

SELECTED REACTIONS OF SOME CYCLIC SULFOXIDES

by

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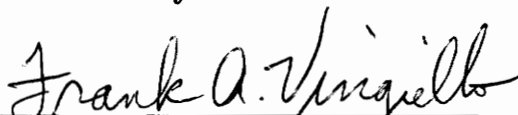
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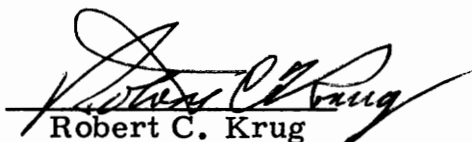
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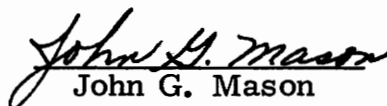
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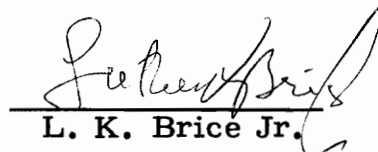
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TO MY PARENTS,
WHOSE HELP AND ENCOURAGEMENT
MADE THIS POSSIBLE

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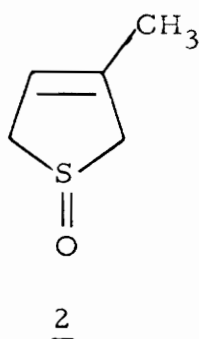
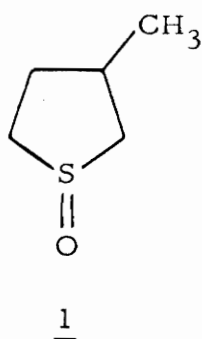
I. INTRODUCTION

Interest in sulfoxides currently assumes a place of major importance in organic chemical research. Investigations in this area stem undoubtedly from the unique and interesting nature of the sulfoxide moiety as well as from discoveries concerning practical application of sulfoxides to man's needs. Theoretical and fundamental interests* range from studies concerning the nature of the sulfur-oxygen bond of sulfoxides,¹ to condensation reactions^{2, 3, 4} and studies of stereochemical phenomena associated with the sulfoxide linkage.^{5, 6} In more practical terms, sulfoxides have been found useful as media for chemical reactions,⁷ as plant preservatives,⁸ insecticides,⁹ dispersing media for dyes and paints,¹⁰ and extraction solvents.¹¹

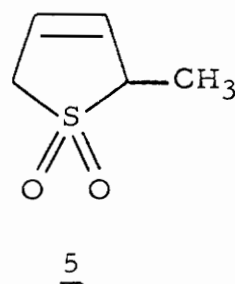
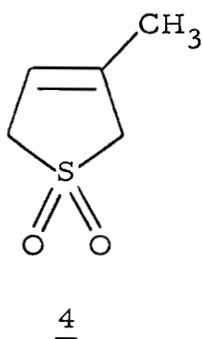
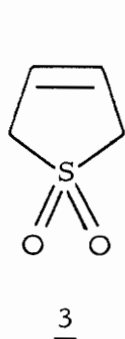
The present investigation contributes new and valuable knowledge to a relatively unexplored area of sulfoxide chemistry--the chemistry of monocyclic five-membered sulfoxides. The synthesis, stereochemical aspects, and selected reactions of the previously unknown 3-methyl-

* References cited in this paragraph were selected from the many publications in these areas and are presented here simply to introduce the reader to some general aspects of sulfoxide chemistry.

tetrahydrothiophene 1-oxide (1)* and 3-methyl-2, 5-dihydrothiophene 1-oxide (2) are discussed in detail in the following sections of this dissertation.



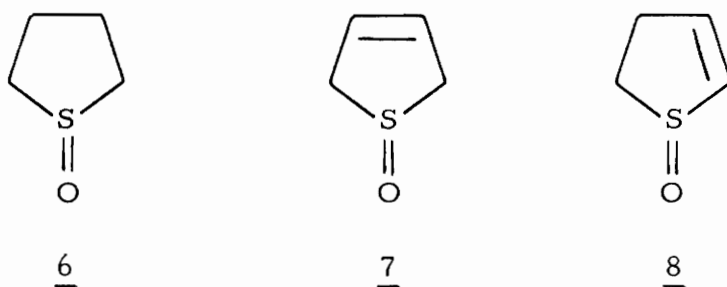
These particular compounds were selected for two reasons. First, studies in this Laboratory by R. C. Krug and co-workers¹² on the monocyclic five-membered sulfones 3, 4, and 5 have provided extensive knowledge concerning these compounds. Similar and related studies in



the corresponding sulfoxide series would enable one to compare the

* In structural formula 1, and in all other cyclic formulas appearing in this dissertation, the hydrogen atoms necessary to complete the covalency of carbon are not shown unless special emphasis is desired.

influence of the sulfoxide and sulfone moiety on other centers of reactivity within these cyclic systems. Secondly, studies in this Laboratory by R. C. Krug and D. E. Boswell¹³ on tetrahydrothiophene 1-oxide (6) and its novel dihydro isomers 7 and 8 have provided significant information concerning the properties and reactivities of these



cyclic sulfoxides. Introduction of a methyl group at position-3, as in 1 and 2, produces nonsymmetric molecules having several possible stereochemical orientations, as well as several nonequivalent centers for chemical reaction. Any alteration in chemical reactivity, due to the presence of the methyl group at position-3, could easily be determined by comparing similar reactions in each series.

Some meaningful comparisons between the present research and these previous studies have been realized and are discussed in the following sections.

II. HISTORICAL*

Although known for 100 years, sulfoxides have received considerably less attention than the related sulfides and sulfones.^{14, 15, 16} Much of the early work with sulfoxides was concerned with acyclic systems and only recently have cyclic sulfoxides been extensively studied. The simplest monocyclic sulfoxide, thiacyclopropane 1-oxide, is even today unreported in the chemical literature. This is of particular interest since the corresponding sulfide¹⁷ and sulfone¹⁸ have been known for many years.

Four cyclic sulfoxides were reported in 1916 by Grishkevich and Trokhimovskii¹⁹ in connection with the preparation of four-, five-, six-, and seven-membered cyclic sulfides. These sulfoxides, 2-methyl- and 2,5-dimethyltetrahydrothiophene 1-oxide, thiacyclohexane 1-oxide and 2-methylthiacyclohexane 1-oxide were described as thick yellow hygroscopic liquids. No further physical or chemical data, however were given for these compounds.

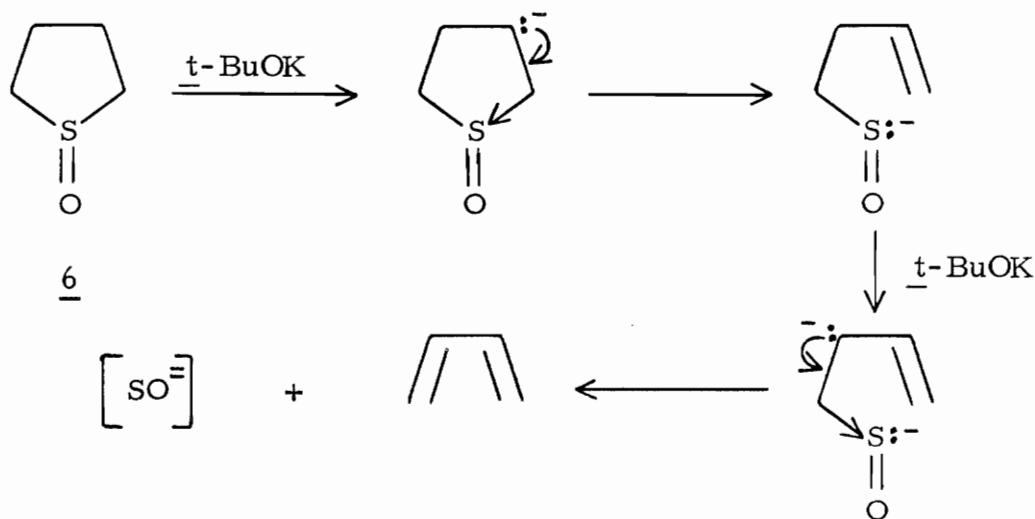
During the next 25 years, few studies concerning cyclic sulfoxides were reported and not until preparation of tetrahydrothiophene 1-oxide (6) by Tarbell and Weaver²⁰ in 1941 was interest in this field intensified.

* Discussion in this section will be limited to monocyclic ring systems having only one sulfoxide moiety, and will include acyclic sulfoxides only when related to research described in this dissertation. A more general review of sulfoxides is found in references 14-16.

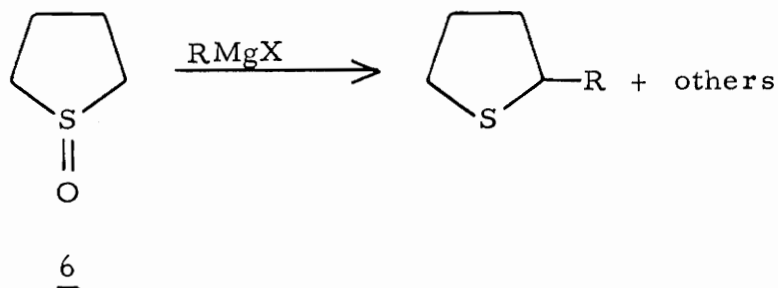
This sulfoxide was prepared simply by oxidation of tetrahydrothiophene with 30% hydrogen peroxide. Derivatives were prepared by condensation of the sulfoxide with p-toluenesulfonamide and substituted acetamides in acetic anhydride--now well known reactions of sulfoxides in general.

Treatment of this sulfoxide with diazo methane under a variety of conditions failed to give a ring expansion as in the case of cyclic ketones.

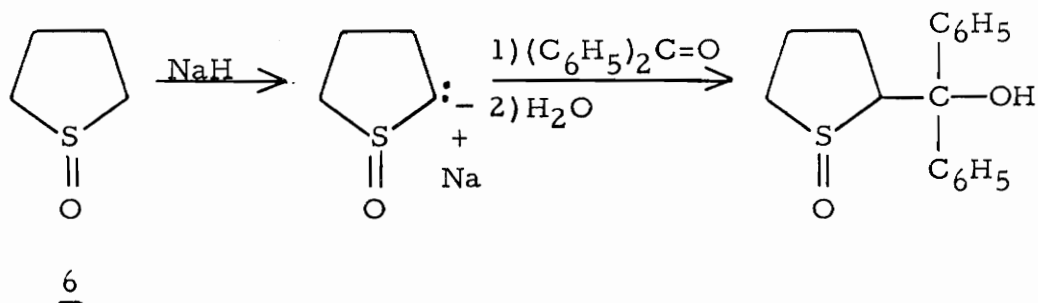
Tetrahydrothiophene 1-oxide is now a commercial product. Dipole moment studies,²¹ oxidation studies,^{22, 23, 24, 25} and industrial problems^{26, 27} represent past and present interest involving this sulfoxide. Reaction of tetrahydrothiophene 1-oxide with potassium t-butoxide in dimethyl sulfoxide has been studied by Wallace and co-workers²⁸ and shown to yield butadiene. Formation of this product was explained by initial removal of a β -hydrogen followed by ring cleavage and further reaction with base to form a β -allylic carbanion which then eliminates the sulfur moiety as shown below:



As mentioned previously, studies in this Laboratory by Krug and Boswell¹³ have provided extremely interesting results on the chemical reactivity of tetrahydrothiophene 1-oxide (6). A series of 2-substituted tetrahydrothiophenes was prepared by reacting 6 with aromatic and aliphatic Grignard reagents. This reaction is of utmost importance to



a portion of the present research and will be discussed fully in the following section. Alkylation of the α -carbanion from 6 with benzophenone, as shown below, was another result of the earlier experiments performed in this Laboratory.

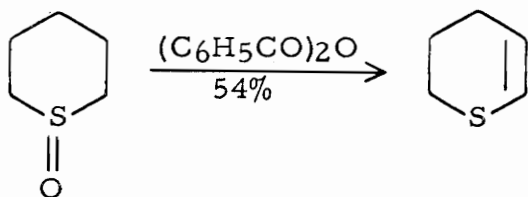


Preparation of a large series of 2-substituted tetrahydrothiophene-1-oxides was reported in 1960.²⁹ Fourteen sulfoxides, having a variety

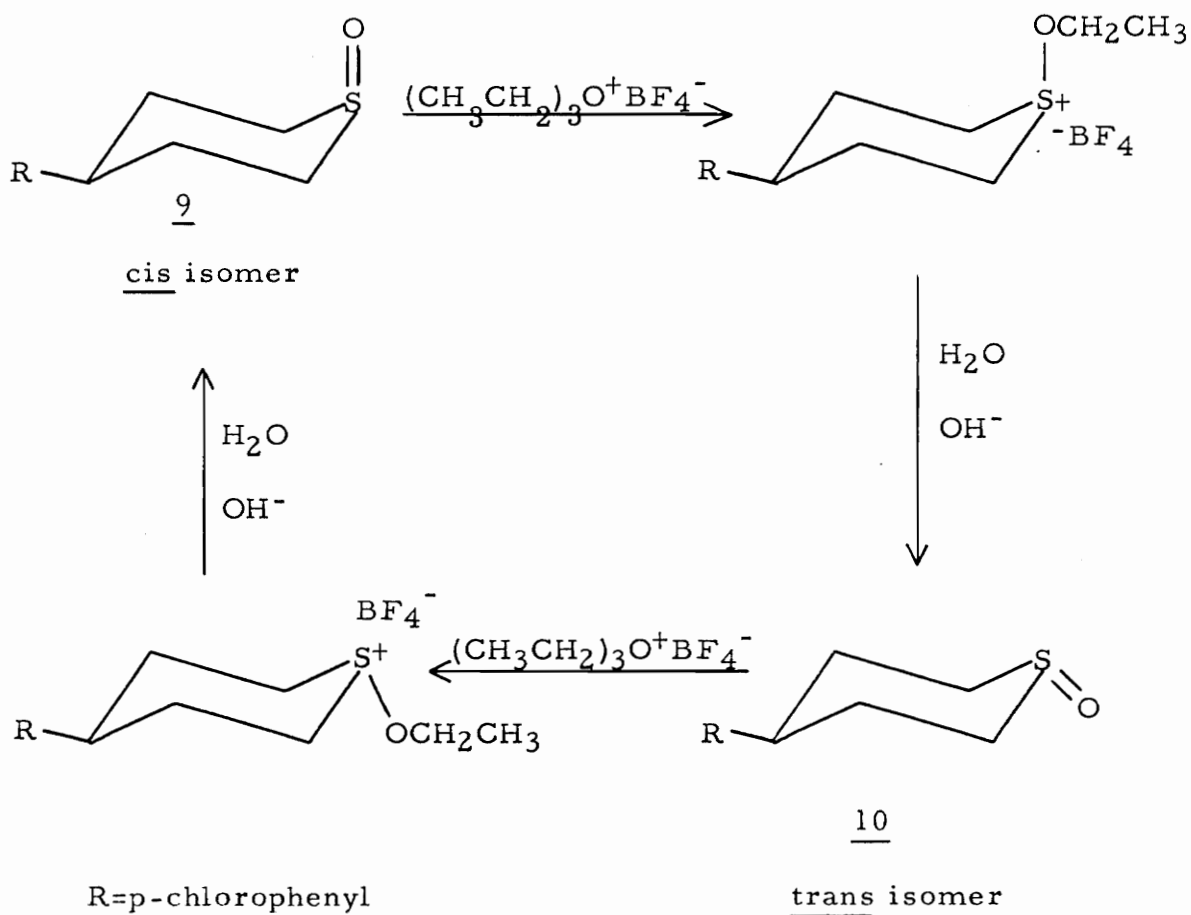
of 2-substituted alkyl groups were prepared by oxidation of the corresponding sulfides with 30% hydrogen peroxide.

