THIOPHENE CHEMISTRY—IX*

PREPARATION AND DEALKYLATION OF 5-SUBSTITUTED 2-t-BUTOXYTHIOPHENES†

H. J. JAKOBSEN, E. H. LARSEN and S.-O. LAWESSON Department of Organic Chemistry, Chemical Institute, University of Aarhus, Denmark

(Received 10 August 1963)

Abstract—Different substituents have been introduced into the 5-position of 2-t-butoxythiophene and by subsequent acid-catalyst dealkylation the corresponding hydroxythiophenes (or their different tautomeric forms) have been isolated in high yields. By NMR, IR and UV-spectroscopy the constitution and the composition of the different tautomeres have been determined. The reaction between carbonyl compounds and 5-t-butoxy-2-thiophenelithium gives carbinols, which upon heating with p-toluenesulphonic acid yielded 5-methylene-3-thiolen-2-ones.

INTRODUCTION

FROM the work of Lawesson and Frisell¹ a convenient method for the preparation of hydroxyaryls is known: The reaction of an aryl-Grignard reagent with a t-butyl perester gives the aryl t-butyl ether smoothly; isobutylene is split off by heating the ether with catalytic amounts of p-toluenesulphonic acid at about 150°, thus giving in high yields the corresponding hydroxyaryl. As the preparation of 2-hydroxythiophene was very promising, an investigation with heterocycles is underway to show in particular the generality of this reaction. This paper deals with the preparation of 2-thiophene t-butylethers with substituents in the 5-position, dealkylation studies of such ethers and determination of the constitution of the hydroxythiophenes formed.[‡]

Synthesis of ethers

In the thiophene series only two t-butyl-ethers were known. Lawesson and Frisell¹ prepared 2-t-butoxythiophene by the reaction of 2-thienylmagnesium bromide with t-butyl perbenzonate and Gronowitz² similarly prepared the 3-substituted ether.

In most of the ether syntheses described here, 2-t-butoxythiophene (I) has been used as starting material. By metalation of I with n-butyllithium 5-t-butoxy-2-thiophenelithium, II is obtained in high yield, which with different reagents yields a series of 5substituted 2-t-butoxythiophenes. Thus, II reacts with dimethylsulphate to give an 87% yield of 5-methyl-2-t-butoxythiophene (IIIa) and it reacts with allylbromide to give 5-allyl-2-t-butoxythiophene (IIIb) in 86% yield. For the introduction of the benzyl

* Part VIII. Jakobsen, H. J., Larsen, E. H. and Lawesson, S.-O., Rec. Trav. Chim. Pay-Bas 82, 791 (1963).

† Presented at the XIXth JUPAC Conference, July 10-17, London (1963).

[‡] For simplicity, the potential tautomeric compounds will be referred to as "hydroxy" without prejudice to the final conclusions.

¹S.-O. Lawesson and C. Frisell, Arkiv Kemi 17, 393 (1961).

* S. Gronowitz, Arkiv Kemi 16, 363 (1960).



group into an aromatic compound a convenient method is to treat the corresponding aryl Grignard reagent with benzyl chloride at 60-70° for some time.³ It has now been found that the coupling between benzyl chloride and II occurs smoothly in boiling ether and a 73% yield of 5-benzyl-2-t-butoxythiophene (IIIc) results. Probably this coupling reaction is general, although side reactions (formations of carbenes) may decrease the yields. Sulphur and dimethyldisulphide react with II yielding 5-mercapto-2-t-butoxythiophene (IVa) and 5-methylmercapto-2-t-butoxythiophene (IVb) respectively. The introduction of another t-butoxygroup into the 5-position of I is achieved by first adding anhydrous magnesium bromide to II, thus forming the Grignard reagent; the reaction with t-butyl perbenzoate then leads to 2,5-di-t-butoxythiophene (V). Treatment of II with Dry Ice yields 2-t-butoxy-5-thiophenecarboxylic acid (VIa) and the corresponding ethylester (VIb) was synthesized from II and ethyl chloroformate. Finally, 5-bromo-2-t-butoxythiophene (VII) was prepared from 2,5dibromothiophene, which after lithium-bromine interconversion and treatment with anhydrous magnesium bromide reacted with t-butyl perbenzoate to give VII.

$$Br \xrightarrow{C_{4}H_{9}Li} Br \xrightarrow{C_{4}H_{9}Li} Br \xrightarrow{S} Li \xrightarrow{Mg Br_{2}} Br \xrightarrow{S} Mg Br \xrightarrow{Mg Br}$$

.VII.

³ F. A. Vingiello, S. G. Quo and J. Sheridan, J. Org. Chem. 26, 3202 (1961).

Finally, II reacts with ketones and aldehydes yielding the corresponding carbinols (VIII).



Infrared absorption of crude VIII shows the presence of hydroxyl groups, but no pure products could be isolated as the compounds decompose during distillation.

Dealkylation of t-butylethers

Very few simple 2-hydroxythiophenes are known; they have been prepared either by oxidation of 2-thiophenemagnesium bromide (2-hydroxythiophene⁴) or through the action of phosphoroustri or pentasulphides with γ -carbonyl acids (2hydroxythiophene,⁵ 5-methyl-2-hydroxythiophene^{5,6}). Some hydroxythiophenes⁷ have also been prepared by oxidation of the corresponding thiopheneboronic acids. By the recent method¹ of dealkylation of t-butylethers, 2-hydroxythiophene has been obtained in high yields and similarly in this investigation the removal of isobutylene from 5substituted-2-t-butoxythiophenes was very smooth. In just one case, a well-defined product could not be isolated: 5-Bromo-2-t-butoxythiophene on dealkylation yields a mixture of products, which has not yet been investigated.

As the carbinols (VIII) could not be isolated in a pure state, they were heated to $150-160^{\circ}$ in the presence of catalytic amounts of *p*-toluenesulphonic acid and a smooth elimination of t-butanol was observed, (t-butanol was formed from isobutylene and water) and the corresponding methylene-3-thiolen-2-ones (IX) were isolated in high yields,



p - TS = p - toluenesulphonic acid

NMR-,* IR-† and UV-studies

2-Hydroxythiophene. This compound may exist in the tautomeric forms X- XII and it has been shown⁸ that it exists exclusively as 3-thiolen-2-one (XI) at room

* Solutions of about 15% hydroxythiophenes in carbon tetrachloride were used for NMR investigations; chemical shifts are all relative to TMS.

[†]IR spectra of the hydroxythiophenes were recorded in the pure (liquid of solid) state and in carbon tetrachloride solution.

- 4 C. D. Hurd and K. L. Kreuz, J. Amer. Chem. Soc. 72, 5543 (1950).
- ⁵ C. Mentzer and D. Billet, Bull. Chim. Fr. 12, 292 (1945).
- * W. Kues and C. Paal, Ber. Dtsch. Chem. Ges. 19, 556 (1886).
- ⁷ S. Gronowitz and A. Hörnfeldt: XIX*th JUPAC Conference* July 10-17 London (1963). Abstract A p. 123.
- ⁸ S. Gronowitz and R. A. Hoffmann, Arkiv Kemi 15, 499 (1960).



temperature. The NMR spectrum of 2-hydroxythiophene, prepared according to our method,¹ shows peaks at 453 cps (hydrogen 4), 374 cps (hydrogen 3) and 246 cps (CH₂ in position 5) with the relative intensities 1:1:2. The coupling constants obtained are $J_{34} = 6.0$ cps, $J_{4-CH_2} = 2.8$ cps, $J_{3-CH_2} = 2.0$ cps, all in good accordance with earlier obtained values.⁸ No peaks corresponding to another tautomer were observed.

