A STUDY OF THE SYNTHESIS AND REARRANGEMENT OF B-HYDROXY ALKYL ARYL SULFIDES, HETEROCYCLIC SULFIDES, AND PHENYL ETHERS

Thesis for the Degree of M. S.

MICHIGAN STATE COLLEGE

Frederick J. McCarty

1953

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By

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A THESIS

Submitted to the School of Graduate Studies of Michigan
State College of Agriculture and Applied Science
in partial fulfillment of the requirements
for the degree of

MASTER OF SCIENCE

Department of Chemistry

1953

12-4-53
8

ACKNOWLEDGMENT

The author wishes to express his sincere appreciation to Professor R. D. Schuetz for his guidance and encouragement throughout the course of this work.

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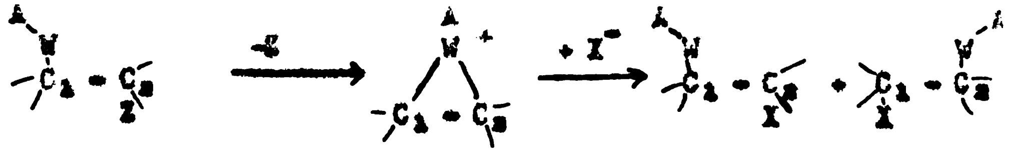
INTRODUCTION

During the past decade, extensive chemical research has been undertaken with the object of elucidating the role of neighboring groups in displacement and rearrangement reactions, particularly those involving a so-called 1,2-shift. In a formal sense, many such transformations can be expressed by the general equation

$$A-W-C_\alpha-C_\beta-Z + X^- \longrightarrow X-C_\alpha-C_\beta-W-A + Z^-$$

Here the group AW which was originally attached to C_α migrates to an adjacent atom, C_β. The above equation is not intended to describe in any way the true mechanism of the rearrangement, but merely to express as simply as possible the significant structural changes involved in such a displacement-rearrangement reaction.

The presently accepted mechanism in these reactions can be formulated as follows

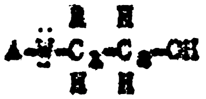


I II III

This involves the participation of the group $A\ddot{W}$ (neighboring Z) in the displacement of Z to yield the cyclic intermediate, II, which on opening yields the product III. The participating group $A\ddot{W}$ may be of the type where W is a hetero atom such as O, N and S, while A may be an alkyl or aryl group. The intermediate II will then be an oxonium, immonium or sulfonium ion.

The important implications of such a mechanism has to do with the stereochemistry of the over-all displacement process. In the formation and opening of the cyclic intermediate a Walden inversion occurs in each step and as a result two such inversions are involved in going from I to III.

The investigation herein reported was undertaken to study some additional cases of displacement-rearrangement reactions involving aromatic and heterocyclic hydroxy sulfides and aromatic hydroxy ethers. These compounds can be represented by the general formula



$$A-\underset{\cdot\cdot}{\overset{\cdot\cdot}{W}}-\underset{H}{\overset{R}{C}}_1-\underset{H}{\overset{H}{C}}_2-OH$$

In the present study, $-\underset{\cdot\cdot}{\overset{\cdot\cdot}{W}}-$ represents either oxygen or sulfur, A is either phenyl, β-naphthyl or 3-thienyl and R was one of three alkyl groups, namely, methyl, ethyl or n-propyl. A systematic attempt was made to determine the effect of variations in A, $\underset{\cdot\cdot}{\overset{\cdot\cdot}{W}}$, and R on the displacement-rearrangement reaction when the hydroxyl group in alcohols of the above general type is replaced by chlorine.

In the present work no attempt has been made to study the actual mechanism of the reaction involved, but only that rearrangement does or does not occur and to what extent.

HISTORICAL

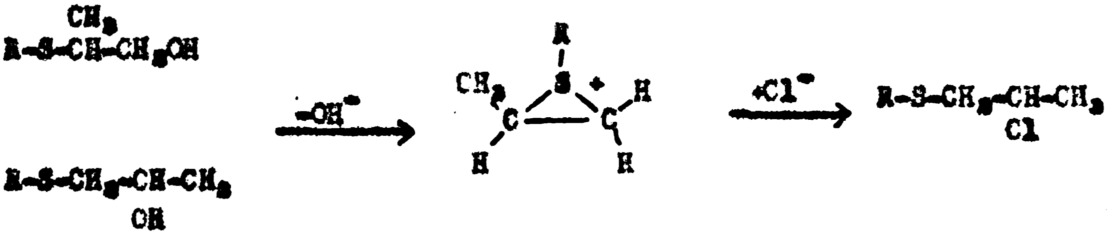
It has been reported recently (2) that when 2-hydroxyethyl-2-hydroxyisopropyl sulfide, $HO-CH_2-CH_2-S-CH(CH_3)-CH_2OH$, is treated with hydrogen chloride to replace the hydroxy group by chlorine,

$$HO-CH_2-CH_2-S-\overset{CH_3}{CH}-CH_2OH \xrightarrow{HCl} Cl-CH_2-CH_2-S-CH_2\underset{Cl}{CH}-CH_3$$

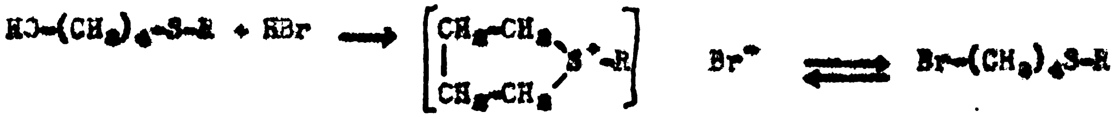
a rearrangement occurs to yield 2-chloroethyl-2-chloro-n-propyl sulfide. That this reaction may be a specific example of a general phenomena was indicated by experiments with ethyl-2-hydroxyisopropyl sulfide and ethyl-2-hydroxy-n-propyl sulfide. These compounds when treated with hydrochloric acid or thionyl chloride resulted in the same product, namely, 2-chloro-n-propyl ethyl sulfide.

$$\begin{matrix} CH_3CH_2-S-\overset{CH_3}{C}HCH_2OH \\ CH_3CH_2-S-CH_2-\underset{OH}{CH}-CH_3 \end{matrix} \xrightarrow[\text{or } SOCl_2]{HCl} CH_3CH_2-S-CH_2-\underset{Cl}{CH}-CH_3$$

The migration of the thioethyl group to the terminal carbon of the propyl group results in the conversion of an isopropyl to a n-propyl structure. This rearrangement can be explained by assuming that nucleophilic replacement reactions in β-hydroxy sulfides of the above type probably occur through a cyclic sulfonium intermediate.

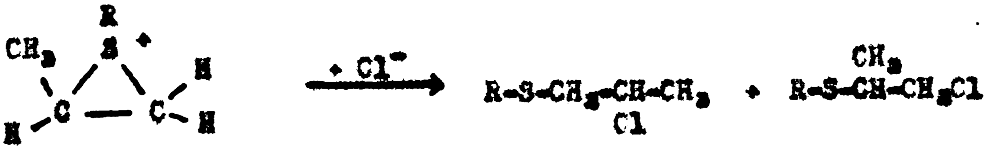


Bennett (3) cites evidence for such a mechanism in his studies on the velocity of the reaction between hydrobromic acid and ω-hydroxy sulfides of varying chain length in which there was observed an extremely high reaction rate when the hydroxyl group was separated from the sulfur atom by four carbon atoms, as in $HO-(CH_2)_4-S-R$. The abnormal reactivity of such sulfides was explained as being due to the ease with which the sulfur atom and the $-CH_2OH$ group could approach one another which could result in a cyclic sulfonium salt as an intermediate.



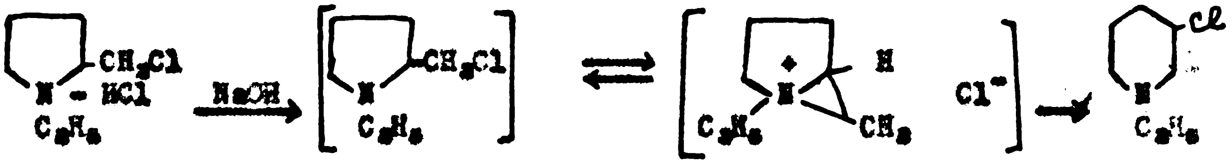
An extension of Bennett's cyclic sulfonium ion intermediate to the replacement of the hydroxyl group by a halogen in β-hydroxy sulfides finds strong support in the theory developed by Winstein and his collaborators in a series of papers (4) to account for the observed stereochemical relationships in certain nucleophilic replacement reactions.

In the nucleophilic attack of the cyclic sulfonium ion intermediate, resulting when ethyl 2-hydroxyisopropyl sulfide is treated with hydrogen chloride, the ring could theoretically be broken on either side of the sulfur atom resulting in the formation of a mixture of two isomeric chloro compounds.



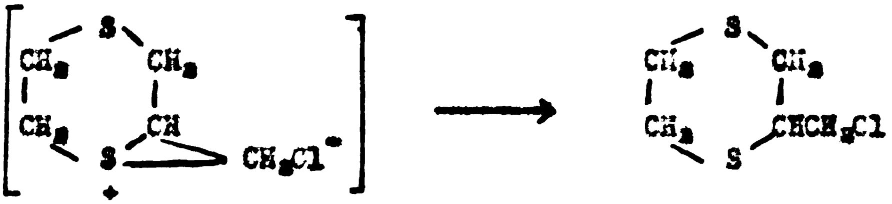
Further, it is conceivable that the two isomeric chloro compounds could occur together as an equilibrium mixture, in which case the isolation of either of them in a pure state might be quite difficult or impossible. However, in the cases cited thus far, the 2-chloroisopropyl sulfides, if formed at all, are themselves intermediates.

Certain 1,2-dialkylaminochloropropanes, nitrogen analogs of the sulfur compounds, have been observed (5) to undergo a similar rearrangement involving the intermediate formation of ethylene immonium compounds. By the use of this type of rearrangement in the nitrogen series it has been possible to effect ring enlargement; 1-ethyl 2-chloromethylpyrrolidine having been found to isomerize to 1-ethyl-3-chloropiperidine (6).



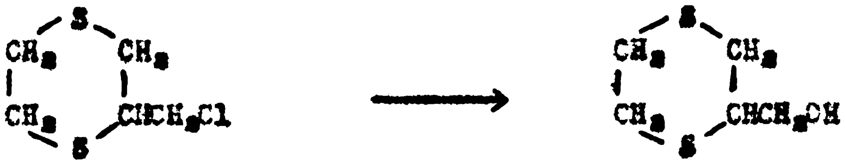
An attempt has been made to carry out a similar ring expansion in the sulfur series, but in the one example so far studied (7), ring contraction occurred instead of ring enlargement. Treatment of 6-hydroxy-1,4-dithiacycloheptane (I) with thionyl chloride in chloroform produced 2-chloromethyl-1,4-dithiane (IV).

(1) (II)



(III) (IV)

It is believed that the 6-chloro-1,4-dithiacycloheptane (II), if formed rearranges to give the bicyclic sulfonium ion intermediate (III). The isomerization of the n-propyl structure to the isopropyl has also been observed in the reactions of 1-dialkylamino-2-chloropropanes (8,9). Hydrolysis of distilled 2-chloromethyl-1,4-dithiane (IV), afforded a 41% yield of the corresponding hydroxy sulfide (V), no other product being isolated.



(IV) (V)

Hence, in this example, a reverse rearrangement of the isopropyl to the n-propyl structure did not occur.

Some observations recorded in the literature (10,11) indicate that the isomerization of the isopropyl structure to the n-propyl structure, encountered in open chain alkyl β-chlorosulfides, may not occur if an aryl group is attached to the sulfur atom. In order to determine whether the presence of an aryl group would prevent rearrangement, Fuson and Koehneke (12) studied the reaction of 2-hydroxyisopropyl phenyl sulfide (VI) with thionyl chloride which resulted in the formation in 63% yield of the rearranged product, 2-chloro-n-propyl phenyl sulfide (VII) instead of 2-chloroisopropyl phenyl sulfide (VIII).

$C_6H_5-S-CH(CH_3)-CH_2OH$

(VI)

$C_6H_5-S-CH_2CH(Cl)CH_3$

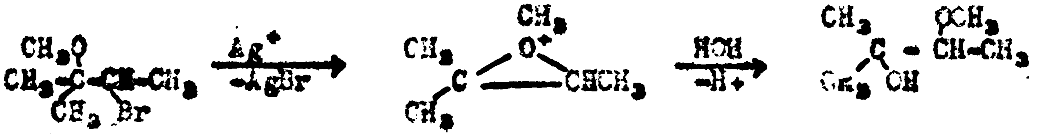
(VII)

$C_6H_5-S-CH(CH_3)-CH_2-Cl$

(VIII)

Thus it has been shown that a phenyl group does not prevent participation of the sulfur atom, to which it is attached, in the nucleophilic displacement of the hydroxyl group with chlorine.

One might expect that in the oxygen analogs of the compounds discussed above, the oxygen atom, which becomes the neighboring group, would be capable of participating in the nucleophilic displacement of an adjacent hydroxyl group. A recent article by Winstein and Ingraham (13) does support this expectation, at least in the case where a methyl group is attached to the oxygen atom. These authors have conducted experiments involving the solvolysis of 2-methyl-2-methoxy-3-bromobutane (XI) to give 3-methoxy-2-methyl-2-butanol (XIII).



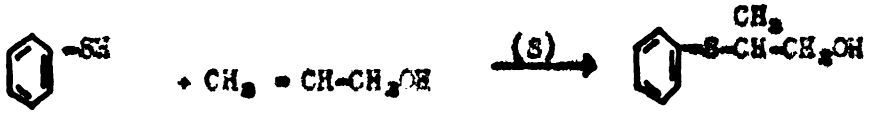
(XI) (XII) (XIII)

Participation of the neighboring methoxyl group to form the intermediate ethylene oxonium ion (XII) easily accounts for its migration. Ions of this type represent structures which are usually preferentially displaced

or opened at the most alkyl substituted carbon atom following an attack by a nucleophilic ion.

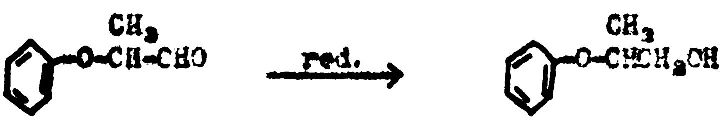
The first concern of this investigation was to find suitable synthetic methods for the preparation of the compounds which were required for a study of the rearrangement of the β-hydroxy sulfides and ethers. A literature search was made in order to find reactions which could be adapted to the preparation of the desired compounds and those which proved to be of some value to the over-all synthetic scheme will be discussed.

The addition of mercapto compounds to olefins is known to proceed according to Markovnikov's rule in the presence of sulfur (14), and thus constitutes a general method of synthesis of β-hydroxy sulfides. Fuson and Koebenke (12) have applied this method to the preparation of 2-hydroxyisopropyl phenyl sulfide.

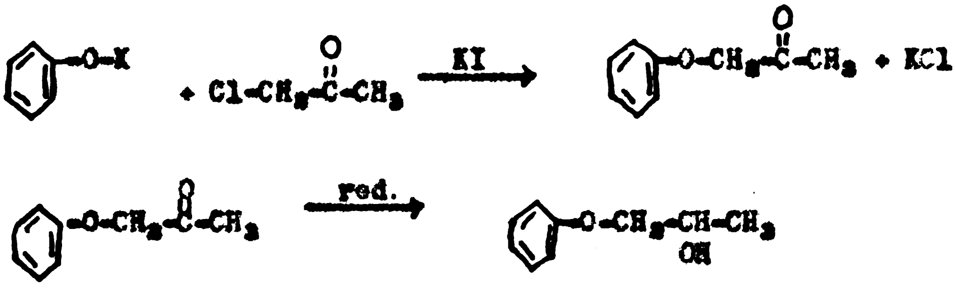


The rearrangement of the primary alcohol was accomplished by treatment with thionyl chloride using chloroform as the solvent.

The preparation of 2-phenoxy-1-propanol by the reduction of α-phenoxypropionaldehyde with hydrogen over platinum oxide has been reported by Sexton and Britton (15) to give a 100% yield of the primary alcohol.