The six-membered sulfoxide, thiacyclohexane 1-oxide, although first mentioned in 1916 was not fully characterized until 1957. Bateman and co-workers³⁰ prepared this compound in connection with a study on the autoxidation of cyclic sulfides found in vulcanized rubber. Two years later, Tamres and Searles³¹ prepared this sulfoxide and were the first to report the preparation of the four-membered thiacyclobutane 1-oxide. These workers studied the effect of ring size on the electron donor ability of an oxygen atom in saturated sulfoxides and ketones. The experimental criterion used was the ability of these compounds to form hydrogen bonds with chloroform, as determined by heats of mixing; and with methanol-d, as determined by the shifts in the O-D frequency of the infrared spectrum. In the sulfoxide series, the basicity decreased in the following manner: 6- \geq 5- > 4-membered ring.

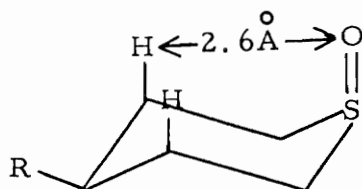
Thiacyclohexane 1-oxide reacts with benzoic anhydride yielding Δ^2 -dihydrothiapyran as shown below.³²



The work of Harrison, Kenyon, and Phillips³³ in 1926 established the configurational stability of sulfoxides. A year later, geometrical isomerism due to the sulfoxide moiety was recognized.³⁴ However, an example of the inversion of the configuration of a sulfoxide group was not provided until 1963. A classic study by Johnson³⁵ involved transformation of cis-4-(p-chlorophenyl)-thian 1-oxide (9) to the corresponding trans isomer 10 by hydrolysis of an intermediate O-alkyl sulfoxide adduct. The trans isomer was likewise transformed to the corresponding cis isomer.



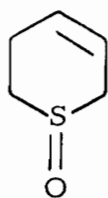
In a later study,³⁶ Johnson and McCants showed that the proportions of cis and trans sulfoxides obtained by oxidation of 4-substituted thianes vary over a wide range with change in the oxidizing agent. These workers also found that a six-membered cyclic sulfoxide is more stable with the oxide in the axial position as shown below. This is



perhaps surprising at first glance, but the greater stability of the axial oxide has also been observed by Martin and Uebel³⁷ with both cis and trans-4-chlorothiane 1-oxide. The 1,3-oxygen-axial hydrogen internuclear distance of these compounds was estimated from models to be 2.6 Å. Van der Waals attractive forces between these centers may outweigh repulsions, thus giving the axial oxide greater stability.

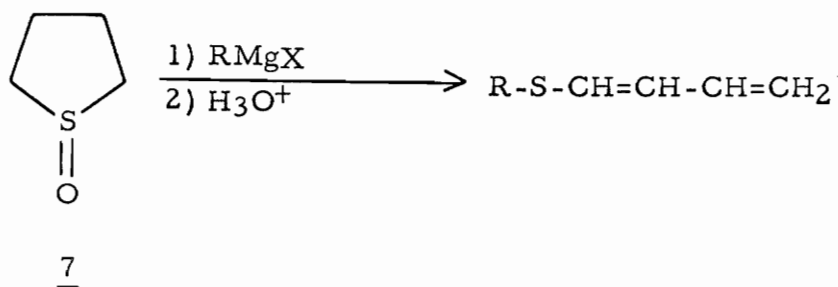
Studies involving saturated cyclic sulfoxides certainly constitute a small portion of sulfoxide chemistry; however, investigations involving unsaturated cyclic sulfoxides are even less numerous. An early example of work in this area was a study concerning the autoxidizability of several six-membered unsaturated cyclic sulfoxides.³⁸ A mixture of products, one of which was the corresponding sulfoxide, was obtained in these reactions. The sulfoxides however were not isolated,

but were simply detected by titration with titanous chloride. Thiacyclohex-3-ene 1-oxide (11) was prepared at a later date in connection with this same study.³⁰



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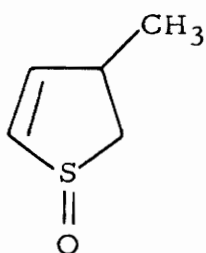
Preparation of the dihydrothiophene 1-oxides 7 and 8 in this Laboratory by Boswell¹³ represents the first synthesis of unsaturated five-membered cyclic sulfoxides. Reaction of 7 with both aromatic and aliphatic Grignard reagents yielded previously unknown dienyl sulfides.



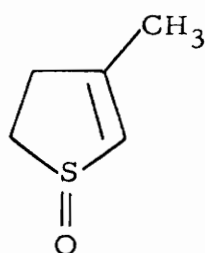
This reaction is also of utmost importance to a portion of the present research.

The unsaturated sulfoxide 2, studied in the present research, is one of three possible 3-methyldihydrothiophene 1-oxides. The other

dihydro sulfoxides, 3-methyl-2, 3-dihydrothiophene 1-oxide (12) and 3-methyl-4, 5-dihydrothiophene 1-oxide (13), are not reported in the literature. Attempts to prepare these sulfoxides during the course of the



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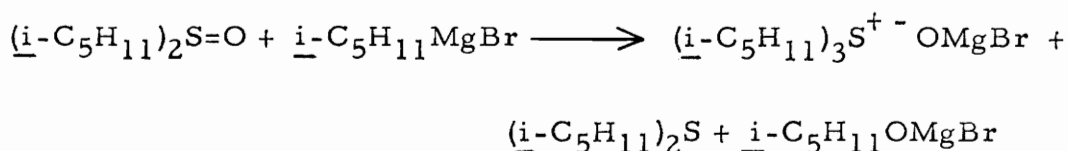
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present research were unsuccessful due to the difficulties encountered in obtaining the precursor sulfides 3-methyl-2, 3-dihydrothiophene and 3-methyl-4, 5-dihydrothiophene respectively. Only the 4, 5-dihydro isomer is reported in the literature.³⁹

The experiments carried out in this Laboratory by Krug and Boswell¹³ represent the first known study concerning the reaction of cyclic sulfoxides with Grignard reagents. In light of this earlier work and research presented in this dissertation, a discussion of past investigations involving the reaction of acyclic sulfoxides with Grignard reagents is worthwhile.

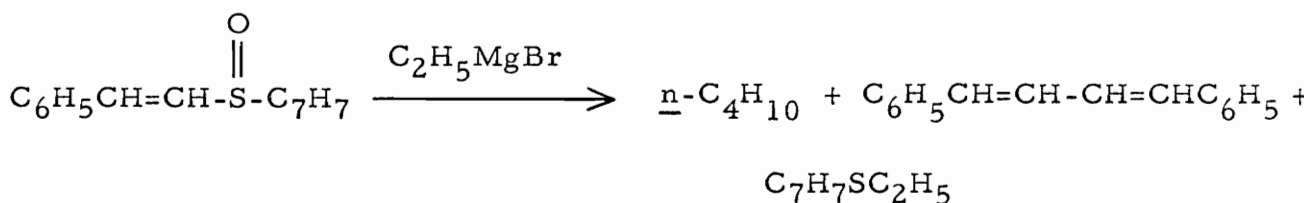
Grignard and Zorn⁴⁰ were the first to recognize that Grignard reagents react in a complex manner with sulfoxides. These workers were preparing sulfoxides by the coupling of Grignard reagents with

thionyl chloride. The appearance of isoamyl sulfide and isoamyl alcohol as by-products in this reaction was explained by considering an attack of the Grignard reagent on the sulfoxide followed by decomposition of the intermediate sulfonium hydroxide derivative. Hepworth and Clapham⁴¹ observed the formation of similar products in the reaction of diaryl

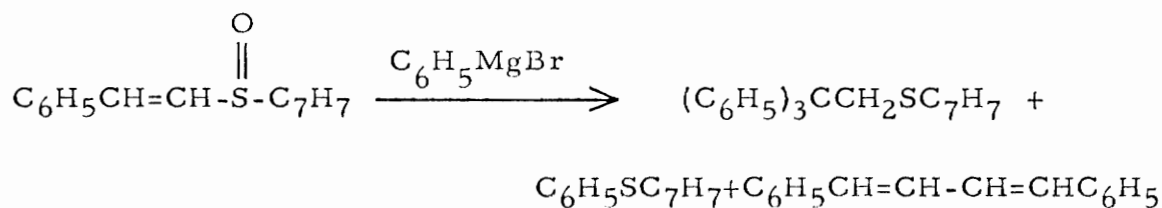


sulfoxides with Grignard reagents.

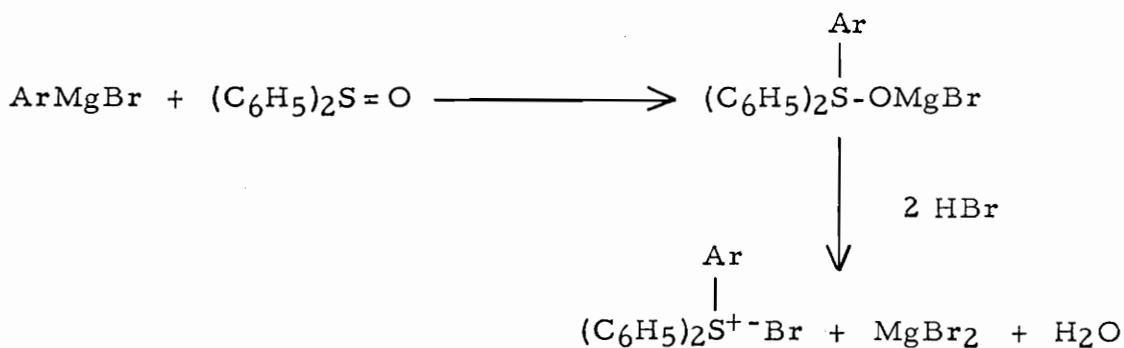
The products observed in these previous experiments were formed as a result of the reduction of the sulfoxide group. In a later experiment⁴² products arising by cleavage as well as reduction of the sulfoxide were observed. This reaction is illustrated, as follows, using 1-p-tolylsulfinyl-2-phenylethylene (14) and ethylmagnesium bromide. Reaction of this same sulfoxide with phenylmagnesium bromide yielded a product in



which the β -carbon atom had been attacked by the Grignard reagent as shown below.



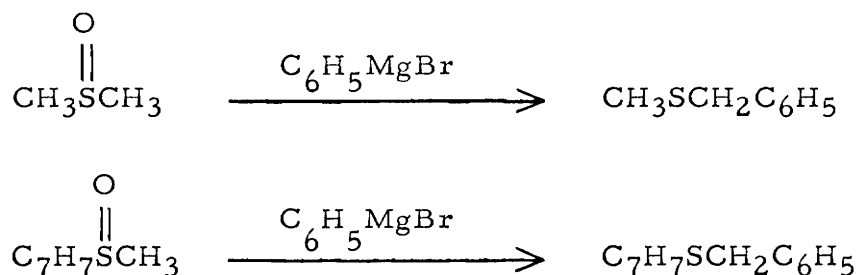
In 1951, Wildi and co-workers⁴³ were successful in preparing sulfonium compounds by reacting various Grignard reagents with diphenyl sulfoxide. These reactions were explained by considering an initial attack of the Grignard reagent upon the sulfur atom to form a magnesium salt which on hydrolysis with aqueous hydrobromic acid yielded the sulfonium bromide.



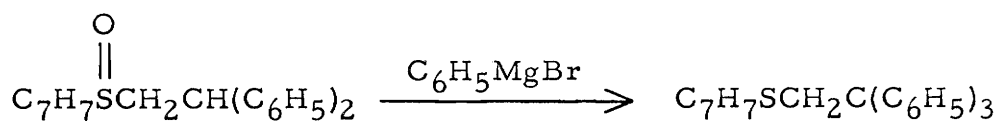
The results of two previous investigations^{44, 45} are most pertinent to the present research. In these studies, sulfoxides bearing α -hydrogens were reacted with Grignard reagents. The major product obtained in these reactions was a sulfide in which the organic group of the Grignard reagent had replaced one of the hydrogens adjacent to the sulfoxide group. The reaction of dimethyl sulfoxide and methyl p-tolyl sulfoxide

with phenylmagnesium bromide illustrates this interesting conversion.

Similar reactions were observed with alkyl and aralkyl Grignard



reagents. The organic portion of the Grignard reagent also replaced a β -hydrogen of the starting sulfoxide as shown below.

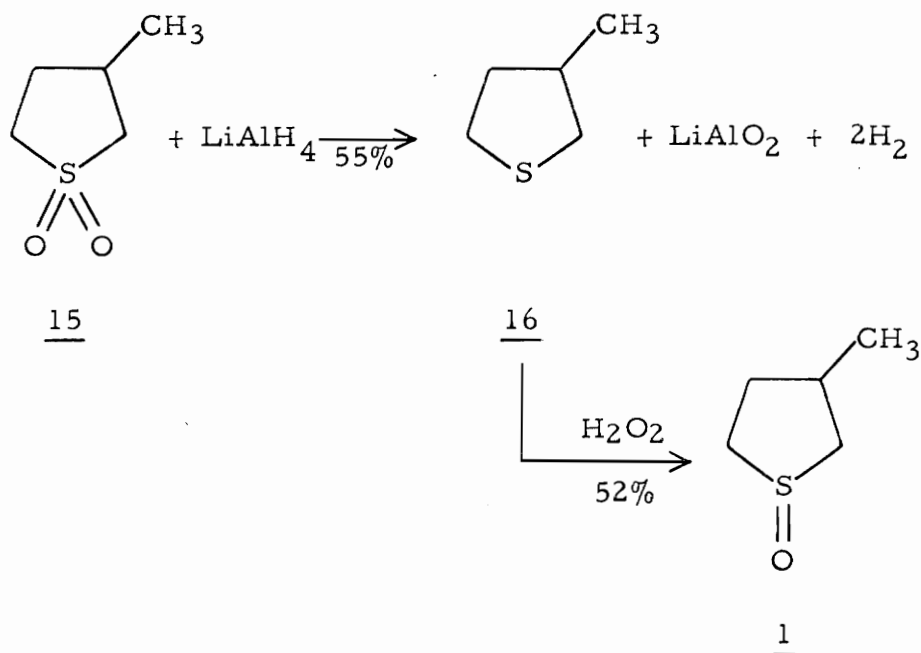


The mechanism of these reactions was not given nor speculated upon. However, work carried out in this Laboratory by Krug and Boswell¹³ and results of the present research have provided a reasonable understanding of this reaction when applied to saturated cyclic sulfoxides.

III. DISCUSSION OF RESULTS

A. The Synthesis and Characterization of 3-Methyltetrahydrothiophene 1-Oxide

The synthesis of 3-methyltetrahydrothiophene 1-oxide was accomplished by a two-step process. First, reduction of the commercially available 3-methyltetrahydrothiophene 1,1-dioxide (15) with lithium aluminum hydride yielded the sulfide precursor 3-methyltetrahydrothiophene (16). Second, oxidation of this sulfide with a slight excess of hydrogen peroxide yielded the colorless hygroscopic sulfoxide 1 in good yield.

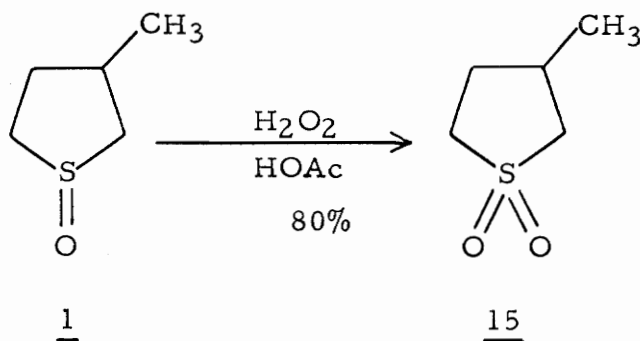


A modification of the procedure of Bordwell and McKellin⁴⁶ was

used for the reduction of 15. Several preliminary small scale reductions showed that the yield of 16 was not significantly increased when employing a large excess of hydride. Therefore, equal molar quantities of hydride and sulfone were used in the preparative scale reductions.

