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THE t-BUTYLATION OF |8|(2,5)THIOPHENOPHANE†

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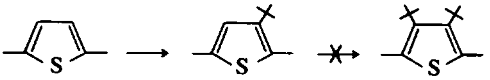
Abstract—When |8|(2,5)thiophenophane (**4**) is treated with an excess of t-BuCl/SnCl$_4$ in CS$_2$ at room temperature, a deepseated rearrangement occurs. t-butyl groups are introduced into the 2- and 5-position of the thiophene nucleus with a concomitant migration of the octamethylene bridge to the 3- and 4-position. In addition to the di-t-butylthiophene (**8**), two mono-t-butylthiophenes (**14** and **16**) are formed under the reaction conditions. These products were isolated and characterized and the course of the reaction is discussed.

INTRODUCTION

During the last decade intensive efforts have been made to prepare *o*-di-t-butyl-(hetero)aromatics. Successful attempts include *inter alia* the synthesis of *o*-di-t-butyl derivatives of benzene,[1] furan,[2] pyrrole[3] and quinoxaline.[4] An *o*-di-t-butylthiophene, however, has not been synthesized up till now, in spite of the fact that several approaches have been tried.[5] Calculations indicate[6] that the interaction of the t-butyl groups in the 2,3- and 3,4-position of thiophene is about equal and that the strain energy of *o*-di-t-butyl derivatives will increase in the series furan-pyrrole < thiophene < benzene.[7]

The *o*-di-t-butyl derivatives of furan[2] and pyrrole[3] have been prepared previously by direct Friedel–Crafts alkylation with t-butylchloride (t-BuCl). Messina *et al.*[8] and Gol'dfarb *et al.*[9] reported that 2,5-dimethylthiophene (**1**) could be converted with t-BuCl/AlCl$_3$ or t-BuCl/FeCl$_3$ in CS$_2$ into the 3-t-butylthiophene **2** in about 90% yield. This result was corroborated and extended by Wynberg and Wiersum[6] who failed in attempts to t-butylate **2** under conditions comparable to those used with furan[2] and pyrrole.[3] The introduction of a second t-butyl group into **2** by direct alkylation clearly is prohibited by steric hindrance.



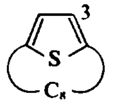
1 **2** **3**

It seemed to us that even a small relief of strain in **2** might allow the *o*-di-t-butylation to succeed. The α-methylenes in |8|(2,5)thiophenophane (**4**) are fixed to some extent.[10] Consequently, there might be some more room for the 3,4-substituents in **4** as compared with **1**.‡

We therefore subjected **4** to alkylation with t-BuCl under Friedel–Crafts conditions.

RESULTS AND DISCUSSION

When **4** was treated with an excess of t-BuCl/SnCl$_4$ in CS$_2$ at room temperature, a mixture of at least three products was obtained as was revealed by GLC analysis. This result is in sharp contrast with the results of the t-butylation of **1**, where—under comparable conditions—**2** was the sole product.[6,8,9]



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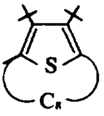
The di-t-butylthiophene 8

The first of the three compounds which was isolated, purified and identified was a solid, m.p. 96–96·4°. Its empirical formula ($C_{20}H_{34}S$), the UV spectrum (λ_{max} 244 mμ, ε 9000) and the PMR spectrum (no aromatic protons) were in agreement with one of the four (**5**, **6**, **7** and **8**) di-t-butylated derivatives of **4**. By analogy with the results obtained with the t-butylation of **1** we were prone to assign structure **5** to this compound. However, it soon became clear that this di-t-butylated product was not the desired *o*-di-t-butylthiophene **5** but the isomer **8**!



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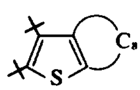

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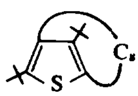

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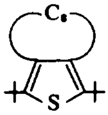

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The assignment of structure **8** to the di-t-butylated product of **4** is based on several pieces of independent evidence namely (a) an NMR analysis, (b) an unambiguous alternate synthesis of **8**, and (c) the analysis of the structure of two mono-t-butylated products.

(a) *NMR analysis.* The PMR (*inter alia* δ 1·40, singlet, t-butyl) and the CMR spectrum showed the product to be symmetrical; consequently the unsymmetrical structures **6** and **7** for our product could be dismissed.

The PMR spectrum of the tetrasubstituted thiophene showed no absorption at $\delta < 0\cdot9$, which indicates this compound to be **8** rather than **5** on the basis of the following reasoning. Bridged thiophene **4** shows an interesting feature in the PMR, viz. some methylene protons absorb at a very high field ($\delta < 0\cdot9$). This shielding has been ascribed[10] to the magnetic anisotropy effect of the aromatic ring and/or the anisotropy of the heteroatom. We expect for **5**, just as it has been found for **4**, methylene protons at $\delta < 0\cdot9$; for **8** no hydrogens are forced close to the thiophene ring and consequently shielded hydrogens are not expected in this case.

The tetrasubstituted thiophene (either **5** or **8**) showed even at −60° a nearly symmetrical triplet for the

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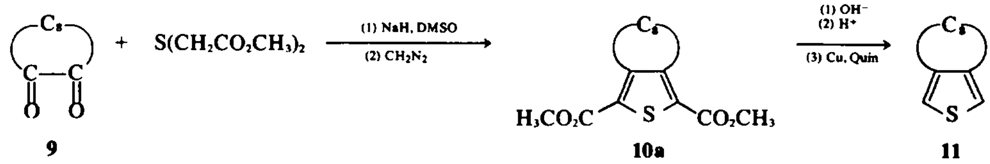
†Taken from the Ph.D. Thesis of R. H., Groningen (1974).

‡Some formal analogy might exist with the work of Leonard[11] and De Groot[4] carried out on quite different systems.