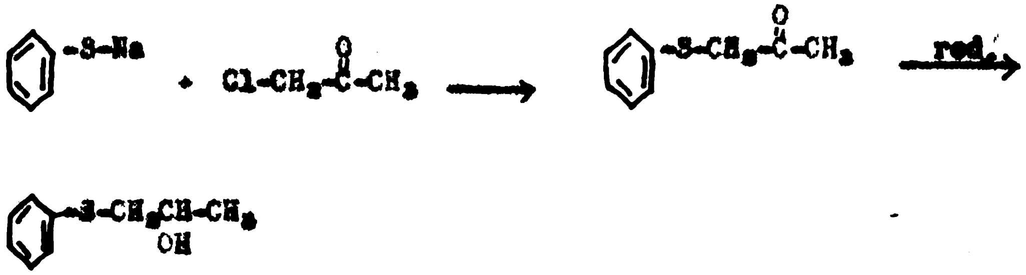


Hurd and Perlets (16) have reported the reaction of phenol and β-naphthol with chloroacetone in the presence of potassium iodide as a catalyst to give good yields of phenoxy acetone and β-naphthoxy acetone. These compounds were subsequently reduced to 1-phenoxy-2-propanol and 1-(β-naphthoxy)-2-propanol by hydrogenation at 100 atmospheres pressure in the presence of a nickel catalyst.

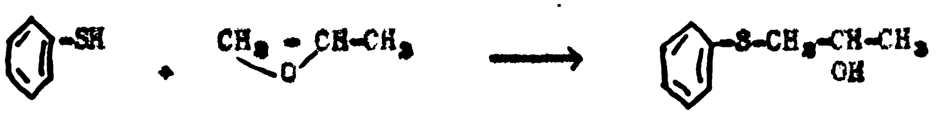


This compound had been previously prepared only by the interaction of 1-chloro-2-propanol and sodium phenoxide (17).

Similarly, Fuson and Koehneke (12) prepared 2-hydroxy-n-propyl phenyl sulfide by a mild aluminum isopropoxide reduction of acetonyl phenyl sulfide obtained from sodium phenyl mercaptide and chloroacetone.



Schuetz (18) has shown that the reaction of thiophenol with propylene oxide in the presence of a basic catalyst produces the pure secondary alcohol.

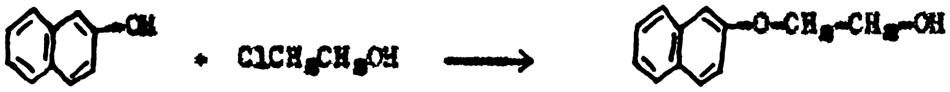


Also the reaction of phenols with propylene oxide in the presence of aqueous sodium hydroxide is reported (15) to give secondary alcohol ethers.

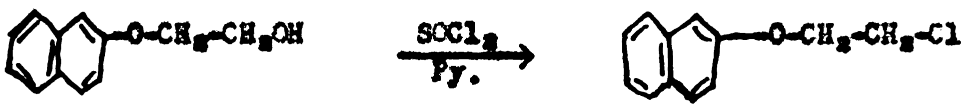
Powell (19) prepared γ-phenoxypropyl alcohol by a modification of the method described by Rindfuss (20) who obtained it in 75% yield by treating an absolute alcoholic solution of sodium phenoxide with trimethylene chlorohydrin. Powell used an aqueous solution of sodium phenoxide in which the chlorohydrin is completely soluble and the reaction was completed in a much shorter time and in better yield.

Kirner and Richter (21) used a similar reaction to prepare β-hydroxyethyl and γ-hydroxypropyl phenyl sulfides.

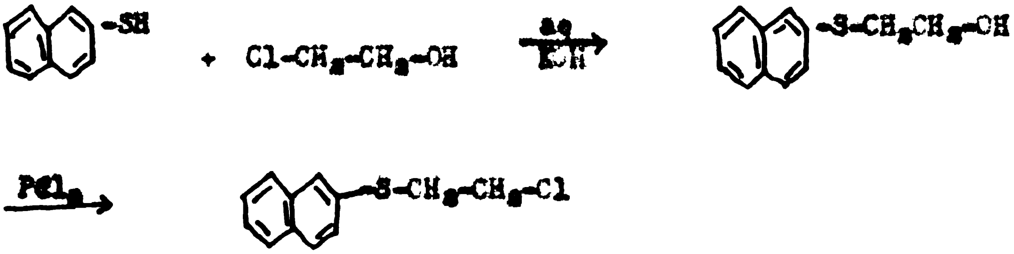
They also prepared the corresponding α and β-naphthoxyl compounds in good yields.



The hydroxy compounds were then converted to the chlorides by Darzens' method (22) using thionyl chloride and pyridine.



Bennett and Baddeley (23) report a similar reaction for the preparation of β-naphthyl-β-hydroxyethyl sulfide by adding ethylene chlorohydrin to a solution of β-thionaphthol in a slight excess of aqueous potassium hydroxide at 60-70°C and heating a short time on a water bath. The hydroxy sulfide was converted to the chloride by the action of phosphorus pentachloride.



Houff and Schuetz (24) prepared 2-hydroxy-n-propyl-3-thienyl sulfide by an analagous reaction of 3-thiophenethiol and propylene chlorohydrin.

The reactions which have just been surveyed were carefully considered in an attempt to develop a general synthetic scheme for preparing the desired sulfide and ether alcohols. It was concluded that the reactions represented by the following general equations should readily lead to an unequivocol synthesis of compounds which were needed for a study of the rearrangement reactions.

$$\text{A-W-H} + \text{X-}\overset{\text{R}}{\text{CH}}\text{-CH}_2\text{-OH} \longrightarrow \text{A-W-}\overset{\text{R}}{\text{CH}}\text{-CH}_2\text{-OH}$$

$$\text{A-W-H} + \text{X-CH}_2\text{-}\underset{\text{OH}}{\text{CH}}\text{-R} \longrightarrow \text{A-W-CH}_2\text{-}\underset{\text{OH}}{\text{CH}}\text{-R}$$

In these equations, [illegible] represents a phenyl, β-naphthyl or 3-thienyl group, W is either a sulfur or oxygen atom, R is an alkyl group and X is a halogen atom.

DISCUSSION

The direct condensation of mercaptans and phenols with 1,2-chlorohydrins in basic solution was considered to lead to an unequivical synthesis of the aryl-2-hydroxy alkyl sulfides and ethers.

$$\mathrm{ArSH} + \underset{\displaystyle\mathrm{OH}}{\mathrm{Cl{-}CH_2{-}CH{-}R}} \xrightarrow{\mathrm{NaOH}} \underset{\displaystyle\mathrm{OH}}{\mathrm{ArS{-}CH_2{-}CH{-}R}}$$

The possibility of a side reaction involving epoxide ring formation and further reaction with mercaptan to yield a mixture of primary and secondary alcohols was discounted. This is in view of the report (16) preferential opening of the alkyl substituted epoxide ring by mercaptans and phenols in the presence of a basic catalyst to produce pure secondary alcohols.

The condensation reaction was carried out both in aqueous alkali and in anhydrous sodium ethoxide solution with comparable yields. The reaction in aqueous alkali has the advantage of eliminating the preparation of sodium ethoxide solutions and allows a somewhat easier isolation of the product. Yields ranging from 56 to 86 percent were obtained by carrying out the reaction in ten percent sodium hydroxide solution with the reactions involving mercaptans giving the higher yields. The mercaptans also gave better results than phenol when the reaction was carried out in alcoholic sodium ethoxide. In the one attempt to prepare 1-phenoxy-2-propanol in sodium ethoxide solution, a considerable quantity of phenol was recovered and a poor yield (20%) of product resulted.

This method was of particular advantage in the condensation of β-thionaphthol with propylene chlorohydrin because of the insolubility of β-thionaphthol in aqueous alkali. In the reactions employing alcoholic medium, sodium chloride precipitated and provided a means of quantitatively estimating the extent of the reaction. A slight excess of chlorohydrin was generally used and the hydroxy sulfides or ethers were obtained as colorless liquids by vacuum distillation.

The hydroxy sulfides were converted to the corresponding chlorosulfides by means of the Darzens' reaction (22) using dry chloroform as a solvent. Yields ranging from 50 to 80 per cent were obtained by treating the hydroxy compound with a slight excess of thionyl chloride which had been purified by distilling from quinoline followed by a second distillation from linseed oil. It was further found to be advantageous to sweep a current of dry air across the reaction surface to remove sulfur dioxide and hydrogen chloride. Two attempts were made to apply this reaction to the conversion of 1-phenoxy-2-propanol to 1-phenoxy-2-chloropropane but in each instance the product gave a negative test for chloride ion after fusion with sodium. However, this conversion was accomplished by carrying out the reaction in pyridine giving a 55 percent yield of the chloroether. Attempts to prepare p-nitro and 3,5 dinitrobenzoates from this chloride by the general method of refluxing the chloride with the sodium salts of the acids in alcohol were unsuccessful. In contrast, the corresponding derivatives of the chlorosulfides were readily obtained by this method. Six of the hydroxy and chloro compounds prepared in the course of this work have not been previously reported and some of their physical properties are recorded in Tables I, II and III.

TABLE I

1-(β-THIOTHIENYL) AND 1-(β-THIONAPHTHYL) ALKYL ALCOHOLS $R_1\text{-}S\text{-}CH_2\text{-}\overset{OH}{CH}\text{-}R_2$

Compound	Formula	b.p.	n_D^{25}	d^{25}	% Sulfide Sulfur Calc'd.	 Found
1-(β-thiothienyl)-2-propanol	$C_7H_{10}S_2O$	116°/5mm[a]	1.5783	1.2011	18.40	18.49 18.40
1-(β-thiothienyl)-2-butanol	$C_8H_{12}S_2O$	115-118°/ 0.5 mm	1.5755	1.1751	17.02	17.31 17.29
1-(β-thiothienyl-2-pentanol	$C_9H_{14}S_2O$	125-127°/ 0.5 mm	1.5635	1.1397	15.83	16.19 16.11
1-(β-thionaphthyl)-2-propanol[b]	$C_{13}H_{14}SO$				14.67	15.13 15.10

[a] Reported only the boiling point, Houff and Schuetz, J. Am. Chem. Soc. 75, 2072 (1953).

[b] The compound melted at 42-44°.

TABLE II

1-(β-THIOTHIENYL) AND 1-(β-THIONAPHTHYL)-2-CHLOROPROPANES $R_1-S-CH_2-\overset{Cl}{CH}-R_2$

Compound	Formula	b.p.	n_D^{25}	d^{25}	% Sulfide Sulfur	
					Calc'd	Found
1-(β-thiothienyl)-2-chloropropane	$C_7H_9S_2Cl$	85-90°/1 mm	1.5794	1.2304	16.62	16.84 17.03
1-(β-thiothienyl)-2-chloropropane[a]	$C_7H_9S_2Cl$	105°/1 mm	1.5780		16.62	16.52 16.66
1-(β-thionaphthyl)-2-chloropropane	$C_{13}H_{13}SCl$	140°/0.5mm	1.6366	1.1711	13.52	13.98 13.91
1-(β-thionaphthyl)-2-chloropropane[a]	$C_{13}H_{13}SCl$		1.6360		13.52	13.90 13.78

[a] Prepared by the rearrangement reaction.

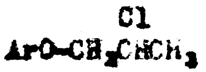
TABLE III

PHENOXYCHLOROPROPANES $Ar\text{-}O\text{-}\overset{CH_3}{CH}\text{-}CH_2Cl$ AND $ArO\text{-}CH_2\overset{Cl}{C}HCH_3$

Compound	Formula	b.p.	n_D^{25}	d^{25}	Analyses[a] %			
					C		H	
					Calc'd.	Found	Calc'd.	Found
1-phenoxy-2-chloropropane	$C_9H_{11}OCl$	95°/5mm	1.5252	1.0939	63.34	64.64	6.45	6.80
2-phenoxy-1-chloropropane	$C_9H_{11}OCl$	62-64°/0.5mm	1.5195	1.0927	63.34	64.32	6.45	6.82
2-phenoxy-1-chloropropane[b]	$C_9H_{11}OCl$	110-113°/ 22 mm	1.5218[c]	1.1020[c]				

[a] Analyses by Micro Tech. Lab., Skokie, Illinois.
[b] Reported by Irwin and Hennion (28).
[c] Reported at 20°C.

TABLE III

PHENOXYCHLOROPROPANES 
$\text{AR-O-}\overset{CH_3}{\text{CH}}\text{-CH}_2\text{Cl}$ AND 
$\text{ArO-CH}_2\overset{Cl}{\text{C}}\text{HCH}_3$

Compound	Formula	b.p.	n_D^{25}	d^{25}	Analyses[a] %			
					C		H	
					Calc'd.	Found	Calc'd.	Found
1-phenoxy-2-chloropropane	$C_9H_{11}OCl$	95°/5mm	1.5252	1.0939	63.34	64.64	6.45	6.80
2-phenoxy-1-chloropropane	$C_9H_{11}OCl$	62-64°/0.5mm	1.5195	1.0927	63.34	64.32	6.45	6.82
2-phenoxy-1-chloropropane[b]	$C_9H_{11}OCl$	110-113°/ 22 mm	1.5218[c]	1.1020[c]				

[a] Analyses by Micro Tech. Lab., Skokie, Illinois.
[b] Reported by Irwin and Hennion (28).
[c] Reported at 20°C.

The only method previously described which was available for the preparation of 2-(β-thioaryl)-1-propanols involved the addition of the appropriate mercaptan to allyl alcohol in the presence of sulfur.

$$\mathrm{ArSH} + \mathrm{CH_2{=}CHCH_2OH} \xrightarrow{(S)} \mathrm{Ar{-}S{-}\overset{CH_3}{CH}{-}CH_2OH}$$

However, application of this method resulted in poor yields and proved to be of limited synthetic value. When 3-thiophenethiol was refluxed with allyl alcohol for periods of twenty-four and forty-eight hours in the presence of sulfur, only a 27% yield of 2-(β-thiothienyl)-1-propanol was obtained. The reaction was also carried out in a nitrogen atmosphere to prevent possible polymerization of the allyl alcohol and disulfide formation from 3-thiophenethiol, but this resulted in only a slight increase in yield. Under the same reaction conditions, β-thionaphthol failed to add to either allyl alcohol or allyl chloride and the unreacted mercaptan was recovered along with some β,β-dinaphthyl disulfide. It would appear that more drastic reaction conditions are necessary to force the addition, such as, carrying out the reaction in a sealed tube.

The preparation of 2-phenoxy-1-propanol using the method employed by Sexton and Britton (15) is difficult and time consuming. It was originally planned to attempt a straightforward synthesis by the interaction of phenol and 2-chloro-1-propanol, the latter compound was prepared from the interaction of chromyl chloride and propylene following the method of Cristol and Eiler (25). The condensation reaction was attempted first in aqueous alkali and then in isopropyl ether containing sodium phenoxide using reflux periods of one hour and eight hours respectively.

Evidently the chlorine of the reverse chlorohydrin cannot be replaced under these conditions since the product isolated from both reactions was primarily unreacted phenol.

At this point it was evident that other synthetic means must be devised in order to obtain the desired compounds. After some deliberation it was envisioned that a very general synthetic method would be available if the esters of the desired alcohols could first be prepared and then reduced to the alcohols by means of lithium aluminum hydride.

(1) 

$$\mathrm{ArSH} + \underset{\mathrm{Br}}{\mathrm{R{-}CH{-}CO_2Et}} \longrightarrow \mathrm{Ar{-}S{-}}\overset{\mathrm{R}}{\mathrm{CH}}\mathrm{{-}CO_2Et}$$

(2) 

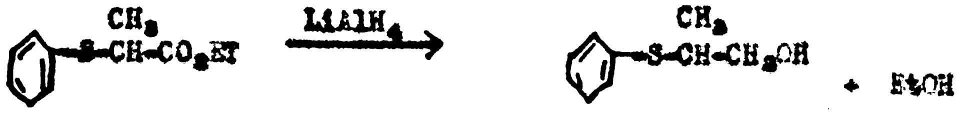
$$\mathrm{Ar{-}S{-}}\overset{\mathrm{R}}{\mathrm{CH}}\mathrm{{-}CO_2Et} \xrightarrow{\mathrm{LiAlH_4}} \mathrm{Ar{-}S{-}}\overset{\mathrm{R}}{\mathrm{CH}}\mathrm{{-}CH_2OH}$$

The reduction step was investigated first using methyl-3-thiophenylpropionate which was easily prepared by the method of Hurd and Gershbein (26). By an application of the general method of Nystrom and Brown (27) for the reduction of ether soluble compounds, and 81% yield of 3-thiophenyl-1-propanol was obtained.

