis of cyclobuteno[c]thiophens. At the outset of this part of our work the only known cyclobutenothiophen was compound **2**. Our first aim, therefore, was to construct a 4-membered ring attached to positions 3 and 4 of a thiophen nucleus (see preliminary report[3]). Our second aim (not yet achieved) was to convert our bicyclic intermediates into the dione (**3**) or a derivative thereof. Since the 2 and 5 positions of thiophen are more reactive towards electrophilic substitution than those at 3 and 4 it was necessary to block the α-positions by starting with 2,5-dichlorothiophen (**4**). Treatment of the latter with iodine and periodic acid gave the diiodothiophen (**5**; 75%) which reacted with *n*-butyl-lithium to give the important intermediate (**6**) in high yield. The dilithio compound was also formed (*ca.* 10%) by reaction of 2,5-dichlorothiophen with butyl-lithium but it was not formed by reaction of the di-iodo compound (**5**) with lithium. Carboxylation of **6** gave the dicarboxylic acid (**7**; 65%) which was reduced with lithium aluminium hydride to the dialcohol (**8**) and then converted into the dibromide (**9**) using hydrobromic acid. In an alternative route to the dibromide (**9**) the dilithio compound (**6**) was treated with dimethyl sulphate thereby giving 2,5-dichloro-4,5-dimethylthiophen (**10**; 45%) together with a red compound (0·17%) which is considered to be a substituted bisthiophenindigo (**11**) (see below). The action of bromine on the dimethyl compound (**10**) gave the dibromide (**9**; 31%) but attempts to make this compound by bromomethylation[4] of 2,5-dichlorothiophen using HBr/HCHO or $BrCH_2OCH_2Br/ZnCl_2$ were unsuccessful. The dibromide (**9**) did not react with N-bromosuccinimide but it did react with bromine (catalysed by UV light) to give the tetrabromide (**12**; 20%). Since the overall yield of tetrabromide (**12**) from the di-iodide (**5**) was very low [6% via compound **8** and 3% via compound **10**] a third route was explored.

The dilithio derivative (**6**), on treatment with N,N-dimethylformamide, gave the dialdehyde (**13**; 25%). Reaction of the latter with phosphorus pentachloride gave the hexachloro compound (**14**) but with phosphorus pentabromide the reaction was more complex. At 40°, 60° and 80° the main products were, respectively, the mono-aldehyde (**15**; 82%), the tetrabromide (**12**; 34%), and



1



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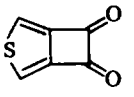

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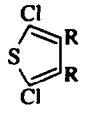
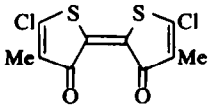


4: R = H
5: R = I
6: R = Li
7: R = CO_2H
8: R = CH_2OH
9: R = CH_2Br
10: R = Me
12: R = $CHBr_2$
13: R = CHO
14: R = $CHCl_2$
29: R = CN



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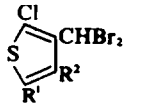
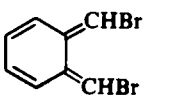


15: R^1 = Cl, R^2 = CHO
16: R^1 = Br, R^2 = $CHBr_2$

the pentabromide (16; 53%). Thus the reaction at 60° completes the best route (8·5% overall) to the tetrabromide (12) from the di-iodide (5). A parallel series of reactions was carried out starting from 2,5-dibromothiophen and proceeding via the 3,4-di-iodo and then the 3,4-dilithio derivative to the 3,4-dialdehyde but this was recovered almost quantitatively even on prolonged treatment with phosphorus pentabromide in boiling benzene. This failure is probably due to the steric compression in the transition states involved in the formation of the desired hexabromothiophen (*cf.* Ref. 5).

In 1910 Finkelstein found that the reaction of *o*-bis-dibromomethylbenzene with sodium iodide gave 1,2-dibromobenzocyclobutene.[6] When this reaction was applied to 2,5-dichloro-3,4-bis-dibromo methylthiophen (12) it gave a mixture of the *trans* (21%) and *cis* (2·4%) dibromides (18 and 19) respectively. Similarly 2-bromo-5-chloro-3,4-bisdibromomethylthiophen (16) yielded the *trans*-compound (20; 13%) and its *cis*-isomer (21; 8%). These reactions are the first examples of the closure of a 4-numbered ring onto a pre-existing thiophen nucleus. The reaction of the hexachloro thiophen (14) with sodium iodide gave a brown, insoluble product which is probably polymeric.