In earlier IR studies of 2-hydroxythiophene,^{4,8} it was stated⁴ that the absorptions at 2.9 μ and 3.2 μ were due to hydroxyl and aromatic C—H linkages, respectively, of the tautomeric form X. (Our observed values were 3360 cm^{-1} and 3055 cm^{-1} respectively.) It is our opinion that the peak at 3360 cm^{-1} is the first overtone of the carbonyl stretching vibration, which is observed at 1682 cm^{-1} . This conclusion is substantiated by the following reasons: The ratio between the intensities (ϵ -values) of the carbonyl peak and the overtone is about 100 which is a reasonable value since it is well-known that this ratio for different carbonyl compounds lies in this region; the IR spectrum of the compound in a pure state shows a very sharp peak at 3360 cm⁻¹, which in the pure state should broaden due to hydrogen bonding if the hydroxyl group actually were present. The peak observed at 3055 cm⁻¹ is ascribed to C--H stretching vibrations of the ethylenic bond in XI and is not due to the aromatic C—H linkages in X. In addition peaks were observed at 2960 cm⁻¹ and 2910 cm⁻¹ which are indications of aliphatic C—H linkages and further a peak at 1605 cm⁻¹ is due to the C=C stretching vibrations. A strong band is recorded at 770 cm⁻¹, probably due to the C=C out-of-plane deformation vibrations.⁹

The UV spectrum of XI in ethanol is similar to that observed by Hurd and Kreuz⁴ $\lambda_{max} = 220 \text{ m}\mu (\log \epsilon = 3.9)$ and $\lambda_{max} = 263 \text{ m}\mu (\log \epsilon = 3.5)$.

5-Methyl-2-hydroxythiophene. According to Gronowitz and Hoffman⁸ this compound consists of about 85% 5-methyl-3-thiolen-2-one (XV) and about 15% 5-methyl-4-thiolen-2-one (XIV). No indications of the presence of XIII could be found.



It was found that the title compound, prepared according to our method, in equilibrium exists as a mixture of about 80% XV and 20% XIV. The same results were obtained when the NMR spectra were recorded 3 days or 3 months after the final distillation. Pure XIV was prepared by the base-extraction method;⁸ the NMR spectrum of XIV was recorded immediately after the final distillation and had three peaks with the relative intensities 3:2:1 with the shifts of the peaks 327 cps (hydrogen 4), 197 cps (CH₂ protons in position 3) and 126 cps (CH₃ protons). The coupling constants were $J_{CH_3-4} = 1.7$ cps, $J_{CH_3-CH_2} = 2.6$ cps and $J_{CH_3-4} = 2.6$ cps in

^{*} L. J. Bellamy: The Infra-red Spectra of Complex Molecules p. 48. London (1958).

accordance with known values.⁸ The solution of XIV in carbon tetrachloride, after standing at room temperature for 14 days, contained 78% XV and 22% X IV. The NMR spectrum of XV showed four peaks with the relative intensities 1:1:1:3, and the shifts of these peaks were 411 cps (hydrogen 4), 366 cps (hydrogen 3), 268 cps (hydrogen 5) and 75 cps (CH₃ protons). The coupling constants were $J_{34} = 5.9$ cps, $J_{35} = 1.9$ cps, $J_{45} = 2.5$ cps and $J_{CH_{2}-5} = 7.2$ cps.

Concerning the IR spectra of XV and XIV, which have been studied earlier,⁸ it is suggested as in the case of 2-hydroxythiophene, that no enol (XIII) is present but that the first overtone of the carbonyl stretching in the region for OH-stretching has earlier lead to some confusion. Thus XV shows a strong carbonyl band at 1687 cm⁻¹ and its overtone at 3370 cm⁻¹. The C—H stretching of the ethylenic bond occurs at 3048 cm⁻¹ and other C—H stretching frequencies are near 2968 cm⁻¹ and 2923 cm⁻¹, the C=C carbonyl conjugated stretching vibration frequency is close to 1605 cm⁻¹. A strong band probably due to the C—H out-of-plane deformation vibrations of the conjugated ethylenic bond⁹ is observed at 795 cm⁻¹.

The non-conjugated form XIV has the carbonyl frequency near 1722 cm^{-1} and its overtone is near 3438 cm^{-1} . The C=C stretching frequency is at 1630 cm^{-1} .

The UV spectrum of the equilibrium mixture (XIV + XV) in ethanol gives $\lambda_{max} = 220 \text{ m}\mu (\log \epsilon = 3.9); \ \lambda_{max} = 268 \text{ m}\mu (\log \epsilon = 3.5).$

5-Allyl-2-hydroxythiophene. Based on the NMR investigations this compound in equilibrium consists of about 85% XVIII and 15% XVII. The aromatic tautomer

$$H_{CH_2 = CH - CH_2} \xrightarrow{H} O \rightleftharpoons CH_2 - CH - CH_2 \xrightarrow{I} O H \rightleftharpoons CH_2 - CH - CH_2 \xrightarrow{I} O H$$

could not be detected. Compound XVIII could easily be transformed to XVII by dissolving in alkali, acidifying and extracting with ether. After 14 days in carbon tetrachloride the mixture consisted of 25% XVIII and 75% XVII.

The NMR spectrum of 5-allyl-3-thiolen-2-one (XVIII) shows seven peaks with the relative intensities 1:1:1:1:1:1:2 and the chemical shifts of the peaks are 444 cps, 369 cps, 344 cps, 311 cps, 299 cps, 267 cps and 153 cps. The peaks at 444 cps and 369 cps are ascribed to hydrogens 4 and 3 respectively; both peaks being split into quartets due to the coupling between hydrogen 3 and 4 and to the coupling of these hydrogens with hydrogen 5, the coupling constants are $J_{34} = 6.0$ cps, $J_{45} = 2.6$ cps and $J_{35} = 2.0$ cps. The peaks at 344 cps, 311 cps and 299 cps are each due to one of the vinyl protons of the allyl group and are without interest in this connection. The band at 267 cps is assigned to hydrogen 5 and consists of a triplet of triplets due to the coupling of hydrogen 5 to the 1'-CH₂ group with $J_{CH_{3}-5} = 7.0$ cps, and to the nearly equal coupling of hydrogen 5 to hydrogen 4 and hydrogen 3; $J_{45} = 2.6$ cps and $J_{35} = 2.0$ cps. The band at 153 cps is assigned to the 1'-CH₂ group with J_{CH_3-5} = 7.0 cps, and to the nearly equal coupling of hydrogen 5 to hydrogen 5 and consists of a triplet of triplets due to the coupling of hydrogen 5 to hydrogen 4 and hydrogen 3; $J_{45} = 2.6$ cps and $J_{35} = 2.0$ cps. The band at 153 cps is assigned to the 1'-CH₂ group and is a triplet due to nearly equal coupling to hydrogen 5 ($J_{CH_3-5} = 7.0$ cps) and to the 2'-proton ($J_{CH_3-CH} = 5.6$ cps); this triplet is further split due to coupling to the 3'-protons.