A slight excess of 30% hydrogen peroxide was used for the straightforward oxidation of 16. This reaction was carried out in redistilled acetone and maintained below 5° in order to prevent sulfone formation. Sulfoxide 1 was obtained as a stable liquid possessing a slight penetrating odor.

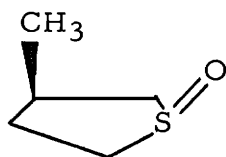
As a proof of structure, 1 was oxidized to the corresponding sulfone 15 by oxidation with excess 30% hydrogen peroxide in refluxing acetic acid. The boiling point, index of refraction, and infrared



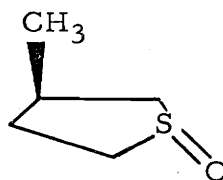
spectrum of this material were in excellent agreement with those of an authentic sample of 15.

It is instructive at this point to consider the stereochemistry of 1. The synthetic approach to this sulfoxide originated with a racemic

mixture of 15 which on reduction afforded a racemic mixture of sulfide precursor 16. The asymmetry of these compounds is due to the asymmetric carbon atom at position-3. Oxidation of 16 is quite interesting since the sulfur atom of the sulfoxide now acts as another center of asymmetry.³³ The carbon atoms and sulfur atom comprising the ring of this cyclic system define a plane. It is important to note that the methyl group and oxygen atom of 1 can be orientated either on the same side or on opposite sides of the ring as shown below. These two compounds can be described as cis-trans isomers.* These sulfoxides are diastereoisomers and thus would have different physical and chemical



cis 1



trans 1

properties. The mirror image of each of these isomers would be formed in a similar manner. Thus, 1 has four possible configurations

* Description of these sulfoxides as cis-trans isomers is in keeping with current nomenclature for substituted cyclic sulfoxides. See for example, references 35, 36, and 37. For a discussion of the stereochemistry of disubstituted planar ring systems, see E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., 1962, chapters 2 and 7. The ring system of these sulfides and sulfoxides is probably not truly planar but is more like the slightly puckered cyclopentane ring system.

(two diastereoisomeric pairs of enantiomers).

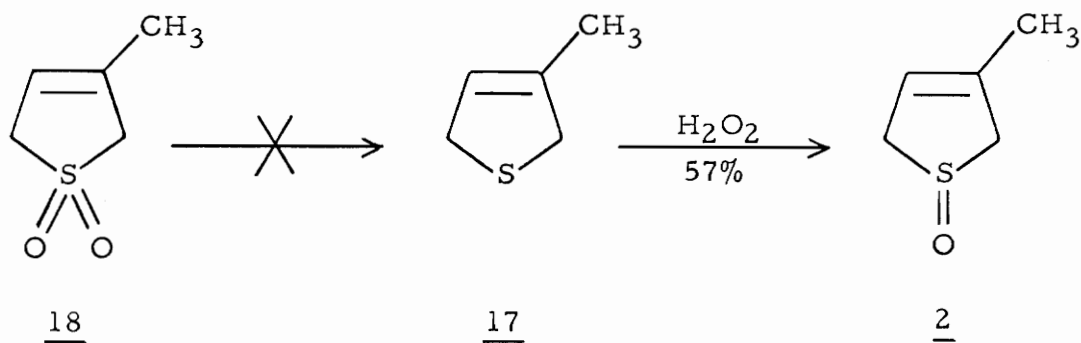
It is now seen that oxidation of sulfide 16 can yield a racemic mixture of cis or trans 1 or a mixture of racemic cis and trans isomers. The nuclear magnetic resonance spectrum of 1 (Figure 8) showed an interesting feature which indicated that this material was a mixture of cis and trans isomers. Absorption due to the methyl group of 16 appeared, as expected, as a doublet centered at 8.85 γ (J=5.5 cps). However, absorption due to the methyl group of 1 appeared somewhat surprisingly as an unsymmetrical triplet centered at 8.88 γ (J=6 cps). This triplet cannot be explained by considering a single sulfoxide isomer. Examination of models has shown that the environment of the methyl group of the cis isomer is considerably different from that of the trans isomer. Therefore, a different chemical shift for the methyl group of each isomer would be expected. Absorption due to the methyl group of each isomer would be expected to appear as a doublet. The observed unsymmetrical triplet is now satisfactorily explained by considering 1 to be a mixture of racemic cis and trans isomers. The triplet apparently results from an overlap of two doublets having a slightly different chemical shift.

The diastereoisomeric cis and trans 1 are theoretically separable by gas chromatography since these isomers would have different physical properties. The gas chromatogram of this sulfoxide strongly

suggested the presence of two components. These appeared to be present in an unequal ratio; however, quantitative measurements were not possible due to extensive tailing of the sample.

B. The Synthesis and Characterization of 3-Methyl-2, 5-dihydrothiophene 1-Oxide

Synthesis of the unsaturated sulfoxide 2 was accomplished in a manner similar to the preparation of the saturated sulfoxide; that is, sulfide precursor 17 was oxidized at 5° in redistilled acetone with a slight excess of 30% hydrogen peroxide.

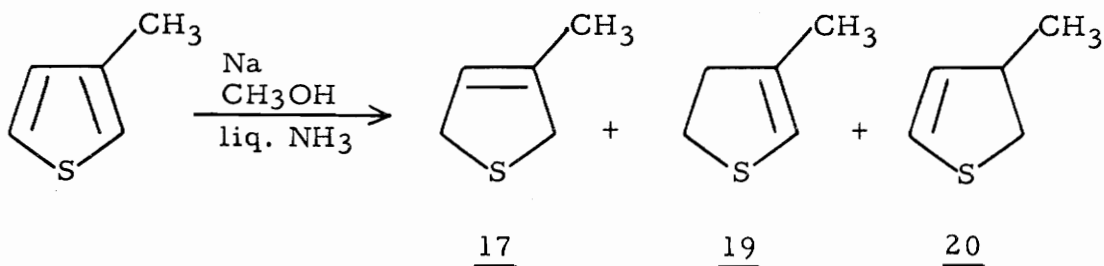


A major problem in obtaining 2 was preparation of the sulfide precursor 17. Although sulfones are known to be resistant to most reducing agents, a successful reduction of the readily available 18 would be the most convenient route to 17. However, all attempts to reduce this sulfone failed. Reaction of 18 with lithium aluminum hydride yielded only polymeric material and hydrogen sulfide. Other systems such as zinc and mineral acids, zinc amalgam, aluminum amalgam, sodium borohydride, and sodium borohydride-aluminum chloride failed to give even a trace of 17. In most cases, unreacted sulfone was recovered.

The successful method for obtaining 17 was a modification of the

now familiar Birch reduction technique using 3-methylthiophene and a sodium-liquid ammonia-methanol reducing system. Birch and McAllen³⁹ reported the reduction of 3-methylthiophene in 1951 and obtained 3-methyl-2, 5-dihydrothiophene (17) and 3-methyl-4, 5-dihydrothiophene (19) along with pentenethiols and hydrogen sulfide. No evidence for the presence of the theoretically possible 2, 3-dihydro isomer (20) was obtained.

The gas chromatogram of the unrefined neutral products obtained from a similar reaction performed in this Laboratory showed, in addition to 3-methylthiophene, the presence of three components in a ratio of 1:3:16. The two minor components of this mixture were identified in



an indirect manner* as 20 and 19 respectively, although actual isolation

* The reaction of 1 with benzoic anhydride yielded a 1.6:1 binary sulfide mixture. The gas chromatographic retention volume of these components was exactly the same as those of the minor two components of the Birch reduction products. These compounds were most probably the dihydro sulfides 20 and 19 respectively since a similar reaction (see reference 30) has been observed with the six-membered sulfoxide thiacyclohexane 1-oxide.

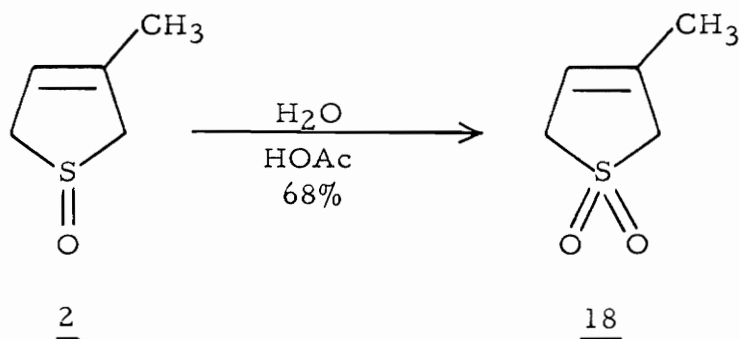
of these compounds was not carried out. The failure of Brich and McAllen to isolate or detect 20, at a time when gas chromatography was in its infancy, is understandable since this material was apparently present in very small quantity. The major component of the Birch reduction products was isolated and identified by its mercurichloride derivative as 17.

An efficient separation of the dihydro sulfides was not realized with the fractionating equipment available in this Laboratory. Excess polymerization of the mixture occurred during the long heating period required for fractional distillation. It was noted however, that the pot residue from these distillations was considerably richer in 17 after a prolonged heating period. This suggested that 19 and 20 were less stable than the 2,5-dihydro isomer (17). This observation, together with previous results in the thiophene series, led to a study of the effect of aqueous phosphoric and sulfuric acid on an isopentane solution of the sulfide mixture. Results of these experiments led to the isolation of 17 in the following manner. A mixture of the unrefined sulfides in isopentane was treated with 50% sulfuric acid while monitoring the composition of the organic phase by periodic gas chromatographic analysis. This unique reaction resulted in removal of 19 and 20 from the mixture without appreciable loss of the desired 17. Fractional distillation of the organic phase gave an efficient separation of the remaining 3-methyl-

thiophene and 17.

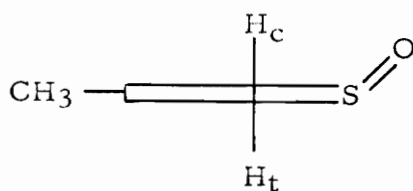
As stated previously, oxidation of 17 was carried out in a straightforward manner. Sulfoxide 2 was obtained as a relatively stable hygroscopic liquid. This sulfoxide also possessed a slight penetrating odor.

As a proof of structure, 2 was oxidized to the corresponding sulfone 18 by oxidation with excess hydrogen peroxide in refluxing acetic acid. Sulfone 18 is a well characterized solid which has been extensively studied in this Laboratory.



The nuclear magnetic resonance study using 2 has provided significant information concerning the stereochemistry of this unsaturated sulfoxide. The sulfur atom of this sulfoxide is an asymmetric center³³ and undoubtedly, oxidation of the planar sulfide 17 would yield a racemic mixture of R and S sulfoxide isomers (oxygen above or below the plane of the ring). Each of the methylenic hydrogens at position-2 and 5 should be distinguishable by nuclear magnetic resonance. These geminal

hydrogens may be considered as being cis or trans (H_c and H_t) to the oxygen of the sulfoxide group and each pair can be considered as an AB system. Position-2 and 5 are probably not equivalent due to the

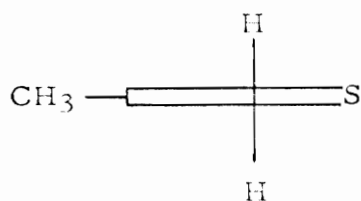


2

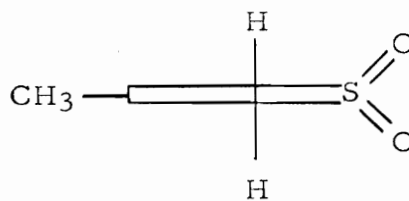
(side view)

methyl group at position-3. Therefore, these positions may best be described as an ABA'B' system rather than as a 2(AB) system.

The quartet (4 H) centered at 6.61τ ($J = 15$ cps) in the nuclear magnetic resonance spectrum of 2 (Figure 9) is typical of an AB system⁴⁷ and shows the nonequivalence of the geminal hydrogens at position-2 and 5. Each peak of the quartet shows fine splitting apparently due to the slightly different AB systems and also spin-spin coupling with the methyl group and methinyl hydrogen at position-3 and 4 respectively. This quartet does not appear in the spectrum of the corresponding symmetrical sulfide 17 or sulfone 18.



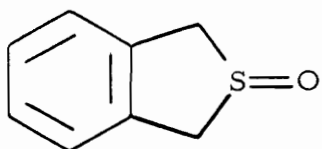
17



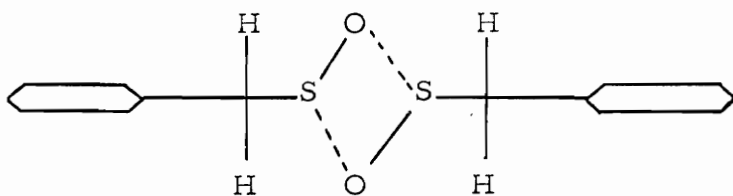
18

(side views)

A similar quartet in the spectrum of 2-thiaindan 2-oxide (21) was found to coalesce to a singlet at -37° . This finding was used as evidence



21



22

(side view)

for the existence of a symmetrical dimer represented as 22.⁴⁸

The spectrum of 2 showed essentially no change when varying the temperature between -34° and 100° . This observation suggested that within this temperature range, there was little or no association of a dimeric nature between molecules of this unsaturated sulfoxide. The additional portions of the spectrum of 2, 4.52τ (1 H multiplet) and 8.27τ (3 H singlet), help substantiate the basic structure of this molecule.

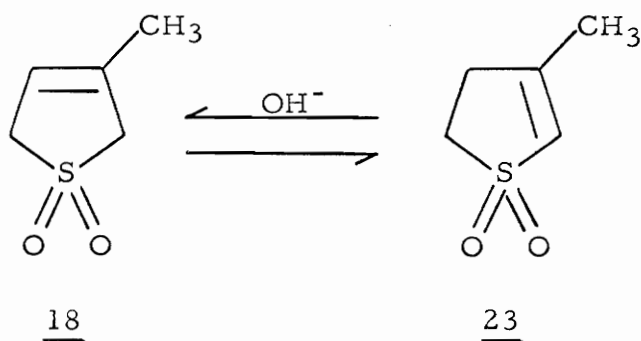
C. Reduction and Base Catalyzed Isomerization of 3-Methyl-2, 5-dihydrothiophene 1-Oxide

The ease with which sulfoxides are reduced contrasts with the relative resistance of sulfones. Previous studies have shown that sulfoxides can be reduced to the corresponding sulfides by a variety of reagents such as zinc in acetic acid,⁴⁹ titanous⁵⁰ or bisulfite ions,⁵¹ butyl lithium,⁵² hydriodic acid,⁵³ and lithium aluminum hydride.⁴⁶

It therefore seemed profitable to ascertain if 2 was likewise easily reduced and also to attempt the base catalyzed isomerization of this unsaturated sulfoxide. These studies were aimed at obtaining additional information concerning the behavior and reactivity of unsaturated cyclic sulfoxides. These objectives have been realized and a meaningful comparison of these results with those of previous studies has been made.

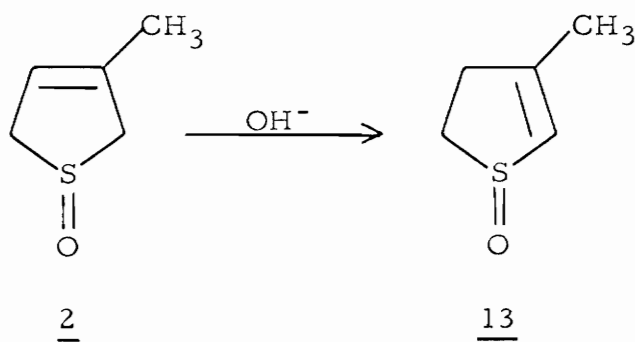
The reduction of 2 was accomplished in a straightforward manner using 48% hydriodic acid. The exothermic reaction immediately produced iodine. The aqueous reaction mixture was extracted with petroleum ether and gas chromatographic analysis of the organic phase showed the presence of only 3-methyl-2, 5-dihydrothiophene. No secondary products arising by attack of the iodine on the olefinic double bond of the sulfide were detected.