A one molar lithium aluminum hydride solution was prepared in anhydrous ethyl ether by crushing the hydride in a mortar in a nitrogen atmosphere, adding it to the ether and stirring for several hours with an efficient wire stirrer. A considerable amount of the material did not dissolve and the hydride solution was used in the form of a slurry.

In order to further test the general applicability of the new synthesis, a few additional known compounds were prepared. Thus ethyl -2-thiophenylpropionate was prepared by refluxing sodium thiophenolate and ethyl α-bromopropionate in anhydrous xylene which resulted in a 58% yield of the desired ester. It was next decided to try the above condensation reaction in anhydrous sodium ethoxide solution in which the reaction proceeded smoothly to give a better yield (74%) of ethyl 2-thiophenylpropionate.

The condensation, when carried out in alcohol, had the advantage of preparing the salt of the mercaptan in situ and the precipitation of sodium halide during the reaction could be used to estimate the extent of reaction. The reduction step was carried out by means of the general procedure and gave a 72% yield of 2-thiophenyl-1-propanol.



The application of this unequivocal synthesis to the desired compounds was successful and greatly facilitated their preparation. Yields of 66 to 85 percent were obtained in the condensation reaction involving mercaptans with 82 to 88 percent yields being obtained in the subsequent reduction reactions. Slightly smaller yields resulted for both reactions when phenol was substituted for the mercaptans. The 2-phenoxy-1-propanol prepared in this manner had a density and refractive index which varied considerably from those reported by Sexton and Britton (15) for the same compound; see Table IV. However, the boiling point and the melting point of the α-naphthylcarbamate derivative of the compound were in good agreement. The density and refractive index of the 2-phenoxy-1-propanol as prepared above was in good agreement with the isomeric 1-phenoxy-2-propanol as is the case when the physical constants of the analogous isomers, 2-hydroxyisopropyl phenyl sulfide and 2-hydroxy-n propyl phenyl sulfide are compared (12). Also three other similar isomeric pairs of alcohols were prepared by the same reactions as those used to prepare 2-phenoxy-1-propanol and they possess physical constants which are very nearly alike. In view of these analogies as well as the unequivocal method of synthesis, it seems likely that the physical constants obtained for 2-phenoxy-1-propanol in this investigation are more reliable than those reported by Sexton and Britton which varies markedly from the physical constants of its isomer, 1-phenoxy-2-propanol. Altogether, in the course of this work, eight new alcohols and esters not previously reported were prepared and some of their physical properties are summarized in Tables V and VI.

The alcohols prepared by the two step synthesis described above were treated with thionyl chloride in order to determine if rearrangement would occur when the hydroxyl group was replaced by chlorine. When 2-(β-thiothienyl)-1-propanol was subjected to the rearrangement reaction conditions,

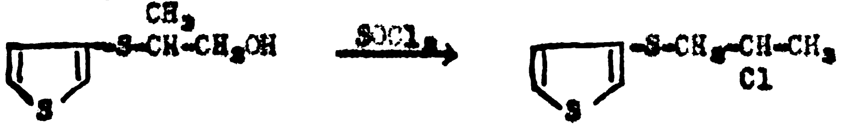


TABLE IV

PHENOXYPROPANOLS $AR{-}O{-}\overset{CH_3}{CH}CH_2OH$ AND $AR{-}O{-}CH_2\overset{OH}{CH}\,CH_3$

Compound	Formula	b.p.	n_D^{25}	d^{25}	p-nitrobenzoate
2-phenoxy-1-propanol	$C_9H_{12}O_2$	122-124°/10 mm	1.5232	1.0632	47-49°
2-phenoxy-1-propanol[a]	$C_9H_{12}O_2$	120°/10 mm	1.4760	0.9030	
1-phenoxy-2-propanol	$C_9H_{12}O_2$	94-96°/0.5mm	1.5220	1.0606	74-75°
1-phenoxy-2-propanol[a]	$C_9H_{12}O_2$	116-117°/10 mm	1.5200	1.0610	

[a] Prepared by Sexton and Britton (15).

TABLE V

2-(β-THIOTHIENYL) AND 2-(β-THIONAPHTHYL)-1-ALKYL ALCOHOLS $R_1 S\text{-}\overset{R_2}{C}H\text{-}CH_2OH$

Compound	Formula	b.p.	n_D^{25}	d^{25}	% Sulfide Sulfur Calc'd.	% Sulfide Sulfur Found
2-(β-thiothienyl)-1-propanol	$C_7H_{10}S_2O$	120-123°/1 mm	1.5844	1.2073	18.39	18.42 18.90
2-(β-thiothienyl)-1-butanol	$C_8H_{12}S_2O$	122-124°/ 0.5 mm	1.5747	1.1743	17.01	17.49 17.40
2-(β-thiothienyl)-1-pentanol	$C_9H_{14}S_2O$	133-135°/ 0.5 mm	1.5632	1.1394	15.83	16.02 16.15
2-(β-thionaphthyl)-1-propanol[a]	$C_{13}H_{14}SO$	160-162°/ 0.5 mm			14.67	14.92 14.99

[a] The melting point of this compound was 26-28°.

TABLE VI

ETHYL 2-(β-THIOTHIENYL) AND ETHYL 2-(β-THIONAPHTHYL) ALKYL ESTERS $R_1\text{-S-}\overset{R_2}{\text{CH}}\text{-CO}_2\text{Et}$

Compound	Formula	b.p.	n_D^{25}	d^{25}	% Sulfide Sulfur Calc'd.	% Sulfide Sulfur Found
Ethyl 2-(β-thiothienyl) propionate	$C_9H_{12}S_2O_2$	115-116°/ 1 mm	1.5410	1.1645	14.81	14.33 14.83
Ethyl 2-(β-thiothienyl) butyrate	$C_{10}H_{14}S_2O_2$	116-118°/ 0.5 mm	1.5357	1.1469	13.91	14.05 14.32
Ethyl 2-(β-thiothienyl) valerate	$C_{11}H_{16}S_2O_2$	120-122°/ 0.5 mm	1.5293	1.1202	13.11	13.28 13.22
Ethyl 2-(β-thionaphthyl) propionate	$C_{15}H_{16}SO_2$	150-151°/ 0.5 mm	1.5991	1.1304	12.30	12.45 12.28

the product had the physical properties (see Table II) of the chlorosulfide prepared by the analogous treatment of 1-(β-thiothienyl)-1-propanol with thionyl chloride.

Both products of the above reactions gave a correct sulfide sulfur (29) analysis for the formula $C_7H_9S_2Cl$. To prove the identity of the two chlorosulfides, both their p-nitro and 3,5 dinitrobenzoate derivatives, see Tables VII and VIII, were prepared by a modification of the general method of Fuson (12). The melting points of the derivatives from the two compounds were identical and a 50-50 mixture caused no depression of the melting point. Furthermore the melting points and mixed melting points of the derivatives prepared from the chlorides and from 1-(β-thiothienyl)-2-propanol were identical which proved the chlorides to be of the same structure as the alcohol containing the β-hydroxy-n-propyl side chain. Thus on the basis of melting point data, it has been established that 2-(β-thiothienyl)-1-propanol upon treatment with thionyl chloride does rearrange to produce 1-(β-thiothienyl)-2-chloropropane. The rearrangement reaction was also carried out using pyridine as a solvent instead of chloroform and resulted in a 26% yield of the chlorosulfide which likewise proved to be identical with the rearranged chlorosulfide prepared in chloroform.

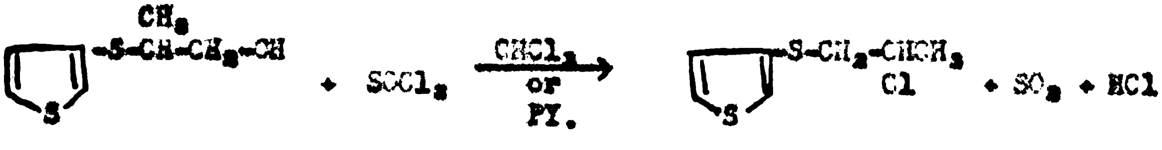


TABLE VII

p-NITROBENZOATES OF β-THIOTHIENYLPROPANOLS AND THEIR CHLORIDES


$C_4H_3S\text{-}S\text{-}CH(CH_3)\text{-}CH_2(OH,Cl)$

and


$C_4H_3S\text{-}S\text{-}CH_2CH(CH_3)\text{-}(OH,Cl)$

p-Nitrobenzoate of	Formula	M. P.
(a) 2-(β-thiothienyl)-1-propanol	$C_{14}H_{13}S_2O_4N$	231-233°
(b) 1-(β-thiothienyl)-2-propanol	$C_{14}H_{13}S_2O_4N$	88-89°
(c) 1-(β-thiothienyl)-2-chloropropane	$C_{14}H_{13}S_2O_4N$	88-89°
(d) 1-(β-thiothienyl)-2-chloropropane	$C_{14}H_{13}S_2O_4N$	87-89°
(e) 50-50 mixture (c) + (d)		87-89°
(f) 50-50 mixture (b) + (d)		88-89°

TABLE VIII

3,5-DINITROBENZOATES OF β-THIOTHIENYLPROPANOLS AND THEIR CHLORIDES

$R_1-S-\overset{R_2}{CH}-CH_2(OH,Cl)$ and $R_1-S-CH_2-\overset{R_2}{CH}-(OH,Cl)$

3,5 Dinitrobenzoate of	Formula	M.P.
a) 2-(β-thiothienyl)-1-propanol	$C_{14}H_{12}S_2O_6N_2$	88-89°
b) 1-(β-thiothienyl)-2-propanol	$C_{14}H_{12}S_2O_6N_2$	82-84°
c) 1-(β-thiothienyl)-2-chloropropane[a]	$C_{14}H_{12}S_2O_6N_2$	82-84°
d) 50-50 mixture (b) + (c)		82-84°

[a] Prepared by the rearrangement reaction.

Similarly, 2-(β-thionaphthyl)-1-propanol was found to rearrange to 1-(β-thionaphthyl)-2-chloropropane in 77% yield when treated with thionyl chloride in chloroform. That rearrangement did occur was again established by a comparison of the 3,5-dinitrobenzoate derivatives of the two isomeric alcohols 1-(β-thionaphthyl)-2-propanol and 2-(β-thionaphthyl)-1-propanol with the same derivatives of the chlorosulfide prepared from the rearrangement reaction; see Table IX. As in the previous case a mixed melting point of the derivative prepared from the chlorosulfide with the same derivative prepared from 1-(β-thionaphthyl)-2-propanol was not depressed, thus proving the derivatives to be identical.

It was not possible to analyse the derivatives from the isomeric alcohols by titration of sulfide sulfur due to their insolubility in acetic acid-water mixtures and their apparent slow reactivity with bromine. A carbon-hydrogen analysis was made of the derivatives and gave good results compared to the calculated values.

As a result of the difficulty encountered in replacing the hydroxy group of 1-phenoxy-2-propanol with chlorine in chloroform, the attempt to rearrange 2-phenoxy-1-propanol was carried out in pyridine. The reaction was carried out in the same manner as has been described for the conversion of 1-phenoxy-2-propanol to 1-phenoxy-2-chloropropane. In both instances attempts to prepare the p-nitro or 3,5-dinitrobenzoates

TABLE II

3,5-DINITROBENZOATES OF β-THIONAPHTHYLPROPANOLS AND THEIR CHLORIDES

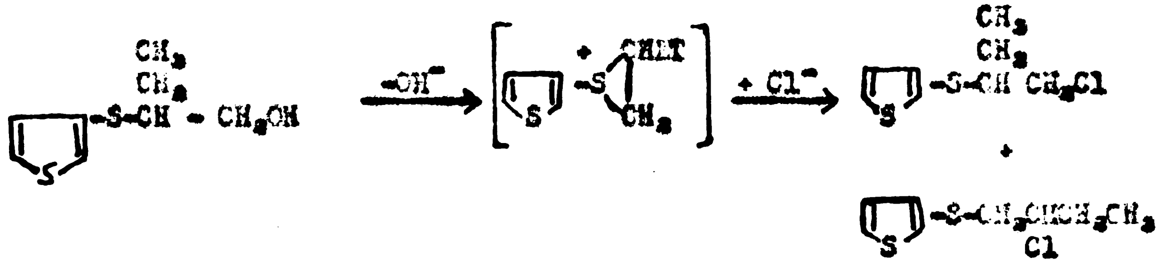
$\beta\text{-}C_{10}H_7\text{-}S\text{-}\overset{CH_3}{CH}\text{-}CH_2\text{-}(OH,Cl)$ and $\beta\text{-}C_{10}H_7\text{-}S\text{-}CH_2\text{-}\overset{CH_3}{CH}\text{-}(OH,Cl)$

3,5 Dinitrobenzoate of	Formula	M.P.	Analyses %			
			C		H	
			Calc'd.	Found	Calc'd.	Found
a) 2-(β-thionaphthyl)-1-propanol	$C_{20}H_{16}SO_6N_2$	144-145°	58.45	58.36	3.88	4.08
b) 1-(β-thionaphthyl)-2-propanol	$C_{20}H_{16}SO_6N_2$	189-190°	58.45	58.36	3.88	3.99
c) 1-(β-thionaphthyl)-2-chloropropane[a]	$C_{20}H_{16}SO_6N_2$	186-187°				
d) 50-50 mixture (b) + (c)		186-188°				

[a] Prepared by the rearrangement reaction.

from the chlorides were unsuccessful. Hence the usual method of comparison of the chlorides from the isomeric alcohols was not available. A carbon-hydrogen analysis of the two chlorides gave results for carbon which were approximately a percent high in both cases. Solely on the basis of physical constants, see Table III, it would appear that the 2-phenoxy-1-propanol did not rearrange since the chloride prepared from it had physical properties which were in better agreement with those reported for 2-phenoxy-1-chloropropane (26) than those determined for 1-phenoxy-2-chloropropane. However, this evidence is not conclusive since the exact purity of the phenoxychlorides is in question, and it would be necessary to first obtain derivatives of the chlorides in order to prove or disprove the rearrangement conclusively. The p-nitrobenzoates of 2-phenoxy-1-propanol and 1-phenoxy-2-propanol were both obtained in small yields and their melting points are reported in Table IV.

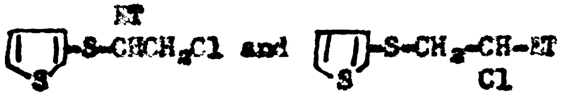
The rearrangement of 2-(β-thiothienyl)-1-butanol when treated with thionyl chloride resulted in the formation of a mixture of the two possible isomeric chlorides, 1-(β-thiothienyl)-2-chlorobutane and 2-(β-thiothienyl)-1-chlorobutane.



Likewise when 1-(β-thiothienyl)-2-butanol was treated with thionyl chloride, a similar mixture resulted having almost identical physical properties, see Table I.

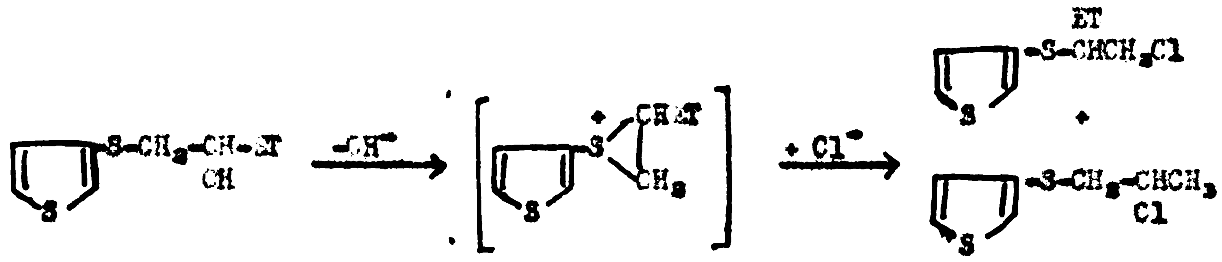
TABLE X

MIXTURES OF 1-(β-THIOTHIENYL)-2-CHLOROALKANES AND 2-(β-THIOTHIENYL)-1-CHLOROALKANES



Compound	Formula	b.p.	n_D^{25}	d^{25}	% Sulfide Sulfur Calc'd.	% Sulfide Sulfur Found
1-(β-thiothienyl)-2-chlorobutane and 2-(β-thiothienyl)-1-chlorobutane	$C_8H_{11}S_2Cl$	92-94°/ 0.5 mm	1.5711	1.2005	15.50	15.70 15.67
1-(β-thiothienyl)-2-chlorobutane[a] and 2-(β-thiothienyl)-1-chlorobutane	$C_8H_{11}S_2Cl$	96-100°/ 0.5 mm	1.5712	1.2008	15.50	15.95 15.77
1-(β-thiothienyl)-2-chloropentane and 2-(β-thiothienyl)-1-chloropentane	$C_9H_{13}S_2Cl$	110-112°/ 0.5 mm	1.5600	1.1593	14.50	14.78 14.79
1-(β-thiothienyl)-2-chloropentane[a] and 2-(β-thiothienyl)-1-chloropentane	$C_9H_{13}S_2Cl$	112-118°/ 0.5 mm	1.5603	1.1594	14.50	14.74 14.87

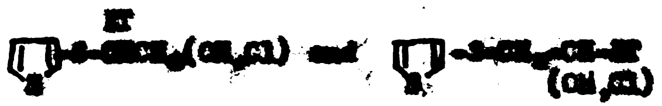
[a] Prepared by the rearrangement reaction.