α-methylene protons. On this basis we conclude that this thiophene has a 3,4-octamethylene bridge instead of a 2,5-bridge, which means that the tetrasubstituted thiophene would be **8**. This conclusion is based on the following. Nozaki *et al.*[10] have studied the temperature dependency of the PMR spectrum of **4**. At +150° the signal of the α-methylene protons strongly resembles a triplet which can be accounted for by assuming a rapid conformational transition of the polymethylene chain over the S atom, resulting in magnetically equivalent α-methylene hydrogens. At room temperature, however, these hydrogens appear as a complex multiplet since this transition becomes relatively slow and two different kinds of α-methylene protons are observed. A comparable behavior would be expected for the 2,5-bridged thiophene **5**. For thiophene **11** which has a highly flexible octamethylene bridge over the 3,4-position we expected and found even at temperatures as low as −30° a triplet for the α-methylene protons, which must be a time averaged signal due to rapidly interconverting conformers. Compound **8** is expected to behave just like **11**.

(b) *Unambiguous synthesis of* **8**. The novel thiophene **11** which was chosen as the starting material for the preparation of **8** was synthesised via a Hinsberg condensation.[12] Reaction of **9** with dimethyl thiodiacetate in DMSO-benzene under the influence of NaH afforded an acid† which was converted into the diester **10a** with the aid of ethereal diazomethane.‡ The yield of **10a** amounted to 36% (based on **9**). Hydrolysis with KOH in ethanol, followed by acidification with hydrochloric acid afforded the diacid **10b**, which was used in the subsequent step without purification. Decarboxylation of **10b** with copper powder in quinoline afforded thiophene **11** in 90% yield. The structure of this thiophene was evident from its elemental analysis and spectroscopic properties (*inter alia* one singlet for the two aromatic protons at δ 6·85).



Treatment of **11** with t-BuCl/SnCl$_4$ in CS$_2$ under conditions comparable to those used in the t-butylation of **4** afforded a tetrasubstituted thiophene which was *identical* to the di-t-butylated product derived from **4** as was concluded from the m.p., mixture m.p. and IR spectrum. The formation of the same di-t-butylated thiophene from **4** as from **11** does not by itself distinguish between **5** and **8** as the reaction product. In principle two possibilities (**a** and **b**) exist (Fig. 1).

In case **a** it is difficult to account for the rearrangement from the unstrained thiophene **11** to **5**, which is expected[7] to be highly strained. In the second case (**b**), **11** is t-butylated in a normal manner, while t-butylation of **4** is accompanied by rearrangement. However, in the latter case the rearrangement can be accounted for since t-butylation without rearrangement would give the thermodynamically unfavorable product **5**.

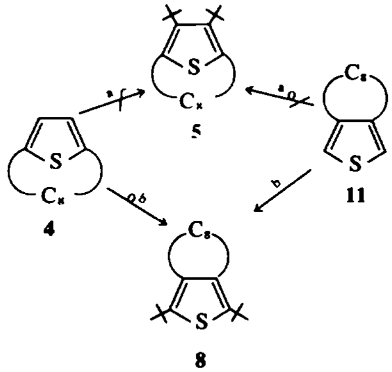
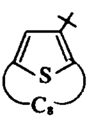


Fig. 1.

(c) *The structure of the mono-t-butylated products.* When the conversion of **4** → **8** was followed with the aid of GLC it turned out that two other compounds were formed in reasonable amounts. Depending on the reaction conditions either of these could be the major product.

The first mono-t-butyl product (14)

Treatment of **4** for 3 hr with an excess of t-BuCl/SnCl$_4$ gave a mixture containing one mono-t-butylated thiophene in 53% yield and an isomeric mono-t-butylthiophene with a slightly longer retention time in 2% yield. In addition, **4** and **8** were present in 40% and 4% yields respectively.§ The major compound was isolated with the aid of preparative GLC and gave a correct elemental analysis for C$_{16}$H$_{26}$S. On the basis of the UV (λ_{max} 246 mμ, ε 7100), the NMR spectra and the chemical evidence presented below it was concluded that this compound was **14**, one of the six possible mono-t-butyl isomers **13–18**.



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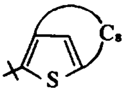

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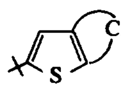

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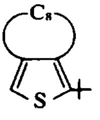

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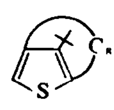

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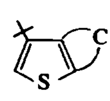

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This structure assignment was based on the following arguments. Thiophenes **13**, **14** and **15** possess an H atom in the β-position of the thiophene nucleus, while the H atom in **16**, **17** and **18** is situated in the α-position. It is well-known that α-hydrogens on thiophene can be replaced by lithium on treatment of the thiophene with n-butyllithium in ether; under these conditions β-

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†On the basis of the mechanism of the Hinsberg condensation a monoacid-monoester is expected.[13]

‡In one case, the mother liquors which were obtained upon recrystallization of the crude **10a** were worked up. The analytical and spectroscopic properties of the obtained product agreed well with those expected for 2-carbomethoxy-3,4-octamethylenethiophene (**12**). This structure was proven by an independent synthesis as shown in the Experimental.

§Trace products were not examined.

hydrogens usually do not exchange.[14] Our thiophene was treated with n-butyllithium under the normal conditions and the mixture quenched with D_2O. PMR spectroscopy showed that little or no deuterium incorporation had taken place. This observation strongly points to the presence of a β-H atom which was supported by CMR spectroscopy as follows. The coupling constant J_{C-H} of a large number of thiophenes has been measured in this laboratory and it turns out that its value gives conclusive information about the position of this C–H. For the α-position a value of about 180 Hz is always found and for the β-position this value is about 160 Hz.† We found J_{C-H} to be 160 Hz and hence the hydrogen must be in the β-position.