The reaction of 2 with 0.5 N sodium hydroxide was carried out in order to determine if an isomerization of the β , γ -double bond would occur. This study was quite intriguing since an isomerization of this unsymmetrical sulfoxide could yield the 2, 3- and/or 4, 5-dihydro sulfoxides (12 and 13 respectively). In the corresponding sulfone series, the equilibrium ratio of 18 and 23 in aqueous potassium hydroxide was found to be 1:10.1 respectively.⁵⁴



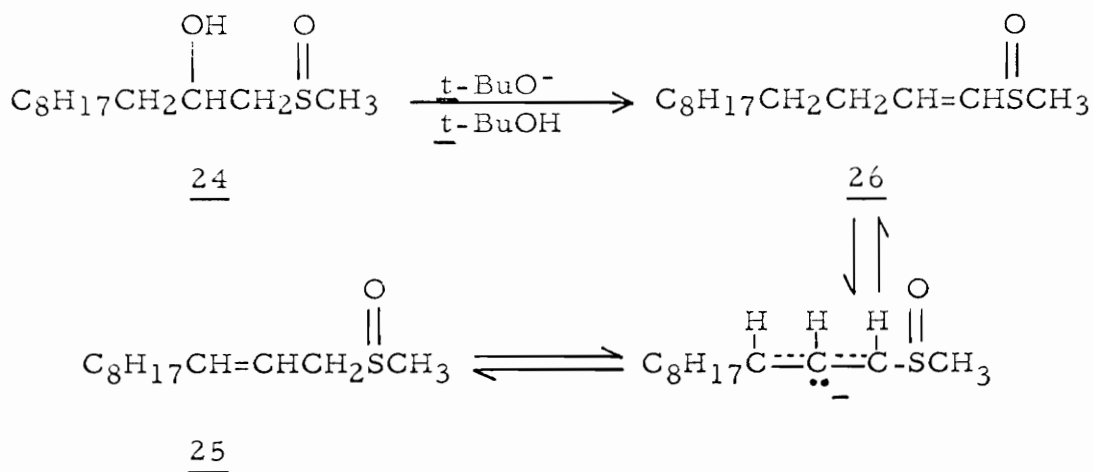
The isomerization of 2 was detected in two ways. First, a portion of the aqueous reaction mixture was worked up and oxidized with excess 30% hydrogen peroxide. The gas chromatogram of this reaction mixture showed the presence of sulfones 18 and 23. Secondly, another portion of the original reaction mixture was reduced with 48% hydriodic acid. The 2, 5- and 4, 5-dihydro sulfides, 17 and 19 respectively, were detected in this reaction mixture by gas chromatographic analysis.

These findings support the isomerization of 2 to 3-methyl-4, 5-dihydrothiophene 1-oxide (13). After a reaction time of 96 hours, 2

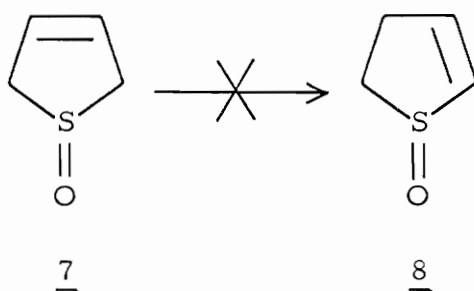


and 13 were present in a ratio of 1.78:1 respectively as shown by gas chromatographic analysis of the reduced reaction mixture. This product ratio did not change when using a reaction time greater than 96 hours. The observed constant ratio of products strongly suggests that an equilibrium between 2 and 13 exists. However, actual isolation of pure 13 and reaction of this material with base under the same conditions would be required to definitely establish this equilibrium.

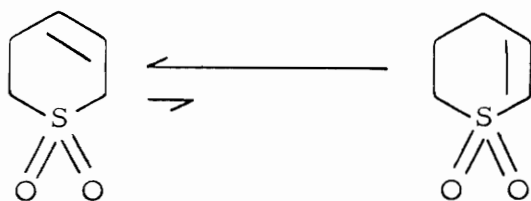
The reaction of 1-methylsulfinyl-2-hydroxyundecane (24) with strong base is pertinent to the present research.⁵⁵ The only product isolated from this reaction was 1-methylsulfinyl-2-undecene (25). Independent deuterium exchange experiments showed that 25 was the thermodynamically controlled product under equilibrium conditions. These findings seem to indicate that the $-\text{SOCH}_3$ group has a destabilizing effect on the olefinic linkage compared to that of the $-\text{CH}_2\text{SOCH}_3$ group. This



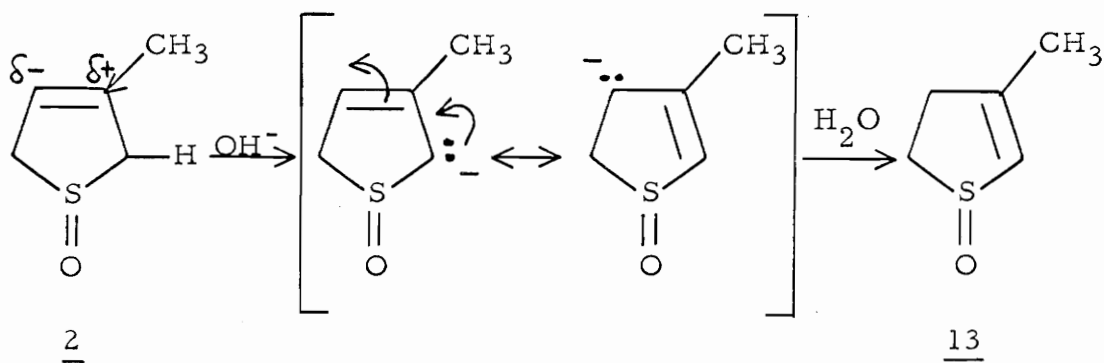
strongly suggests that the ground state resonance between the sulfur atom and the adjacent unsaturated system is unimportant, since conjugation would favor the α , β -unsaturated isomer 26. These experiments and conclusions support the lack of base catalyzed isomerization observed by Boswell¹³ with 2, 5-dihydrothiophene 1-oxide (7).



Apparently the ground state resonance between the sulfur atom and the adjacent olefinic linkage is also unimportant in the dihydrothiopyran 1, 1-dioxides. In this series, the Δ^3 -isomer is greatly favored over the Δ^2 -isomer at equilibrium.⁵⁶



The observed isomerization of 2 can be explained by considering the electronic effect of the methyl group at position-3. The inductive and hyperconjugative effects of the methyl group would tend to polarize the olefinic linkage so that carbon-4 was more negatively charged than carbon-3. As a result of this polarized olefinic linkage, position-2 would be more activated for proton abstraction than position-5. Abstraction of a proton from the activated position-2, and a subsequent shift of electrons as shown, would afford the isomeric sulfoxide 13. Thus, the electron donating ability of the methyl group serves as a driving force for the isomerization. Exclusive formation of 13 is readily



understood since a similar reaction at position-5 would be directly opposed to the electronic effect of the methyl group. A similar reasoning has been used to explain addition reactions to the olefinic bond of the

corresponding sulfone 18.⁵⁷

The electronic effect of the methyl group and the resulting polarization of the β , γ -double bond also serve to explain the results obtained when reacting 2 with Grignard reagents. These results are discussed in a later section.

D. The Reaction of 3-Methyltetrahydrothiophene 1-Oxide with Grignard Reagents

It has previously been stated that a series of 2-substituted tetrahydrothiophenes was prepared in this Laboratory by reaction of tetrahydrothiophene 1-oxide with various Grignard reagents. Boswell¹³ showed that reactions of this type are best carried out in tetrahydrofuran using a 4:1 molar excess of Grignard reagent. An extension of this study using 3-methyltetrahydrothiophene 1-oxide (1) was undertaken in order to ascertain the influence of the methyl group at position-3. Also, information and technique gained from this study could then be used in the studies on the less readily available 3-methyl-2, 5-dihydrothiophene 1-oxide (2).

Phenylmagnesium bromide was treated with 1 in tetrahydrofuran at 25° and the resulting solution was stirred for 20 hours. Gas chromatographic analysis of the organic phase after hydrolysis showed the presence of eight identifiable components. Four of these were readily identified* as benzene, phenol, 3-methyltetrahydrothiophene, and biphenyl. The presence of 3-methyl-2, 3- and 3-methyl-4, 5-dihydrothio-

* The identity of these compounds was established using gas chromatography by 1) comparing the retention volume of an authentic sample of each compound with the observed retention volumes of the experimental chromatogram (isothermal conditions) and by 2) comparing the temperature of elution of these authentic samples with those of the experimental chromatogram (linear temperature programming).

phene was established in an indirect manner.* The presence of these dihydro sulfides was expected since 2, 3-dihydrothiophene had previously been detected as a by-product in the reaction of 6 with phenylmagnesium bromide. The following discussion concerns identification of the two additional components.

Distillation of the unrefined reaction products yielded a mixture containing biphenyl and the two unidentified components as shown by gas chromatographic analysis. The interpretation of the infrared spectrum of this mixture supported the presence of biphenyl and suggested that the additional components were substituted 3-methyltetrahydrothiophenes. Separation of this mixture by distillation was not realized; however, removal of the biphenyl was effected using the procedure of Whitehead.⁵⁸ This involved formation of the mercurichloride salt of each sulfide and subsequent steam distillation of this mixture from dilute hydrochloric acid. Work-up of the steam distillate afforded a 1.04:1 binary sulfide mixture** having the molecular formula $C_{11}H_{14}S$. These results showed the sulfide mixture to be composed of isomeric phenyl substituted 3-methyltetrahydrothiophenes.

* See the discussion concerning the 3-methyl-dihydrothiophenes in Section IIIB.

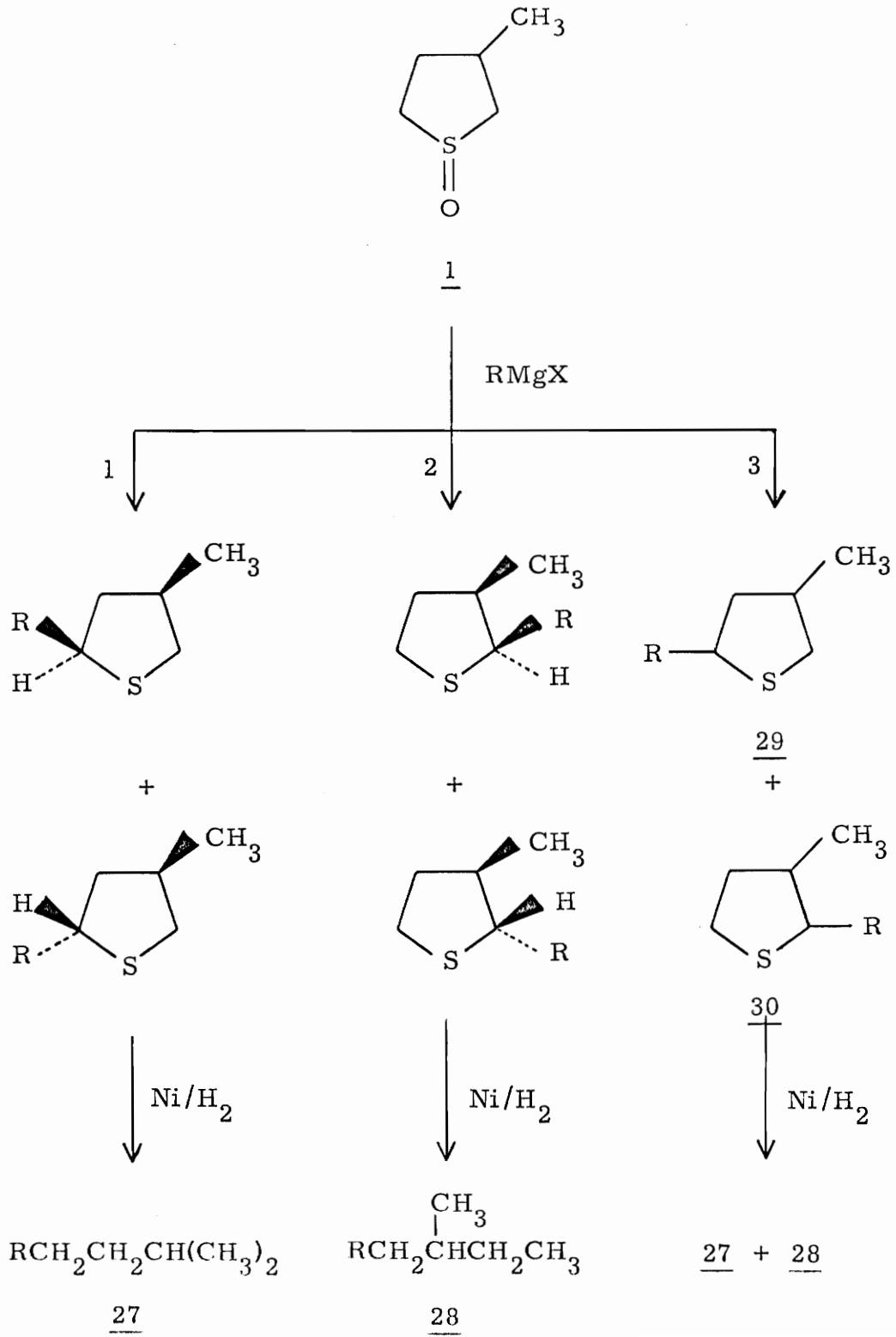
** The ratio of these components in the crude reaction mixture following hydrolysis was 1.33:1 respectively.

The reaction of 1 with phenylmagnesium bromide could conceivably yield three different binary sulfide mixtures by attack of the Grignard reagent at position-2 or 5. An attack at position-3 or 4 will not be considered for this discussion since the previous study by Boswell¹³ showed this type of reaction to occur at the carbon atom adjacent to the sulfoxide group. The present research has shown that 1 undergoes a similar reaction at the α -carbon atoms.

In light of the previous discussion concerning the stereochemical aspects of 16 and 1, several comments concerning the stereochemistry of the possible sulfide products of the present reaction should be mentioned here. The atoms comprising the ring of these sulfides, shown in Chart A, are planar and as a result, cis-trans isomerization of this disubstituted ring system is possible. Also, certain of these compounds may be described as position isomers.⁵⁸

Attack of the Grignard reagent at position-5 of 1 could yield the cis-trans isomers shown in reaction 1 of Chart A. Gas chromatographic separation of these isomers would theoretically be possible since these compounds are diastereoisomers. The mirror image of each diastereoisomer would also exist in this mixture since the original 3-methyltetrahydrothiophene, from which 1 was obtained, was a racemic mixture. The products shown in reaction 2 are also cis-trans isomers. Attack of the Grignard reagent at position-2 of 1 would lead to these diastereo-

CHART A



isomers and likewise, the mirror image of each of these compounds. Attack of the Grignard reagent at position-2 or 5 would yield the position isomers shown in reaction 3.

Identification of the individual isomers was accomplished by desulfurization of the sulfide mixture. Desulfurization of the mixtures shown in reactions 1 and 2 would yield only one hydrocarbon while the mixture shown in reaction 3 would yield two different hydrocarbons.