The fact that the products are mixtures of the isomeric chlorides was established by preparing the 3,5-dinitrobenzoate derivatives, see Table XI, of the two mixtures and taking a mixed melting point of these derivatives with the 3,5-dinitrobenzoate prepared from 1-(β-thiothienyl)-2-butanol. The derivatives prepared from the two chloride mixtures each had a melting point of 103-105°C and a 50-50 mixture of the two had the same melting point which proves the mixtures to be identical. This is to be expected since the postulated intermediate sulfonium ion which forms during the conversion of the alcohols to the chlorides would be the same regardless of which alcohol was involved. The 3,5-dinitrobenzoate prepared from 1-(β-thiothienyl)-2-butanol had a melting point of 104-105°C and a 50-50 mixture of this derivative with either of the derivatives from the chloride mixtures resulted in a depression of the melting point to 96-98°C. A study of the Table XI and the melting point curve in Figure 1 indicates that such a lowering is possible only if the derivative from the chloride mixture consists roughly of 70% of the unrearranged chloride and 30% of the rearranged chloride. The mixture of derivatives which melts at 103-105°C corresponds to two possible points on the melting point curve, C and C'. Point (a) represents the melting point of the pure 3,5-dinitrobenzoate of 2-(β-thiothienyl)-1-butanol

TABLE XI

3,5-DINITROBENZOATES OF β-THIOTHIENYLBUTANOLS AND THEIR CHLORIDES



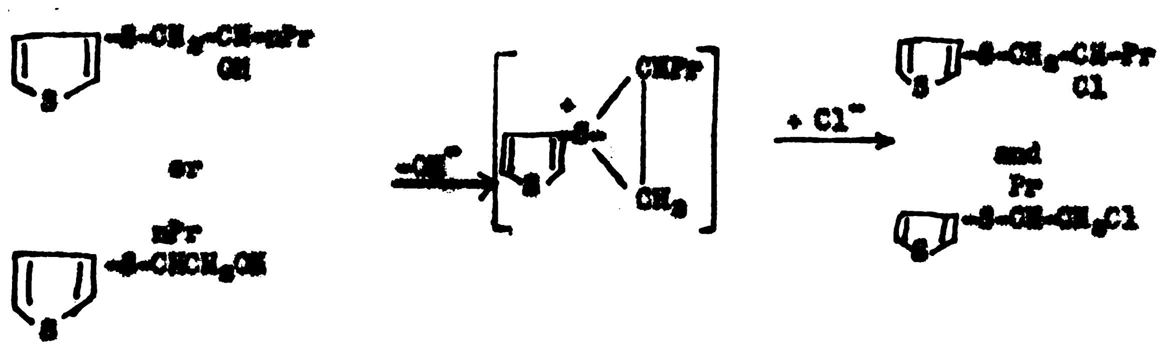
$\mathrm{C_4H_3S{-}S{-}\overset{Et}{C}H{-}CH_2(OH,Cl)}$ and $\mathrm{C_4H_3S{-}S{-}CH_2{-}\underset{(OH,Cl)}{C}H{-}Et}$

3,5-Dinitrobenzoate of	Formula	M.P.	Analyses - % C Calc'd.	C Found	H Calc'd.	H Found	N Calc'd.	N Found	S Calc'd.	S Found
a) 2-(β-thiothienyl)-1-butanol	$C_{15}H_{14}S_2O_6N_2$	120-121°							8.38[b]	8.48 —
b) 1-(β-thiothienyl)-2-butanol	$C_{15}H_{14}S_2O_6N_2$	104-105°							8.38[b]	8.14 8.48
c) 1-(β-thiothienyl)-2-chlorobutane and 2-(β-thiothienyl -1-chlorobutane	$C_{15}H_{14}S_2O_6N_2$	103-105°	47.12	47.26 47.26	3.66	3.64 3.74	7.33	7.35 7.48	16.75	16.79 16.70
d) 1-(β-thiothienyl)-2-chlorobutane[a] and 2-(β-thiothienyl) -1-chlorobutane	$C_{15}H_{14}S_2O_6N_2$	103-105°	47.12	47.22 47.21	3.66	3.56 3.48	7.33	7.43 7.54	16.75	16.68 16.79
e) 50-50 mixture (c) + (d)		103-105°								
f) 50-50 mixture (b) + (c) or (d)		96-98°								
g) 50-50 mixture (a) + (b)		95-97°								
h) 50-50 mixture (a) + (d)		101-115°								

[a] Prepared by the rearrangement reaction.
[b] Calculated for sulfide sulfur.
[c] Analysis by Micro Tech Laboratories, Skokie, Illinois.

and (b) corresponds to the melting point of the pure 3,5-dinitrobenzoate of 1-(β-thiothienyl)-2-butanol. If the mixture is of the composition represented by C then further addition of (b) should cause a slight increase in the melting point since (a), acting as an impurity in (b), would become less concentrated. However, if C' represents the true composition of the mixture, the addition of more (b) should cause a lowering of the melting point and the addition of more (a) should cause an elevation of the melting point. The latter was actually found to be the case, on addition of (a) and (b) to the mixtures obtained. A sulfide sulfur (29) analysis was made on all of the derivatives and in each case, a good analysis was obtained. An elemental analysis of the two derivatives obtained from the two chloride mixtures gave correct results for percentages of C, H, N and S, see Table II.

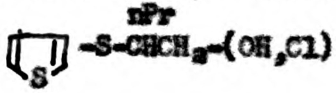
Similar results were encountered when the isomeric alcohols, 2-(β-thiothienyl)-1-pentanol and 1-(β-thiothienyl)-2-pentanol were treated with thionyl chloride. The formation of the mixture of isomeric chlorides from either of the alcohols may be represented as follows



The melting points of the 3,5-dinitrobenzoates, see Table III, prepared from the mixture of chlorides obtained from either of the isomeric

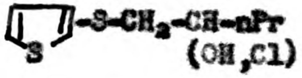
TABLE XII

3,5-DINITROBENZOATES OF β-THIOTHIENYLPENTANOLS AND THEIR CHLORIDES



$\text{C}_4\text{H}_3\text{S}\text{-S-CH(nPr)CH}_2\text{-(OH,Cl)}$

and



$\text{C}_4\text{H}_3\text{S}\text{-S-CH}_2\text{-CH(OH,Cl)-nPr}$

3,5 Dinitrobenzoate of	Formula	M.P.	Analyses % [c] C Calc'd.	 C Found	 H Calc'd.	 H Found	 N Calc'd.	 N Found	 S Calc'd.	 S Found
a) 2-(β-thiothienyl)-1-pentanol	$C_{16}H_{16}S_2O_6N_2$	97-98°							8.08[b]	8.19
b) 1-(β-thiothienyl)-2-pentanol	$C_{16}H_{16}S_2O_6N_2$	94-95°							8.08[b]	8.25 8.13
c) 1-(β-thiothienyl-2-chloropentane and 2-(β-thiothienyl)-1-chloropentane	$C_{16}H_{16}S_2O_6N_2$	79-81°	48.73	48.84 48.73	4.04	4.30 4.27	7.07	7.23 7.12	16.16	16.05 16.20
d) 1-(β-thiothienyl)-2-chloropentane[a] and 2-(β-thiothienyl)-1-chloropentane	$C_{16}H_{16}S_2O_6N_2$	79-81°	48.73	48.61 48.77	4.04	4.23 4.17	7.07	6.87 7.08	16.16	16.40 16.44
e) 50-50 mixture (c) + (d)		78-80°								
f) 50-50 mixture (b) + (c) or (d)		80-86°								
g) 50-50 mixture (a) + (b)		80-82°								
h) 50-50 mixture (a) + (d)		80-85°								

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[a] Prepared by the rearrangement reaction.
[b] Calculated for Sulfide Sulfur.
[c] Analysis by Micro Tech Laboratories, Skokie, Illinois.

alcohols were the same (79-81°C), and a mixture of these two derivatives melted at 79-81°C which proves that the two derivatives were identical and of course that the two chloride mixtures from which they were prepared must have been identical. This is confirmed by the physical properties of the two chloride mixtures which are identical within the limits of experimental error; see Table I. As in the preceding case, the formation of identical intermediate sulfonium ions during the conversion of the alcohols to the chlorides accounts for the identity of the chloride mixtures obtained. A study of Table XII and the melting point curve, Figure II, for the mixture indicates that the mixture must be of approximately 50-50 in composition, corresponding to point C" on the graph. Points (a) and (b) represent the pure 3,5-dinitrobenzoate derivatives of 2-(β-thiothienyl)-1-pentanol and 1-(β-thiothienyl)-2-pentanol respectively. It can be seen that an approximate 50-50 mixture of pure (a) and (b) has a melting point of 80-82° (determined experimentally) which corresponds favorably with the 79-81 melting point of the mixture in question, indicated by point C" on the curve. Further, the addition of either (a) or (b) to (d) causes an elevation of the melting point (80-86°) which is to be expected if (d) is of an approximate 50-50 composition. All of the derivatives gave a correct analysis for sulfide sulfur and the two derivatives prepared from the chloride mixtures were analysed for C, H, N, and S giving results which were in very good agreement with the calculated values, see Table XII. The possibility was considered that the derivatives obtained from the chlorides (m.p. 79-81°) might be isomorphic forms of the derivatives obtained from

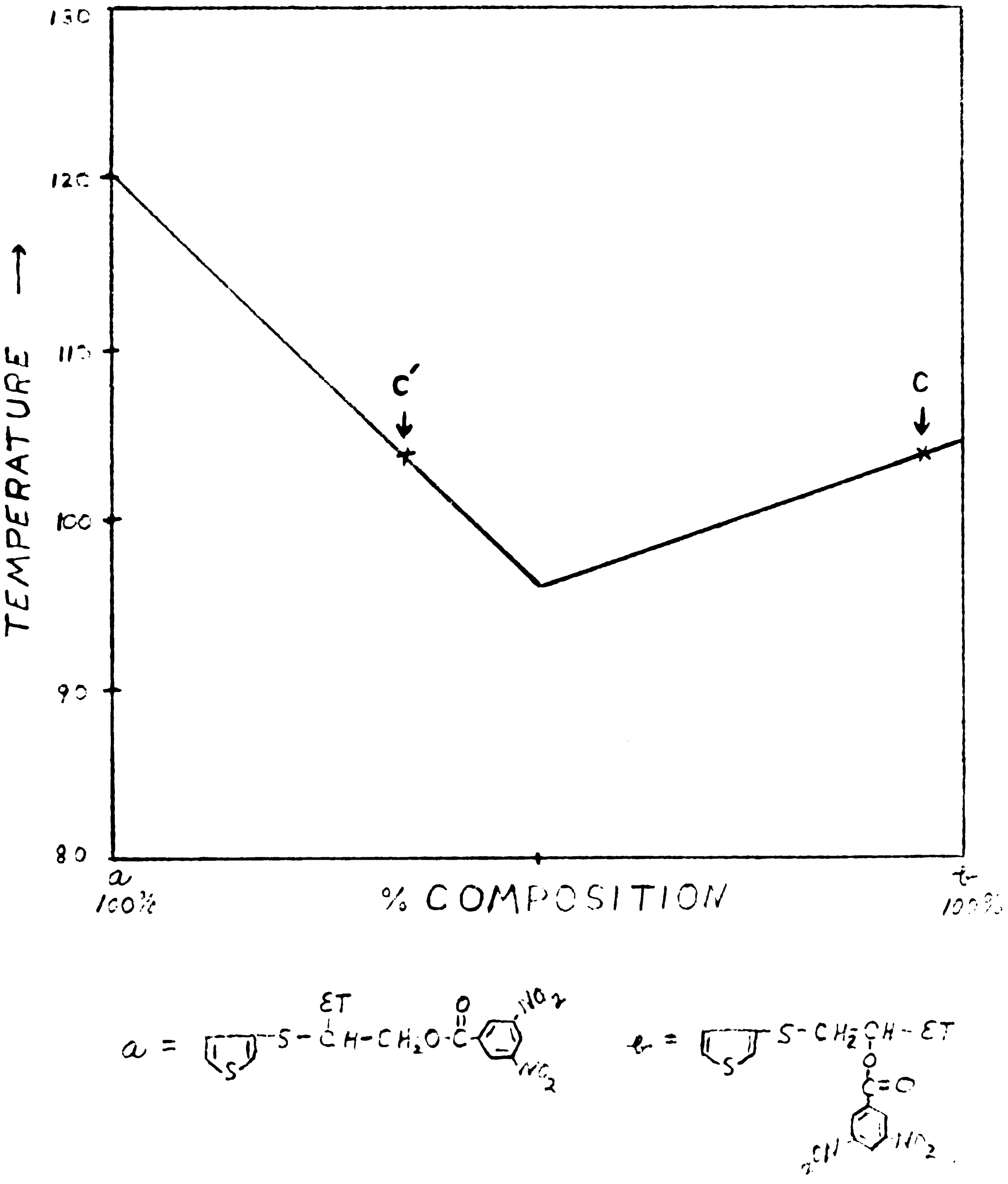


FIG. I MELTING POINT CURVE

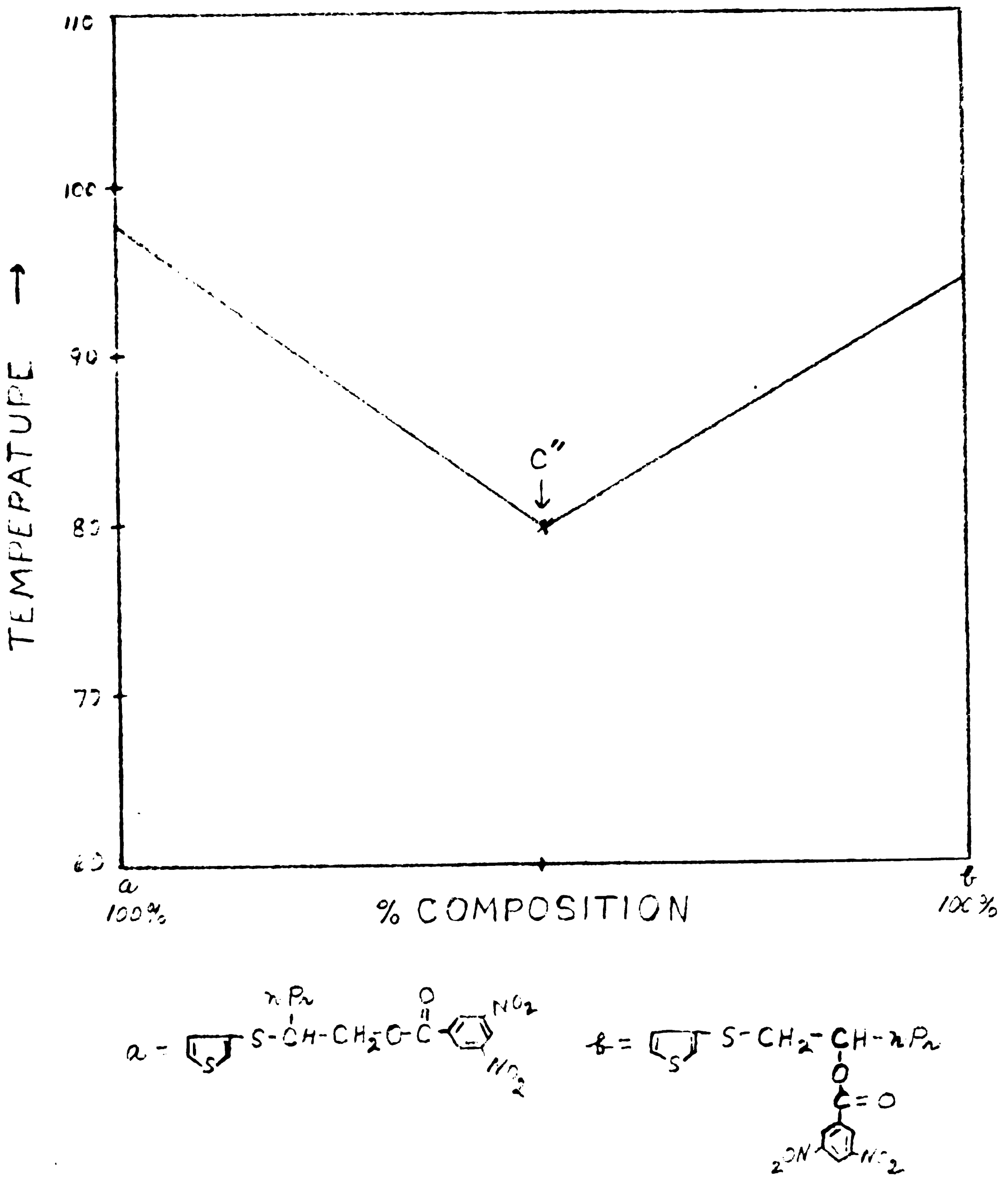


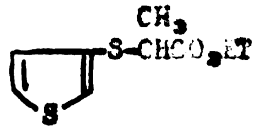
FIG.II MELTING POINT CURVE

the alcohols (m.p. 94-95°). The derivatives melting at 79-81° were melted, allowed to cool and crystallize, remelted and the process repeated. In each case the melting point was 79-81° and there was no indication of a change to the higher melting point. Furthermore, the 3,5-dinitrobenzoate derivative prepared from the product obtained from the treatment of 2-(β-thiothienyl)-1-pentanol with thionyl chloride, was hydrolyzed with alcoholic potash, and the mixture of alcohols thereby isolated were converted back to the 3,5-dinitrobenzoates by the usual method of preparing the derivatives from the alcohols. The melting point of this derivative was 81-83° and when mixed with the original derivative melting at 79-81°, there was no depression of the melting point.