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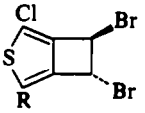
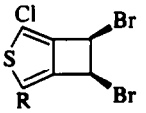
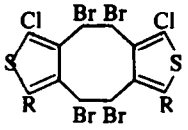


18: R = Cl
20: R = Br



19: R = Cl
21: R = Br



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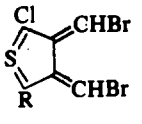

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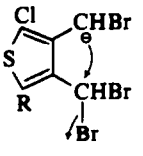

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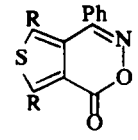
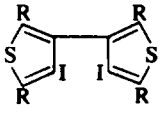


27: R = H
28: R = Cl



25: R = Me
26: R = Cl

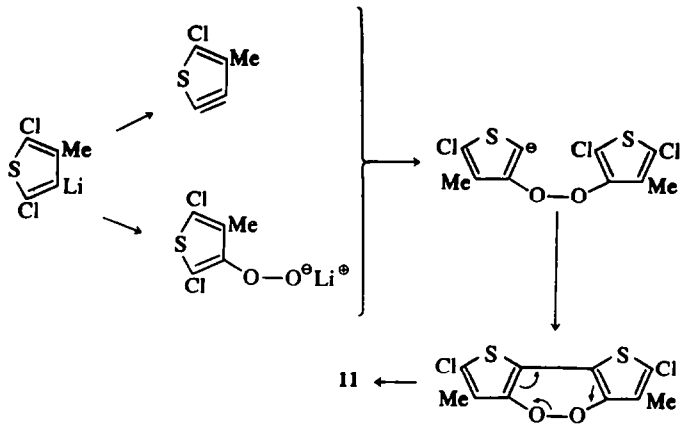
18–21

The molecular ions of compounds (18–21) show that the molecules are monomeric and not dimeric such as structure 22. The four compounds are colourless and they do not undergo cycloaddition when heated with N-phenylmaleimide in ethanol, hence they do not possess the possible alternative type of structure (23). Attempts to brominate the dibromide (18) with N-bromosuccinimide to give the 3,3,4,4-tetrabromide, which might have given the dichloro derivative of the dione (3) on hydrolysis (*cf.* Ref. 7) were unsuccessful. Instead the product was 2,5-dichloro-3,4-bisdibromomethylthiophen (12). Clearly the 4-membered ring in the bicyclic compound (18) is more highly strained (and hence more reactive) than that in 1,2-dibromobenzocyclobutene which readily undergoes substitution to give the 1,1,2,2-tetrabromide[7] and only undergoes ring cleavage to give *o*-bis-dibromomethylbenzene on heating with bromine at 160°.[6] The *cis*- or *trans*-structure of compounds (18–21) is assigned on the basis of their NMR spectra since it is known that the chemical shift (τ value) of the benzylic hydrogens in the *trans*-1,2-disubstituted benzocyclobutenes is 0·01–0·76 ppm larger than for the corresponding *cis*-isomer.[8–10] In the dibromides (20 and 21) the protons are non-equivalent and their J values (8 and 3 Hz respectively) confirm the assignments based on τ values (*cf.* Ref. 11). In our preliminary communication[3] the J values were interchanged by error.

The mechanism of the debromination of the bisdibromomethyl thiophens to give bicyclic systems is uncertain but it probably does not involve the intermediate formation of tetracovalent-sulphur species such as 23 which we attempted to trap by carrying out the reaction in the presence of N-phenylmaleimide. In the benzene series, Cava was able to trap the *o*-quinodimethane intermediate (17) in high yield.[12] We suggest that the reaction involves an intermediate carbanion (24) which displaces a bromide ion from the adjacent $-CHBr_2$ group (*cf.* discussion in Ref. 12). When *trans*-1,2-dibromobenzocyclobutene is treated with zinc dust it generates benzocyclobutadiene which can be trapped with 1,3-diphenylisobenzofuran.[13] A similar reaction with the *trans*-dibromide (20) gave a mixture of at least seven products but no pure compound could be isolated. Since the completion of our work a few derivatives of cyclobuteno- and cyclobutadieno-[*c*]thiophen have been made by methods which are completely different from that described above.[14]

Structure of the bisthiophenindigo (11). The structure proposed for this compound was deduced from spectroscopic evidence since only 10 mg of it were obtained. High resolution mass spectrometry gave the molecular formula as $C_{10}H_6Cl_2O_2S_2$ and the NMR spectrum showed one sharp singlet at τ 8·03. The IR spectrum showed one band at 1650 (C=O) and a band at 1575 (ring C=C) with a shoulder at 1560 cm^{-1} (central C=C bond) and the visible spectrum has λ_{max} (C_6H_5Cl) 484 nm (ϵ_{max} 3630). This evidence suggests a structure consisting of two symmetrically-substituted thiophen units joined together. Of all the various possibilities the most likely one is structure 11. The *cis*-configuration is assigned by analogy with the parent *cis*-bisthiophenindigo (11, with H in place of Me and Cl) which has λ_{max} ($CHCl_3$) 476 whereas the *trans*-isomer has λ_{max} at 505 nm.[15] In compound 11 the Me and Cl substituents would be expected to exert a bathochromic effect and hence the λ_{max} would be greater than 476 nm. The parent *trans*-compound has $\nu_{C=O}$ ($CHCl_3$) 1641 cm^{-1} but unfortunately the IR spectrum of the *cis*-isomer has not been recorded, however the $\nu_{C=O}$ would be expected to be higher (*cf. trans*- and *cis*-thioindigo, 1656 and 1702 cm^{-1} respectively[16]) and, of course, the central C=C bond in the *trans*-isomer would be IR inactive. The compound 11 was probably formed by aerial oxidation of some 2,5-dichloro-4-lithio-5-methylthiophen to give the 4-peroxythiophen which could add to the thiophyne (Scheme A) and thence by ring-closure and subsequent rearrangement of electrons to give directly the *cis*-compound (11).