The number of possible structures was now restricted to three, viz. **13**, **14** and **15**. The 100 MHz PMR spectrum (Fig. 2) showed absorptions at a very high field (δ 0·4 and δ 0·8), in accord with meta bridged structures such as **13** and **14** which possess hydrogens closely forced to the thiophene ring.[10,15,16] At δ 2·66, a signal approximately consisting of two triplets was evident. This signal is in agreement with two slightly different methylene groups, each of them carrying two mutually equal protons. In analogy with the situation in **4**, the protons at each of the α-methylene carbons of **13** would be mutually different due to the inhibition of free inversion of the polymethylene bridge. Consequently, the PMR of **13** is expected to exhibit a broad multiplet for the α-methylene protons. Hence the NMR data suggest that the thiophene under consideration is **14** rather than **13**.

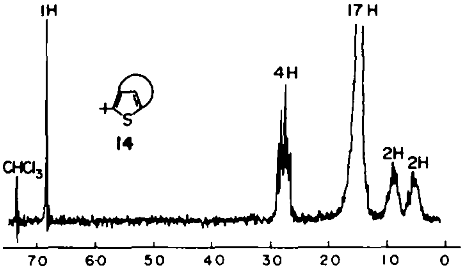


Fig. 2.

Desulfurization. In order to prove the structure of thiophene **14** it was treated with Raney-nickel.[18] This reagent is known to effect reductive desulfurization of thiophenes to the corresponding saturated hydrocarbons without concomitant rearrangement. Numerous examples of structure proofs based on this procedure do exist.[18]

In this way, **13** was expected to give t-butylcyclododecane (**19**) upon treatment with Ra–Ni; neopentylcycloundecane (**20**) was anticipated as the desulfurization product derived from **14**.

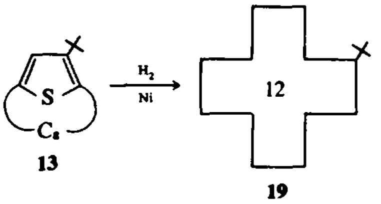
Hydrocarbon **20** was synthesised via an unambiguous route. Addition of neopentyllithium‡ to **21** gave, after work-up, a mixture of an alcohol and the starting ketone. This mixture was distilled from anhydrous copper sulfate in order to dehydrate the alcohol. Chromatography of the distillate gave the alkene **22**§ which was hydrogenated to afford neopentylcycloundecane (**20**).

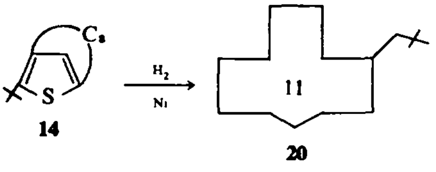
According to GLC, 100 MHz PMR, IR and MS the hydrocarbon which was obtained on desulfurization of the thiophene with Ra–Ni was identical to **20** prepared from cycloundecanone (**21**) as described above. Hence we conclude that the first mono-t-butylthiophene is 5-t-butyl|8|(2,4)thiophenophane (**14**) indeed.‖

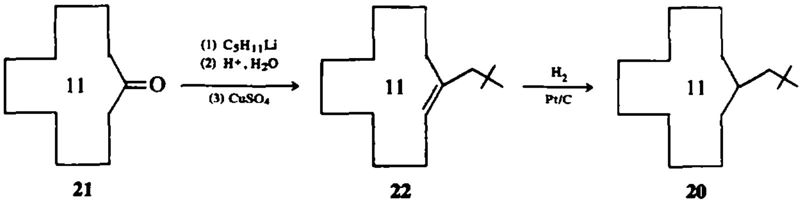
The second mono-t-butyl product (**16**)

In order to isolate the second mono-t-butylthiophene, its yield was optimized. Thus treatment of **4** with t-BuCl/$SnCl_4$ for 20 hr afforded a crystalline thiophene (m.p. 51–51·5°) as the major product. Its elemental analysis and spectroscopic properties showed it to be one of the isomers **13**–**18**. An exchange experiment with n-butyllithium (*vide supra*) resulted in a complete deuterium incorporation, pointing to an α-H atom on the thiophene nucleus.[14] The J_{C-H} (180 Hz) was also in agreement with one of the isomers **16**–**18**. The absence of absorptions in the PMR spectrum between δ 0–1 restricted the possible structures to **16** and **18**. The CMR spectrum showed that the thiophene carbon to which the hydrogen is attached is not only coupled with this hydrogen but also with the hydrogens of the neighboring methylene group of the bridge. Wieringa pointed out¶ that this coupling is strong evidence for **16** rather than for **18** especially since about the same coupling (6 Hz) was present in the CMR spectrum of **11**.

We realize that again Ra–Ni desulfurization of the







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†Drs. J. Runsink, personal communication; see also Ref. 17.

‡The use of neopentylmagnesiumbromide in this reaction led to dimerization of **21** to the corresponding ketol.

§According to PMR probably a *cis–trans* mixture; no attempts were made to effect separation.

‖On the basis of the results of the t-butylation of 2,5-dimethylthiophene (**1**), thiophene **13** would be expected[6,8,9] as the primary t-butylthiophene!

¶Dr. J. H. Wieringa, personal communication.


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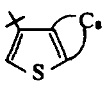
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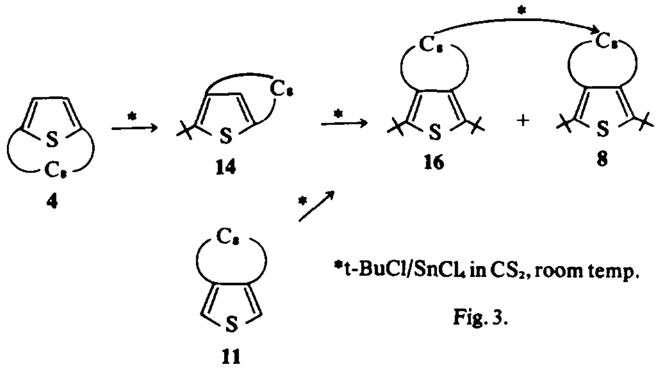
11

thiophene should give conclusive information about its structure. However, a conclusion was drawn from other chemical evidence (see below) avoiding in this way the laborious synthesis of the hydrocarbon which was expected as the desulfurization product. Under the appropriate conditions we could isolate a mono-t-butylthiophene from the reaction of 11 with t-BuCl/$SnCl_4$. This product was identical to the mono-t-butyl thiophene (16 or 18) which was obtained from 4 upon treatment with t-BuCl/$SnCl_4$ for 20 hr. Since 18 can not be imagined as an intermediate in the conversion 11→8 and since 16 is the thiophene which we would expect as the intermediate product in this conversion, structure 16 was assigned to this mono-t-butylthiophene.