Desulfurization of a 1.04:1 binary sulfide mixture was carried out with Raney nickel catalyst and a 1:1.37 binary hydrocarbon mixture was obtained. Gas chromatographic analysis using an internal standard showed these components to be 1-phenyl-3-methylbutane (27) and 1-phenyl-2-methylbutane (28). Further identification of these hydrocarbons was obtained by preparing a mixture of authentic 27 and 28 in a weight ratio of 1:1.37 respectively. The infrared spectrum and index of refraction of the authentic sample were in good agreement with those of the mixture obtained in the desulfurization reaction.

These findings thus showed that the reaction of 1 with phenyl-magnesium bromide yielded a mixture of 2-phenyl-4-methyltetrahydrothiophene (29) and 2-phenyl-3-methyltetrahydrothiophene (30) as shown in reaction 3 of Chart A. The stereochemistry of 29 and 30 is intriguing since each compound has four possible configurations (two diastereoisomeric pairs of enantiomers).⁵⁹ The present research however, does

not solve this problem and the presence of cis and/or trans isomers can only be speculated upon.

The unequal mixture of hydrocarbons 27 and 28 obtained on desulfurization of the essentially 1:1 sulfide mixture of 29 and 30 was not readily explained. Further information concerning the desulfurization was obtained using a semimicroquantity of the 1.04:1 sulfide mixture and a 10-fold excess of Raney nickel catalyst. This desulfurization was carried out in a test tube. The reactants were periodically mixed simply by shaking the tube and progress of the reaction was followed by periodic gas chromatographic analysis of the clear nickel free solution. The unreacted sulfides remaining after 35 minutes were present in a ratio of 1:1.60 and hydrocarbons 27 and 28 were present in a ratio of 1:1.44 respectively. No sulfides were detected after 40 minutes. The unequal ratio of unreacted sulfides observed during the reaction was at first thought to be due to a selective adsorption of one of the sulfide isomers on the nickel catalyst. This phenomenon could conceivably lead to the unequal ratio of hydrocarbons obtained. However, subsequent experiments proved this assumption to be incorrect.

The 1.04:1 sulfide mixture was separated by preparative-scale gas chromatography and a semimicroquantity of each component was obtained in 100% purity. A semimicrodesulfurization of the minor component of the original mixture was carried out in the manner previously

described. Gas chromatographic analysis during the reaction showed the presence of only 28 and the original unreacted sulfide. This experiment thus established the identity of the minor sulfide component of the original mixture as 30.

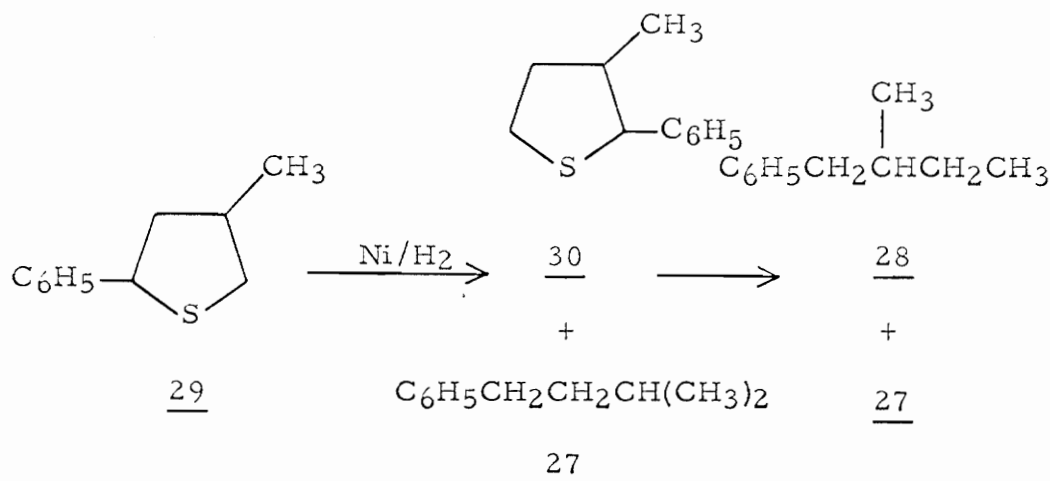
Semimicrodesulfurization of the major component of the original mixture led to an important discovery. After a contact time of only 5 minutes with the Raney nickel catalyst, the unknown sulfide and surprisingly a small percentage of 30 were detected. After 10 minutes, these sulfides were present in a ratio of 2.20:1 respectively. No sulfides were detected after 15 minutes. Both hydrocarbons 27 and 28 were present in these samples in ratios ranging from 2.03:1 to 1.70:1 respectively.

Results of these semimicrodesulfurization experiments are summarized in Table I. These studies have shown the 1.04:1 binary sulfide mixture to be composed of 29 and 30. It has also been shown that sulfide 29 not only undergoes desulfurization with Raney nickel to yield hydrocarbon 27, but also undergoes isomerization yielding sulfide 30. This isomerization and subsequent desulfurization of the isomerized products explains the high percentage of hydrocarbon 28 obtained when desulfurizing the essentially 1:1 mixture of 29 and 30.

TABLE I

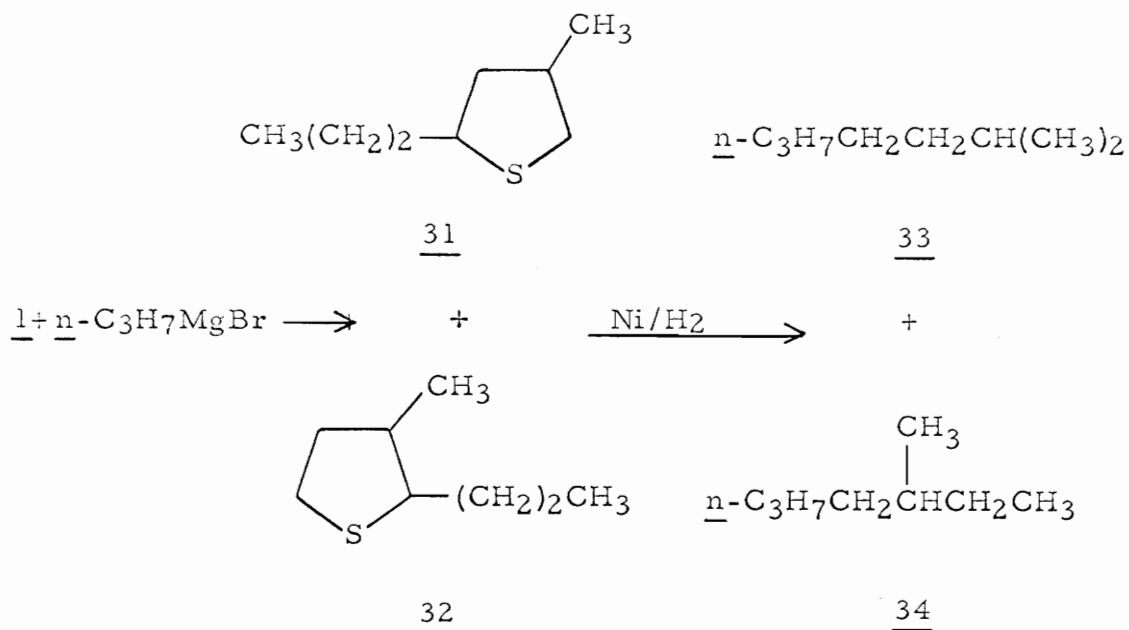
Semimicrodesulfurization of 2-Phenyl-4-methyltetrahydrothiophene (29) and/or 2-Phenyl-3-methyltetrahydrothiophene (30)

Compound(s)	Time (min)	Remaining Sulfide (s)	Hydrocarbon (s)
		<u>29</u> and/or <u>30</u>	<u>27</u> and/or <u>28</u>
1.04:1 Mixture of <u>29</u> and <u>30</u> respec- tively	5	1:1.08	1:1.13
	15	1:1.35	1:1.29
	35	1:1.60	1:1.44
pure <u>30</u>	5	<u>30</u>	<u>28</u>
	20	<u>30</u>	<u>28</u>
	35	<u>30</u>	<u>28</u>
pure <u>29</u>	5	8.10:1	2.03:1
	10	2.20:1	1.94:1
	15	none	1.70:1



A portion of Raney nickel catalyst was treated to remove the adsorbed hydrogen from the metal surface. This "deactivated nickel catalyst" was placed in contact with a semimicroquantity of the 1.04:1 sulfide mixture of 29 and 30 to ascertain if isomerization of 29 would occur under conditions where desulfurization would not occur. No isomerization occurred under these conditions even after a contact time of 8 hours. Desulfurizations using Raney nickel catalyst are known to be free radical in nature.⁶⁰ The fact that an active catalyst is required for isomerization of 29 strongly suggests that this isomerization is a free radical reaction.

The reaction of 1 with n-propylmagnesium bromide was carried out to obtain information concerning reaction of this sulfoxide with an aliphatic Grignard reagent. A 7.34:1 binary sulfide mixture composed of 2-n-propyl-4-methyltetrahydrothiophene (31) and 2-n-propyl-3-methyltetrahydrothiophene (32) was obtained from this reaction. By-products of this reaction were identified as n-propyl alcohol, 3-methyltetrahydro-



thiophene (16), and the 3-methyldihydrothiophenes 19 and 20. The 16 obtained from this reaction represented 25% of the starting sulfoxide. Propene was also detected as a by-product of this reaction. This olefin was trapped in bromine and identified as its dibromide.

Identification of this binary mixture was also accomplished by desulfurization. A 3:1 sulfide mixture was desulfurized and a 1:1.44 binary mixture of 2-methylheptane (33) and 3-methylheptane (34) was obtained. The identity of this hydrocarbon mixture was established by preparing a sample of authentic 33 and 34 in a weight ratio of 1:1.44 respectively. The gas chromatogram, index of refraction, and infrared spectrum of the authentic sample were in excellent agreement with those of the mixture obtained in the desulfurization reaction.

The results obtained in a semimicrodesulfurization of a 5.24:1

mixture of 31 and 32 respectively were very surprising when compared to the results of the earlier reaction with a mixture of the aromatic sulfides 29 and 30. In the present reaction, the ratio of remaining unreacted sulfides did not change during the reaction and a constant ratio of hydrocarbons 33 and 34 was obtained. These findings are summarized in Table II.

The results of these two desulfurization experiments employing a mixture of 31 and 32 did not agree. That is, the major hydrocarbon detected in each experiment was not the same compound. It should be pointed out however, that the semimicrodesulfurization reaction was carried out with a large excess of catalyst whereas the preparative-scale reaction was not.

This mixture was also separated by preparative-scale gas chromatography and the individual components were isolated in 100% purity. Results of the semimicrodesulfurization of each of these components are summarized in Table II. These experiments have established the identity of the major and minor alkylated 3-methyltetrahydrothiophenes as 31 and 32 respectively. These experiments have also shown that both sulfides 31 and 32 undergo isomerization during the desulfurization reaction. It is important to note that an essentially constant ratio of hydrocarbons was formed in each reaction. Also, no isomerized sulfide product was detected in either reaction. The failure of a mixture of

TABLE II

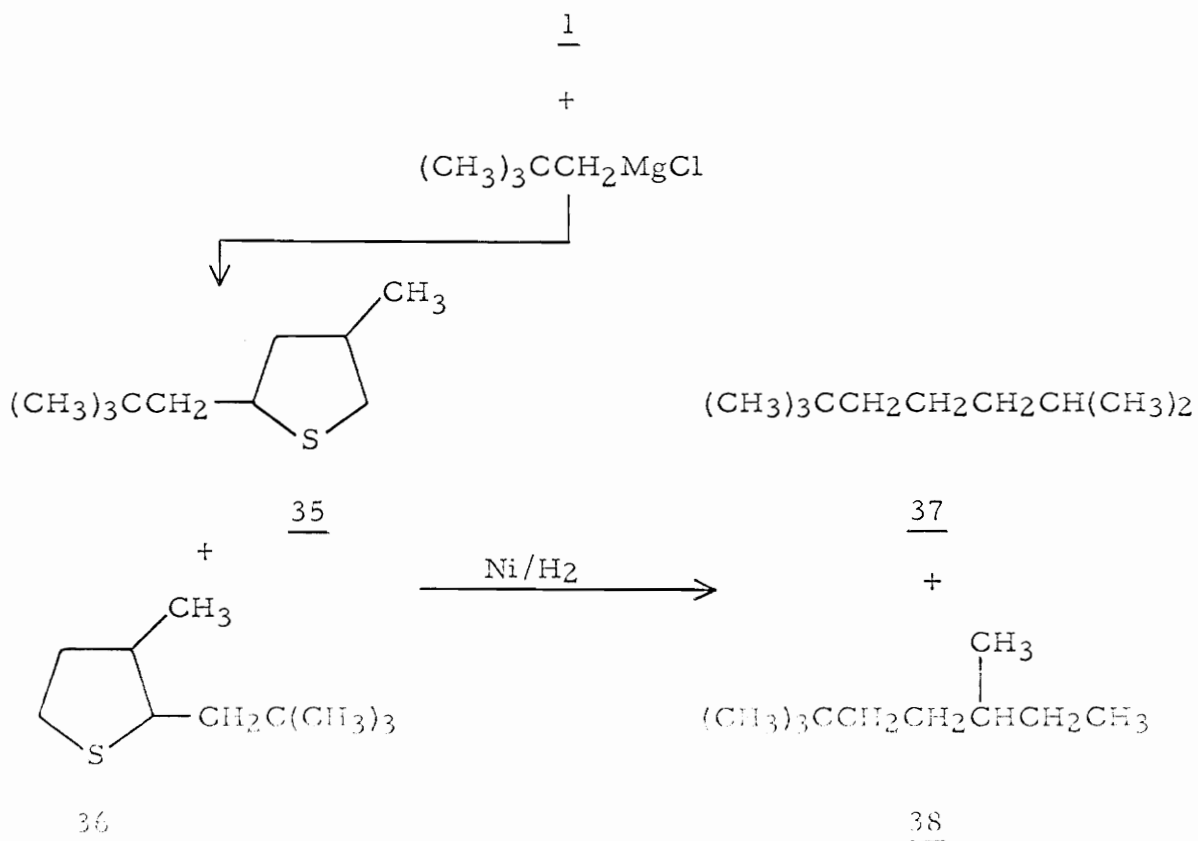
Semimicrodesulfurization of 2-n-propyl-4-methyltetrahydrothiophene (31) and/or 2-n-propyl-3-methyltetrahydrothiophene (32)

Compound (s)	Time (min)	Remaining Sulfide (s)	Hydrocarbons
		<u>31</u> and/or <u>32</u>	<u>33</u> and <u>34</u>
5.24:1 Mixture of <u>31</u> and <u>32</u> respectively	20	5.25:1	2.33:1
	40	5.67:1	2.57:1
	60	none	2.23:1
pure <u>31</u>	10	<u>29</u>	6.14:1
	20	<u>29</u>	5.25:1
	40	none	4.88:1
pure <u>32</u>	6	<u>30</u>	1:2.57
	17	<u>30</u>	1:2.84
	40	none	1:3.17

31 and 32 to isomerize with "deactivated nickel catalyst" was also observed.