Attempted syntheses of dithiabisnorbiphenylenes. We have made many attempts to synthesise the dithiabisnorbiphenylene (1) and its tetrachloro and tetramethyl derivatives mostly by methods which are known to give biphenylenes. Thus the first, and probably still the most general synthesis of biphenylenes, involves heating a 2,2'-di-iodobiphenyl with cuprous oxide[17,18] or with copper powder[19] at *ca.* 350°. When the di-iodobithienyls (25[20] and 26) were heated with copper bronze no reaction occurred and the bithienyls simply sublimed out of the mixture.



Scheme A.

When the tetrachlorodi-iodobithienyl (**26**) was passed through a heated tube[21] at 800° and 0·15 torr it gave iodine, a small amount of white solid, m.p. 115–119°, *m/e* 464, of unknown structure, together with starting material. 2,5-Dichloro- and 2,5-dimethyl-3,4-di-iodothiophen sublimed unchanged when heated with copper bronze. The former thiophen, when heated with copper bronze in N,N-dimethylformamide, gave a low yield (7%) of the bithienyl (**26**) but the dimethyl thiophen gave no isolable product in a similar reaction (*cf.* Ref. 22). Flash vapour pyrolysis of both di-iodothiophens at 800° and 0·1 torr gave a small amount of iodine, and over 90% of each starting material was recovered. Other unsuccessful experiments included the pyrolysis of thiophen-3,4-dicarboxylic acid anhydride, and its 2,5-dichloro derivative, at 750° and 0·1–0·5 torr (*cf.* Ref. 21); pyrolysis of the bicyclic thiophens (**27** and **28**),[23] and pyrolysis of 2,5-dichloro-3-iodothiophen-4-carboxylic acid at 850° and 0·005 torr (*cf.* Ref. 21). An attempt to prepare and to trap a 3,4-thiophyne by heating silver 2,5-dichloro-3-iodothiophen-4-carboxylate in anthracene at 210° gave no isolable product.

During our work on the dialdehyde (**13**) we decided to convert it into the previously unknown dinitrile (**29**). The preparation of the latter and of some nitrogen-containing intermediates are described in the Experimental.

EXPERIMENTAL

NMR spectra were measured in $CDCl_3$ at 100 or 60 MHz. IR spectra were measured in Nujol mulls. Silica gel M.F.C. and Kieselgel G were used for column and TLC respectively. Petroleum refers to light petroleum (b.p. 40–60°) unless stated otherwise. Flash vacuum pyrolyses were carried out using a horizontal silica tube (35 × 2·6 cm, i.d.) heated by an external electric furnace. The temp. was measured by a chromel-alumel thermocouple in a silica sheath placed concentrically within the pyrolysis tube.

2,5-Dichloro-3,4-di-iodothiophen (**5**)

A mixture of 2,5-dichlorothiophen[24] (30·6 g), I_2 (42·5 g), periodic acid dihydrate (19·3 g), AcOH (110 ml), water (22 ml), and conc. H_2SO_4 (3·3 ml) was stirred at 85–90° for 4·5 hr. The soln was poured into a dil. $NaHSO_3$ aq and stirred vigorously at 85–90° for 30 min. The soln, allowed to cool while still being stirred, deposited granular crystals. Recrystallisation from EtOH gave the di-iodothiophen (60·7 g, 75%) as very pale yellow plates, m.p. 80–81° (lit.,[25] 83°).

2,5-Dichlorothiophen-3,4-dicarboxylic acid (**7**)

(a) A soln of 2,5-dichloro-3,4-di-iodothiophen (74 g) in sodium-dried ether (370 ml) was added during 3 min to 1·1M BuLi (280 ml) (made by Gilman's method[26]) under N_2 at −60° to −70°. The mixture was stirred for 30 min at −70° then poured onto an excess of powdered solid CO_2 under dry ether, and the whole allowed to reach room temp. Water (500 ml) was added and the aqueous layer was discarded. The ethereal layer was extracted with 10% NaOH aq which, on acidification gave the dicarboxylic acid (28·5 g, 65% after being twice recrystallised from water) as needles, m.p. 205–206° (lit.,[25] m.p. > 200°).

(b) BuLi (1·0M, 100 ml) was added slowly to a soln of 2,5-dichlorothiophen (7·6 g) in dry ether (20 ml). After being kept at room temp. for 4 hr, the mixture was poured onto crushed solid CO_2. The product was isolated as above and gave the dicarboxylic acid (1·0 g, 8%) as needles, m.p. 203–204°.