The reaction path given in Fig. 3 is in agreement with the obtained results. The following observations are in accordance with the proposed reaction scheme. When 4 was treated for a short period with t-BuCl/$SnCl_4$ in CS_2 (the usual conditions), 14 was formed contaminated with only minor amounts of 16 and 8; when the reaction was carried out for a longer period, 14 disappeared while 16 and 8 were formed. Treatment of pure 14 with t-BuCl/$SnCl_4$ in CS_2 also led to the formation of 16 and 8; on the other hand, treatment of 16 with t-BuCl/$SnCl_4$ did not result in the formation of 14. Finally, 4 did not rearrange upon treatment with $SnCl_4$ (no t-BuCl present).† All these observations are in agreement with the t-butylation/isomerization 4→14 as the first step.



*t-BuCl/$SnCl_4$ in CS_2, room temp.

Fig. 3.

Having in mind the conversion 4→14 as the initial step, we can imagine in principle 14 as well as 8 as the precursors of 16.

In order to find out whether 16 might be formed by de-t-butylation of 8, the di-t-butylthiophene 8 was treated with $SnCl_4/CS_2$ in the presence of 4 and 14 as the possible t-butyl acceptors. No evidence was obtained for the formation of 16 under these conditions.‡ A control experiment (a mixture of 4, 14, 16 and 8 was treated with $SnCl_4$ in CS_2) showed clearly that the fact that 16 was not detected was not due to a fast disappearance under these reaction conditions.

As mentioned, when 14 was treated with t-BuCl/$SnCl_4$ in CS_2 the isomerization 14→16 was evident. So it seems plausible to suppose that 16 is formed (at least for a large part) from 14. The conversion 14→16 did not occur in the absence of t-BuCl.

The formation of 8 must occur from 14 and/or 16. When 16 was treated with t-BuCl/$SnCl_4$ in CS_2, 8 was formed indeed. Under these conditions, 14 gave rise to the formation of 16 and 8. These data do not answer the question whether 8 can be formed from 14 directly, since 8 might arise from 16 under these circumstances. Hence, the direct formation of 8 from 14 is neither proven nor excluded. This conversion is mentioned here because of its analogy with the conversion 4→14.

The mild conditions under which the conversion 4→8 occurs and the dramatic difference in behavior between 2,5-dimethylthiophene (1) and 4 must be emphasised. On the basis of the scarce literature data on the isomerization of alkylthiophenes§ we do not know whether the difference in behavior between 1 and 4 is due to the strain in the bridged thiophene 4, to the difference in the migrating group (CH_3 *vs* CH_2R) or to a combination of these facts. The acylation of |9|- and |10|paracyclophane, as carried out by Blomquist *et al.*[20] is of interest in connection with our work.

We hope that the results reported above will initiate further studies of the rearrangements of bridged heterocyclic compounds.

Synthesis of 1,4-*cyclododecanedione* (26)

We needed large (30–40 g) amounts of compound 26 which was used as the starting material for the synthesis of |8|(2,5)thiophenophane (4) and its oxygen analog, |8|(2,5)furanophane.[10] Since the literature procedures described for 26 were unsatisfactory, its synthesis was reinvestigated.

Cyclododecanedione 26 was first prepared by Camerino and Patelli[21] in 1964 as shown in Fig. 4; the yields and the experimental procedures were not given. Nozaki *et al.*[22,23] reinvestigated the synthesis of 26. Irradiation of cyclododecanone (23) gave 87% of a mixture of the cyclobutanols 24. Dehydration of 24 gave the alkene 25 in 35% yield. Oxidation of 25 gave the diketone 26 in an unspecified yield.

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†Since we did not attempt to exclude traces of moisture from the reaction mixture the presence of small amounts of HCl, a compound which will also be present when 4 reacts with t-BuCl/$SnCl_4$, is probable. The reaction of 4 with $SnCl_4$ in CS_2 in the presence of larger amounts of HCl has not yet been studied. When 4 was treated with H_2SO_4 no rearrangement occurred.

‡The influence of large amounts of HCl has not yet been studied. Treatment of pure 8 with H_2SO_4 gave, after work-up, the mono-t-butylthiophene 16.

§The isomerization of 2,5-di-t-butylthiophene to the 2,4-isomer under the influence of $AlCl_3$ is the first example[19] of an isomerization of an alkylthiophene under Friedel–Crafts conditions.

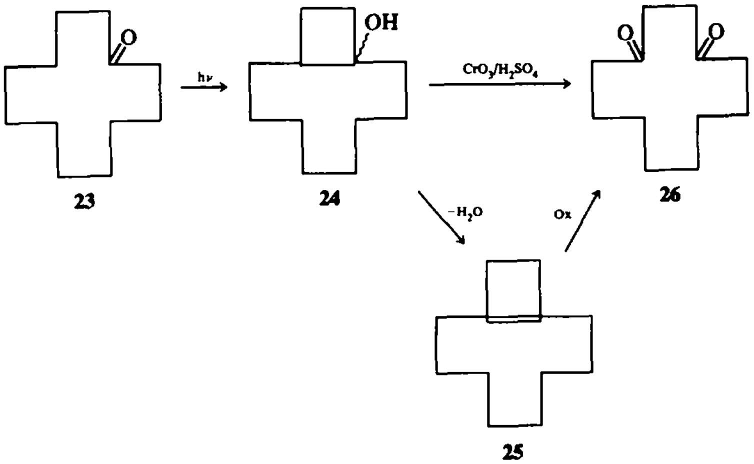

Fig. 4.