The NMR spectrum of 5-allyl-4-thiolen-2-one (XVII) shows six bands with relative intensities 1:1:1:1:2:2 and the shifts of these bands are 344 cps, 329 cps,

311 cps, 299 cps, 199 cps and 187 cps. The peaks at 344 cps, 311 cps and 299 cps are as for XVIII each due to one of the vinyl protons of the allyl group. The band at 329 cps is assigned to the ethylenic hydrogen 4 of XVII, and it consists of a triplet, which is due to the coupling to the CH₂ group in position 3, $J_{CH_3-4} = 2.5$ cps, each of the peaks within the triplet is further split into a triplet due to the coupling between hydrogen 4 and the 1'-CH₂ group, $J_{1C'H_3-4} - 4_1' = 1.5$ cps. The band at 199 cps is ascribed to the CH₂ group in position 3, and it consists of a quartet with the relative intensities of 1:3:3:1 within the band; this is due to equal coupling of the CH₂ protons (pos. 3) to the 1'-CH₂ protons and to hydrogen 4; $J_{CH_3-1'CH} = J_{CH_3-4} = 2.4$ cps. Finally the band at 187 cps is ascribed to the 1'-CH₂ protons, but it is badly resolved; it consists mainly of two peaks due to the coupling to the 2'-proton, and these peaks are further split, but no good resolution of the band could be obtained.

An IR investigation of the conjugated system 5-allyl-3-thiolen-2-one (XVIII) shows C=O stretching frequency at 1686 cm⁻¹, and a peak due to its first overtone at 3368 cm⁻¹. The C=C stretching frequency of the allyl-group (2'-3' double bond) is found at 1638 cm⁻¹ and the C=C stretching frequency of the ethylenic bond in the thiolactone ring occurs at 1607 cm⁻¹. The C-H stretching vibrations of the CH₂ = CH-group occurs in the expected¹⁰ region at 3081 cm⁻¹ and at 3005 cm⁻¹. A sharp shoulder at 3064 cm⁻¹ is ascribed to C-H stretching of the ethylenic bond of the thiolactone ring. C-H stretching frequencies are also found at 2979 cm⁻¹, 2930 cm⁻¹ and 2905 cm⁻¹. A broad band at 793 cm⁻¹ is probably due to the out-of-plane deformation of the CH=CH group in the lactone ring (compare with the analogous band of the spectrum of 5-methyl-3-thiolen-2-one, XV).

The IR spectrum of 5-allyl-4-thiolen-2-one (XVII) which was recorded immediately after isolation shows, as in the spectrum of 5-methyl-4-thiolene-2-one (XIV), a shift of the C=O frequency and of the thiolactone ring double bond frequency towards higher frequencies due to non-conjugation. The observed frequencies are: C=O at 1718 cm⁻¹ and its first overtone at 3428 cm⁻¹; C=C (thiolactone ring) at 1622 cm⁻¹; ethylenic C-H stretching at 3082 cm⁻¹ and 3008 cm⁻¹; C-H stretching at 2980 cm⁻¹ and 2892 cm⁻¹. The spectrum shows characteristic bands at 760 cm⁻¹ and at 715 cm⁻¹. The UV spectrum of the equilibrium mixture (XVIII + XVII) gives $\lambda_{max}^{\text{Ethanol}} = 220 \text{ m}\mu (\log \epsilon = 3.8), \lambda_{max}^{\text{Ethanol}} = 263 \text{ m}\mu (\log \epsilon = 3.6).$ UV spectrum of XVII gives $\lambda_{max}^{\text{Ethanol}} = 220 \text{ m}\mu (\log \epsilon = 3.6), \lambda_{max}^{\text{Ethanol}} 268 \text{ m}\mu (\log \epsilon = 3.2).$

5-Benzyl-2-hydroxythiophene. The NMR investigation of this compound shows that the equilibrium mixture contained about 70% 5-benzyl-3-thiolen-2-one, (XXI) and about 30% 5-benzyl-4-thiolen-2-one (XX).

$$\begin{array}{cccc} & & H \\ & & & \swarrow \\ & & & & \downarrow \\ & & &$$

It was not possible to transform XXI to XX by treatment with base, etc.: The mixture, investigated immediately after the distillation, consisted of about ¹⁰ Ref. 9: p. 43. 55% XXI and 45% XX. In the NMR spectrum of the equilibrium mixture the bands corresponding to XXI have the relative intensities 1:5:1:1:2, and the shifts of these bands (relative to TMS) are 434 cps, 428 cps, 364. cps, 271 cps, and 180 cps respectively. The bands at 434 cps and 364 cps are ascribed to hydrogens 4 and 3 respectively; both bands are split into quartets due to the coupling between hydrogen 3 and 4, $J_{34} = 6.0$ cps, and to the coupling of these hydrogens with hydrogen 5, $J_{45} = 2.5$ cps and $J_{35} = 1.9$ cps. The single peak at 428 cps is assigned to the phenyl protons; this peak contains also the resonance signal from the phenyl protons of the tautomer form XX. The broad band at 271 cps is ascribed to hydrogen 5; it consists of a triplet of tiplets due to coupling to the CH₂ group, $J_{CH_4-5} = 7.4$ cps and to the nearly equal coupling of hydrogen 5 to hydrogen 4 and hydrogen 3. The band at 180 cps consists of two lines and is ascribed to the CH₂ group; its coupling to hydrogen 5 is $J_{CH_{*}-5} = 7.4$ cps.

The bands of the NMR spectrum corresponding to the tautomer form XX have the relative intensities 5:1:2:2 and the shifts of the bands are 428 cps, 321 cps, 216 cps and 194 cps, respectively. The single peak at 428 cps is due to the phenyl protons. The band at 321 cps is ascribed to the ethylenic hydrogen 4; it is split into a triplet due to the coupling to the CH₂ group in positions 3, $J_{CH_2-4} = 2.4$ cps, and each of the lines within the triplet is further split into a triplet due to the coupling of hydrogen 4 to the 1'CH₂ group, $J_{1'CH_2-4} = 1.5$ cps. The band at 216 cps is ascribed to the 1'CH₂ group; the coupling to the CH₂ group (position 3) $J_{1'CH_2-CH_2} = 2.4$ cps causes a triplet, which is further split due to the coupling to hydrogen 4 $J_{1'CH_2-4} = 1.5$ cps; the picture of the band is almost like a quartet (1:3:3:1) due to the nearly equal coupling constants. Finally the band at 194 cps is assigned to the CH₂-group (position 3); it consists of a quartet (1:3:3:1) due to the equal coupling constants of the CH₂ protons ($J_{CH_2-1'CH_2} = J_{CH_2-4} = 2.4$ cps) to the 1'CH₂ protons and to hydrogen 4.

The IR spectrum of the equilibrium mixture of XXI and XX shows bands corresponding to both tautomeric forms. Only some of the bands corresponding to the form XXI can easily be determined, and the following characteristic frequencies for this tautomeric form are found: C=O stretching vibration at 1690 cm⁻¹ and its overtone at 3375 cm⁻¹; the C—C band of the thiolactone ring stretching at 1605 cm⁻¹; a strong band at 790 cm⁻¹, which may be the C-H out-of-plane deformation of the ethylenic bond. For the tautomeric form XX, the C-O stretching was found at 1722 cm^{-1} and its overtone at 3435 cm^{-1} . The C—C double bond of the thiolactone ring is stretching at 1625 cm⁻¹. Besides these characteristic bands the spectrum also shows the following sharp bands in the region of C-H stretching frequencies 3088 cm^{-1} , 3062 cm^{-1} and 3030 cm^{-1} all probably due to the aromatic part of the molecule; the weak absorption for the ethylenic C—H stretching is probably overlapped by these sharp bands. The bands, probably due to the C = C stretching of the aromatic double bonds are found at $1595 \,\mathrm{cm}^{-1}$, $1490 \,\mathrm{cm}^{-1}$ and at $1450 \,\mathrm{cm}^{-1}$ (the last band is partially overlapped by the CH_2 deformation band). The UV spectreum of the equilibrium mixture gives: $\lambda_{\max}^{\text{Ethanol}} = 216 \text{ m} \mu (\log \epsilon = 4.0); \ \lambda_{\max}^{\text{Ethanol}} = 268 \text{ m} \mu (\log \epsilon = 3.7).$

5-Methylmercapto-2-hydroxythiophene. The NMR spectrum of the equilibrium mixture of the tautomeric forms shows that this mixture contains 85% 5-methylmercapto-3-thiolen-2-one (XXIV) and 15% 5-methylmercapto-4-thiolen-2-one (XXIII).