2,5-Dichlorothiophen-3-carboxylic acid

During one attempt to make the dicarboxylic acid by method (a) above no precautions were taken to prevent moisture from condensing on the solid CO_2 before the dilithiothiophen was added to it. The only solid product isolated was 2,5-dichlorothiophen-3-carboxylic acid (89%), needles, m.p. 146–147° (lit.,[27] 147–148°) (Found: C, 30·4; H, 1·1; Cl, 36·15. Calc. for $C_5H_2Cl_2O_2S$: C, 30·4; H, 1·0; Cl, 36·0%).

Anhydride of 2,5-dichlorothiophen-3,4-dicarboxylic acid

The dicarboxylic acid (6·0 g) was heated in Ac_2O (15 ml) under reflux for 4 hr. Some of the solvent (7–8 ml) was distilled off and the remaining soln allowed to cool. The crystals which separated were collected and washed with petroleum (b.p. 30–40°) then recrystallised from benzene–hexane (1:1) to give the *anhydride* (4·0 g, 72%) as prisms, m.p. 142–143° (Found: C, 32·8; H, nil. $C_6Cl_2O_3S$ requires: C, 32·3; H, nil %), IR 1855 and 1786 cm^{-1} (anhydride C=O).

2,5-Dichloro-3,4-bishydroxymethylthiophen (**8**)

(a) The above anhydride (11·2 g) was added in portions to a boiling suspension of LAH (3 g) in ether (200 ml) and boiling was continued for 2 hr more. Water was added to the cooled mixture and the dialcohol collected in ether. Recrystallisation of the solid from aqueous MeOH gave the dialcohol (6·0 g, 56%) as platelets, m.p. 134–135° (Found: C, 34·0; H, 3·0; Cl, 33·0. Calc. for $C_6H_6Cl_2O_2S$: C, 33·8; H, 2·8; Cl, 33·3%), NMR τ 5·45 (CH_2, S) and 6·84 (OH, S). Zwanenberg and Wynberg[5] give m.p. 105–106° for the dialcohol prepared by hydrolysis of 2,5-dichloro-3,4-bischloromethylthiophen. We have repeated the hydrolysis and we obtained material m.p. 134–135°.

(b) Reduction of the dicarboxylic acid (28·5 g) with LAH (6·75 g) as above gave the dialcohol (14·6 g, 58%), m.p. 134–135° after recrystallisation from aqueous MeOH.

(c) Reduction of 2,5-dichlorothiophen-3,4-dialdehyde (210 mg) in THF (7 ml) with LAH (50 mg) as above gave the dialcohol (158 mg, 74%), m.p. 134–135° after recrystallisation from aqueous MeOH.

2,5-Dichloro-3,4-bischloromethylthiophen

The above dialcohol (100 mg) was suspended in conc. HCl (5 ml) and stirred at room temp. for 16 hr. The ppt was collected and recrystallised from petroleum (b.p. 30–40°) to give the bischloromethylthiophen (40 mg, 34%) as needles, m.p. 40–41° (lit.,[28] 41–42°) (Found: C, 29·0; H, 1·3; Cl, 56·6. Calc. for $C_6H_4Cl_4S$: C, 28·8; H, 1·6; Cl, 56·8%).

3,4-Bisbromomethyl-2,5-dichlorothiophen (**9**)

(a) A suspension of the dialcohol (1·01 g) in 48% aqueous HBr (15 ml) was stirred at room temp. for 4 hr. The ppt was collected in ether and gave the *bisbromomethylthiophen* (0·59 g, 35%) as needles, m.p. 53·5–54° [from petroleum (b.p. 30–40°)] (Found: C, 21·5; H, 1·3; Br, 47·3; Cl, 20·9. $C_6H_4Br_2Cl_2S$ requires: C, 21·3; H, 1·2; Br, 47·2; Cl, 20·95%), NMR τ 5·56 (CH_2, S).

(b) A soln of 2,5-dichloro-3,4-dimethylthiophen (1·8 g) and Br_2 (7·2 g) in CCl_4 (2 ml) was heated under reflux for 4 days whilst being irradiated with UV light from a medium pressure UV lamp. The cooled mixture was poured into dilute $NaHSO_3$ aq and stirred for 30 min. The organic layer yielded a solid which on crystallisation from petroleum (b.p. 30–40°) gave the bisbromomethyl thiophen (1·05 g, 31%), m.p. 52–53°.

2,5-Dichloro-3,4-dimethylthiophen (**10**) *and bisthiophenindigo* (**11**)

An ethereal soln of 2,5-dichloro-3,4-dilithiothiophen, prepared from 2,5-dichloro-3,4-di-iodothiophen (20·25 g) and 1·2M BuLi (85 ml), was stirred in an ice-bath under N_2 while a soln of Me_2SO_4 (13 g) in ether (20 ml) was added dropwise during 15 min. The mixture was stirred at room temp. for 20 hr then poured into 2M NaOH (250 ml) and stirred for 30 min. The ethereal layer yielded an oil which was purified by column chromatography on silica gel (petroleum, b.p. 40–6°, as eluent) and then by distillation. The product, b.p. 208–210° was *2,5-dichloro-3,4-dimethylthiophen* (4·1 g, 45%) (Found: M^+, 179·957 and $(M+2)^+$ 181·954. $C_6H_6{}^{35}Cl_2S$ and $C_6H_6{}^{35}Cl^{37}ClS$ require: 179·957 and 181·954 respectively), NMR τ 7·9 (CH_3).