We obtained only moderate yields upon repetition of the routes described for **26**, but found a new route which was superior to the published procedures. Direct oxidation of the cyclobutanol mixture **24** with Jones reagent in acetone gave **26** in 55% yield (relative to **23**). As much as 59 g of **26** was easily prepared by this method. The experimental part illustrates the simplicity of this procedure. The detailed mechanism of the conversion **24**→**26** is not clear. This reaction is of interest in connection with the recent mechanistic work on the oxidative cleavage of bridgehead alcohols[24] and the oxidation of 1-methylcyclobutanol.[25] The oxidation of **24** was carried out in pursuance of the work of Fieser and Szmuszkovicz[26] on the oxidation of t-cyclohexanols.

EXPERIMENTAL

Microanalyses were performed in the analytical section of our department. M.ps were determined with a Mettler apparatus and are corrected. Mass spectra were obtained on an AEI MS-902. UV spectra were obtained on a Zeiss PMQ II. IR spectra were taken on a PE 125 and a PE 257. PMR spectra were taken on Varian A-60 and T-60 spectrophotometers. Some of these spectra were recorded by Mr. A. Kiewiet. Columnchromatography was done with Al_2O_3 (Merck) or silicagel (BDH). Gaschromatography was carried out on a HP F&M Scientific 5750 Research Chromatograph with FID (analytical GLC), or on a HP F&M Scientific 700 Laboratory Chromatograph with TCD (preparative GLC) with technical assistance from Mr. M. L. Suijkerbuijk. SE-30 columns were used. Peak-area ratios were considered to be approximately proportional to product ratios: no attempts were made to correct for differences in detector response of the thiophenes. A Varian XL-100 was used for the CMR and 100 MHz PMR spectra. These spectra were recorded by and discussed with Drs. J. Runsink, Dr. J. de Wit, and Dr. J. H. Wieringa.

|8|(2,5)*Thiophenophane* (**4**). The procedure of Nozaki[10] was modified as follows. A soln of 40 g of **26** in 1 l of EtOH was cooled in an ice-bath and HCl and H_2S were led into the soln. After 8 hr most of the solvent was evaporated. The crude product was dissolved in hexane and washed with $NaHCO_3$ aq. Drying followed by distillation afforded 32 g (80%) of **4**.

2,5-Di-t-butyl-3,4-octamethylenethiophene (**8**) *starting from* **4**. A mixture of **4** (3·49 g; 18 mmole), t-BuCl, (5·55 g; 60 mmole), $SnCl_4$ (15·63 g; 60 mmole) and CS_2 (60 ml) was stirred for 16 hr. Work-up (addition of H_2O and CH_2Cl_2 followed by subsequent treatment of the organic layer with 10% HCl, H_2O and $NaHCO_3$ aq, drying of the organic layer on Na_2SO_4 and evaporation of the solvents) afforded 3·7 g of a mixture containing **14** (30%), **16** (57%) and **8** (12%) as the major components. This mixture, t-BuCl (27·8 g; 300 mmole), $SnCl_4$ (62·5 g; 240 mmole) and CS_2 (90 ml) were stirred for 1·75 hr. Work-up (*vide supra*) gave 3·12 g of an oil which solidified upon standing for a short time. Composition: **14** (8%), **16** (14%) and **8** (78%); yield of **8** 52%, corrected for **14** and **16**. Crystallization from MeOH/EtOH (2x) afforded 1·6 g of **8**, m.p. 95·5–96·5°. The preparation of the analytically pure sample gave some difficulties; crystallization from MeOH (3x) and sublimation (2x) gave m.p. 96–96·4°. (Found: C, 78·41, 78·66; H, 11·09, 11·12; S, 9·58, 9·72. Calcd for $C_{20}H_{34}S$: C, 78·36; H, 11·18; S, 10·46% MW (osm, C_6H_6): 306·2, 303·2; calcd 306·554). PMR (CCl_4): δ 2·67 (t, 4H) and δ 1·2–2·0 (30 H); the t-Bu signal at δ 1·40 (s) could not be integrated separately. UV (96% C_2H_5OH): λ_{max} 244 mμ (ϵ 9000). MS: *m/e* 306, $M^{+\cdot}$ (33%); 291 (100). CMR ($CDCl_3$): δ 142·6, 137·7, 34·9, 32·6, 28·9, 28·7, 26·6.

Compound **8**, *starting from* **11**. A mixture of **11** (120 mg; 0·62 mmole), CS_2 (1 ml), t-BuCl (1 ml) and $SnCl_4$ (1 ml) was stirred for 19 hr. Work-up (*vide supra*) afforded 120 mg of a dark-colored oil. GLC showed that **16** made out about 90% of the volatile part of the mixture. This oil (120 mg) was stirred with 1 ml of CS_2, 1 ml of t-BuCl and 1 ml of $SnCl_4$ for 2·5 hr. Work-up gave 130 mg of a slightly yellow oil, containing **16** and **8** in the ratio 1:2 next to minor amounts of impurities. Yield of **8** about 56% when corrected for **16**. Careful crystallization from MeOH/EtOH at low temp. afforded 30 mg (21%) of **8** (nearly pure, m.p. 92–94·5°) which was recrystallized from MeOH to give 25 mg, m.p. 94–94·5°. The IR was identical to the IR of **8** obtained earlier using **4** as the starting material. A 1 : 1 mixture of these samples showed no depression of m.p.