Transformations of XXIV to XXIII also failed in this case: Only a mixture of 80% XXIV and 20% XXIII was obtained.

The NMR spectrum of the equilibrium mixture was investigated, and the bands corresponding to the form XXIV had the relative intensities 1:1:1:3 and the shifts of these bands are 434 cps, 371 cps, 326 cps and 118 cps, respectively. The bands at 434 cps, 371 cps and 326 cps are assigned to the hydrogen 4, 3 and 5 respectively. All bands are split into 4 lines due to the coupling of the hydrogen in question with two other hydrogen atoms; the coupling constants observed are $J_{34} = 5.9$ cps, $J_{45} = 2.8$ cps and $J_{35} = 1.8$ cps. The methyl groups show resonance at 118 cps, giving a single peak.

The spectrum also gives the bands corresponding to the tautomeric form XXIII and the relative intensities observed are 1:2:3, the shifts corresponding to these bands are 336 cps, 207 cps and 143 cps. The band at 336 cps, due to the ethylenic hydrogen 4, is split into a triplet due to the coupling with the CH₂ group, $J_{CH_2-4} = 2.8$ cps. The CH₂ resonance band at 207 cps is a doublet (coupling to hydrogen 4) and finally the CH₃ group appears as a single peak at 143 cps.

The IR spectrum of the equilibrium mixture shows bands due to both tautomeric forms, XXIV and XXIII. For the tautomer XXIV the following bands occur: The C=O stretching band occurs at 1697 cm⁻¹ and its first overtone at 3380 cm⁻¹, the C=C frequency is found at 1600 cm⁻¹. The corresponding frequencies for XXIII are 1725 cm⁻¹ and 1630 cm⁻¹. The C-H stretching of the ethylenic bonds of the thiolactones XXIV and XXIII occur at 3060 cm⁻¹ and 3030 cm⁻¹. C-H stretching frequencies are also found at 2985 cm¹ and 2920 cm⁻¹. A strong band at 795 cm⁻¹ is probably due to the C-H out-of-plane deformation vibration of the ethylenic bond of XXIV.

The UV spectrum of the equilibrium mixture (XXIV + XXIII) gives: $\lambda_{\max}^{\text{Ethanol}} = 220 \text{ m}\mu (\log \epsilon = 3.8); \lambda_{\max}^{\text{Ethanol}} = 263 \text{ m}\mu (\log \epsilon = 3.5).$

5-Carbethoxy-2-hydroxythiophene. The NMR spectrum of this compound in 10% carbon tetrachloride solution shows that it exists mainly in the aromatic (enol) form and consists of about 85% of the enol form (XXV) and 15% of XXVI. No peaks corresponding to the form XVII have been recorded.

ц.

The bands of the NMR spectrum corresponding to the form XXV have relative intensities 1:1:1:2:3 and the shifts of these bands are 572 cps, 443 cps, 366 cps, 255 cps and 81 cps, respectively. The band at 572 cps occurs as a single peak and is assigned to the hydrogen of the O—H group. The bands at 443 cps and 366 cps are both doublets and are ascribed to the hydrogens 3 and 4, $J_{34} = 4.2$ cps. The CH₂ group

of the C_2H_5 group occurs at 255 cps as a quartet and the CH₃ group at 81 cps as a triplet, $J_{CH_5-CH_5} = 7.1$ cps.

The bands of the spectrum corresponding to the form XXVI have the relative intensities 1:2:2:3 and the shifts of the bands are 402 cps, 255 cps, 213 cps and 76 cps. The band at 402 cps is assigned to the ethylenic hydrogen 4 and is split into a triplet owing to the coupling with the CH₂ hydrogens in position 3, $J_{CH_2-4} = 2.8$ cps. The band at 213 cps is assigned to the CH₂ hydrogens of position 3 and is split into a doublet ($J_{CH_2-4} = 2.8$) cps. The quartet at 255 cps and the triplet at 76 cps are due to the CH₂ and CH₃ group of the carbethoxy group, respectively.

Before discussing the IR spectrum of XXV it should be mentioned that the IR spectrum of the corresponding t-butyl ether shows absorption for C=O near 1700 cm⁻¹ and for aromatic C—C stretching near 1540 cm⁻¹. The IR spectrum of XXV has been of interest. In pure liquid state (before crystallization) it shows a broad band extending from 3500-3050 cm⁻¹ with maximum near 3200 cm⁻¹ (characteristic for bonded O_{H} groups). In the region for C_{H} stretching frequencies, a strong band near 1650 cm⁻¹ was observed and a less strong band could be seen near 1710 cm⁻¹. Bands in the C—C stretching region were observed near 1560 cm⁻¹ and 1540 cm⁻¹. These observatons are probably due to intermolecular hydrogen bonding between the O-H and C=O groups; this was confirmed by recording IR spectra of XXV in carbon tetrachloride solution at different concentrations. A 10% solution of XXV in carbon tetrachloride showed a broad band (3500-3050 cm⁻¹) with maximum near 3225 cm⁻¹. In the region for $C \rightarrow O$ two bands with nearly equal intensities were observed at 1710 cm⁻¹ and 1660 cm⁻¹. A 1% solution of XXV in carbon tetrachloride still showed a broad band (3500-3050 cm¹) with maximum at 3275 cm⁻¹. but now also a sharp band appears at 3580 cm⁻¹ due to free hydroxyl groups; the intensity of this band is much less than that of the bonded O-H groups. The C=O band at 1715 cm^{-1} is now much stronger than the band at 1660 cm^{-1} . In a 0.2% solution the bonded O-H band occurs at 3350-3500 cm⁻¹. The peak for free O-H groups at 3580 cm⁻¹ has increased in intensity relative to the bonded O-H band. The C=O band at 1715 cm⁻¹ is the only carbonyl band that can be observed. In a 0.04% solution the O-H bonded band has completely disappeared and the peak for free O-H is very weak; the C=O band occurs at 1717 cm⁻¹.

This indicates that by hydrogen bonding of the O—H group with the C=O group of the carbethoxy group the frequency of the C=O group is lowered from 1715 cm⁻¹ to 1660 cm⁻¹.

By breaking the intermolecular hydrogen bonding of XXV on dilution the ketoenol equilibrium is probably changed, but investigations in this direction have not been made. UV: $\lambda_{\max}^{\text{Ethanol}}$ 217, 240, 302 and 349 m μ (log $\epsilon = 3.7$, 3.6, 4.1 and 3.0).