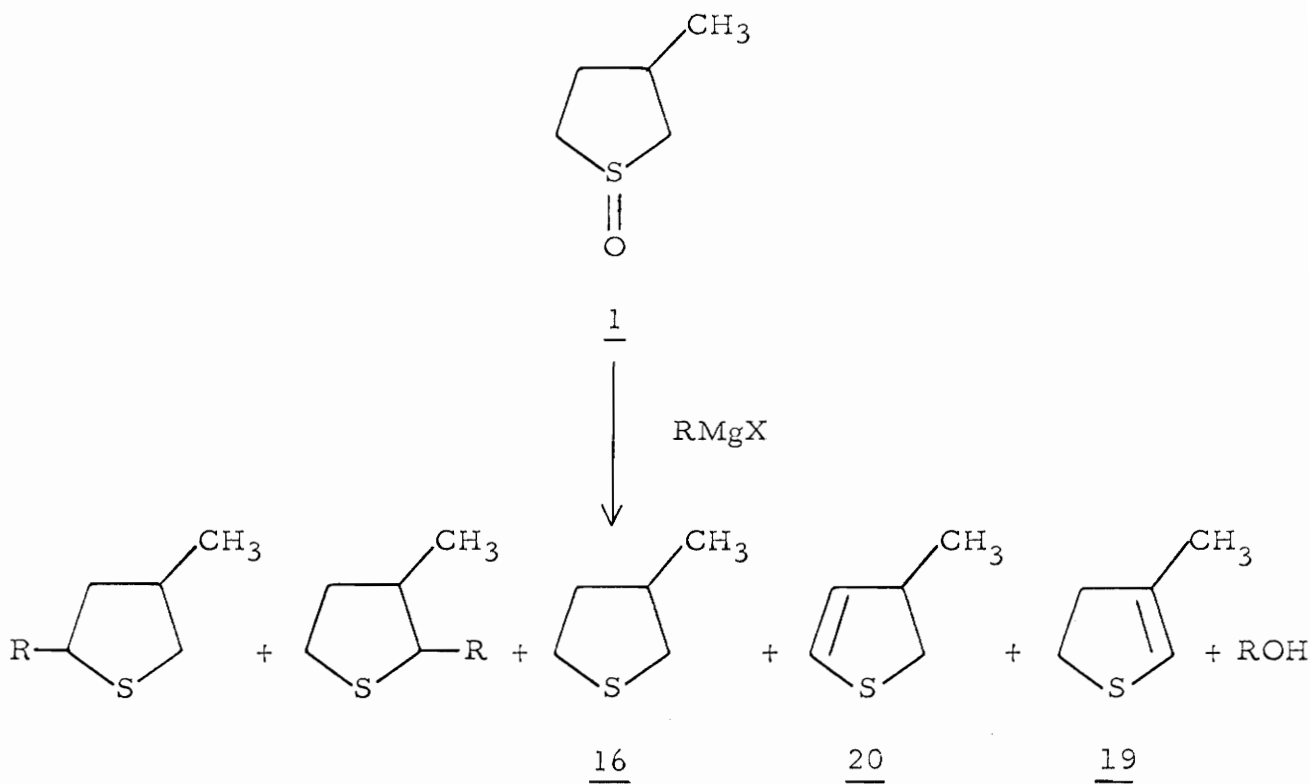
The main purpose of the desulfurization experiments with the arylated and alkylated 3-methyltetrahydrothiophene mixtures was identification of the isomeric sulfides. It is evident from the preceding discussion that this objective was realized. Discovery of the isomerization reactions occurring during these desulfurizations was quite surprising and certainly merits further investigation. It appears however from the present research, that maximum desulfurization and minimum isomerization occur when using a large excess of very active nickel catalyst.

Reaction of 1 with the "bulky" Grignard reagent 2, 2-dimethyl



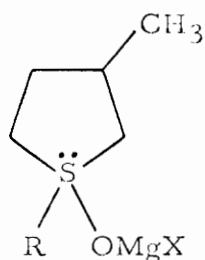
propylmagnesium chloride yielded a 8.09:1 mixture of 2-(2,2-dimethylpropyl)-4-methyltetrahydrothiophene (35) and 2-(2,2-dimethylpropyl)-3-methyltetrahydrothiophene (36) in 29% yield. The identity of these sulfides was established by semimicrodesulfurization of the 8.09:1 binary sulfide mixture. Gas chromatographic analysis during the reaction showed the presence of two components in a 5.25:1 ratio. The major component of this mixture was identified as 2,2,6-trimethylheptane (37) by comparing the retention volume, relative to an internal standard 3-methylheptane, of an authentic sample of 37 with that of the experimental chromatogram. The minor component of the desulfurization product was shown to be 2,2,5-trimethylheptane (38) by comparing the retention volumes of a ternary hydrocarbon mixture containing 38 with that of the minor component of the experimental chromatogram.

The reaction of 1 with Grignard reagents can be summarized in the following manner:

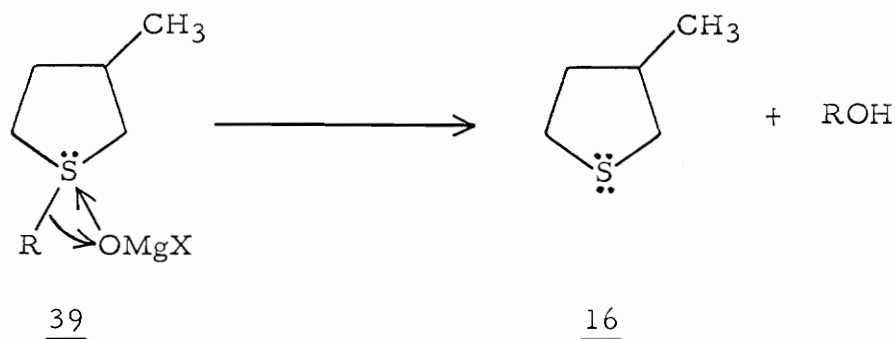


In all reactions studied, a binary mixture of substituted 3-methyltetrahydrothiophenes was obtained. The major component of each of these mixtures was the sulfide produced by attack of the Grignard reagent at position-5 of 1. The most significant data concerning the composition of these mixtures was obtained from the gas chromatogram of the unrefined reaction mixture following hydrolysis since the composition of the mixtures actually obtained was affected by the rate of distillation.

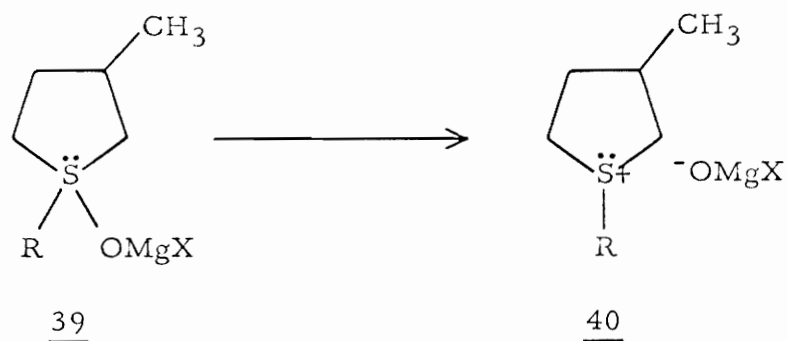
The observed products of these reactions can be explained by considering an initial complex formed by attack of the Grignard reagent upon the sulfoxide moiety to give an intermediate such as 39:



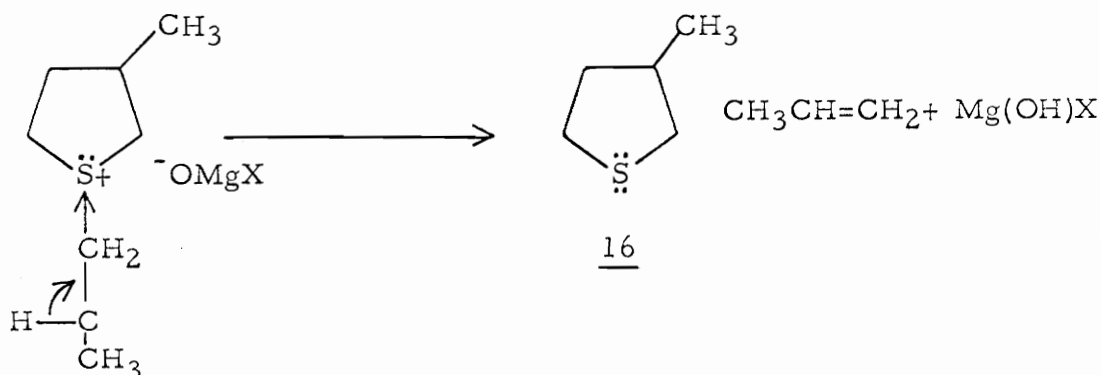
A compound of this nature was isolated by Boswell¹³ when using a 1:1 molar ratio of ethylmagnesium bromide and 6 in ethyl ether. The trace amounts of alcohols detected in these reactions could be formed by a collapse of 39. This would also lead to the observed 3-methyltetrahydrothiophene (16).



The additional products of these reactions can be rationalized by considering the dissociation of 39 to the sulfonium salt 40. If R in 40 is CH₃CH₂CH₂-, the sulfonium salt could undergo a β-elimination with sub-

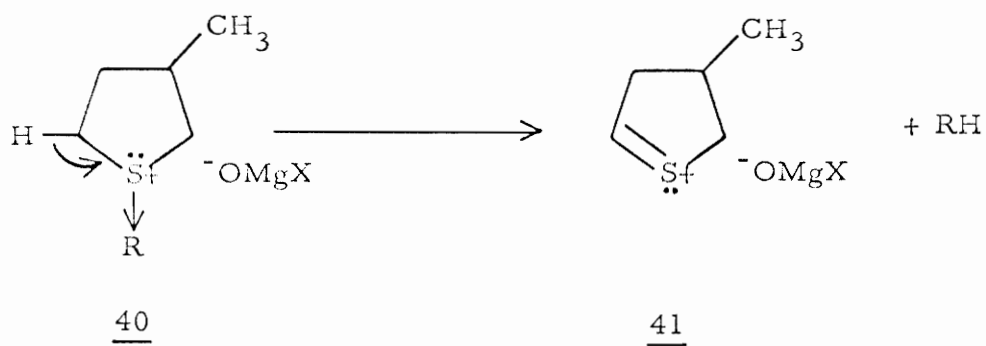


sequent formation of propene and 16. This type of reaction serves to explain the formation of propene and the large percentage of 16

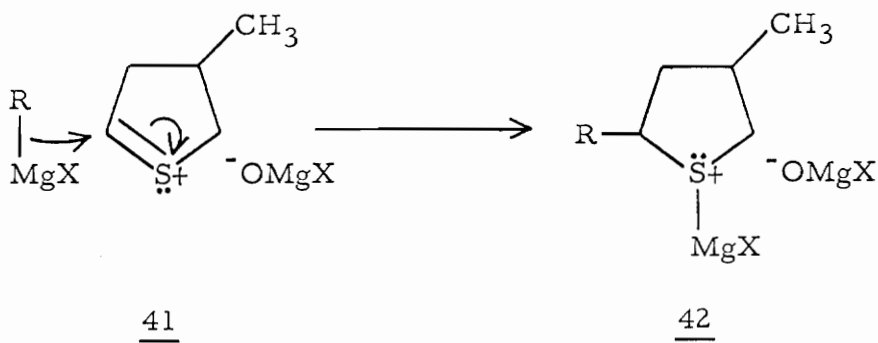


obtained when using the propyl Grignard reagent.

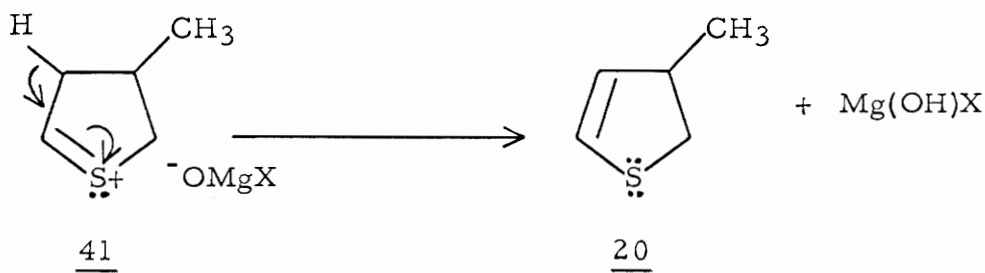
The formal positive charge on the sulfur atom of 40 would certainly increase the acidity of the hydrogens at position-2 and 5. Abstraction of a hydrogen from position-5 by the excess Grignard reagent could yield the transition state represented as 41. This reactive species could then undergo further reaction in two ways. Attack of the nucleophilic



Grignard reagent at position-5, and subsequent hydrolysis or dissociation of 42 would lead to the 2-substituted-4-methyltetrahydrothiophene.

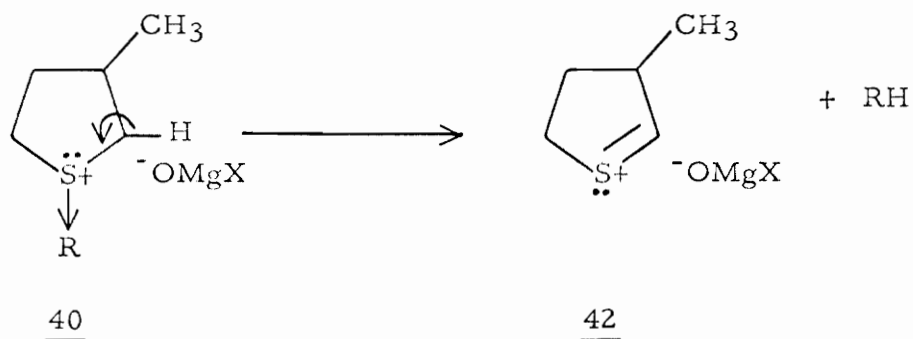


The observed 3-methyl-2,3-dihydrothiophene (20) could be formed from 41 by loss of an allylic hydrogen and shift of electrons as shown:



Similar abstraction of a proton from position-2 of 40 could yield

the reactive species 42 from which the 2-substituted-3-methyltetrahydro-



thiophene and 3-methyl-4,5-dihydrothiophene could be formed in like manner.

The ratio of products obtained when using the n-propyl and neopentyl Grignard reagents suggest that there is a considerable steric factor which prevents significant abstraction of the proton from position-2 of the proposed intermediate 40.

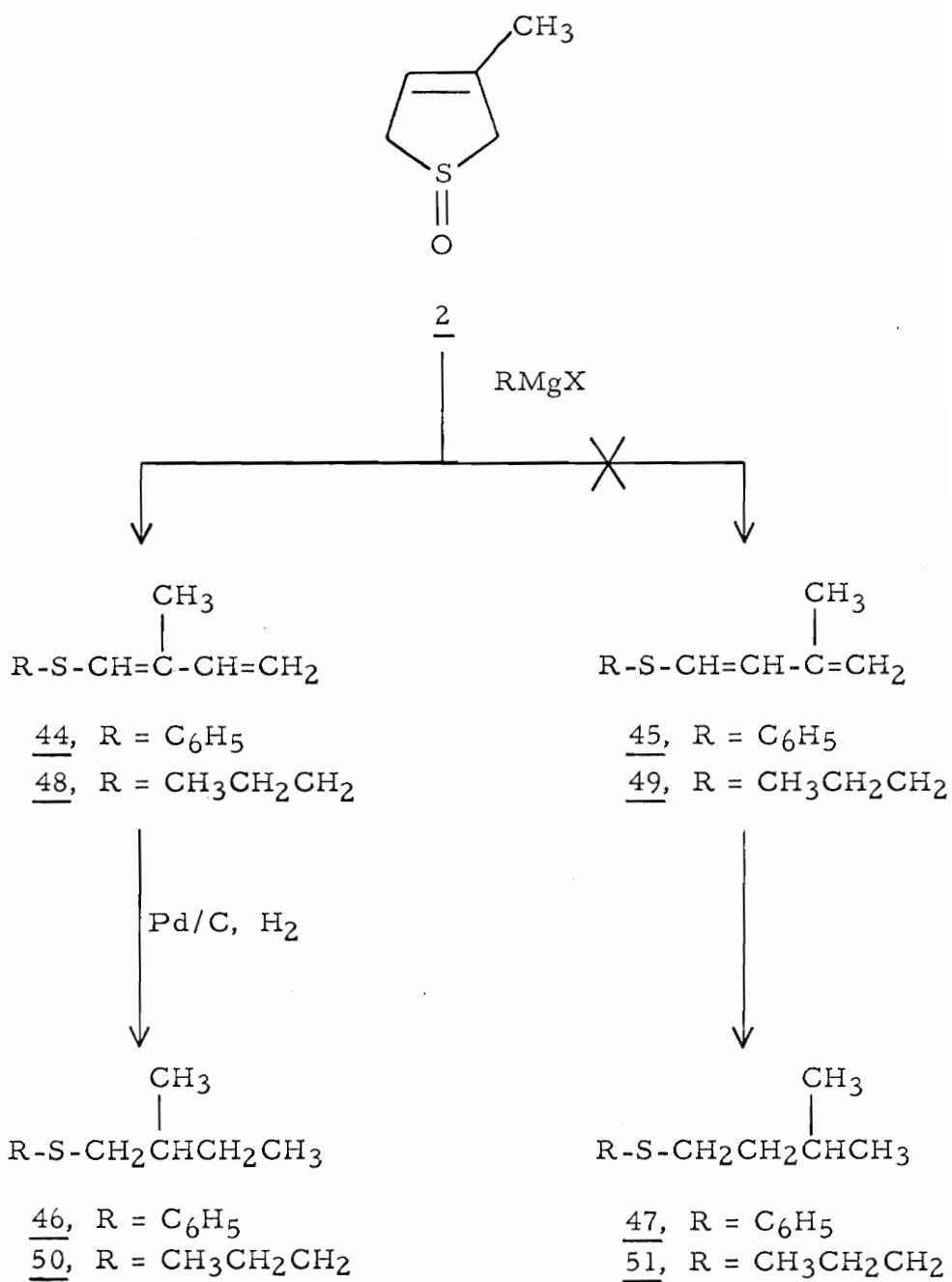
The preceding mechanistic discussion is an attempt to explain the experimental data obtained. Actual participation of these species remains to be proved and presently is strictly a matter of speculation.