2,5-Dicarbomethoxy-3,4-octamethylenethiophene (**10a**). A mixture of DMSO (50 ml) and NaH (768 mg, 32 mmole) was heated for 50 min at 70° under N_2. After cooling to 20°, 50 ml dry C_6H_6 was added and the mixture was cooled to 3°. A soln of **9** (2·688 g; 16 mmole) and dimethyl thiodiacetate (3·026 g; 17 mmole) in 5 ml of C_6H_6 was added. The mixture was cooled for a few min with an ice-salt bath and stirred for another 40 min at 0°. Work-up afforded 2·5 g of an acid which was esterified with CH_2N_2 in ether. Crystallization from MeOH afforded 1·8 g (36%) of **10a**, m.p. 120–121°. After another three crystallizations the product was analytically pure, m.p. 129·5–130·5°. (Found: C, 62·17, 61·86; H, 7·25, 7·11; S, 10·06, 10·16. Calcd for $C_{16}H_{22}O_4S$: C, 61·91; H, 7·14; S, 10·33%). PMR ($CDCl_3$): δ 0·9–2·2 (m, 12H), δ 3·10 (t, 4H) and δ 3·90 (s, 6H); UV (96% C_2H_5OH): λ_{max} 286 mμ (ϵ 15000). MS: *m/e* 310, M^+ (100%).

3,4-Octamethylenethiophene (**11**). A mixture of **10a** (992 mg; 32 mmole), KOH (1000 mg) and EtOH (250 ml) was refluxed for 18 hr. The solvent was evaporated and 10% HCl was added to the residue. Filtration followed by drying gave 970 mg of the acid which was used without purification and characterization in the following step. A mixture of 970 mg of the acid, 25 ml quinoline and 250 mg Cu powder was refluxed for 2 hr. After cooling the Cu was separated from the soln and washed with hexane. The organic layer was washed several times with 10% HCl and dried.

Kugelrohr distillation (30 torr) afforded 600 mg (96%) of **11**, purity 95% according to GLC. The analytically pure sample was obtained with the aid of preparative GLC. (Found: C, 73·93, 74·16; H, 9·28, 9·14; S, 16·37, 16·52. Calcd for $C_{12}H_{18}S$: C, 74·17; H, 9·33; S, 16·50%) PMR (CCl_4): δ 0·95–2·15 (m, 12H), δ 2·75 (t, 4H) and δ 6·85 (s, 2H); UV (96% C_2H_5OH): λ_{max} 248 mμ (ϵ 6400). MS: *m/e* 194, M^+.

2-*Carbomethoxy*-3,4-*octamethylenethiophene* (**12**). The synthesis of **10a** was carried out as described above. Crystallization of the esterfied material afforded 990 mg of **10a** (m.p. 119–124°) and, after crystallization 415 mg of **12** (m.p. 60–62°). Recrystallization from MeOH gave analytically pure **12**, m.p. 63–65°. (Found: C, 66·09, 66·03; H, 8·00, 8·10; S, 12·47, 12·66. Calcd for $C_{14}H_{20}O_2S$: C, 66·63; H, 7·99; S, 12·70%). PMR ($CDCl_3$): δ 0·9–2·1 (m, 12H), δ 2·8 (t, 2H), δ 3·1 (t, 2H), δ 3·85 (s, 3H) and δ 7·20 (s, 1H); UV (96% C_2H_5OH): λ_{max} 265 mμ (ϵ 10700). MS: *m/e* 252, M^+.

Compound **12**, *starting from* **11**. Thiophene **11** (133 mg, 0·68 mmole) was dissolved in 10 ml ether, and 2 ml 2N n-BuLi was added. The soln was refluxed for 1 hr, cooled and added to an excess of solid CO_2/ether. Work-up gave the crude acid which was esterified with CH_2N_2 to give, after crystallization from MeOH, 122 mg (71%) of **12**, m.p. 62–64·5°. The PMR and the IR (more than thirty absorptions) were identical to the spectra of **12** obtained as described above.

5-*t*-*Butyl*|8|(2,4)*thiophenophane* (**14**). A mixture of **4** (5·04 g; 26 mmole), t-BuCl (16·65 g; 185 mmole), $SnCl_4$ (15·6 g; 60 mmole) and CS_2 (90 ml) was stirred magnetically. The reaction was followed by GLC and stopped by pouring on ice. In a typical run, a reaction time of 5 hr resulted in 5·1 g of an oil consisting of **4** (5%), **14** (67%), **16**, (17%) and **8** (12%). Distillation gave 4·4 g of a slightly yellow oil having about the same composition. The yield of **14** amounted to 59% (corrected for **4**, **16** and **8** and after distillation). In another run the reaction was stopped after 3 hr. Distillation gave 4·4 g of colorless material containing **4** (40%), **14** (53%), **16** (2%) and **8** (4%). In this case the corrected yield of **14** amounted to 58%. Purification of **14** was accomplished by preparative GLC. Since **14** can easier be separated from large amounts of **4** than from **16**, relatively short reaction times (2–3 hr) are recommended for the preparation of **14**. Analytically pure **14**, a colorless liquid, was obtained after a second purification (GLC). (Found: C, 76·94, 76·63; H, 10·42, 10·31; S, 12·84, 12·66. Calcd for $C_{16}H_{26}S$: C, 76·73; H, 10·46; S, 12·80%) PMR (100 MHz, $CDCl_3$): δ 6·76 (1H), δ 2·68 (4H), δ 1·4 (17H), δ 0·8 (2H) and δ 0·4 (2H); See also Fig. 2. The PMR strongly changed upon cooling; UV (96% EtOH): λ_{max} 246 mμ (ϵ 7100). MS: *m/e* 250, M^+ (41%); 235 (100); CMR ($CHCl_3$): δ 145·3, 137·4, 136·2, 131·6 (thiophene carbons); J_{C-H} 160 Hz (131·6). The sp^3 carbons and some peaks due to minor amounts of impurities are not mentioned.