5-Isopropylidene-3-thiolen-2-one. The proof of the structure XXVIII was fully



established by the NMR spectrum of the compound. It shows bands with the relative intensities 1:1:3:3. No bands corresponding to the tautomeric forms XXIX, XXX and

XXXI were observed. The shifts of the bands are 465 cps, 368 cps, 128 cps and 122 cps. The bands at 465 cps and 368 cps are both doublets and are ascribed to the ethylenic hydrogens of the thiolactone ring, $J_{34} = 6.0$ cps. By comparison with spectra of other α,β -unsaturated thiolactones, it may be concluded from the shifts that the band at 465 cps is due to hydrogen 4 and that the band at 368 cps is due to hydrogen 3. Each of the bands at 128 cps and 122 cps corresponds to one of the CH₃ groups.

The IR spectrum of XXVIII shows the C=O stretching frequency at 1677 cm⁻¹ lit.¹¹, 1675 cm⁻¹ and its overtone occurs at 3345 cm⁻¹. In the IR spectrum of the reaction product obtained by Biggerstaff and Stevens¹¹ they describe a strong band near 1725 cm⁻¹. The spectrum of pure XXVIII shows no band in that region and we believe that the observed band is due to the C=O group of acetone and not to the CH₂=HC(CH₃) group of the methyl ether of XXXI as suggested by the authors. C=C stretching frequencies of the ethylenic bonds of XXVIII are observed at 1615 cm⁻¹ and 1560 cm⁻¹. The C-H stretching frequency of the thiolactone double bond occurs as a weak band at 3065 cm⁻¹. Other C-H stretchings are found at 2980 cm⁻¹, 2912 cm⁻¹ and 2850 cm⁻¹. A strong band at 840 cm⁻¹ may be due to C-H out-of-plane deformation vibrations of the CH=CH bond. UV: $\lambda_{max}^{Ethanol} = 230 \text{ m}\mu (\log \epsilon = 3.5)$; shoulder near 281 m μ (log $\epsilon = 3.8$); $\lambda_{max}^{Ethanol} = 322 \text{ m}\mu$ (log $\epsilon = 4.1$).

5-Ethylidene-3-thiolen-2-one. The NMR spectrum shows only peaks corresponding to the structure XXXII. The spectrum has four bands with the relative intensities

XXXII

1:1:1:3 and the shifts of these bands are 447 cps, 376 cps, 370 cps and 120 cps. The bands at 447 cps and 370 cps are assigned to the hydrogens 4 and 3, respectively, and are both split into doublets, $J_{34} = 5.9$ cps. The bands at 376 cps is assigned to the hydrogen 1' and is split into a quartet owing to the coupling with the hydrogens of the CH₃ group, $J_{CH_3-CH} = 7.0$ cps. The doublet at 370 cps partly overlaps this quartet. The CH₃ resonance band at 120 cps is split into a doublet ($J_{CH_3-CH} = 7.0$ cps).

The IR spectrum of XXXII shows the following characteristic bands: The C=O group at 1688 cm⁻¹ and its first overtone at 3365 cm⁻¹; C=C stretchings occur at 1623 cm⁻¹ and 1560 cm⁻¹. =C-H stretching vibrations are seen at 3020 cm⁻¹, C-H stretchings also occur at 2965 cm⁻¹, 2935 cm⁻¹ and 2910 cm⁻¹ (all weak). UV: $\lambda_{\text{max}}^{\text{Ethanol}} = 222 \text{ m}\mu \text{ (log } \epsilon = 3.45);$ shoulder near at 232 m $\mu \text{ (log } \epsilon = 3.40);$ broad shoulder near 282 m $\mu \text{ (log } \epsilon = 4.38);$ $\lambda_{\text{max}}^{\text{Ethanol}} = 308 \text{ m}\mu \text{ (log } \epsilon = 4.44).$

5-Cyclopentylidene-3-thiolen-2-one. The NMR spectrum shows only bands corresponding to the structure XX. The bands have the relative intensities



XXXII

1:1:4:4 and the shifts are at 453 cps, 364 cps, 153 cps and 110 cps. The bands ¹¹ W. R. Biggerstaff and K. L. Stevens, J. Org. Chem. 28, 733 (1963). at 453 cps and 364 cps, which are due to the hydrogens 4 and 3, respectively, are split into doublets and the coupling constant is found to be $J_{34} = 5.8$ cps. The bands at 153 cps and 110 cps are each assigned to four hydrogens of the cyclopentylidene ring.

The IR spectrum of XXXIII shows the following absorptions: The C=O stretching vibrations at 1675 cm⁻¹ and its overtone at 3340 cm⁻¹; C=C stretchings at 1625 cm⁻¹ and 1560 cm⁻¹; =C-H stretching at 3055 cm⁻¹ and finally the C-H stretchings at 2960 cm⁻¹ and 2860 cm⁻¹.

UV: $\lambda_{\max}^{\text{Ethanol}} = 229 \text{ m}\mu \text{ (log } = 3.54); \text{ shoulder at } 239 \text{ m}\mu \text{ (log } \epsilon = 3.45); \text{ shoulder at near } 282 \text{ m}\mu \text{ (log } \epsilon = 3.85); \lambda_{\max}^{\text{Ethanol}} = 3.28 \text{ m}\mu \text{ (log } \epsilon = 4.13).$

5-Benzylidene-3-thiolen-2-one. In this compound, prepared by Hurd and Kreuz⁴ and by Biggerstaff and Stevens,¹¹ it appears that the structure is XXXIV.



These authors have studied the IR and UV spectra of XXXIV; and in addition we have also studied the NMR spectrum.

This spectrum contains four bands with the relative intensities 1:5:1:1 and the shifts of these bands are 456 cps, 443 cps, 418 cps and 375 cps respectively. The bands at 456 cps and 375 cps are assigned to the hydrogens 4 and 3, respectively, and both bands are split into doublets with the coupling constant $J_{34} = 5.9$ cps. The band at 443 cps is ascribed to the five protons of the phenyl ring. The single peak at 418 cps is ascribed to hydrogen 1'.

The IR spectrum of XXXIV shows the following absorptions: C=O stretching vibration at 1683 cm⁻¹ (lit. 1675 cm⁻¹) and its first overtone at 3360 cm⁻¹. C=C stretching vibrations (aromatic C=C skeletal in-plane vibrations) at 1590 cm⁻¹, 1489 cm⁻¹ and 1443 cm⁻¹. The spectrum also shows a sharp band at 1560 cm⁻¹. C=H stretching modes are found at 3060 cm⁻¹, 3023 cm⁻¹ and 3005 cm⁻¹.

UV: $\lambda_{\max}^{\text{Ethanol}} = 239 \text{ m}\mu (\log \epsilon = 3.9); \lambda_{\max}^{\text{Ethanol}} = 246 \text{ m}\mu (\log \epsilon = 3.9); \lambda_{\max}^{\text{Ethanol}} = 351 \text{ m}\mu (\log \epsilon = 4.3).$

2,5-Dihydroxythiophene. The NMR spectrum of the dealkylation product of 2,5-di-t-butoxythiophene shows only one single peak, observed at 182 cps. From this

XXXV

it may be concluded that the structure of the compound is XXXV. The same compound (thiosuccinic acid anhydride or 2,5-di-ketotetrahydrothiophene) was prepared earlier and its physical data are identical with those obtained by us for XXXV.