During another preparation of the dimethylthiophen on two fifth of the above scale the mixture was allowed to stand overnight at room temp. open to the atmosphere. Purification of the crude product by column chromatography on silica gel gave on elution with petroleum (b.p. 40–60°) the dimethylthiophen (23%) and then elution with methylene dichloride gave the *bisthiophen indigo* (**11**; 10 mg, 0·17%) as orange-red needles, m.p. 239° (Found: M^+ 291·917 and $(M+2)^+$ 293·915. $C_{10}H_6{}^{35}Cl_2O_2S_2$ and $C_{10}H_6{}^{35}Cl^{37}Cl$ O_2S_2 require: 291·919 and 293·916 respectively), IR 1650 m, 1575 m, 1560 sh, 1300 s, 1100 w, 955 w, and 900 w cm^{-1}, UV (C_6H_5Cl) λ_{max} 295 sh (log ϵ 3·80), 304 (3·90), 317 (3·92), 330 sh (3·77) and 484 (3·56) nm.

2,5-Dichloro-3,4-bisdibromomethylthiophen (**12**)

(a) A soln of **9** (31 mg) and Br_2 (36 mg) in CCl_4 (5 ml) was irradiated with UV light whilst being boiled under reflux until the Br_2 colour disappeared (18 hr). The straw-coloured soln was poured into dil. $NaHSO_3$ aq and stirred for 30 min. The product was collected in methylene dichloride and, after two crystallisations from EtOH, gave the *tetrabromide* (**12**; 9 mg, 20%) as platelets, m.p. 168–169° (Found: C, 14·5; H, 0·7; Br, 64·3; Cl, 14·1. $C_6H_2Br_4Cl_2S$ requires: C, 14·5; H, 0·4; Br, 64·4; Cl, 14·3%).

(b) 2,5-Dichloro-3,4-bishydroxymethylthiophen (15 g) was suspended in 48% aqueous HBr (25 ml) and stirred at room temp. for 16 hr. The ppt was extracted with CCl_4 (100 ml) and the organic layer washed with water and then dried over $MgSO_4$. Br_2 (36 g) was added to the filtered soln and the mixture heated under reflux for 3 days whilst being irradiated with UV light. The mixture was worked up as in (a) above and gave **12** (5·5 g, 16%), m.p. 166–167°.

(c) A mixture of **15** (5·7 g) and PBr_5 (8·2 g) in benzene (100 ml) was stirred at room temp. for 72 hr, then at 40° for 7 hr, followed by stirring at 55° for 8 hr. More PBr_5 (5 g) was added and the mixture was refluxed for 5 hr. The cooled mixture was stirred with 2M NaOH for 1 hr and the product was isolated from the benzene layer by evaporation: it was purified by column chromatography on alumina with petroleum and gave **12** (3·25 g, 41%), m.p. 166–167°.

2,5-Dichlorothiophen-3,4-dialdehyde (**13**)

(a) An ethereal soln of 2,5-dichloro-3,4-dilithiothiophen, prepared from 2,5-dichloro-3,4-di-iodothiophen (32·4 g) and 0·9M BuLi (176 ml), was added dropwise under N_2 to a well-cooled, stirred soln of purified N,N-dimethylformamide (17·6 g, 1·5 molar equivs) in Na-dried ether (400 ml) at such a rate that the temp. of the mixture remained between −50° and −55°. After being stirred at −70° for 2 hr the suspension was allowed to warm up to room temp., and the solid collected by filtration. It was washed with ether, then stirred with 2N HCl (800 ml) for 1 hr. The resulting oily product was purified by chromatography on a silica gel column. Elution with methylene dichloride gave first pentanal then the *thiophendialdehyde* which formed needles (4·2 g, 25%) (from aqueous MeOH) m.p. 89–90° (Found: C, 34·0; H, 1·2; Cl, 34·2. $C_6H_2Cl_2O_2S$ requires: C, 34·5; H, 1·0; Cl, 33·9%), NMR τ −0·22 (CHO). When BuLi in hexane (instead of in ether) was used to prepare the dilithiothiophen the yield of dialdehyde was reduced to 7%. The dialdehyde gave a *bis-dinitrophenylhydrazone* as yellow platelets, m.p. 299° (dec.) (from N,N-dimethylformamide) (Found: C, 37·7; H, 2·2; Cl, 12·2; N, 19·6. $C_{18}H_{10}Cl_2N_8O_8S$ requires: C, 38·0; H, 1·8; Cl, 12·5; N, 19·7%).