2-*t*-*Butyl*-3,4-*octamethylenethiophene* (**16**), *starting from* **4**. A mixture of **4** (2·33 g; 12 mmole), $SnCl_4$ (10·42 g; 40 mmole), t-BuCl (3·70 g; 40 mmole) and CS_2 (25 ml) was stirred for 24 hr. Work-up (*vide supra*) afforded, after distillation, 2·24 g of a colorless oil which was analyzed by GLC. The mixture contained two compounds having about the same retention time as **4** (each amounted to 1%, the presence of **4** was neither proven, nor excluded), **14** (12%), **16** (74%) and **8** (12%). The yield of **16** amounted to 58% relative to **4**, and to 69% when corrected for the known byproducts. Purification was effected by crystallization from EtOH and elution on silicagel with pentane. In this way 1·6 g of distillate gave 890 mg of reasonably pure **16**. The analytically pure sample was obtained after crystallization from MeOH, m.p. 51–51·5°. (Found: C, 76·67, 76·44; H, 10·49, 10·39; S, 12·65, 12·72. Calcd for $C_{16}H_{26}S$: C, 76·73; H, 10·46; S, 12·80%). PMR (CCl_4): δ 6·67 (s, 1H), δ 2·70 (m, 4H) and δ 1·1–2·1 (21H, the t-Bu signal at δ 1·43 could not be integrated separately), UV (96% EtOH): λ_{max} 246 mμ (ϵ 7600). MS: *m/e* 250, M^+ (40%); 235 (100). CMR ($CHCl_3$): δ 148·5, 144·3, 135·1, 115·4 (thiophene carbons); J_{C-H} 180 Hz (115·4), J_{C-CH_2} 6 Hz. The sp^3 carbons are not mentioned.

Compound **16**, *starting from* **11**. A mixture of **11** (116 mg; 0·60 mmole), CS_2 (1 ml), t-BuCl (1 ml) and $SnCl_4$ (0·5 ml) was stirred for 4 hr. Work-up afforded a violet semi-solid containing **16** as the major component. Elution on silicagel (hexane) and preparative TLC (Al_2O_3, hexane) gave 80 mg of a colorless oil containing **16** and **8** in a 2 : 1 ratio as the major components (yield of **16** about 40%, when corrected for **8**). Preparative GLC gave 12 mg of **16** which afforded 5 mg, m.p. 50–51·5° upon crystallization from MeOH. The IR was identical to that of **16** prepared from **4**. A mixture of both samples did not show a depression of m.p.

Dimerization of cycloundecanone (**21**). A soln of neopentylmagnesiumbromide in 15 ml ether was prepared from 170 mg (7 mmole) Mg and 1057 mg (7 mmole) neopentylbromide. The soln was cooled to 0° and 840 mg (5 mmole) of **21** in 5 ml of ether was added. The mixture was stirred for 16 hr at room temp. and cooled again to 0°. Ice was added and then NH_4Cl aq. After addition of ether (50 ml), the organic layer was separated, dried and concentrated to give 801 mg of a white solid exhibiting no t-Bu absorption in the PMR. Crystallization from hexane (3×) gave the analytically pure sample, m.p. 139·5–141° (dec). (Found: C, 78·35, 78·45; H, 11·81, 11·87. Calcd for $C_{22}H_{40}O_2$: C, 78·51, H, 11·98%). IR (Nujol): 1695, 3550 cm^{-1}; MS: *m/e* 336, M^+ (8%), 318 (12), 168 (74), 55 (100).

1-*Neopentylcycloundecene* (**22**). A soln of neopentyllithium in pentane was prepared from 880 mg (127 mmole) of Li sand and 7·55 g (50 mmole) neopentylbromide. The soln was cooled to −80° and 6·2 g (37 mmole) of **21** was added. After stirring for 2 hr at room temp. the mixture was treated with ice. The organic layer was separated, dried and concentrated to give 8·1 g of a mixture containing **21** and the alcohol as the major components. This mixture was distilled from anhyd $CuSO_4$ (Kugelrohr, 150–180°, 30 torr) to give 6·8 g of a liquid containing **21** and **22** as the major products. Chromatography on silicagel (pentane) was carried out in order to remove the polar substances. There resulted 2·8 g of crude **22** which was purified by preparative GLC. (Found: C, 86·46, 86·07; H, 13·49, 13·50. Calcd for $C_{16}H_{30}$: C, 86·40; H, 13·60%). PMR (CCl_4): δ 0·8–2·6 (m), δ 0·88 (s), δ 5·1 (t) and δ 5·4 (t). Because of overlap of peaks no exact integration was determined. The ratio of the triplets in the vinylic region was about 4 : 1. MS: *m/e* 222, M^+ (9%), 166 (22), 151 (13), 57 (100) and several other fragments of a reasonable intensity.

Neopentylcycloundecane (**20**). A mixture of **22** (500 mg), 96% EtOH (50 ml), HOAc (20 ml) and 50 mg of Pt/C was shaken for 24 hr in a Parr apparatus (3 atu H_2). Work-up afforded 460 mg of **20**. The presence of residual **22** was not evident from the PMR. However, to be sure of the absence of trace quantities hereof, **20** was treated with O_3 in CH_2Cl_2. Work-up and chromatography (silicagel, hexane) gave 370 mg of **20**. The analytically pure sample was obtained by preparative GLC. (Found: C, 85·72, 85·45; H, 14·38, 14·15. Calcd for $C_{16}H_{32}$: C, 85·63; H, 14·37%). The PMR, IR, MS and GLC of this compound were identical to the corresponding of **20** obtained from **14** (see below).