The IR spectrum of XXXV shows only one C—O stretching frequency in contrast to ordinary anhydrides which show two C—O absorptions bands (succinic acid anhydride absorbs at 1865 cm⁻¹ and at 1782 cm⁻¹). The C—O stretching frequency of XXXV occurs at 1715 cm⁻¹ and its overtone at 3450 cm⁻¹. C—H stretching vibration is found at 2922 cm⁻¹. UV: $\lambda_{max}^{Ethanol} = 222 \text{ m}\mu (\log \epsilon = 4.0)$. 5-Mercapto-2-hydroxythiophene. The NMR and IR spectra of 5-mercapto-2-tbutoxythiophene (IVa) show that this compound exists as such. After dealkylation the NMR spectrum showed that the fraction contained 90% 5-mercapto-2-hydroxythiophene and 10% 5-t-butylmercapto-2-hydroxythiophene (as 5-t-butylmercapto-3 (or/and 4)-thiolen-2-one). The NMR spectrum of 5-mercapto-2-hydroxythiophene showed only one peak at 195 cps which means that it exists exclusively as 2-keto-5thioketotetrahydrothiophene (XXXVI).

<u>IV X X X I</u>

The IR spectrum also confirms the structure XXXVI for 5-mercapto-2-hydroxythiophene. The SH stretching of IVa near 2510 cm⁻¹ has completely disappeared in the spectrum of XXXVI. It has the C=O stretching at 1735 cm⁻¹ and its overtone at 3470 cm⁻¹. A strong band at 1160 cm⁻¹ probably indicates the C=S stretching vibration which is generally found between 1200 and 1000 cm⁻¹.¹² C--H stretchings are observed at 2960 cm⁻¹, 2920 cm⁻¹ and 2860 cm⁻¹.

DISCUSSION

One of the main synthetic problems when studying keto-enol equilibrium in heterocyclic chemistry is the introduction of the hydroxyl group under such mild conditions that no destruction of the nucleus occurs. As the Grignard or lithium reagents are generally the starting materials in the so-called mild methods (for pertinent references, see Ref.¹) no substituents, which can react with organometallic reagents, may be introduced first. The limitation of these methods has been avoided by first preparing the t-butyl ether, then introducing the different substituents and finally eliminating isobutylene. Generally, high yields have been obtained.

From Table 1, where some of the results from the NMR investigations are recorded, is seen that a carbethoxy group in the 5-positions completely changes the character

R	R-SOH	R - S = 0	R S 0
CH3		20 %	80 %
СН ₂ =СН-СН ₂	······	15 🔏	85 %
С ₆ Н ₅ – С Н ₂		30 %	70 🔏
С Н ₃ — S		15 %	85 🔏
с ₂ н ₅ оос	85 %	15 %	

TABLE 1

¹² A. R. Katritzky: *Physical Methods in Heterocyclic Chemistry* Vol. II p. 220. New York and London (1963).

1878

Thiophene chemistry-IX

of the hydroxythiophene in that the aromaticity of the thiophene is maintained. The NMR spectrum was recorded on a 10% solution and unequivocal proof of the hydroxy-form was obtained. Studying the IR spectra at different concentrations revealed, however, the existence of intermolecular hydrogen bonding, which might account for the tautomer 5-carbethoxy-2-hydroxythiophene. Similar findings have recently been obtained on 3-actyl-2-hydroxyfuran.¹³ Further studies on similar types of hydroxythiophenes are being planned.

Quite recently a paper¹¹ appeared concerning 5-methylene-3-thiolen-2-ones, prepared according to the following scheme:

The corresponding diarylmethylene derivatives are obtained in high yields but dialkylmethylene- and aralkylmethylene derivatives are accessible in poor yields only. After dealkylation under drastic conditions the 5-benzylidene derivatives are obtained in low yields.

Independently of the studies by Biggerstaff and Stevens, we have studied similar reactions, starting from 5-t-butoxy-2-thiophenelithium, which then reacted with different carbonyl compounds. In all cases we found high yields of 5-methylene-3-thiolen-2-ones indicating that t-butoxythiophenes are convenient starting materials for the syntheses of hydroxythiophenes. General studies are in progress.

EXPERIMENTAL

2-t-Butoxythiophene was prepared according to Lawesson and Frisell.¹ The Grignard and lithium reagents were prepared under nitrogen. t-Butylperbenzoate from Light and Co. was used without further purification beyond drying (Na_2SO_4) . IR curves were recorded on a Perkin-Elmer model 221 spectrophotometer, UV spectra on a Perkin-Elmer model 137 UV spectrophotometer and the NMR spectra on a Varian A-60 spectrophotometer. Analyses were made by Dr. A. Bernhardt, Mülheim (Ruhr), Germany and by Dr. Ing. A. Schoeller, Kronach, Germany. B.ps. and m.ps. are uncorrected.

Preparation of 5-substituted 2-t-butoxythiophenes and 5-substituted 2-hydroxythiophenes

5-Methyl-2-t-butoxythiophene (IIIa). To a solution of 33 g (0.21 mole) 2-t-butoxythiophene in 75 ml ether, 160 ml 1.60N butyllithium (0.25 mole) was added without cooling during 15 min. The mixture which turned yellow-orange was gently refluxed for 2 hr until evolution of butane had ceased. The solution was cooled in ice-water and 29 g (0.23 mole) dimethyl sulphate in 75 ml ether was added dropwise. After stirring for 3 hr the reaction mixture was poured into ice water and the phases separated. The water phase was extracted with ether, the combined ether phases washed with water until neutral and dried (Na₂SO₄). After removal of the solvent the product was distilled (red. press.) and yielded 30.9 g (87%) 5-methyl-2-t-butoxythiophene as a colourless liquid, b.p. 77-78°/7 mm. $n_{D^0}^{20} = 1.4970$. (Found: C, 63.32; H, 8.05; Calc, C, 63.51; H, 8.29%).

¹³ R. E. Rosenkranz, K. Allner, R. Good, W. U. Philipsborn and C. H. Eugster, *Helv. Chim. Acta* 46, 1259 (1963).

5-Methyl-2-hydroxythiophene. In a 50 ml distillation flask, 27.4 g (0.16 mole) 5-methyl-2-tbutoxythiophene and 0.1 g p-toluenesulphonic was placed in an oil bath at 155° and evolution of isobutylene began at once. After 5-10 min gas evolution had ceased and the product was distilled (red. press.) while N₂ was drawn through the capillary. A fraction b.p. 78-81°/8 mm was collected. $n_D^{10} = 1.5320$, yield 17.0 g (93%). The product was redistilled after 1 hr giving a small fraction (1 g) b.p. 71-73°/8 mm, $n_D^{10} = 1.5290$, of 5-methyl-4-thiolene-2-one mixed with some of the tautomer 5-methyl-3-thiolene-2-one (lit⁸: for 97-98% pure 5-methyl-4-thiolene-2-one b.p. 65-66°/13 mm; $n_D^{10} = 1.5278$). The main fraction distilled at 79-80°/8mm; $n_D^{20} = 1.5340$; (lit⁸: for 92% pure 5-methyl-3-thiolene-2-one b.p. 89-91°/13 mm; $n_D^{30} = 1.5346$). A sample of this fraction was analyzed by NMR.

5-Methyl-4-thiolen-2-one (XIV). The rearrangement of the tautomer mixture of 5-methyl-2hydroxythiophene to 5-methyl-4-thiolen-2-one was carried out according to the known method.⁸ We obtained the b.p. 65-66°/13 mm, $n_D^{36} = 1.5249$. Spectra of this tautomeric form were recorded immediately after isolation.