E. The Reaction of 3-Methyl-2, 5-dihydrothiophene 1-Oxide with Grignard Reagents.

The reactivity of cyclic sulfoxides was pursued further by studying the reaction of the unsaturated sulfoxide, 3-methyl-2, 5-dihydrothiophene 1-oxide (2) with Grignard reagents. This investigation was an extension of the earlier study¹³ employing the simple unsaturated sulfoxide 6. Boswell showed that 6 underwent a ring cleavage with Grignard reagents yielding previously unknown dienyl sulfides. Similar reactions employing 2 were especially intriguing since this unsymmetrical sulfoxide could yield two different dienyl sulfides, as shown in Chart B. The present research has shown that 2 undergoes a stereospecific ring cleavage with Grignard reagents yielding a single dienyl sulfide. These results, together with a comparison of similar reactions with the corresponding sulfone 18, are presented in the following discussion.

Phenylmagnesium bromide was treated with 2 in the manner previously described for reaction of the saturated sulfoxide 1. Gas chromatographic analysis of the organic phase following hydrolysis showed the presence of only three components. Two of these were identified as 3-methyl-2, 5-dihydrothiophene (17), and biphenyl. Distillation yielded the pure unknown component. The interpretation of the infrared and nuclear magnetic resonance spectra (Figures 3b and 10 respectively) suggested that the molecule contained a phenyl group, a methyl group

CHART B



and an olefinic linkage. The ultraviolet spectrum (Figure 7a) suggested extensive conjugation within the molecule and quantitative analytical data supported the molecular formula $C_{11}H_{12}S$. It was thus apparent that this material was either 1-phenylthio-2-methyl-1,3-butadiene (44) or 1-phenylthio-3-methyl-1,3-butadiene (45) as shown in Chart B.

Identification of the dienyl sulfide was accomplished by catalytically reducing this material to the fully saturated sulfide. Authentic samples of the two possible isomeric sulfides 1-phenylthio-2-methylbutane (46) and 1-phenylthio-3-methylbutane (47) were prepared. The boiling point, index of refraction, infrared spectrum (Figure 4a), and nuclear magnetic resonance spectrum (Figure 11) of the catalytic reduction product were in excellent agreement with those of the authentic sulfide 46. This finding thus established the identity of the original dienyl sulfide as 1-phenylthio-2-methyl-1,3-butadiene (44). This material was obtained in 70% yield.

Several comments concerning the infrared and nuclear magnetic resonance spectra of the saturated sulfides 46 and 47 should be mentioned here. The presence of the isopropyl group in sulfide 47 was shown by the asymmetric CH_3 bending absorption appearing as a doublet at 1379 cm^{-1} (Figure 4b).⁶¹ This contrasts with the singlet appearing at 1377 cm^{-1} in the spectrum of sulfide 46. The chain branching in these sulfides was further confirmed by the nuclear magnetic resonance spectrum of each of

these compounds. The octet ($J = 6.5$ cps) centered at 7.56τ in the spectrum of 46 shows the methyl group to be attached at position-2. The carbon atom at position-2 is an asymmetric center and as a consequence, the methylene hydrogens adjacent to the sulfur atom are nuclear magnetically nonequivalent. Absorption due to these hydrogens would be expected to appear as an octet.^{62, 63} This contrasts with the unsymmetrical triplet appearing in the spectrum of 47 (Figure 12).⁶⁴ These spectral interpretations are summarized in Tables III and IV.

The reaction of 2 with n-propylmagnesium bromide also yielded a similar dienyl sulfide. This material, 1-n-propylthio-2-methyl-1,3-butadiene (48), was obtained in 49% yield. The structure of this dienyl sulfide was confirmed by infrared and nuclear magnetic resonance analysis and by catalytic reduction to the previously unreported saturated sulfide 1-n-propylthio-2-methylbutane (50). The boiling point, index of refraction, infrared spectrum (Figure 5b), and nuclear magnetic resonance spectrum (Figure 14) of the reduced product were in excellent agreement with those of an authentic sample of 50. The other possible sulfide, 1-n-propylthio-3-methylbutane (51), was also prepared for comparison purposes. Spectral data concerning these compounds are also summarized in Tables III and IV.

Isolation of a single dienyl sulfide from each of these Grignard reactions supports a stereospecific ring cleavage of 2 under these condi-

TABLE III
Infrared Spectral Interpretations

Compound	Absorption Frequency cm ⁻¹	Structural Assignment
<u>44</u> (Figure 3b)	1799	-CH=CH ₂
	1616	-C=C-C=C-
	1585	aromatic -C=C-
	1439, 1379	-CH ₃
	1029, 729, 690	mono substituted benzene
	989, 905	-CH=CH ₂
<u>46</u> (Figure 4a)	1585	aromatic -C=C-
	1437, 1379	-CH ₃
	1028, 725, 688	mono substituted benzene
<u>47</u> (Figure 4b)	1587	aromatic -C=C-
	1445	-CH ₃
	1379 (doublet) 1171	-CH(CH ₃) ₂
	1030, 727, 688	mono substituted benzene

TABLE III (cont'd)
Infrared Spectral Interpretations

Compound	Absorption Frequency cm ⁻¹	Structural Assignment
<u>48</u> (Figure 5a)	1805	-CH=CH ₂
	1618	-C=C-C=C-
	1420, 1379	-CH ₃
	990, 900	-CH=CH ₂
<u>50</u> (Figure 5b)	1379	-CH ₃
<u>51</u> (Figure 6)	1377 (doublet)	-CH(CH ₃) ₂

TABLE IV

Nuclear Magnetic Resonance Spectral Interpretations

Compound	Chemical Shift γ^*	Multiplicity, J cps	Number of Hydrogens	Structural Assignment
<u>44</u> (Figure 10)	8.62	doublet 1.0	3	$-\text{CH}=\overset{\text{1}}{\text{C}}-\text{CH}_3$
	8.58	doublet 1.0		
	5.30	multiplet		
<u>46</u> (Figure 11)	3.10	multiplet	5	$\text{C}_6\text{H}_5-\text{S}-$
	7.56	octet 6.5	2	$-\text{S}-\text{CH}_2\overset{\text{1}}{\text{C}}\text{H}(\text{CH}_3)$
	9.42	triplet 6.0	6	$-\text{CH}_3$, two groups
<u>47</u> (Figure 12)	3.08	multiplet	5	$\text{C}_6\text{H}_5-\text{S}-$
	7.47	triplet 7.5	2	$-\text{S}-\text{CH}_2\text{CH}_2-$
	9.46	doublet 6.0	6	$-\text{CH}(\text{CH}_3)_2$
<u>48</u> (Figure 13)	3.37	quartet 10.0	1	$-\text{S}-\text{CH}=\overset{\text{1}}{\text{C}}-\text{CH}_3$
	4.37	singlet (broad)	1	$-\text{CH}=\text{CH}_2$
	5.11	multiplet	2	$-\text{CH}=\text{CH}_2$
	7.65	triplet 8.0	2	$-\text{CH}_2\text{CH}_2-\text{S}-$
	8.44	doublet 1.0	3	$-\text{CH}=\overset{\text{1}}{\text{C}}-\text{CH}_3$
	9.30	triplet 8.0	3	$-\text{CH}_2\text{CH}_3$

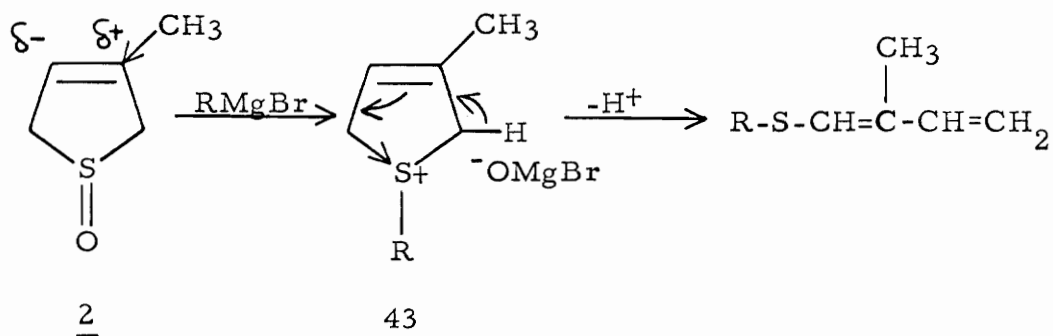
TABLE IV (cont'd)

Nuclear Magnetic Resonance Spectral Interpretations

Compound	Chemical Shift τ^*	Multiplicity, J cps	Number of Hydrogens	Structural Assignment
<u>50</u> (Figure 14)	7.72	multiplet	4	$-\text{CH}_2-\text{S}-\text{CH}_2\overset{1}{\text{C}}\text{H}(\text{CH}_3)$
	9.21	multiplet	6	$-\text{CH}_3$, two groups
<u>51</u> (Figure 15)	7.70	triplet 7.5	4	$-\text{CH}_2\text{CH}_2-\text{S}-\text{CH}_2\text{CH}_2-$
	9.25	doublet 5.0	6	$-\text{CH}(\text{CH}_3)_2$

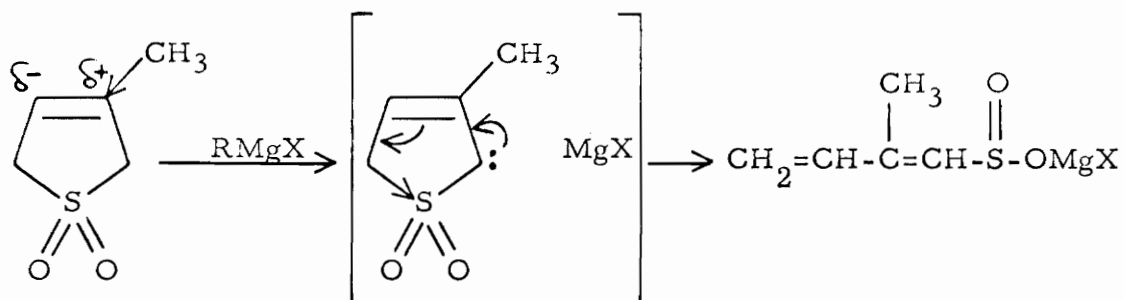
* Relative to tetramethylsilane

tions. These products, and the lack of by-products as observed with the similar reactions of 1, can be explained by considering the formation of a sulfonium salt such as 43. This intermediate apparently undergoes a rapid reaction with the excess Grignard reagent. Abstraction of a proton from position-2 and subsequent rupture of the bond between carbon-5 and the sulfur atom would yield the observed dienyl sulfide. Exclusive reaction at position-2 is apparently due to the electronic effect of the methyl group at position-3. The inductive and hyperconjugative effects of the methyl group would tend to polarize the olefinic linkage so that carbon-4 was more negatively charged than carbon-3. The relative acidity of the α -hydrogens would certainly be different due to the polarized olefinic linkage, and as a result, position-2 would be more activated for proton abstraction than position-5.



The results of the present research are similar to those observed when reacting the corresponding sulfone 18 with Grignard reagents.⁶⁵ This unsymmetrical sulfone also underwent a similar stereospecific

ring cleavage. A single dienyl sulfonic acid salt, as shown below, was isolated from these reactions.



18

It is interesting to note from steric considerations that the Grignard reagent attacked the sterically hindered position-2 in both the sulfoxide and sulfone.

IV. EXPERIMENTAL

A. General

The infrared spectra were recorded on a Beckman IR-5 infrared spectrophotometer using 0.1 mm matched sodium chloride cells. All spectra were run in carbon tetrachloride solution with compensation for the solvent.

The ultraviolet spectra were recorded on a Beckman DK-2A ratio recording spectrophotometer using 95% ethyl alcohol as solvent.

The nuclear magnetic resonance spectra were obtained from neat liquids or dilute carbon tetrachloride or deuteriochloroform solution using a Varian A-60 spectrometer. Resonance positions were determined by pre-calibrated charts using tetramethylsilane as an external standard.

The gas chromatographic analyses were run on an Aerograph model 204 gas chromatograph equipped with a Sargent model SR 1-millivolt full scale recorder. The columns employed were 1/8-in. o. d. aluminum or stainless steel packed columns as described in Table V. Peak area was determined by the method of Cremer (area = height x width at half height) and the composition of mixtures was determined by measuring the ratio of the individual peak areas.

The drying of organic extracts in reaction work-ups was carried

TABLE V
Gas-Liquid Partition Chromatographic Columns

<u>Column</u>	<u>Description*</u>		
A	5' SS	5%	SE-30 on 60/80 Chrom W (HMDS)
B	5' Al	15%	Dow 550 on 80/100 Gas Chrom Z
C	15' Al	15%	Dow 550 on 80/100 Gas Chrom Z
D	15' Al	16%	Dow 200/550, 3% Bentone 34 on 80/100 Gas Chrom Z
E	5' Al	15%	TCP (80% para, 20% meta) on 80/100 Gas Chrom Z
F	5' Al	15%	Carbowax 20M on 30/60 Gas Chrom Z
G	3' SS	6.3%	Carbowax 1500 on 80/100 Gas Chrom Z

* All column packings were prepared by making a slurry of the liquid phase and solid support in a suitable solvent. The solvent was removed by flash evaporation and the coated support was dried in an oven at 110°.

out with anhydrous magnesium sulfate and solutions were concentrated by flash evaporation.

Melting points were determined on a Thomas Hoover capillary melting point apparatus and are corrected. Boiling points are uncorrected. Pressure is reported in millimeters of mercury.

The elemental analyses were carried out by Galbraith Laboratories, Inc., Knoxville 21, Tenn.