Desulfurization of **14**. A mixture of **14** (1002 mg; 4 mmole), 6 g of Ra–Ni (W-2) and 250 ml of EtOH was refluxed for 60 hr. Work-up gave 624 mg (70%) of crude **20**. The PMR showed weak absorptions due to vinylic hydrogens. In order to remove the unsaturated material the crude **20** was treated with O_3 in CH_2Cl_2. Work-up gave an oil which was chromatographed on silicagel. With pentane 320 mg of **20** was obtained; with ether 400 mg of unidentified material (IR: C=O, OH) came from the column. Compound **20** was further purified by preparative GLC. IR (CCl_4): 1360, 1390, 1440, 1470, 2845, 2860, 2925 and 2950 cm^{-1}. PMR ($CDCl_3$, 100 MHz): δ 0·94, δ 1·15, δ 1·19 and δ 1·49. GLC: an equimolar mixture of the hydrocarbon obtained from **14** and the hydrocarbon obtained from **22** was used. Columns: UCW 98, 6 ft, 10%, 1/8": SE 30, 10 ft, 15%, 1/8". UCW 98, 50 ft Hi-Pack; Apiezon L, 12 ft, 10%, 1/8". Oven temp. 100–265°; retention time from a few minutes to several hr. In all cases only one peak could be detected. MS: except for one example, only peaks with *m/e* > 50 and with a relative intensity >1% are given; the second number between brackets gives the relative intensity of the corresponding peak in the MS of **20** derived from **22**. *m/e* 250 (0·3%, 0%), 235 (1, 0), 225 (2, 2), 224 (8, 10), 209 (2, 2), 181 (1, 1), 168 (4, 5), 167 (3, 3), 166 (8, 10), 153 (3, 3), 152 (1, 1), 151 (1, 2), 139 (1, 1), 125 (4, 4), 124 (1, 2), 123 (1, 1), 112 (2, 2), 111 (10, 11), 110 (3, 3), 109 (3, 3), 99 (1, 1), 98 (3, 3), 97 (22, 24), 96 (5, 6), 95 (6, 6), 91 (1, 1), 85 (7, 7), 84 (13, 14), 83 (28, 30), 82 (6, 6), 81 (7, 6), 79 (2, 2), 77 (1, 1), 71 (10, 11), 70 (28, 32), 69 (27, 28), 68 (5, 5), 67 (10, 10), 65 (1, 1), 58 (5, 4), 57 (100, 100), 56 (36, 41), 55 (40, 42), 54 (7, 7), 53 (5, 5).

Attempted reaction of **14** *with n*-BuLi. A mixture of **14** (48 mg), 1N n-BuLi in hexane (3 ml) and 15 ml dry ether was refluxed for 4·5 hr. The mixture was cooled and 1 ml of D_2O was slowly added. Work-up gave back **14**. According to PMR, little or no D incorporation has occurred.

Reaction of **16** *with n*-BuLi. A mixture of **16** (40 mg), 2N n-BuLi in hexane (2 ml), and 10 ml dry ether was refluxed for 1·5 hr. The mixture was cooled and 1 ml of D_2O was slowly added. Work-up gave back **16**. According to PMR, a virtually complete D incorporation has occurred.

Treatment of **4** *with* $SnCl_4$ *in* CS_2. A mixture of **4** (116 mg), CS_2 (2 ml) and $SnCl_4$ (0·1 ml) was stirred for 21 hr. About 1 ml of the mixture was removed from the flask and worked up. No isomerization was detected (GLC, IR, PMR). In a control experiment, 0·1 ml of t-BuCl was added to the remainder of the mixture. After stirring for 2·5 hr, **14** was the major component.

Treatment of **4** *with* H_2SO_4. A soln of **4** (170 mg) in 1·5 ml H_2SO_4 was stirred for 20 hr. Work-up gave a colorless oil (120 mg). GLC, IR and PMR were as expected for **4**. Some decomposition might have occurred.

Treatment of **8** *with* H_2SO_4. A soln of **8** (50 mg) in 0·5 ml H_2SO_4 was kept for 4 weeks at 5°. Work-up gave an oil, which contained, according to GLC, **16** as the major component and no **8**.

Treatment of **14** *with* $SnCl_4$ *in* CS_2. A mixture of **14** (34 mg), CS_2 (2 ml) and 4 drops $SnCl_4$ was stirred for 21 hr. According to GLC, no reaction occurred under these conditions.

Treatment of **8** *with* $SnCl_4$ *in* CS_2 *in the presence of* **4** *and* **14**. To a soln of **4** (57 mg), **14** (30 mg) and **8** (30 mg) in 1 ml CS_2 was added 0·1 ml of $SnCl_4$. The yellow soln was stirred for 12 hr; GLC showed that at most trace amounts of **16** had been formed. The soln was divided in two portions. To the first portion, 0·1 ml t-BuCl was added. After stirring for 24 hr, **16** was the major component in the mixture. To the second portion, 16 mg of **16** was added and the mixture was stirred for 24 hr. Although the amount of **16** was not accurately estimated, it was clear that the largest part of this compound was still present.

Bicyclo|8.2.0|*dodecanol* (**24**). A soln of **23** (50 g) (m.p. 59–61°, EGA) in 450 ml light petroleum 60–80 was irradiated for 24 hr (Q 700, quartz, no attempts were made to exclude O_2). The solvent was evaporated to give 50 g of a colorless oil. The IR showed the presence of small amounts of **23**. This crude material was used without purification in the following step.

1,4-*Cyclododecanedione* (**26**). Jones reagent[27] was added dropwise to a mechanically stirred soln of **24** (100 g) in 2 l acetone, cooled in an ice bath. When the orange color persisted for a few min, an excess of about 15% was added. After 30 min the ice bath was removed and stirring was continued for 1 hr. Most of the acetone was evaporated, ether and H_2O were added. Work-up gave a slightly green–yellow solid. Crystallization from hexane gave 59 g of pure **26**, m.p. 74–76° reported[21] 78–80°). Sometimes another crystallization was necessary to remove small amounts of **23**.

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