(b) 2,5-Dichloro-3,4-bisdibromomethylthiophen (75 mg) and silver trifluoroacetate (145 mg) were heated under reflux in a mixture of acetonitrile (5 ml) and water (0·2 ml) for 12 hr in a flask which was protected from light. The soln was evaporated to dryness and the residue extracted with methylene dichloride. This extract gave 2,5-dichlorothiophen-3,4-dialdehyde (29 mg, 92%) as needles, m.p. 89–90° from aqueous MeOH.

Reaction of phosphorus pentachloride with 2,5-dichlorothiophen-3,4-dialdehyde

A soln of the dialdehyde (2·1 g) and PCl_5 (4·5 g) in benzene (100 ml) was kept at room temp. for 5·5 hr. The mixture was stirred with 2M NaOH then the benzene layer was evaporated. The residue was recrystallised from petroleum (b.p. 30–40°) and gave *2,5-dichloro-3,4-bisdichloromethylthiophen* (**14**; 1·52 g, 47%) as plates, m.p. 129–130° (Found: C, 22·9; H, 0·8; Cl, 66·5. $C_6H_2Cl_6S$ requires: C, 22·8; H, 0·6; Cl, 66·8%).

Reaction of phosphorus pentabromide with 2,5-dichlorothiophen-3,4-dialdehyde

(a) A mixture of the dialdehyde (4·2 g) and PBr_5 (17·25 g) in benzene (100 ml) was stirred at 40° for 13 hr. After hydrolysis of the phosphorus halides with 2M NaOH the benzene layer was evaporated and the residue recrystallised twice from petroleum to give *2,5-dichloro-3-dibromomethylthiophen-4-aldehyde* (**15**; 5·83 g, 82%) as needles, m.p. 82–83° (Found: C, 20·2; H, 0·6; Br, 45·6; Cl, 19·8. $C_6H_2Br_2Cl_2OS$ requires: C, 20·4; H, 0·6; Br, 45·3; Cl, 20·1%).

(b) A soln of the dialdehyde (1·4 g) and PBr_5 (6 g) in benzene 100 ml) was stirred at 60° for 10 hr. The product was separated from some dialdehyde by chromatography on a column of alumina with petroleum as eluent. The first fraction gave 2,5-dichloro-3,4-bisdibromomethylthiophen (1·13 g, 34%) as plates, m.p. 166–167°.

(c) A mixture of the dialdehyde (0·84 g) and PBr_5 (5 g) in benzene (5 ml) was refluxed for 48 hr. The product was recrystallised from N,N-dimethylformamide and gave *2-bromo-5-chloro-3,4-bisdibromo methylthiophen* (**16**; 1·14 g, 53%) as plates, m.p. 164–165° (Found: C, 13·2; H, 0·4; Br, 73·6; Cl, 6·6. $C_6H_2Br_5ClS$ requires: C, 13·3; H, 0·4; Br, 73·8; Cl, 6·6%), NMR τ 2·95 and 3·30.

2,5-Dibromo-3,4-di-iodothiophen

A mixture of 2,5-dibromo thiophen[29] (9·7 g), I_2 (8·55 g), periodic acid dihydrate (3·86 g), AcOH (25 ml), water (5 ml) and conc. H_2SO_4 (0·7 ml) was stirred at 85–90° for 4 hr. The cooled mixture was added to dil. $NaHSO_3$ aq then stirred for 30 min. The ppt was recrystallised from EtOH and gave the di-iodothiophen (14·5 g, 73%) as needles, m.p. 141–142° (lit.,[30] 141–142°).

2,5-Dibromothiophen-3,4-dialdehyde

A soln of 2,5-dibromo-3,4-di-iodothiophen (9·9 g) in THF (400 ml) was added, during 25 min, to a stirred soln of 1·2M BuLi (33·5 ml) in ether (60 ml) at −70°, under N_2. This mixture was stirred for 30 min at −70° and then added dropwise to a stirred soln of N,N-dimethylformamide (6 g) in ether (100 ml) under N_2. A sticky cream-coloured mass formed which prevented further stirring so the mixture was kept at −50° for 1 hr before being allowed to warm up to room temp. 2M HCl (200 ml) was added and the organic layer separated. The crude product was chromatographed on a silica gel column in benzene. The second fraction yielded the *dialdehyde* (3·75 g, 63%) as needles, m.p. 149–150° after two recrystallisations from aqueous MeOH (Found: C, 23·9; H, 0·7; Br, 53·8. $C_6H_2Br_2O_2S$ requires: C, 24·2; H, 0·7; Br, 53·6%).

cis- and trans-3,4-Dibromo-2,5-dichlorocyclobuteno[c]thiophen (**19** and **18**)