5-Allyl-2-t-butoxythiophene (IIIb). 2-t-Butoxythiophene (33 g, 0.21 mole) in 50 ml ether was metallated with 180 ml 1.42 M (0.25 mole) butyllithium as in the preceding experiment. Allyl bromide (34 g, 0.28 mole) in 50 ml ether was added to the thiophene-lithium reagent during 15 min without cooling and the mixture heated under gentle reflux of ether overnight with stirring. It was then poured into water, the phases separated and the water phase shaken several times with ether. The combined extracts were washed neutral with water, dried (Na₂SO₄) and then concentrated. The residue was distilled *in vacuo* yielding 35.4 g (86%) 5-allyl-2-t-butoxythiophene; b.p. 61-63°/0.2 mm; $n_{10}^{30} = 1.5048$. (Found: C, 66.89; H, 8.23; Calc: C, 67.32; H, 8.22%).

5-Allyl-2-hydroxythiophene. 5-Allyl-2-t-butoxythiophene (34.7 g, 0.18 mole) was pyrolyzed in the presence of 0.1 g p-toluenesulphonic acid in an oil bath at 150-160° as in the preparation of 5-methyl-2-hydroxythiophene. Distillation gave a fraction of 5-allyl-2-hydroxythiophene, b.p. 59-60°/0.05 mm; $n_D^{00} = 1.5472$, yield 22.6 g (91%). Upon redistillation a small forerun, b.p. 50-57°/0.05 mm was observed. (Found: C, 59.39; H, 5.55; Calc; 59.99; H, 5.75%). A sample of the analyzed fraction was examined by NMR.

5-Allyl-4-thiolen-2-one (XVII). The rearrangement of the equilibrium mixture of the tautomer forms of 5-allyl-2-hydroxythiophene to 5-allyl-4-thiolen-2-one was carried out following the usual procedure. For 5-allyl-4-thiolen-2-one the b.p. was 54-55°/0.5 mm. $n_D^{50} = 1.5350$. Spectra were recorded immediately after isolation.

5-Benzyl-2-t-butoxythiophene (IIIc) 2-t-Butoxythiophene (23 g, 0.21 mole) was metallated with 0.25 mole butyllithium in ether in the usual way. Benzyl chloride (35 g, 0.28 mole) in 50 ml ether was added dropwise without cooling and the reaction mixture was gently refluxed overnight with stirring and worked up as described for 5-allyl-2-t-butoxythiophene. Distillation gave a fraction of 5-benzyl; 2-t-butoxythiophene, b.p. 112–114°/0.08 mm; $n_D^{s0} = 1.5541$, yield 37.5 g (73%). (Found: C, 72.37-H, 6.93; Calc: C, 73.14; H, 7.37%).

5-Benzyl-2-hydroxythiophene. 5-Benzyl-2-t-butoxythiophene (23.5 g, 0.096 mole) was pyrolyzed in an oil bath (150–160°) in the presence of 0.1 g p-toluene-sulphonic acid. When evolution of isobutylene ceased the product was distilled in an atm of N₁. 5-Benzyl-2-hydroxythiophene was obtained as an almost colourless liquid, b.p. 130–132°/0.3 mm; $n_D^{10} = 1.6075$, yield 16.6 g (91%). On standing, the refractive index decreases. (Found: C, 70.62; H, 5.43; Calc: C, 69.46; H, 5.30%).

5-Mercapto-2-t-butoxythiophene (IVa) 2-t-Butoxythiophene (33 g, 0.21 mole) was metallated using 195 ml 1.34M (0.25 mole) butyllithium in ether. Then the reaction flask was cooled in ice-water and 8 g (0.26 g atoms) sulphur was added to the mixture in 3 portions over a period of 3 min. After stirring $\frac{1}{2}$ hr at 0° the mixture was poured into ice-water and the phases separated. The water-phase was acidified and extracted with ether; the combined ether phases were extracted with 2N NaOH aq; the basic extracts were acidified under cooling with ice and then extracted with ether. The combined ether extracts were finally washed neutral with water and dried (Na₂SO₄). The ether was removed and the residue fractionated giving the main fraction at 59–61°/0·1 mm; $n_{10}^{20} = 1.5485$, yield of 5mercapto-2-t-butoxythiophene was 29.0 g (73%). (Found: C, 50.03; H, 6.14; Calc: C, 51.06; H, 6.43%).

5-Mercapto-2-hydroxythiophene. 5-Mercapto-2-t-butoxythiophene (25.7 g, 0.14 mole) was pyrolyzed in the presence of 0.1 g p-toluenesulphonic acid and the product was distilled under N_a immediately after the gas evolution had ceased. The main fraction, b.p. 67-71°/0.3 mm, was

obtained as a red-orange liquid. Redistillation gave b.p. 67-69°/0.3 mm; $n_D^{20} = 1.6520$, yield 11.8 g.

The main fraction always contained about 10% of 5-t-butylmercapto-3 (or/and 4)-thiolen-2-oneand a pure product for analysis could not be obtained.

5-Methylmercapto-2-t-butoxythiophene. (IVb). To an ether solution of 5-lithium-2-t-butoxythiophene [prepared from 33 g (0.21 mole) 2-t-butoxythiophene and 165 ml 1.58M (0.26 mole) butyllithium] 25.4 g (0.27 mole) dimethyldisulphide in 100 ml ether was added. The mixture was stirred 3 hr and then poured into water. The phases were separated and the water phase extracted with ether; the combined ether phases were extracted 4 times with 2N NaOH aq, washed neutral with water and dried (Na₂SO₄). Distillation gave a main fraction, b.p. 68-69°/0.2 mm; $n_D^{s0} = 1.5426$, yield 36.6 g (87%). (Found: C, 52.30; H, 6.82; Calc: C, 53.46; H, 6.98%).

5-Methylmercapto-2-hydroxythiophene. 5-Methylmercapto-2-t-butoxythiophene (30 g, 0.15 mole) was pyrolyzed in the presence of 0.1 g p-toluenesulphonic acid at 150–160°, and then the product was distilled immediately, b.p. 70–72°/01 mm; $n_D^{10} = 1.6040$, yield 13.8 g (63%). (Found: C, 41.13; H, 4.11; Calc: C, 41.10; H, 4.14%).

5-Ethylidene-3-thiolen-2-one. 2-t-Butoxythiophene (33 g, 0.21 mole) was metallated with butyllithium (0.25 mole) in ether following the usual procedure. Acetaldehyde (9.3 g, 0.21 mole) in 50 ml ether was added dropwise to the cooled solution during $\frac{1}{2}$ hr. The mixture was then stirred for 2 hr at room temp and thereafter poured into water. The phases were separated, the water phase extracted with ether, the combined ether extracts washed with water until neutral and dried (Na₂SO₄). The solution was concentrated and distillation gave a fraction, b.p. 96–98°/0.3 mm. The IR spectrum showed bands corresponding to hydroxyl, carbonyl, ethylenic and aromatic double bonds and t-butyl group showing that the fraction consisted of a mixture of 5-ethylidene-3-thiolen-2-one and 2-t-butoxy-5-(1' ethanol)-thiophene. The fraction was then immediately pyrolyzed with *p*-toluenesulphonic acid at 150–160° and a fraction consisting of t-butanol distilled from the flask during the pyrolysis. When the elimination was complete (5-10 min) the product was distilled and gave a main fraction, b.p. 58–60°/0.1 mm of 5-ethylidene-3-thiolen-2-one which crystallized. Recrystallization from ethanol-water gave white plates, m.p. 47–49°. The crystals turned red on standing, yield 15.0 g (57%) (based on 2-t-butoxythiophene). (Found: C, 56.85; H, 4.77; Calc. C, 57.14; H, 4.80%).