EXPERIMENTAL

Ethyl-2-(β-Thiothienyl) and (β-Thionaphthyl) and (Thiophenyl) and (Phenoxy) Alkyl Esters

Ethyl 2-(β-thiothienyl) propionate



Into a 300 ml three necked flask fitted with a stirrer, reflux condenser and dropping funnel was placed 120 ml of absolute ethanol. The flask was cooled in an ice bath and 6.9 g (0.30 mole) of metallic sodium was added while stirring. After the sodium had dissolved, 34.8 g (0.30 mole) of 3-thiophenethiol was added rapidly and stirring was continued a half hour. The solution was then heated to its reflux temperature and 60 g (0.33 mole) of ethyl α-bromopropionate was added dropwise to the stirred solution in a one hour period. Precipitation of sodium bromide ensued after the first few drops of the halo ester had been added. Following the addition of the halo ester the mixture was refluxed gently for two hours to complete the reaction. The reaction mixture was then cooled and filtered to remove salt. Additional salt was removed by evaporating alcohol until dissolved salt again began precipitating, allowing the solution to cool and filtering a second time. The filtrate was taken up in 300 ml of ether, washed first with 50 ml of water, then with two 50 ml portions of a 5% sodium hydroxide solution, and finally with 50 ml of water. After drying the ether solution with anhydrous sodium sulfate overnight, and removal of the ether, the product was distilled through a small Vigreux column under vacuum to yield 44 g (0.20 mole, 68%) of an almost colorless liquid having a pleasant odor. Its physical constants were: b.p. 115-116°/1 mm; n_D^{25} 1.5410; d^{25} 1.1645. Analysis of the compound for sulfide sulfur (29) gave the following results:

Calc'd. for $C_9H_{12}S_2O_2$: S, 14.81. Found: S, 14.33; 14.83.

In a second preparation of the same compound, 250 ml of absolute alcohol was heated with 13.8 g (0.60 mole) of metallic sodium. To this solution of sodium ethoxide were added 69.6 g (0.60 mole) of 3-thiophenethiol and 127 g (0.70 mole) of ethyl α-bromopropionate. After removal of sodium bromide and concentration of the above reaction mixture, the product was extracted with ether, washed with water and 5% sodium hydroxide solution, dried and vacuum distilled. The yield of ethyl 2-(β-thiothienyl) propionate was 111 g (0.52 mole, 85%). Its physical constants were: b.p. 132-134°/5 mm; n_D^{25} 1.5410.

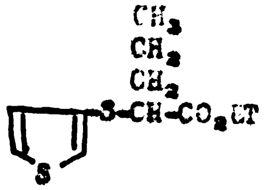
In a third preparation of ethyl 2-(β-thiothienyl) propionate, a solution of 6.9 g (0.30 mole) of sodium in 150 ml of absolute alcohol was treated with 34.8 g (0.30 mole) of 3-thiophenethiol followed by the addition of 63.5 g (0.35 mole) of ethyl α-bromopropionate. The reaction was carried out and the product isolated as was described above to yield 54.5 g (0.25 mole, 84.2%) of a pure material which had a boiling point of 113-115°/1 mm.

Ethyl 2-(β-thiothienyl) butyrate

Using the apparatus and procedure described above, 16 g (0.70 mole) of metallic sodium were dissolved in 350 ml of absolute ethanol and 81 g (0.70 mole) of 3-thiophenethiol was added to the solution. After stirring for fifteen minutes, 145 g (0.74 mole) of ethyl α-bromobutyrate was added slowly to the hot solution. The mixture was refluxed gently for an hour and a half, cooled and filtered to remove the inorganic salt. The sodium bromide was washed with ether and after drying it weighed 65 g (90% of the theoretical amount). The filtrate was concentrated to 150 ml, taken up in 300 ml of ether, and washed with two 80 ml portions of 5% sodium hydroxide solution and one 100 ml portion of water. After drying with sodium sulfate, and removing the ether, the product was vacuum distilled through a small Vigreux column to yield 133 g (0.58 mole, 83%) of an almost colorless liquid having a pleasant odor. Its physical constants were: b.p. 116-118°C/0.5 mm (oil bath temperature 160-170°C); n_D^{25} 1.5357; d^{25} 1.1469. Analysis of the compound for sulfide sulfur (29) gave the following results:

Calc'd. for $C_{10}H_{14}S_2O_2$: S, 13.91. Found: S, 14.05; 14.32.

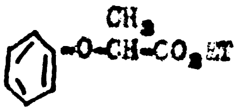
Ethyl 2-(β-thiothienyl) valerate



By following the same general procedure discussed above, 23 g (1.0 mole) of sodium was dissolved in 450 ml of absolute alcohol, and 116 g (1.0 mole) of 3-thiophenethiol was added to the hot sodium ethoxide solution. Following the addition of the α-bromovalerate and a reflux period of two and one half hours, the solution was cooled, filtered and the filtrate concentrated to 150 ml. The crude product was extracted with ether, washed and dried. After removal of the ether, the ester was distilled under reduced pressure in a small Vigreux column. A forerun of 25 g of ethyl α-bromovalerate was recovered boiling at 55°C/0.5 mm. The remaining material was distilled using an oil bath (temperature, 175-190°C) and boiled at 120-122°C/0.5 mm to yield 160 g (0.66 mole, 66%) of pure product. The pure ester possessed a pleasant odor and a light yellow color. Its density and index of refraction were as follows: n_D^{25} 1.5293; d^{25} 1.1202. Analysis of the compound for sulfide sulfur (29) gave the following results:

Calc'd. for $C_{11}H_{18}S_2O_2$: S, 13.11. Found: S, 13.28; 13.22.

Ethyl 2-phenoxypropionate



The same technique was employed as described previously for the analogous thio esters. A quantity, 2.7 g (0.12 mole), of sodium was dissolved in 50 ml of absolute ethanol and 10.9 g (0.12 mole) of phenol was added to the hot solution. The mixture was stirred for twenty minutes to assure complete formation of sodium phenoxide and then 23.8 g (0.13 mole) of ethyl α-bromopropionate was added dropwise to the sodium phenoxide solution. Precipitation of sodium bromide did not become apparent until most of the α-halo ester had been added. The mixture was refluxed for one hour, cooled and filtered to remove sodium bromide. The filtrate was taken up in ether and washed with three 30 ml portions of 5% sodium hydroxide solution and once with water. After allowing the ether solution to stand in contact with anhydrous sodium sulfate overnight, the ether was removed and the residual product distilled. A small forerun of 2 g was collected which boiled over a broad range, 80-120°/6 mm. The remaining material was distilled and yielded 11.2 g (0.06 mole, 50%) of ester having a pleasant odor. It possessed the following physical constants: b.p. 120-122°/6 mm; n_D^{25} 1.4932. The previously reported (30) boiling point for this ester was 120°/6 mm.

A second preparation of the ester was carried out under slightly different conditions. The quantity, 11.8 g (0.52 mole), of sodium was added to 225 ml of anhydrous ethyl alcohol, followed by the addition with stirring of 48.5 g (0.52 mole) of phenol to the sodium ethylate solution, stirring being continued for an additional half hour after the addition of the phenol. The solution of sodium phenylate was heated to its reflux temperature and 107 g (0.59 mole) of α-halo ester added slowly. After completing the addition of ester the reaction mixture was refluxed for four and a half hours. The mixture was then cooled, filtered, washed, and dried in the same manner as the first run. Following removal of the ether, the impure product was distilled to yield 65.4 g (0.34 mole, 65.4%) of the pure ester. The compound boiled at 128-130°/10 mm (oil bath temperature 165-170°C).

Ethyl-2-Thiophenylpropionate

The procedure used was the same as that employed in the previous preparations. A quantity of 2.90 g (0.13 mole) of sodium was dissolved in 40 ml of absolute ethanol, and 14.1 g (0.13 mole) of thiophenol was added to the solution. The condensation reaction was then carried out by adding 29 g (0.16 mole) of ethyl α-bromopropionate slowly while the mixture was being stirred. The rapid reaction resulted in the immediate precipitation of sodium bromide with the evolution of heat. Following the addition of the α-halo ester, the mixture was refluxed gently for one hour, then cooled, and filtered to remove the inorganic salt. The filtrate was dissolved in 150 ml of ether and washed in the usual manner, followed by drying over anhydrous sodium sulfate. The ether was removed by distillation and the yellow oil remaining was distilled under reduced pressure. There were 3 g of forerun followed by 20 g (0.09 mole, 74%

yield) of a slightly yellow, clear oil which boiled at 149°/13 mm. The refractive index of the compound was also determined, n_D^{20} 1.5323. Its previously reported (31) boiling point is: b.p. 139°/14 mm.

A second preparation of the ester was carried out by a modification of the general condensation reaction used previously, with a resultant decrease in the yield. The quantity, 3 g (0.13 mole), of sodium was placed in a 3-necked, 300 ml flask which contained 100 ml of anhydrous xylene. The flask was fitted with a reflux condenser, dropping funnel, and an efficient wire stirrer. The flask was heated to melt the metallic sodium and stirred vigorously while the xylene was allowed to cool slowly. The finely powdered metallic sodium was then treated with 14.1 g (0.13 mole) of thiophenol and warmed carefully to complete the salt formation of the thiophenol. To this was added, from a dropping funnel, 27 g (0.15 mole) of ethyl α-bromopropionate and the mixture was refluxed gently for three and one half hours. The solution was then cooled and the sodium bromide removed by filtration. A quantity of 100 ml of ether was added to the filtrate and the solution was washed with two 30 ml portions of 5% sodium hydroxide solution and one 50 ml portion of water followed by drying over anhydrous sodium sulfate. The ether and xylene were removed by distillation and the yellow oil remaining was distilled under vacuum to give 15.7 g (0.07 mole, 58%) of an almost colorless oil boiling at 140-145°/14 mm. The product was redistilled and boiled at 149-150°/12 mm. Its reported boiling point is 139°/14 mm (31). Analysis of the product for sulfide sulfur (29) gave the following results:

Calc'd. for $C_{11}H_{14}O_2S$: S, 15.24. Found: S, 15.03; 15.13.

Ethyl 2-(β-thionaphthyl) propionate

Into a 500 ml three necked flask fitted with a stirrer, reflux condenser and dropping funnel were placed 250 ml of anhydrous ethanol (distilled from magnesium alloy) and 32 g (0.20 mole) of β-thionaphthol which was previously crushed in a mortar. Provision was made to bubble dry nitrogen gas through the reaction mixture and after sweeping the system for ten minutes, the mixture was warmed to dissolve the β-thionaphthol. A solution of sodium ethoxide was prepared by dissolving 4.6 g (0.20 mole) of sodium in 100 ml of absolute alcohol. The sodium ethoxide solution was added through the dropping funnel and the mixture was warmed and stirred for fifteen minutes following the addition of sodium ethoxide solution. The nitrogen was continuously passed into the solution throughout the reaction. The stirred solution was heated to its reflux temperature and 41.5 g (0.23 mole) of ethyl α-bromopropionate was added slowly and resulted in an immediate precipitation of sodium bromide. Following the addition of the α-halo ester, the mixture was refluxed for one and a half hours, and filtered while still hot to remove the sodium bromide. On cooling the reaction mixture, 1.5 g of β,β-dinaphthyl disulfide precipitated and this was removed by filtration. The filtrate was concentrated to a 100 ml volume, during which it was necessary twice to remove the sodium bromide by filtering to prevent vigorous bumping. To the crude product was then added 60 ml of water to dissolve the last of the salt; followed by extraction with 200 ml of benzene to remove the product. The benzene extract was washed with two 30 ml portions of water, and dried over anhydrous sodium sulfate. The dry benzene solution was then refluxed with Norite for fifteen minutes, filtered and the benzene was removed on the steam bath. After removal of the solvent, the yellow liquid was distilled in vacuo to yield 40 g (0.15 mole, 77%) of a clear yellowish oil boiling at 150-151°/0.5 mm (oil bath temperature 220-230°C). Its physical constants were as follows: n_D^{25} 1.5991; d^{25} 1.1304. Analysis of the compound for sulfide sulfur (29) gave the following results:

Calc'd. for $C_{15}H_{16}SO_2$: S, 12.30. Found: S, 12.45; 12.28.

Methyl 3-thiophenyl propionate

The quantity, 7.4 g (0.86 mole) of methyl acrylate was added dropwise to 44 g (0.40 mole) of chilled thiophenol containing 0.40 g of suspended sodium methoxide as a catalyst. The reaction was carried out in an apparatus consisting of a three necked flask fitted with a stirrer, dropping funnel and reflux condenser. Following complete addition of the methyl acrylate, the reaction mixture was stirred for a period of sixteen hours at room temperature, and then filtered to remove the basic catalyst, and a small amount of polymerized ester. The unreacted ester was removed under reduced pressure and the residue was distilled to yield 72 g (0.37 mole, 92%) of the ester boiling at 150-153°/12 mm. The refractive index of the compound was: n_D^{20} 1.5510. Its reported (26) physical constants are: b.p. 153-155°/13 mm; n_D^{20} 1.5510.

2-(β-Thiothienyl) and (β-Thionaphthyl) and (Thiophenyl) and (Phenoxy)-1-Alkyl Alcohols

2-(β-thiothienyl)-1-propanol

Into a three necked liter flask fitted with a stirrer, reflux condenser and dropping funnel was placed 235 ml (0.24 mole) of a one molar solution of lithium aluminum hydride. The quantity, 34 g (0.16 mole) of ethyl 2-(β-thiothienyl) propionate was dissolved in 100 ml of dry ether and added with vigorous stirring to the flask as quickly as the refluxing ether would allow. It was necessary at various time intervals to immerse the reaction flask in an ice bath to control the exothermic reaction. After the addition of the ester, the mixture was stirred for a one hour period and the excess hydride was then destroyed by cooling the solution in an ice bath and cautiously adding 25 ml of ethyl acetate. At this point the mixture became very viscous and an additional quantity of 200 ml of ether was added. The contents of the flask was then poured into 300 ml of ice water, and 700 ml of 10% sulfuric acid was added to decompose the complex alcoholate. The ether layer was separated and the aqueous portion was extracted twice with 150 ml quantities of ether. The combined ether layers were washed with 100 ml of 10% sodium bicarbonate solution, then with 100 ml of water and dried over anhydrous sodium sulfate. After removal of the ether, the compound was distilled under vacuum to obtain 22.3 g (0.13 mole, 81.5%) of an almost colorless oil boiling at 120-123°/1 mm. The physical constants of the compound were: n_D^{25} 1.5864; d^{25} 1.2073. Analysis of the compound for sulfide sulfur (29) gave the following results:

Calc'd. for $C_7H_{10}S_2O$: S, 18.39. Found: 18.42; 18.90.