2,5-Dichloro-3,4-bis-dibromomethylthiophen (2·5 g) and NaI (5 g) were heated in N,N-dimethylformamide (25 ml) at 65° for 7 hr, during which time I_2 was liberated. The soln was poured into dil. $NaHSO_3$ aq, the mixture was stirred for 30 min and then extracted with methylene dichloride. The organic layer yielded a brown solid, which was dissolved in CCl_4 (25 ml), and Br_2 (5 ml) added. After being kept for 24 hr the soln was stirred with dil. $NaHSO_3$ aq for 30 min. The organic layer yielded a pale orange solid which was chromatographed in petroleum on a column of alumina. The first fraction was recrystallised from petroleum (b.p. 60–80°) and gave trans-*3,4-dibromo-2,5-dichlorocyclobuteno[c]thiophen* (**18**; 360 mg, 21%) as platelets, m.p. 95°. Similar treatment of the second fraction gave the cis-*isomer* (**19**; 40 mg, 2·4%) as needles, m.p. 149–150°. Both isomers had the same mass spectrum and gave peaks for the parent ion at *m/e* 334, 336, 338, 340, and 342 in ratios consistent with a molecule containing two atoms each of Br and Cl (*trans*-isomer-Found: M^+, 335·7595 and $(M+2)^+$, 337·7562. $C_6H_2Br_2Cl_2S$ requires: 335·7598 and 337·7574 allowing for weighted mean of halogen isotopes). *trans*-isomer, NMR τ 4·43, *cis*-isomer, τ 3·98.

cis- and trans-2,3,4-Tribromo-5-chlorocyclobuteno[c]thiophen (**21** *and* **20**)

2-Bromo-5-chloro-3,4-bis-dibromomethylthiophen (1·0 g) and NaI (2·0 g) were heated at 60° in N,N-dimethyl formamide (10 ml) for 6 hr, then the mixture was worked up as in the preceding experiment. The first fraction gave trans-2,3,4-*tribromo-5-chlorocyclobuteno[c]thiophen* (**20**; 93 mg, 13%) as platelets, m.p. 91–92° and the second fraction gave the cis-*isomer* (**21**; 58 mg, 8%) as needles, m.p. 138–139°. Both isomers had the same mass spectrum and gave peaks for the parent ion at *m/e* 378, 380, 382, 384, and 386 in the relative intensities expected for a molecule with one Cl and three Br atoms (*trans*-isomer-Found: M^+, 379·7076 and $(M+2)^+$ 381·7043. $C_6H_2Br_3ClS$ requires: 379·7094 and 381·7072 allowing for weighted mean of halogen isotopes). *trans*-Isomer, IR 3225 w, 1442 s, 1265 s, 1130 s, 925 m and 670 s cm^{-1}, NMR τ 4·02 d and 4·36 d, *J* 3 Hz. *cis*-Isomer, IR 3220 m, 1440 s, 1240 m, 1140 s, 905 m and 705 s cm^{-1}, NMR τ 3·64 d and 3·92 d, *J* 8 Hz.

Reaction of 3,4-dibromo-2,5-dichlorocyclobuteno[c]thiophen with N-bromosuccinimide

The dibromide (157 mg of mixed isomers), N-bromosuccinimide (167 mg), and dibenzoyl peroxide (10 mg) were heated under reflux in CCl_4 (5 ml) for 24 hr. Further portions of N-bromosuccinimide (167 mg) and dibenzoyl peroxide (10 mg) were added and heating was continued for another 24 hr. The hot soln was filtered and the filtrate, on evaporation, gave 2,5-dichloro-3,4-bisdibromomethylthiophen (75 mg, 32%) as plates, m.p. 164–165° after recrystallisation from petroleum (b.p. 60–80°).

2,2',5,5'-Tetrachloro-4,4'-di-iodo-3,3'-bithienyl (**26**)

A soln of 2,5-dichloro-3,4-di-iodothiophen (20 g, 50 mmole) in ether (75 ml) was added dropwise to 1·15M BuLi (43·5 ml, 50 mmole) with stirring under N_2. After 15 min at −70°, anhyd cupric chloride (6·5 g, 50 mmole) was added, and stirring continued at −70° for 4 hr more. The mixture was allowed to warm to room temp. then 4 N HCl (200 ml) added. The ethereal layer gave the *bithienyl* (3·8 g, 28%), m.p. 126° from MeOH. (Found: M^+ etc 554, 556, 558, 560, 562 in correct ratio for 4 Cl. $C_8{}^{35}Cl_4I_2S$ requires: *M*, 554).

When the same reaction was carried out except that only half as much of the thiophen was used the product was *2,2',5,5'-tetrachloro-3,3'bithienyl* (41%) which formed pale yellow needles from MeOH, m.p. 122–123° (Found: C, 31·9; H, 0·7. $C_8H_2Cl_4S_2$ requires: C, 31·6; 0·7%).

Reaction of 2,5-dichloro-3,4-di-iodothiophen with copper

The thiophen (1 g), copper bronze (1 g), and N,N-dimethylformamide (20 ml) were boiled under reflux for 3 hr, then the mixture was cooled and poured into water. Extraction with ether gave **26** (46 mg, 7%) as needles from MeOH, m.p. and m. m.p. 126°.