5-Benzylidene-3-thiolen-2-one. 2-t-Butoxythiophene (16 g, 0·10 mole) was metallated with butyllithium (0·12 mole) in ether and to the solution 12·8 g (0·12 mole) benzaldehyde in 30 ml of ether was added dropwise. After stirring for 3 hr, the reaction mixture was worked up as in the preceding experiment. Pyrolysis in a beaker with p-toluenesulphonic acid gave 15·3 g (81%) crude product. Purification on an aluminium oxide column and recrystallization from ethanol gave beautiful light yellow needles, m.p. 97–98·5° (lit. m.p. 97·5–98·5°). (Found: C, 70·22; H, 4·33; Calc: C, 70·21; H, 4·29%).

5-Isopropylidene-3-thiolen-2-one. 2-t-Butoxythiophene (33 g, 0.21 mole) in 75 ml ether was metallated with 0.25 mole butyllithium. The lithium reagent was cooled in ice-water and 16 g (0.28 mole) acetone in 50 ml ether was added during 15 min. The mixture was stirred for 4 hr and then worked up as usual. After pyrolyzing with p-toluenesulphonic acid, the product was distilled *in vacuo*, b.p. 76–78°/0.2 mm. The product crystallized and after recrystallization from ethanol gave white crystals, m.p. 61.5–63°, yield 24.0 g (82%). (Found: 60.17; H, 5.77; Calc: C, 59.99; H, 5.75%).

5-Cyclopentylidene-3-thiolen-2-one. 2-t-Butoxythiophene (17 g, 0.11 mole) was metallated with 0.13 moles butyllithium and 12.6 g (0.15 mole) cyclopentanone in 30 ml ether was added dropwise at about 0°. After stirring for 2 hr the mixture was worked up as usual. Pyrolysis with p-toluene-sulphonic acid of the tertiary alcohol in a beaker gave a crystalline product, yield 14.5 g (80%). Recrystallization from ethanol gave grey-white crystals, m.p. 121.5–122.5°. (Found: C, 64.88; H, 6.31; Calc: C, 65.05; H, 6.07%).

2,5-Di-t-butoxythiophene (V). 2-t-Butoxythiophene (33 g, 0.21 mole) was metallated with 0.25 mole butyllithium in ether. To the lithium reagent, an ethereal solution of anhydrous MgBr₁ (prepared by dropping 43 g (0.27 mole) Br₂ to 10 g (0.41 g atoms) Mg in 200 ml of anhydrous ether) was added. After stirring for $\frac{1}{2}$ hr, 0.20 mole t-butylperbenzoate in 50 ml ether was added dropwise to the Grignard reagent at 0° and stirred overnight. It was then poured into ice water and the complex dissolved by adding conc HCl. The acidic water phase was extracted with ether and the combined ether phases extracted with 2N NaOH aq. to remove benzoic acid (23 g crude benzoic acid was obtained by

acidifying the basic extract), and finally washed neutral with water and dried (Na₂SO₄). The ether was removed and the residue fractionated *in vacuo*. The main fraction, b.p. 74–76°/0·2 mm, crystallized on standing. Recrystallization from alcohol gave fine white crystals, m.p. 38·0–39·5°, yield 35·5 g (78%). (Found: C, 63·15; H, 8·74; Calc: C, 63·13; H, 8·83%).

2,5-Dihydroxythiophene. 2,5-Di-t-butoxythiophene (28 g, 0.12 mole) in a distillation flask was pyrolyzed at 150–160° in the presence of 0.1 g p-toluenesulphonic acid. The product was distilled at once under N₂ and gave a main fraction that immediately crystallized, b.p. 58–63°/0.15 mm. n_{2}^{10} = 1.5430. Recrystallization from ethanol gave white crystals, m.p. 30–31°, yield 11.9 g (83%). (Lit. m.p. 31° for thiosuccinic acid anhydride). (Found: C, 41.32; H, 3.71; Calc: C, 41.39; H, 3.47%).

5-Bromo-2-t-butoxythiophene. To 60.5 g (0.25 mole) 2,5-dibromothiophene in 150 ml ether cooled to 70°, 185 ml 1.42 M (0.26 mole) butyllithium in ether was added during 45 min; 0.30 moles anhydrous MgBr₂ in ether was added rapidly and the mixture stirred at room temp for $\frac{1}{2}$ hr; 0.21 mole t-butylperbenzoate in 50 ml ether was added dropwise to the Grignard reagent cooled to 0°. After stirring 1 hr, the reaction mixture was worked up as described for 2,5-di-t-butoxythiophene. The ether was removed and the residue distilled under N₂ giving 5-bromo-2-t-butoxythiophene as a light yellow liquid, b.p. 57-59°/0.2 mm, Redistillation gave b.p. 52-53°/0.08 mm. $n_D^{20} = 1.5340$, yield 39.0 g (79%). (Found: C, 41.45; H, 4.80; Calc: C, 40.88; H, 4.72%).

5-Carbethoxy-2-t-butoxythiophene (VIb). 2-t-Butoxythiophene (29 g, 0.186 mole) was metallated with 0.22 mole butyllithium in ether by the usual procedure. The organolithium reagent was added dropwise to 33 g (0.30 mole) ethyl chloroformate in 80 ml ether under cooling in an ice-water bath and the mixture stirred at room temp overnight. Water (100 ml) saturated with Na₂CO₃ was added and the mixture worked up by extracting the water phase with ether: the combined ether extracts were washed neutral and dried (Na₂SO₄). Distillation gave the main fraction of 5-carbethoxy-2-t-butoxythiophene, b.p. 90–92°/0·1 mm. $n_D^{20} = 1.5145$, yield 19·2 g (46%). (Found: C, 57·83; H, 7·11; Calc: C, 57·88; H, 7·07%).

5-Carbethoxy-2-hydroxythiophene. 5-Carbethoxy-2-t-butoxythiophene (14·4 g, 0.063 mole) was pyrolyzed in the usual way and then immediately fractionated under N_2 , b.p. 95–97°/0·1 mm, yield 9·7 g (89%). On standing overnight in a refrigerator the fraction crystallized, recrystallization from benzene gave colourless plates, m.p. 66–67.5°. (Found: C, 48·91; H, 4·61; Calc: C, 48·84; H, 4·68%).

2-t-Butoxythiophene-5-carboxylic acid (VIa). 2-t-Butoxythiophene (33 g, 0·21 mole) was metallated with 0·25 mole butyllithium in ether. The mixture was cooled and poured on solid CO_2 covered with ether. After the Dry Ice had evaporated the mixture was hydrolyzed with water. The water phase was acidified with dil HCl and extracted with ether. The combined ether layers were extracted with dil NaOH. Upon acidification of the alkaline solution a white powder precipitated. Recrystallization from methanol-water gave small fine plates, m.p. 114–116°, yield 32 g (75%). (Found: C, 54·03; H, 6·06; Calc: C, 53·99; H, 6·04%).

Acknowledgements—Our thanks are due to Professor Hakon Lund for his interest in this investigation and to Dr. J. Eggers for helpful discussions. Acknowledgements are also expressed to Dr. John Rastrup-Andersen and Miss E. Cruse for help with the NMR-investigation and to Mrs. S. Andersen for recording the IR spectra. Grants were obtained from Statens Almindelige Videnskabsfond and from Lucidol Division, Wallace and Tiernan, Inc., Buffalo, N.Y., U.S.A.