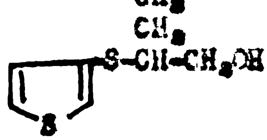
A second preparation of the compound carried out as described above, gave a yield which was a little better than the first case, 87.5 percent of the theoretical, and the product boiled at 140°/5 mm.

An alternative procedure was also used to prepare the same compound. Into a 100 ml flask fitted with a reflux condenser were placed 29 g (0.25 mole) of 3-thiophenethiol, 17.4 g (0.30 mole) of freshly distilled allyl alcohol and 0.25 g of sulfur. The mixture was heated under reflux for twenty-four hours. The reaction mixture was dissolved in 50 ml of ether and washed first with three 40 ml portions of a 5% solution of sodium hydroxide, then with one 40 ml portion of water, followed by drying over anhydrous magnesium sulfate. Removal of the ether and distillation of the product yielded 11.6 g (0.067 mole, 26.6%) of the hydroxy sulfide boiling at 120-123°/1 mm. The compound had the following physical constants: n_D^{25} 1.5852; d^{25} 1.2078. Analysis of the compound for sulfide sulfur (29) provided the following results:

Calc'd. for $C_7H_{10}S_2O$: S, 18.40. Found: 17.94; 17.90.

A second preparation of this compound was carried out in a nitrogen atmosphere and resulted in a 30% yield of the desired product which distilled at 123-125°/1 mm.

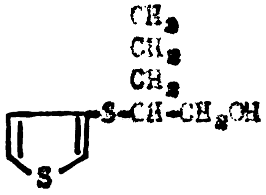
2-(β -thiothienyl)-1-butanol



Using the same apparatus as was described above, 500 ml (0.50 mole) of a one molar lithium aluminum hydride solution was placed in the flask and treated with 108 g (0.47 mole of ethyl 2-(β -thiothienyl) propionate at such a rate as to maintain gentle refluxing of the ether. The reaction mixture was stirred for forty-five minutes, cooled, and ethyl acetate cautiously added to destroy the excess hydride, after which the mixture was poured into 250 ml of ice water. The complex alcoholate was decomposed with 1500 ml of a ten percent solution of sulfuric acid and the ether layer was separated. The aqueous layer was extracted with three 125 ml portions of ether. The combined ether layers were dried and the ether removed. Subsequent distillation of the product yielded 74 g (0.40 mole, 84%) of a light yellow oil which boiled at 122-124°/0.5 mm (oil bath temperature 155-170°C). The physical properties of the hydroxy sulfide were determined: n_D^{25} 1.5747; d^{25} 1.1743. Analysis of the compound for sulfide sulfur (29) gave the following results:

Calc'd. for $C_8H_{12}S_2O$: S, 17.01. Found: S, 17.49; 17.40.

2-(β-thiothienyl)-1-pentanol



The same general procedure as previously described was employed, using 600 ml (0.60 mole) of a lithium aluminum hydride solution and 130 g (0.53 mole) of ethyl 2-(β-thiothienyl) valerate dissolved in 150 ml of anhydrous ether. The excess hydride and complex alcoholate were decomposed in the usual manner. After the ether extraction of the hydroxy sulfide, the ether layers were combined, washed with sodium bicarbonate and water, dried, and the ether removed. Fractionation of the crude product gave 88 g (0.44 mole, 82%) of the pure compound which distilled at 133-135°C/0.5 mm (oil bath temperature 160-180°C). Its physical properties were: n_D^{25} 1.5632; d^{25} 1.1394. The sulfide sulfur (29) analysis of the product gave the following results:

Calc'd. for $C_9H_{14}S_2O$: S, 15.83. Found: 16.02; 16.15.

2-phenoxy-1-propanol

Using the same technique as that used in the foregoing experiments, 60 g (0.31 mole) of ethyl α-phenoxy propionate was added to 310 ml

(0.31 mole) of a cooled molar solution of lithium aluminum hydride. The reaction mixture was stirred for a one hour period and the excess hydride was decomposed with ethyl acetate. After allowing the mixture to stand overnight, the complex alcoholate was decomposed by pouring it into 300 ml of ice water and adding 1200 ml of a ten percent sulfuric acid solution. The ether layer was separated and the aqueous layer extracted with two 150 ml portions of ether. The combined ether layers were washed with 200 ml of a five percent sodium bicarbonate solution and then dried. After removing the ether, the product was distilled to obtain 40.5 g (0.27 mole, 86.5%) of the phenoxy alcohol boiling at 125°/10 mm (oil bath temperature 160-165°C). The physical constants of the compound were: n_D^{25} 1.5239; d^{25} 1.0632. The reported (15) values are: b.p. 120°/10 mm; n_D^{25} 1.4760; d^{25} 0.9830.

A second preparation of the compound on a small scale (0.05 mole) resulted in a 6 g yield (79% of the theoretical) of the phenoxy alcohol possessing the following physical constants: b.p. 122-125°/10 mm; n_D^{25} 1.5232; d^{25} 1.0632.

In order to test a second general method of synthesis, 4.2 g (0.18 mole) of sodium and 100 ml of anhydrous isopropyl ether were placed in the apparatus previously described and a solution of 22 g (0.23 mole) of phenol dissolved in anhydrous isopropyl ether was added slowly. The flask was warmed slightly to initiate the reaction. After the sodium had reacted, 20 g (0.21 mole) of 2-chloro-1-propanol was added and the mixture was refluxed for an eight hour period. It was then transferred to a separatory funnel, washed with 100 ml of water, next with two 50 ml portions of a five percent sodium hydroxide solution and again with water. After the ether solution had been dried over anhydrous sodium sulfate, the ether was removed and the product distilled to yield 19 g of a material boiling at 80-83°/10 mm. The physical properties of the liquid were: n_D^{25} 1.5253; d^{25} 1.0409. The material evidently consisted primarily of unreacted phenol as several extractions with a solution of sodium hydroxide greatly reduced its volume.

2-thiophenyl-1-propanol

Following the same procedure as in the previous preparations, 95 ml (0.095 mole) of a one molar solution of lithium aluminum hydride was placed in the flask, cooled and treated slowly with 20 g (0.095 mole) of ethyl 2-thiophenyl propionate. Following the addition of the ester, the contents of the flask were stirred for a period of one hour and a half. A 13 ml volume of ethyl acetate was added to decompose the excess hydride and additional ether was added to increase the fluidity of the viscous mixture. The complex alcoholate was decomposed by using 200 ml of ice water and 500 ml of a ten percent sulfuric acid solution. The product was extracted, washed and dried in the usual manner. Removal of the ether and distillation of the residual liquid yielded a forerun of 3 g and 11.5 g (0.07 mole, 72%) of the desired compound boiling at

114-118°/ 1 mm. The refractive index of the product was: n_D^{20} 1.5722. The reported (12) properties of this compound are: b.p. 98-100°/0.5 mm; n_D^{20} 1.5710.

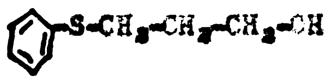
2-(β-thionaphthyl)-1-propanol

Following the same general procedure discussed above, 26 g (0.10 mole) of ethyl 2-(β-thionaphthyl) propionate dissolved in 50 ml of anhydrous ether was added dropwise to 125 ml (0.13 mole) of lithium aluminum hydride solution. The mixture was stirred for one half hour after which ethyl acetate was added to decompose the excess hydride. The viscous reaction mixture was poured into 100 ml of ice water and decomposed with 600 ml of a ten percent sulfuric acid solution. The product was extracted with ether, washed, and dried as before. The ether was removed by distillation and the residual oil solidified when cooled in an ice bath. The compound melted at room temperature and was distilled in vacuo to yield 18 g (0.08 mole, 83%) of a pure compound which boiled at 160-162°/0.5 mm. The refractive index of the liquid was: n_D^{25} 1.6444. The liquid solidified to a waxlike solid upon cooling and its melting point determined: m.p. 26-28°C. Analysis for sulfide sulfur (29) of the product gave the following results:

Calc'd. for $C_{13}H_{14}SO$: S, 14.67. Found: 14.92; 14.99.

An attempt was made to prepare the compound by refluxing a mixture of β-thionaphthol and allyl alcohol in the presence of sulfur for twenty-four hours but resulted only in the recovery of some β,β-dinaphthyldisulfide and unreacted β-thionaphthol.

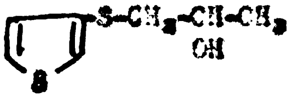
3-thiophenyl-1-propanol



By a similar procedure involving the interaction of 127 ml (0.127 mole) of lithium aluminum hydride solution and 25 g (0.127 mole) of methyl (3-thiophenyl) propionate dissolved in 100 ml of absolute ether followed by decomposition of the excess hydride with ethyl acetate there was obtained a viscous solution of the complex alcoholate. Decomposition of the complex was accomplished as described previously and the ether extract of the compound was washed and dried. After removing the ether, the product was distilled to yield 17.3 g (0.10 mole, 18%) of a clear oil boiling at 133-135°/1 mm. Its refractive index was: n_D^{20} 1.5807. The reported (21) physical constants for this compound are: b.p. 134-135°/2 mm; n_D^{20} 1.5813.

1-(β-Thiothienyl) and (β-Thionaphthyl) and (Phenoxy)-2-Alkyl Alcohols

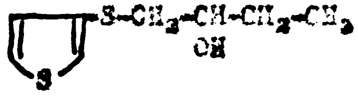
1-(β-thiothienyl)-2-propanol



Into a three necked flask fitted with a stirrer, reflux condenser and dropping funnel, were placed 46.4 g (0.40 mole) of 3-thiophenethiol and 120 ml of a twenty percent solution of sodium hydroxide. A quantity, 45.5 g (0.48 mole), of propylene chlorohydrin was added dropwise over a one-half hour period. The reaction mixture was refluxed for a period of one hour and allowed to cool to room temperature during which time a yellow oil separated. The oily layer was separated and the aqueous layer extracted with two 50 ml portions of ether. The ether extracts were combined with the oily layer, washed twice with 50 ml portions of water, and dried over anhydrous sodium sulfate. After removing the ether, the compound was distilled under reduced pressure and gave 59.6 g (0.34 mole, 85.6%) of clear yellowish oil boiling at 116°/5 mm. Its physical constants were: n_D^{25} 1.5783; d^{25} 1.2011. The reported boiling point is: 116°/5 mm. Analysis of the compound for sulfide sulfur (29) gave the following data:

Calc'd. for $C_7H_{10}S_2O$: S, 18.40. Found: 18.49; 18.40.

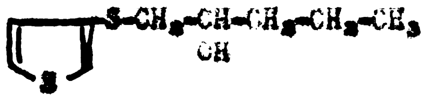
1-(β-thiothienyl)-2-butanol



Using the same apparatus as was employed in the previous preparations, 21 g (0.18 mole) of 3-thiophenethiol was dissolved in 50 ml of absolute ethanol and treated with 100 ml of a solution prepared by adding 4.2 g (0.18 mole) of sodium to 100 ml of absolute alcohol. The resulting solution was then warmed and 20 g (0.18 mole) of butylene chlorohydrin added dropwise with stirring. The temperature of the reaction mixture was then raised to its reflux temperature and refluxed gently for an hour and a half. After allowing the reaction to stand overnight, the heterogeneous mixture was filtered to remove sodium chloride which was subsequently dried and weighed to give 9.5 g of salt (90% of the theoretical). The filtrate was then concentrated, dissolved in ether, washed with three 50 ml portions of a five percent solution of sodium hydroxide and two 50 ml quantities of water. The ether layer was dried over anhydrous sodium sulfate and after removing the ether the product was distilled to yield 18 g (0.09 mole, 53%) of a light yellow liquid boiling at 116-118°/0.5 mm (oil bath temperature 180-190°C). Its physical constants were: n_D^{25} 1.5755; d^{25} 1.1751. Sulfide sulfur (29) analysis of the compound gave the following results:

Calc'd. for $C_8H_{12}S_2O$: S, 17.02. Found: S, 17.31, 17.29.

1-(β-thiothienyl)-2-pentanol



The procedure and apparatus for the reaction was the same as that used in the preceding preparation. A quantity, 26.6 g (0.23 mole) of 3-thiophenethiol was dissolved in 50 ml of absolute alcohol, placed in the flask and treated rapidly with a solution of sodium ethoxide prepared by dissolving 5.3 g (0.23 mole) of sodium in 100 ml of absolute alcohol.

The reaction mixture was heated and stirred for a period of twenty minutes followed by treatment with 32 g (0.26 mole) of 1-chloro-2-pentanol which was added over a ten minute period. The reaction mixture was maintained at its reflux temperature for a period of one hour, cooled, filtered and the alcohol removed by distillation which left a dark colored liquid. The crude product was dissolved in ether, washed, dried, and after removing the ether, the compound was distilled to yield 33 g (0.16 mole, 71%) of a yellowish oil which boiled at 125-127°/0.5 mm. The refractive index and density of the compound were: n_D^{25} 1.5636; d^{25} 1.1397. Analysis of the compound for sulfide sulfur (29) gave the following results:

Calc'd. for $C_9H_{14}S_2O$: S, 15.83. Found: S, 16.19; 16.11.

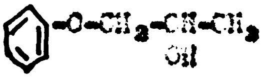
1-(β-thionaphthyl)-2-propanol

$$\text{-S-CH}_2\text{-}\underset{\text{OH}}{\text{CH}}\text{-CH}_3$$

The same apparatus as previously described was used and provision was made to bubble a stream of dry nitrogen gas through the reaction mixture. A quantity, 16g (0.16 mole) of β-thionaphthol was crushed in a mortar and added to a flask containing 150 ml of absolute alcohol. Nitrogen was bubbled through the system and continued throughout the reaction. The mixture was kept at 60-70°C and stirred until the β-thionaphthol had completely dissolved. A solution of sodium ethoxide was prepared by dissolving 2.3 g (0.10 mole) of sodium in 100 ml of absolute ethanol and added to the reaction flask. After stirring the hot solution for a half hour period, 11.4 g (0.12 mole) of propylene chlorohydrin was added quickly and the mixture was refluxed for a period of an hour and a half. The hot solution was filtered to yield 5.5 g of sodium chloride (94% of the theoretical) and upon cooling the filtrate, 1 g of β,β-dinaphthyldisulfide crystallized from the reaction mixture in the form of silvery plates (m.p. 139-140°). The disulfide was removed by filtration followed by removal of most of the alcohol by distillation. Upon cooling, the product crystallized, was filtered and dried. It melted at 41-43°C. After crystallization from a 50-50 mixture of ethyl alcohol and water there was obtained 19 g (0.09 mole, 67%) of light yellow crystals melting at 42-44°C. Analysis of the material for sulfide sulfur (29) gave the following results:

Calc'd. for $C_{13}H_{14}SO$: S, 14.67. Found: S, 15.13; 15.10.

1-phenoxy-2-propanol

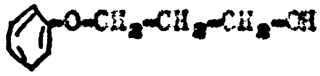


$C_6H_5{-}O{-}CH_2{-}\underset{OH}{CH}{-}CH_3$

A quantity, 42 g (0.45 mole), of phenol was dissolved in 180 ml of a ten percent sodium hydroxide solution and interacted with slightly more than the theoretical amount (45 g, 0.47 mole) of propylene chlorohydrin. The reaction proceeded rapidly under reflux with the separation of an oily layer and was complete in a half hour. The oily layer of the product was separated and the aqueous layer extracted with ether. The ether extracts and oily layer were combined, washed with a five percent sodium hydroxide solution, followed by water, dried and the ether removed. Distillation of the product gave 38 g (0.25 mole, 55.5%) of a colorless oil boiling at 116-117°/10 mm. Its physical constants were: n_D^{25} 1.5220; d^{25} 1.0606. Literature (15) values for its physical constants are: b.p. 116-117°/10 mm; n_D^{25} 1.5200; d^{25} 1.0610.

A second preparation of the compound resulted in a 60% yield of a colorless liquid boiling at 115°/1 mm. Its refractive index was: n_D^{25} 1.5220.