2,5-Dichloro-3-iodothiophen-4-carboxylic acid

A mixture of 2,5-dichlorothiophen-3-carboxylic acid (10·8 g), I_2 (10·6 g), and periodic acid dihydrate (4·9 g) in AcOH (41 ml), water (8 ml), and conc. H_2SO_4 (1·2 ml) was stirred at 85–90° for 13 hr. The cooled mixture was added to dil $NaHSO_3$ aq and stirred for 30 min. The white solid was extracted with 2M NaOH leaving a yellow solid which, on recrystallisation from EtOH, gave 2,5-dichloro-3,4-di-iodothiophen (1·6 g, 7%) as plates, m.p. 80–81°. The alkaline extract was acidified and gave *2,5-dichloro-3-iodothiophen-4-carboxylic acid* (3·7 g, 21%) as needles from aqueous MeOH, m.p. 163–164°. (Found: C, 18·7; H, 0·4; Cl, 21·9; I, 39·5. C_5HCl_2IOS requires: C, 18·6; H, 0·3; Cl, 22·0; I, 39·3%).

The Ag-salt (2·25 g, 52%) was made by adding $AgNO_3$ (1·8 g) in water to the thiophen acid (3·2 g) in 0·1M NaOH (100 ml). The first formed white ppt rapidly turned brown. It was washed with water and with MeOH, and then dried at room temp.

3-Iodo-2,5-dimethylthiophen-4-carboxylic acid

3,4-Di-iodo-2,5-dimethylthiophen (18·2 g, 0·05 mole) in ether (100 ml) was added to a stirred soln of 1·0M BuLi (100 ml) in ether at −70° during 15 min, then the mixture was poured onto a slurry of solid CO_2 in ether. The acidic product was isolated and recrystallised from aqueous MeOH to give the *carboxylic acid* (10·1 g, 72%), m.p. 199°. (Found: C, 30·0; H, 2·6. $C_7H_7IO_2S$ requires: C, 29·8; H, 2·5%).

Derivatives of 2,5-dichlorothiophen-3,4-dialdehyde

The following sequence was carried out in an attempt to prepare 2,5-dichloro-3,4-dicyanothiophen (*cf.* Ref. 31). The dialdehyde (1 mmole) and N,N-dimethylhydrazine (3 mmole) were heated under reflux in benzene and the water formed removed by a Dean–Stark apparatus. The oily product was recrystallised from hexane, and gave the *bis-N,N-dimethylhydrazone* (67%) as pale cream needles, m.p. 34·5–35°. (Found: C, 41·0; H, 4·9; N, 18·7. $C_{10}H_{14}Cl_2N_4S$ requires: C, 41·0; H, 4·8; N, 19·1%). Treatment of the bishydrazone with an excess of MeI in benzene gave the corresponding N,N-*dimethylhydrazone-N,N,N-trimethyl hydrazonium iodide* (74%) as a pale brown powder, m.p. 180–181° (Found: C, 29·7; H, 3·9. $C_{11}H_{17}Cl_2IN_4S$ requires: C, 30·3; H, 3·9%). The latter compound (580 mg) was added in portions to NaOMe (250 mg) in MeOH (25 ml) and the mixture boiled under reflux until the evolution of trimethylamine ceased (4 hr). The crude product after being chromatographed in silica gel (eluting with benzene) gave the N,N-*dimethylhydrazone of 2,5-dichloro-3-cyanothiophen-4-aldehyde* (145 mg, 44%) as needles, m.p. 74–75° (Found: M^+, 246·974 and 248·971. $C_8H_7{}^{35}Cl_2N_3S$ and $C_8H_7{}^{35}Cl^{37}ClN_3S$ require: 246·974 and 248·971 respectively.

2,5-Dichloro-3,4-dicyanothiophen (**29**)

2,5-Dichlorothiophen-3,4-dialdehyde (2·1 g) and hydroxylamine hydrochloride (2·1 g) were stirred in pyridine (50 ml) at room temp. for 2 hr. The soln was poured into 4M HCl (150 ml) and the product collected in ether. The *dioxime* (2·05 g, 86%) formed cream needles (from aqueous EtOH), m.p. 175–176° (Found: C, 30·6; H, 1·8; N, 11·3. $C_6H_4Cl_2N_2O_2S$ requires: C, 30·2; H, 1·7; N, 11·7%).

The dioxime (2·05 g) in Ac_2O (20 ml) was boiled under reflux for

13 hr. The cooled soln was poured into stirred $NaHCO_3$ aq, and solid $NaHCO_3$ added until all the anhydride has been hydrolysed and neutralised. The product was collected in ether then recrystallised twice from EtOH, giving 2,5-*dichloro*-3,4-*dicyanothiophen* (**29**) (1·0 g, 58%) as pale cream needles, m.p. 139–140°. (Found: C, 36·0; Cl, 34·9; N, 14·2. $C_6Cl_2N_2S$ requires: C, 35·5; Cl, 35·0; N, 13·6%), IR 2240 s, 2235 s, 1160 s, 963 s and 754 s cm^{-1}.

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