3-phenoxy-1-propanol



Following the previous general procedure, 21 g (0.22 mole) of phenol was dissolved in 90 ml of a ten percent solution of sodium hydroxide and treated with 22.5 g (0.24 mole) of trimethylene chlorohydrin. The mixture was refluxed for an hour during which an oily layer separated. This was removed and the water layer extracted with ether. After combining the oily layer and ether extracts, they were washed, dried, and the ether removed. Vacuum distillation of the product yielded 20 g (0.13 mole, 60%) of a colorless liquid boiling at 140-143°/10 mm. Its refractive index was: n_D^{25} 1.5244. The reported (32) boiling point for this compound is: 249-250°/754 mm.

(β-Thiothienyl) and (β-Thionaphthyl) and (Phenoxy) Chloroalkanes

1-(β-thiothienyl)-2-chloropropane

Into a 300 ml three necked flask fitted with a stirrer, reflux condenser, and dropping funnel was placed 25 g (0.14 mole) of 1-(β-thiothienyl)-2-propanol dissolved in 15 ml of pyridine. To this solution was added with stirring 20.6 g (0.17 mole) of purified thionyl chloride during an hour. Provision was also made to pass a slow stream of dry air across the surface of the mixture during the reaction. Stirring was continued for fifteen minutes after the addition of thionyl chloride was complete. The reaction mixture was then taken up in 80 ml of ether, washed twice with 40 ml portions of water and dried over anhydrous sodium sulfate. Following the removal of the ether, the product was distilled in vacuum to yield 10 g (0.05 mole, 37%) of yellowish oil boiling at 85-90°/1 mm. The physical constants of the compound were: n_D^{25} 1.5794; d^{25} 1.2304. Analysis for sulfide sulfur (29) gave the following results:

Calc'd. for $C_7H_9S_2Cl$: S, 16.62. Found: S, 16.84; 17.03.

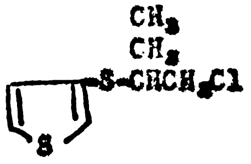
The compound was also prepared by the rearrangement reaction using dry chloroform as the solvent. A quantity 17.4 g (0.10 mole) of 2-(β-thiothienyl)-1-propanol was dissolved in 25 ml of dry chloroform and treated with 14.3 g (0.12 mole) of purified thionyl chloride dissolved in 15 ml of chloroform. The mixture was then refluxed gently for an hour during which the volume of chloroform was kept constant by occasional addition of solvent. The chloroform was then removed and the product dissolved in ether, washed with water, dried and the solvent again removed. Distillation of the product gave 13 g (0.07 mole, 68%) of an almost colorless liquid boiling at 105°/1 mm. Its refractive index was: n_D^{25} 1.5800. Analysis of the chlorosulfide for sulfide sulfur (29) gave the following data:

Calc'd. for $C_7H_9S_2Cl$: S, 16.62. Found: S, 16.52; 16.66.

A second preparation using the same quantities of materials gave a 58% yield of the rearranged chlorosulfide boiling at 115-117°/3 mm. Its refractive index was: n_D^{25} 1.5793.

A third preparation of the compound in which dry pyridine was employed as the solvent gave a 26% yield of the rearranged chlorosulfide boiling at 90-94°/0.5 mm. Its refractive index was: n_D^{25} 1.5800.

1-(β-thiothienyl)-2-chlorobutane and 2-(β-thiothienyl)-1-chlorobutane



The procedure and apparatus was the same as previously described and consisted of dissolving 10 g (0.053 mole) of 1-(β-thiothienyl)-2-butanol in 25 ml of dry carbon tetrachloride followed by treatment with 7.1 g (0.06 mole) of purified thionyl chloride dissolved in 5 ml of carbon tetrachloride. At the end of the addition, the mixture was refluxed gently on the steam bath for a forty-five minute period. After dissolving the reaction mixture in ether, it was washed with three 20 ml quantities of water, dried and the solvent removed. The product was distilled under vacuum to yield 11 g (0.05 mole, 50%) of a light yellowish oil boiling at 92-94°/0.5 mm (oil bath temperature 175-195°C). The physical constants of the mixture of isomers were: n_D^{25} 1.5711; d^{25} 1.2005. The sulfide sulfur analysis gave the following results.

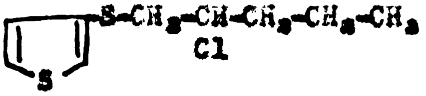
Calc'd. for $C_8H_{11}S_2Cl$: S, 15.50. Found: S, 15.70; 15.67.

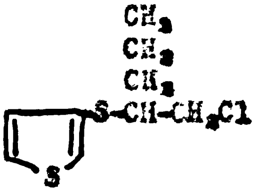
The mixture was also prepared by the rearrangement of 2-(β-thiothienyl)-1-butanol by treating 18.8 g (0.10 mole) of the hydroxy sulfide dissolved in 40 ml of dry carbon tetrachloride with 14.2 g (0.12 mole) of purified thionyl chloride dissolved in 10 ml of carbon tetrachloride. The usual operations were carried out and distillation of the product yielded 13 g (0.06 mole, 63%) of a mixture of the rearranged and unrearranged chlorosulfides boiling at 100-102°/0.5 mm. The refractive index and density were: n_D^{25} 1.5712; d^{25} 1.2008. Analysis of the mixture for sulfide sulfur (29) gave the following results:

Calc'd. for $C_8H_{11}S_2Cl$: S, 15.50. Found: S, 15.95; 15.77.

A second preparation of the compounds by the rearrangement reaction resulted in a 65.5% yield of the chlorosulfides boiling at 96-100°/0.5 mm. The refractive index was: n_D^{25} 1.5707.

1-(β-thiothienyl)-2-chloropentane and 2-(β-thiothienyl)-1-chloropentane





Using the same apparatus and technique as described above, 16 g (0.08 mole) of 1-(β-thiothienyl)-2-pentanol were dissolved in 30 ml of dry carbon tetrachloride and reacted with 7.6 g (0.07 mole) of purified thionyl chloride dissolved in 5 ml of carbon tetrachloride. Identical operations were carried out as previously described and distillation yielded 10 g (0.05 mole, 57%) of a mixture of chlorosulfides which boiled at 110-112°/0.5 mm (oil bath temperature 175-190°C). The physical constants were: n_D^{25} 1.5600; d^{25} 1.1593. Analysis of the mixture for sulfide sulfur is indicated below.

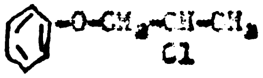
Calc'd. for $C_9H_{13}S_2Cl$: S, 14.50. Found: S, 14.78; 14.79.

The preparation was also carried out by the partial rearrangement of 2-(β-thiothienyl)-1-pentanol. A quantity, 14.2 g (0.12 mole), of purified thionyl chloride was dissolved in 10 ml of carbon tetrachloride and added dropwise to 20.2 g (0.10 mole) of the hydroxy sulfide dissolved in 40 ml of dry carbon tetrachloride. The product was isolated by carrying out the previously discussed operations and resulted in the preparation of 16 g (0.07 mole, 73%) of the mixture of isomers boiling at 122-124°/0.5 mm (oil bath temperature 170-185°C). The following physical properties were determined: n_D^{25} 1.5603; d^{25} 1.1594. A sulfide sulfur analysis gave the following results:

Calc'd. for $C_9H_{13}S_2Cl$: S, 14.50. Found: S, 14.75; 14.87.

A second and third runs were made involving the partial rearrangement of 2-(β-thiothienyl)-1-pentanol with thionyl chloride and resulted in yields of 83.5% and 69% respectively of the chlorosulfides. The boiling points and refractive indices were respectively: 112-118°/0.5 mm; n_D^{25} 1.5601 and 118-122°/0.5 mm; n_D^{25} 1.5593.

1-phenoxy-2-chloropropane



$$C_6H_5-O-CH_2-\underset{Cl}{CH}-CH_3$$

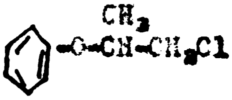
Following the general procedure discussed above for the conversion of hydroxy sulfides to chlorosulfides, 23 g (0.15 mole) of 1-phenoxy-2 propanol were dissolved in 40 ml of dry pyridine and treated slowly with 20 g (0.17 mole of purified thionyl chloride. The reaction mixture became warm from the exothermic reaction and the precipitation of pyridine hydrochloride became noticeable after about half of the thionyl chloride had been added. The mixture was stirred and warmed for a half hour following the addition of thionyl chloride. It was then taken up in ether, washed with water, dried and the ether removed by distillation. The product on distillation boiled at 95°/5 mm yielding 14 g (0.08 mole, 55%) of the desired compound. Its physical constants were as follows: n_D^{25} 1.5252; d^{25} 1.0939. Analysis of the compound for carbon and hydrogen gave the following results:

Calc'd. for $C_9H_{11}OCl$: C, 63.34; H, 6.45. Found: C, 64.04; H, 6.80.

Another preparation of the same compound gave a 47% yield of product boiling at 95°/5 mm. Its refractive index was: n_D^{25} 1.5221.

Two attempts were made to prepare the chloride by a similar reaction in which the pyridine solvent was replaced by chloroform and in each instance the product obtained gave a negative test for chloride ion in the sodium fusion test and was evidently unreacted phenoxy propanol.

1-Chloro-2-Phenoxy propane



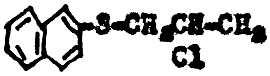
$C_6H_5-O-CH(CH_3)-CH_2Cl$

Using pyridine (35 ml) as a solvent, and employing the general procedure and apparatus used in the preceding preparation, 12 g (0.08 mole) of 2-phenoxy-1-propanol were treated with 12 g (0.10 mole) of purified thionyl chloride. An ice bath was used to moderate the exothermic reaction which was stirred for a half hour following the thionyl chloride addition. After gently heating for an hour, the thick reaction mixture was poured into 50 ml of water to dissolve the pyridine hydrochloride. A 100 ml quantity of ether was added and the mixture transferred to a separatory funnel, and the water layer removed. The latter was extracted with ether. The ether layers were combined, washed with three 40 ml portions of a dilute solution of hydrochloric acid, twice with water, dried and the ether removed. The product was distilled in vacuo to give

7 g (0.04 mole, 52%) of a colorless oil boiling at 62-64°/0.5 mm. The physical constants of the compound were: n_D^{25} 1.5195; n_D^{20} 1.5216; d^{25} 1.0927. The reported values are: b.p. 110-113°/22 mm; n_D^{20} 1.5218; d^{20} 1.102. A carbon and hydrogen analysis of the compound gave the following results:

Calc'd. for $C_9H_{11}OCl$: C, 63.34; H, 6.45. Found: C, 64.32; H, 6.82.

1-(β-thionaphthyl)-2-chloropropane



Into a 200 ml Erlenmeyer flask were placed 15 ml of dry chloroform containing 4 g (0.018 mole) of 1-(β-thionaphthyl)-2-propanol and treated dropwise with 2.5 g (0.021 mole) of purified thionyl chloride. The flask was shaken continuously during the addition of thionyl chloride. A slow stream of dry air was directed across the surface of the reaction mixture at frequent intervals throughout the reaction, to facilitate removal of sulfur dioxide and hydrogen chloride. The reaction mixture turned brownish in color and was warmed on the steam bath for a ten minute period to complete the removal of gases. The mixture was then dissolved in 50 ml of ether, washed with three 20 ml portions of water, dried, the ether removed and the product distilled under vacuum to yield 3.3 g (0.014 mole, 80%) of a light yellow liquid boiling at 140°/0.5 mm. Its refractive index and density were: n_D^{25} 1.6366; d^{25} 1.1711. Analyses of the compound for sulfide sulfur (29) gave the following results:

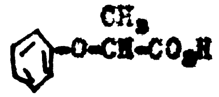
Calc'd. for $C_{13}H_{13}SCl$: S, 13.52. Found: S, 13.98; 13.91.

The same compound was also prepared by the rearrangement of 2-(β-thionaphthyl)-1-propanol using a similar procedure as was employed in the previously described reaction. A quantity, 7 g (0.032 mole) of the hydroxy sulfide was dissolved in 25 ml of dry chloroform and treated with 4.2 g (0.036 mole) of purified thionyl chloride. The mixture was warmed on the steam bath for five minutes to complete the reaction and to drive off reaction gases. It was then dissolved in ether, washed with water, dried, refluxed for a few minutes with Norite, filtered, and the ether removed by distillation. The residual product was placed under a 0.5 mm vacuum for one hour (while heating on a steam bath) to remove the last traces of thionyl chloride and solvent. The chlorosulfide weighed 6 g (0.025 mole, 79%) and its refractive index was: n_D^{25} 1.6360. Analysis of the compound gave the following results for sulfide sulfur (29):

Calc'd. for $C_{13}H_{13}SCl$: S, 13.52. Found: S, 13.90; 13.76.

Intermediates

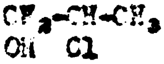
-Phenoxy propionic acid



$C_6H_5-O-CH(CH_3)-CO_2H$

A 300 ml three necked flask was fitted with a reflux condenser, stirrer, and dropping funnel. A quantity, 10 g (0.45 mole), of sodium were placed in the flask and treated with 42 g (0.45 mole) of phenol dissolved in anhydrous isopropyl ether. The heterogeneous mixture was refluxed until all the sodium had dissolved and 66 g (0.45 mole) of α-bromopropionic acid dissolved in 50 ml of anhydrous isopropyl ether was added, after which the mixture was refluxed for eight hours. A solution of 2 ml of concentrated hydrochloric acid in 200 ml water was added, the mixture shaken, and the ether layer separated. The aqueous layer was extracted with ether. The combined ether extracts were dried, and the ether removed by distillation. The remaining material was fractionated and the unreacted phenol collected at 55-65°/1 mm leaving a residue in the distillation flask which crystallised upon cooling. This material was dissolved in ether, heated with Norite, filtered, and the ether removed. Recrystallization of the compound from carbon tetrachloride yielded 3 g (0.02 mole, 4%) of the pure acid. Its melting point was: 116-118°C. The reported value (33) is: 115-116°C.

2-Chloro-1-Propanol



$$\underset{OH}{CH_2}-\underset{Cl}{CH}-CH_3$$

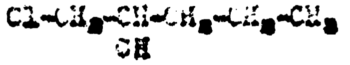
Into a one liter three necked flask, immersed in an ice bath, was placed a solution of 155 g (1.00 mole) of chromyl chloride contained in 300 ml of carbon tetrachloride. The flask was fitted with a stirrer, reflux condenser and a piece of glass tubing which extended below the surface of the solution. Into this rapidly stirred cold solution, propylene was bubbled until the color of the chromyl chloride discharged and the flask had gained 29.4 g which corresponded to 0.70 mole of propylene. The solid was filtered, washed and hydrolyzed with cold sodium bisulfite solution. The aqueous solution was saturated with salt, extracted with ether and the extract dried over anhydrous sodium sulfate. Removal of the ether and distillation at atmospheric pressure gave 26 g (43%) of the chlorohydrin boiling at 131-132°C. Its refractive index was: n_D^{25} 1.4368. The 3,5-dinitrobenzoate of the compound melted at: 73-75°C. The previously reported properties of this compound are: b.p. 121-124°C/613 mm; n_D^{20} 1.4377; m.p. of its 3,5-dinitrobenzoate, 76.5-77.5°C.

1-Chloro-2-Butanol

$$CH_3CH_2\underset{OH}{C}HCH_2Cl$$

A quantity, 100 g (0.80 mole), of dimethyl chloroacetal and 72 g (0.80 mole) of anhydrous oxalic acid were placed in a 500 ml round bottom flask fitted with a 12 inch Vigreux column arranged for distillation. The flask was covered completely with a heating mantle and a safety glass was placed in front of the apparatus as a precaution against peroxide explosion. The reaction mixture was heated moderately allowing the slow collection of a distillate boiling in the range 90-100°C. The distillate was dissolved in 100 ml of anhydrous ether, placed in a one liter bottle containing 60 g of powdered calcium chloride dihydrate. The bottle was stoppered with a cork having a small hole to relieve pressure and shaken for three and a half hours in a mechanical shaker. The heterogeneous mixture was filtered and the filtrate allowed to drop into a chilled Grignard reagent prepared from 87.2 g (0.80 mole) of redistilled ethyl bromide and 20 g (0.83 mole) of magnesium. The addition compound was decomposed in the usual manner with 500 ml of a one to one hydrochloric acid solution containing an equal volume of cracked ice. The acidic solution was extracted with four, 150 ml portions of ether, which were combined, washed first with 150 ml of a dilute hydrochloric acid solution, then with 150 ml of water, next with 150 ml of a ten percent potassium carbonate solution and finally with 150 ml of water. The ether solution was dried over anhydrous potassium carbonate for two hours and then over anhydrous sodium sulfate for eight hours. The ether was removed and the product distilled in vacuo to yield 20 g (0.19 mole, 23%) of the colorless chlorohydrin boiling at 50-55°/15 mm. Its refractive index was: n_D^{25} 1.4427. The reported (34) physical constants are: b.p. 52°/15 mm; n_D^{25} 1.4410.

1-Chloro-2-Pentanol



$$\underset{\displaystyle OH}{\text{Cl-CH}_2\text{-CH}}\text{-CH}_2\text{-CH}_2\text{-CH}_3$$

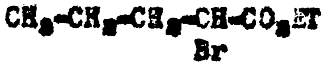
The procedure and apparatus were the same as that described in the preceding preparation. A quantity, 124 g (1.00 mole) of dimethyl chloroacetal and 90 g (1.00 mole) of anhydrous oxalic acid were allowed to interact. The fraction boiling in the range 90-95°C was collected, diluted with 100 ml of absolute ether and shaken for a period of four hours with powdered calcium chloride dihydrate. The resulting anhydrous chloroacetaldehyde was filtered directly into a well cooled Grignard solution which had been prepared by the interaction, in 450 ml of absolute ether, of 26 g (1.10 moles) of magnesium and 123 g (1.00 mole) of redistilled n-propyl bromide. The mixture was decomposed with 500 ml of a one to one hydrochloric acid solution containing cracked ice. The acidic solution was extracted with ether, washed and dried as before. Removal of the ether and distillation of the product yielded 32 g (0.26 mole, 26%) of the colorless chlorohydrin which turned a reddish violet color after being set aside overnight. The boiling point of the material was: 60-64°/14 mm, and its reported value (35) is: 59-62°/14 mm.

Ethyl α-Bromopropionate

$$CH_3\,\underset{Br}{CH}\,CO_2Et$$

A quantity, 198 g (1.20 mole) of α-bromopropionic acid and 153 g (1.50 mole) of thionyl chloride was placed in a 500 ml round bottom flask fitted with a reflux condenser. The mixture was refluxed for a two hour period and the unreacted thionyl chloride removed by arranging the apparatus for distillation and evacuating the system with an aspirator for a one hour period. The residual α-bromopropionyl chloride weighed 194 g (1.13 moles, 95%). The acid chloride was transferred to a three neck flask fitted with a stirrer, reflux condenser and dropping funnel and treated dropwise with 65 g (1.42 moles) of absolute ethanol. Following the addition of alcohol, the mixture was warmed for a fifteen minute period to complete the reaction, and the compound distilled using a water aspirator to give 30 g of a forerun and 183 g (1.01 moles, 91%) of the α-bromo ester boiling at 60°/12 mm. Its reported (36) boiling point is 159-161°/atm.

Ethyl α-Bromovalerate

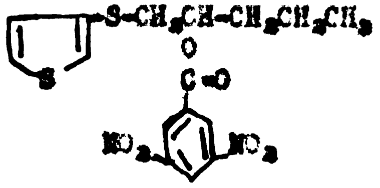


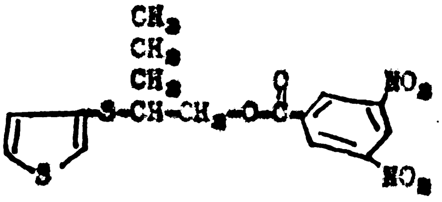
$$CH_3-CH_2-CH_2-\underset{Br}{CH}-CO_2Et$$

Into a one liter three necked flask fitted with a stirrer, an efficient reflux condenser and dropping funnel were placed 204 g (2.00 moles) of n-valeric acid and 5 g of phosphorus pentachloride. A quantity, 336 g (2.10 moles) of bromine was added cautiously to the flask while it was kept hot on a steam bath. The reaction mixture was stirred and heated for twenty-five hours during which time hydrogen bromide was continuously evolved as well as a little bromine. The condenser was removed and the heating continued for three additional hours to drive off excess bromine. A quantity, 284 g (2.4 moles), of thionyl chloride was added quickly through the dropping funnel after which the reaction mixture was refluxed on the steam bath for a two and one-half hour period. The excess thionyl chloride was removed by distillation and 115 g (2.50 moles) of absolute ethanol were added at such a rate as to maintain gentle refluxing of the reaction mixture. Following the addition of ethanol, the mixture was heated at its reflux temperature for a half hour. The material was then transferred to a one liter round bottom flask and the low boiling material removed under reduced pressure using a water aspirator. A vacuum pump was then connected and the α-bromo ester distilled to yield

253 g (1.20 moles, 61%) of a material boiling at 71-73°/10 mm. Its reported (37) boiling point is: b.p. 84-86°/16 mm.

3,5-Dinitrobenzoate derivative of 1-(β-thiothienyl)-2-chloropentane and 2-(β-thiothienyl)-1-chloropentane



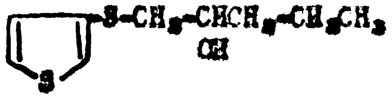


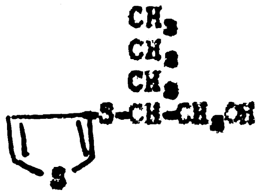
The quantity, 1.6 g (0.018 mole), of sodium was dissolved in 100 ml of absolute ethanol and 14.5 g (0.068 mole) of 3,5-dinitrobenzoic acid was added to the sodium ethoxide solution contained in a 200 ml Erlenmeyer flask. The mixture was swirled for ten minutes to complete salt formation and 15 g (0.068 mole) of a mixture of 1-(β-thiothienyl)-2-chloropentane and 2-(β-thiothienyl)-1-chloropentane were added. The heterogeneous mixture was heated at its reflux temperature for a period of five hours. The yellow colored mixture was filtered to remove salts, concentrated to a volume of 60 ml, taken up in 200 ml of benzene and washed with three 80 ml portions of a ten percent solution of sodium carbonate and then with water. The benzene was removed by distillation and a 300 ml quantity of ethanol added. The derivative was allowed to crystallize overnight and then cooled in the refrigerator for a period of one hour, giving rise to a heavy precipitate which was filtered and dried to yield 13 g (0.033 mole, 50%) of yellow crystals, melting at

79-81°C. Analysis of the derivative for sulfide sulfur (29) gave the following results:

Calc'd. for $C_{16}H_{16}S_2O_6N_2$: S, 8.08. Found: S, 7.86.

1-(β -thiothienyl)-2-pentanol and 2-(β -thiothienyl)-1-pentanol





The saponification of a mixture of the 3,5-Dinitrobenzoates of 1-(β-thiothienyl)-2-chloropentane and 2-(β-thiothienyl)-1-chloropentane was carried out in the following manner. A 300 ml quantity of ethyl alcohol was placed in a 500 ml beaker and 20 g of potassium hydroxide added and stirred for several minutes. The alcoholic potash was decanted from the sediment into a 500 ml Erlenmeyer flask containing 13 g (0.033 mole) of a mixture of the 3,5-dinitrobenzoates of 1-(β-thiothienyl) and 2-(β thiothienyl-1-chloropentane. The mixture was warmed on the steam bath for an hour and a half, filtered, and the filtrate concentrated to a volume of 100 ml, and taken up in ether. This resulted in the precipitation of additional salt which was removed by filtration. The filtrate was concentrated a second time on the steam bath, dissolved in ether, washed four times with 50 ml portions of water and the ether removed. The reddish liquid was then poured into an Erlenmeyer flask and 150 ml of absolute ether was added followed by drying with anhydrous sodium sulfate. The ether was removed and the product distilled using an oil bath temperature of 190-200°C. A 3 g quantity of light yellow liquid was obtained. Its refractive index was: n_D^{25} 1.5617, and its 3,5-dinitrobenzoate melted at 81-83°C. Analysis of the mixture for sulfide (29) sulfur gave the following results:

Calc'd. for $C_9H_{14}S_2O$: S, 15.83. Found: S, 16.01.

SUMMARY

1. Three ethyl 2-(β-thiothienyl) alkyl esters and one ethyl-2-(β-thionaphthyl) alkyl ester were synthesized for the first time and their physical properties determined.

2. Three 2-(β-thiothienyl)-1-alkyl alcohols and one 2-(β thionaphthyl)-1-alkyl alcohol were synthesized for the first time and their physical properties were determined. The 3,5-dinitrobenzoate derivatives of these alcohols were prepared, analyzed, and their melting points determined.

3. Two 1-(β-thiothienyl)-2-alkyl alcohols and one 1-(β-thionaphthyl)-2-alkyl alcohol were synthesized for the first time and their physical properties were determined. Their 3,5-dinitrobenzoate derivatives were prepared, analyzed and the melting points are reported.

4. One 1-(β-thiothienyl)-2-chloroalkane, one 1-(β-thionaphthyl)-2-chloroalkane, and one phenoxychloroalkane were synthesized for the first time and their physical properties were determined. The 3,5-dinitrobenzoates of the chlorosulfides were prepared and the melting points of these derivatives were compared with those prepared from the corresponding alcohol.

5. Two hydroxy sulfides, 2-(β-thiothienyl)-1-propanol and 2-(β-thionaphthyl)-1-propanol, were found to rearrange totally to form

1-(β-thiothienyl)-2-chloropropane and 1-(β-thionaphthyl)-2-chloropropane respectively when treated with thionyl chloride. 2-(β-thiothienyl)-1-butanol was found to undergo partial rearrangement to produce a mixture of the isomeric chlorobutanes, when treated with thionyl chloride. Likewise, 2-(β-thiothienyl)-1-pentanol was found to partially rearrange to produce a mixture of the isomeric chloropentanes.

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A STUDY OF THE SYNTHESIS AND REARRANGEMENT OF β-HYDROXY ALKYL ARYL SULFIDES, HETEROCYCLIC SULFIDES, AND PHENYL ETHERS

By

Frederick J. McCarty

AN ABSTRACT

Submitted to the School of Graduate Studies of Michigan
State College of Agriculture and Applied Science
in partial fulfillment of the requirements
for the degree of

MASTER OF SCIENCE

Department of Chemistry

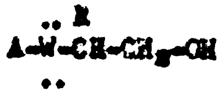
Year 1953

Approved ______________________________

Frederick J. McCarty

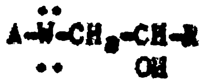
THESIS ABSTRACT

Several β-hydroxy sulfides and ethers have been prepared in order to investigate their behavior in displacement reactions which very presumably proceed through an intermediate sulfonium or oxonium ion. The primary and secondary alcohols studied may be represented by the general formulas,



$$A\text{-}\overset{\cdot\cdot}{\underset{\cdot\cdot}{W}}\text{-}\overset{R}{CH}\text{-}CH_2\text{-}OH$$

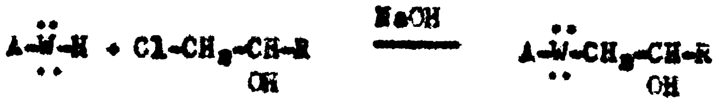
and



$$A\text{-}\overset{\cdot\cdot}{\underset{\cdot\cdot}{W}}\text{-}CH_2\text{-}\underset{OH}{CH}\text{-}R$$

where $\overset{\cdot\cdot}{\underset{\cdot\cdot}{W}}$ is either an oxygen or sulfur atom, A is a phenyl, β-naphthyl, or β-thienyl group and R is methyl, ethyl or n-propyl.

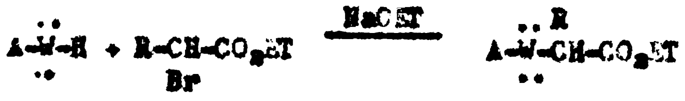
The general method of synthesis of the secondary alcohols involved a condensation of the appropriate mercaptan and chlorohydrin in aqueous alkali



$$A\text{-}\overset{\cdot\cdot}{\underset{\cdot\cdot}{W}}\text{-}H + Cl\text{-}CH_2\text{-}\underset{OH}{CH}\text{-}R \xrightarrow{NaOH} A\text{-}\overset{\cdot\cdot}{\underset{\cdot\cdot}{W}}\text{-}CH_2\text{-}\underset{OH}{CH}\text{-}R$$

A new general method of synthesis for preparing the isomeric primary alcohols was developed and consisted of two steps.

I



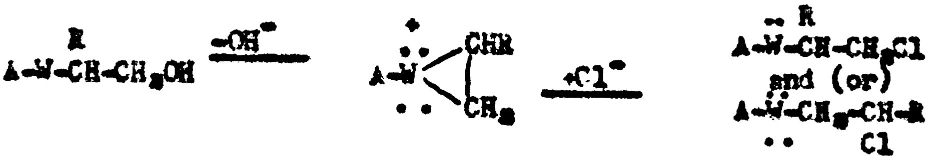
$$A\text{-}\overset{\cdot\cdot}{\underset{\cdot\cdot}{W}}\text{-}H + R\text{-}\underset{Br}{CH}\text{-}CO_2ET \xrightarrow{NaOET} A\text{-}\overset{\cdot\cdot}{\underset{\cdot\cdot}{W}}\text{-}\overset{R}{CH}\text{-}CO_2ET$$

II

$$A\text{-}\overset{\cdot\cdot}{\underset{\cdot\cdot}{W}}\text{-}\overset{R}{CH}\text{-}CO_2ET \xrightarrow{LiAlH_4} A\text{-}\overset{\cdot\cdot}{\underset{\cdot\cdot}{W}}\text{-}\overset{R}{CH}\text{-}CH_2OH$$

Altogether, seven hydroxy sulfides and four esters which have not been previously reported were prepared and their physical properties determined. The alcohols were further characterized by converting them into their 3,5-dinitrobenzoate derivatives.

The hydroxy sulfides and ethers were converted into their chlorides by treatment with thionyl chloride. Theoretically this reaction presumably proceeds through the formation of an intermediate ion which forms as a result of the participation of the oxygen or sulfur atom in the nucleophilic displacement of the neighboring hydroxyl group. The over-all process involves two Walden inversions and may yield either a single compound or a mixture of two compounds.



When 2-(β-thiothienyl)-1-propanol was treated with thionyl chloride in chloroform it was found to rearrange completely to give a single product, namely, 1-(β-thiothienyl)-2-chloropropane. The structure of the rearranged compound was established by preparing its 3,5-dinitrobenzoate and comparing this with the same derivative prepared from 1-(β-thiothienyl)-2-propanol. It was found that a mixed melting point of these two derivatives was not depressed, thereby proving that rearrangement had occurred in the replacement of the hydroxyl group by chlorine.

Likewise when 2-(β-thionaphthyl)-1-propanol was treated with thionyl chloride in chloroform, the only product isolated was 1-(β-thionaphthyl)

-2-chloropropane. The identity of the product was established by the preparation and comparison of the 3,5-dinitrobenzoate derivatives of the compounds involved.

The replacement of the hydroxyl group of 2-phenoxy-1-propanol and 1-phenoxy-2-propanol was accomplished by treating these compounds with thionyl chloride in pyridine. The phenoxychlorides prepared in this manner could not be converted into their p-nitro or 3,5-dinitrobenzoates by the usual methods. Thus, it was not possible to conclusively prove or disprove the rearrangement of 2-phenoxy-1-propanol.

The treatment of 2-(β-thiothienyl)-1-butanol or 1-(β-thiothienyl)-2-butanol with thionyl chloride in chloroform resulted in the formation of identical mixtures of the isomeric chlorides. The 3,5-dinitrobenzoates of these chloride mixtures were found to be identical and this observation is in accord with the postulated intermediate sulfonium ion, which could be converted into identical products by an attack of chloride ion, regardless of which alcohol it had originated from. By taking several mixed melting points of the pure derivatives comprising the mixture, it was established with the aid of a melting point diagram of the pure components and their mixtures, that the composition of the mixtures obtained in the displacement reaction consisted approximately of 70% unrearranged and 30% rearranged chloride.

Similar results were obtained when 2-(β-thiothienyl)-1-pentanol and 1-(β-thiothienyl)-2-pentanol were treated with thionyl chloride. By the interpretation and correlation of mixed melting point data of the pure derivatives comprising the mixture, it was estimated that the mixture was of approximately a 50-50 composition. The rearrangement reactions investigated here also resulted in the preparation of two chlorosulfides and one phenoxychloride not previously reported and these new compounds were further characterized by determining several of their physical properties.