B. The Synthesis and Characterization of 3-Methyltetrahydrothiophene 1-Oxide

3-Methyltetrahydrothiophene (16). Into a 3-l. flask equipped with a nitrogen inlet, a paddle stirrer, and a reflux condenser, was placed 37.94 g (1.0 mole) of lithium aluminum hydride in 600 ml of dry peroxide free ethyl ether. To this stirred slurry was slowly added 120.8 g (0.90 mole) of 3-methyltetrahydrothiophene 1,1-dioxide* in 200 ml of ethyl ether. The reaction mixture was refluxed for 3 hr and then cooled to room temperature. Unreacted hydride was decomposed by slow addition of 35 ml of ethyl acetate followed by 75 ml of wet ethyl ether and finally 35 ml of water. The aluminum salts were dissolved by addition of 600 ml of dilute hydrochloric acid. The two phases were separated and the aqueous layer was saturated with sodium chloride and extracted with one 100 ml portion of ethyl ether. The ether layers were combined, dried, and concentrated. Distillation of the residue afforded crude yellow sulfide which upon redistillation through a 12-in. Vigreux column yielded 49.6 g (55%) of colorless 16: bp 132-134° (720 mm); n_D^{25} 1.4889 [lit⁵⁸ bp 138.2°, n_D^{20} 1.4929]. Vacuum distillation of the pot residue from the first distillation resulted in

* This material was purchased from Phillips Petroleum Co., Bartlesville, Oklahoma and was redistilled before use: bp 140° (4 mm); n_D^{20} 1.4778.

recovery of 16.3 g (13%) of pale yellow 15: bp 140-141° (4 mm);
 n_D^{25} 1.4764.

Mercurichloride of 3-Methyltetrahydrothiophene. A saturated solution of mercuric chloride in 95% ethyl alcohol was added dropwise to a warm stirred solution of 1.02 g (0.01 mole) of 16 in 10 ml of 95% ethyl alcohol until the resulting solution became turbid. The warm mixture was stirred for 0.5 hr, cooled to room temperature, and filtered. One recrystallization of the material obtained gave 2.9 g (78%) of finely divided white crystals: mp 109-110° [lit⁵⁸ mp 109.5°].

3-Methyltetrahydrothiophene 1-Oxide (1). A solution of 10.2 g (0.10 mole) of 16 in 40 ml of redistilled acetone was cooled to 0° in an ice bath. This stirred solution was treated with 14.73 g of 30% hydrogen peroxide (4.42 g, 0.13 mole hydrogen peroxide) while maintaining the reaction below 5°. The ice bath was removed and the solution was allowed to stand for 60 hr. The solution was concentrated by flash evaporation and then extracted with two 30 ml portions of chloroform. The extracts were combined, dried, and concentrated. Vacuum distillation yielded a total of 7.2 g of colorless liquid: bp 108-114° (4 mm). Two redistillations from powdered calcium hydride afforded 6.2 g (52%) of colorless 1: bp 112-113° (6 mm); n_D^{25} 1.5037; d_4^{25} 1.101. The infrared and nmr spectra of 1 are shown in Figures 1a

and 8 respectively.

Anal. Calcd for $C_5H_{10}OS$: C, 50.80; H, 8.54; S, 27.12.

Found: C, 50.71; H, 8.73; S, 26.90.

A similar oxidation carried out on a preparative scale using 80.8 g (0.79 mole) of 16 and 94.06 g of 30% hydrogen peroxide gave 1 in 67% yield.

3-Methyltetrahydrothiophene 1,1-Dioxide (15). To a cooled solution of 7.0 g (0.059 mole) of 1 in 25 ml of glacial acetic acid was added 26.7 g of 30% hydrogen peroxide (8.02 g, 0.236 mole hydrogen peroxide). This solution was refluxed for 4 hr, cooled, and diluted with 25 ml of chloroform. The aqueous layer was separated and extracted with three 25 ml portions of chloroform. The combined extracts were washed with ferrous ammonium sulfate solution, dried, and concentrated. Vacuum distillation of the residue yielded 6.3 g (80%) of colorless 15: bp 95-97° (0.8 mm); n_D^{25} 1.4758. The infrared spectrum of this material was superimposable with that of an authentic sample of 15.

C. The Synthesis and Characterization of 3-Methyl-2, 5-dihydrothiophene 1-Oxide

3-Methyl-2, 5-dihydrothiophene (17). 3-Methylthiophene (490.8 g, 5.0 moles) and 1.5-l. of methyl alcohol were placed in a 5-l. flask equipped with a paddle stirrer, a toluene thermometer, and a large Dry Ice cooled condenser. The flask was surrounded by a Dry Ice-acetone bath and 1.5-l. of anhydrous ammonia was added through the side arm. A 500 ml Erlenmyer flask containing 230 g (10.0 moles) of sodium (small cubes about 0.5 cm on an edge) was attached to the side arm of the reaction vessel with Gooch tubing. The sodium was added in small portions over a 5 hr period while maintaining the cooling bath at -30° to -40° . The reaction mixture was stirred an additional 5 hr during which time the cooling bath was allowed to warm naturally. The cooling bath was removed and the mixture was left standing over night. The flask was then surrounded by an ice bath and the paddle stirrer was carefully operated by hand to release trapped ammonia gas. Mechanical stirring was begun and the mixture was treated with 1.5-l. of ice water while maintaining the reaction below 25° . The resulting solution was separated into two equal portions. Each aqueous alkaline portion was extracted with four 200 ml portions of cold isopentane. The isopentane extracts were combined and dried.

The procedure described above was repeated twice and the isopentane extracts from the three separate runs were combined. The isopentane was distilled under a low flow of nitrogen and the residue was distilled through a 12-in. Vigreux column. A total of 569.3 g of colorless liquid, bp 127-147° was collected. The gas chromatogram (column E, 75°) of this unrefined material showed the presence of 3-methylthiophene and its three dihydro isomers 17, 19, and 20.

The unrefined sulfide mixture was diluted with 500 ml of isopentane. This solution was cooled to 20° and 100 ml of cold 50% sulfuric acid was slowly added with vigorous stirring while monitoring the reaction by periodic gas-liquid partition chromatography (glpc) analysis. After 5 hr, the gas chromatogram (column E, 75°) showed the presence of only 3-methylthiophene and 17. The isopentane layer was separated and the aqueous layer was extracted with one 100 ml portion of isopentane. The combined organic layers were washed with 100 ml of water and dried. The isopentane was again distilled under a low flow of nitrogen. The residue was then distilled, at a reflux ratio of 2:1, through a 45 cm x 1.2 cm i. d. vacuum jacketed vigreux column. A 126 g (13%) fraction of colorless 3-methyl-2, 5-dihydrothiophene (17) was collected: bp 144° (718 mm); n_D^{20} 1.5192 [lit ³⁹ bp 147.5° (760 mm), n_D^{20} 1.5196]. The purity of this material was greater than 98% as shown by glpc analysis (column E, 75°).

Mercurichloride of 3-Methyl-2, 5-dihydrothiophene. A saturated solution of mercuric chloride in 95% ethyl alcohol was added dropwise to a warm stirred solution of 2.0 g (0.02 mole) of 17 in 15 ml of 95% ethyl alcohol until the resulting solution became cloudy. The warm solution was stirred for 0.75 hr, cooled to room temperature, and filtered. The solid material obtained was recrystallized twice from 95% ethyl alcohol and 6.3 g (84%) of finely divided white crystals was obtained: mp 125-127° [lit³⁹ mp 127.5-128°].

3-Methyl-2, 5-dihydrothiophene 1-Oxide (2). A solution of 10.0 g (0.10 mole) of 17 in 40 ml of redistilled acetone was cooled to 0° in an ice bath. To this well-stirred solution was added 14.73 g of 30% hydrogen peroxide (4.42 g, 0.13 mole hydrogen peroxide) while maintaining the reaction mixture below 8°. The ice bath was removed and the solution was allowed to stand for 60 hr. The solution was concentrated by flash evaporation and the residue was extracted with two 35 ml portions of chloroform. The organic extracts were combined, dried, and concentrated. Vacuum distillation of the residue yielded 8.2 g of colorless distillate: bp 60-62.5° (0.12 mm). Two redistillations afforded 6.6 g (57%) of colorless 2: bp 94-96° (0.95 mm); n_D^{25} 1.5296. Redistillation of this material from powdered calcium hydride gave an analytical sample: bp 123° (4.7 mm); n_D^{25} 1.5298; d_4^{25} 1.159. The infrared and

nmr spectra of 2 are shown in Figures 1b and 9 respectively.

Anal. Calcd for C_5H_8OS : C, 51.69; H, 6.94; S, 27.60.

Found: C, 51.37; H, 7.19; S, 27.83.

A similar experiment carried out on a preparative scale using 73.4 g (0.73 mole) of 17 and 99.0 g of 30% hydrogen peroxide afforded 2 in 64% yield.

3-Methyl-2,5-dihydrothiophene 1,1-Dioxide (18). A 3.1 g (0.027 mole) sample of 2 in 25 ml of glacial acetic acid was treated with 3.98 g of 30% hydrogen peroxide (1.19 g, 0.035 mole hydrogen peroxide). The resulting solution was heated at reflux for 1.5 hr. Volatile material was removed on the steam bath at ca. 25 mm and the residue was dissolved in benzene. The solution was dried, filtered, and warmed on a hot plate. Petroleum ether (bp 30-60°) was added until the solution became turbid. Filtration of the chilled solution afforded 2.4 g (68%) of crude sulfone. A single recrystallization from methyl alcohol gave white flakey crystals of 18: mp 62-63° [lit⁶⁶ mp 63.5-64]. A mixture melting point of this material with an authentic sample of 18 showed no depression.

D. Reduction and Base Catalyzed Isomerization of 3-Methyl-2, 5-dihydrothiophene 1-Oxide

Reduction of 3-Methyl-2, 5-dihydrothiophene 1-Oxide by Hydriodic Acid. A solution of 0.579 g (5×10^{-3} mole) of 2 in 10 ml of water was treated slowly with 2.66 g of 48% hydriodic acid (1.27 g, 0.01 mole hydrogen iodide). This solution was stirred for 0.5 hr, cooled and extracted with a single 30 ml portion of petroleum ether (bp 30-60°). The gas chromatogram (column E, 75°) of this extract showed the presence of only 3-methyl-2, 5-dihydrothiophene (17).

Base Catalyzed Isomerization of 3-Methyl-2, 5-dihydrothiophene 1-Oxide. A solution of 2.2 g (0.02 mole) of 2 in 100 ml of 0.5 N sodium hydroxide was stirred periodically and maintained at 25°. After 72 hr, a 25 ml portion of the alkaline solution was withdrawn and extracted with three 25 ml portions of chloroform. The combined extracts were divided into two equal portions. One portion was concentrated by flash evaporation and the residue was dissolved in 10 ml of acetone. This solution was treated with 0.40 g of 30% hydrogen peroxide (0.12 g, 3.5×10^{-3} mole hydrogen peroxide) and refluxed for 4 hr. The gas chromatogram (column G, 135°) of this cooled solution showed the presence of two components in a 3.0:1 ratio. These were identified as 3-methyl-2, 5- and 3-methyl-4, 5-dihydrothiophene (18 and 23)

respectively by comparing the retention volumes of the experimental chromatogram with those of authentic samples 18 and 23.

The second portion of the original chloroform extract was also concentrated by flash evaporation. The residue was dissolved in 10 ml of water and treated with 1.34 g of 48% hydriodic acid (0.64 g, 5×10^{-3} mole hydrogen iodide). This solution was stirred for 0.5 hr, cooled and extracted with 10 ml of petroleum ether. The gas chromatogram (column E, 75°) of this solution showed the presence of 17 and 3-methyl-4,5-dihydrothiophene (19) in a ratio of 2.84:1 respectively.

Another 25 ml portion of the original reaction mixture was withdrawn after 96 hr and worked up and reduced in the previous manner. Gas chromatographic analysis of the reduced products showed the presence of 17 and 19 in a ratio of 1.78:1 respectively. The relative percentage of sulfides 17 and 19 detected after a reaction time of 120 hr was unchanged.

E. The Reaction of 3-Methyltetrahydrothiophene 1-Oxide with Grignard Reagents

Description of the Reaction Vessel. All Grignard reactions were carried out in a 1000 ml flask with three vertical necks. The flask was equipped with a paddle stirrer, a condenser, and a pressure equilibrated dropping funnel with a nitrogen inlet. The system was thoroughly purged with nitrogen and dried with an open flame.

Purification of Starting Materials. The 3-methyltetrahydrothiophene 1-oxide was purified by vacuum distillation from powdered calcium hydride immediately before use. The tetrahydrofuran was refluxed over sodium for 48 hr, distilled, and stored over molecular sieves. This solvent was then distilled from lithium aluminum hydride immediately before use. The organic halides were obtained commercially and were distilled prior to use. The magnesium turnings were obtained from Fisher Scientific Company and were used as received.

2-Phenyl-4-methyltetrahydrothiophene (29) and 2-Phenyl-3-methyltetrahydrothiophene (30). A Grignard reagent was prepared from 94.2 g (0.60 mole) of bromobenzene and 14.6 g (0.60 g-atom) of magnesium turnings in 525 ml of tetrahydrofuran. The resulting mixture was refluxed for 3 hr and then cooled to room temperature.

To this well-stirred reagent was added 17.7 g (0.15 mole) of 1 in 75 ml of tetrahydrofuran during a 20 min period. The dark mixture was stirred at room temperature for 20 hr, then cooled in an ice bath and carefully hydrolyzed with 30 g of concd sulfuric acid in 400 ml of ice water. The two phase mixture was allowed to warm to room temperature and was then separated. The aqueous layer was extracted with a single 100 ml portion of ethyl ether. The combined organic layers were washed with 50 ml of water, dried, and concentrated. Vacuum distillation of the residue yielded 7.7 g of colorless liquid: bp 70-77° (0.1 mm). The gas chromatogram (column B, 50-200° at 10°/min) of this material showed the presence of biphenyl, 29, and 30.

The contaminated sulfide mixture was dissolved in 30 ml of 95% ethyl alcohol and added dropwise to 185 ml of warm 1 M mercuric chloride solution in 95% ethyl alcohol. A white precipitate quickly formed and the mixture was stirred at 60° for 0.5 hr. The mixture was set aside for 5 hr and then filtered to yield 22.7 g of fine white powder: mp 143-146°. This powder was added to 450 ml of 5% hydrochloric acid and the resulting mixture was steam distilled until the distillate was no longer cloudy. The distillate was extracted with two 100 ml portions of ethyl ether and the extracts were combined, dried and concentrated. Vacuum distillation of the residue afforded 4.7 g (17%) of colorless liquid: bp 78-80° (0.1 mm); n_D^{25} 1.5690. The gas

chromatogram showed this material to be a 1.04:1 binary sulfide mixture composed of 29 and 30. A previous reaction yielded an analytical sample composed of 29 and 30 in a ratio of 1.50:1 respectively: bp 83-83.5° (0.35 mm); n_D^{25} 1.5686; d_4^{25} 1.0501. The infrared spectrum of this mixture is shown in Figure 2a.

Anal. Calcd for $C_{11}H_{14}S$: C, 74.09; H, 7.93; S, 17.98.

Found: C, 74.04; H, 8.06; S, 18.05.

Desulfurization of a Mixture Containing 29 and 30. This reaction was carried out using both preparative-scale and semimicroquantities of sulfide mixture.

(a) Preparative-scale Desulfurization. A solution containing 2.2 g (0.012 mole) of a 1.04:1 sulfide mixture composed of 29 and 30 in 10 ml of 95% ethyl alcohol was added to a stirred suspension of ca. 25 g of No. 28 Raney nickel catalyst (Raney Catalyst Co., Chattanooga, Tenn.) in 50 ml of 95% ethyl alcohol. This mixture was stirred at reflux for 4 hr, cooled, and filtered through Celite. The clear filtrate was placed in a 200 ml volumetric flask and ca. 150 ml of 85% phosphoric acid was added with cooling. A clear insoluble upper layer was removed from the acid solution: 1.6 g (87%); n_D^{20} 1.4896. The gas chromatogram (column D, 100°) of this material, using p-cymene as an internal standard, showed the presence of 27 and 28 in a ratio of 1:1.37 respectively. An

authentic sample of 27 and 28* in a ratio of 1:1.37 was prepared. The infrared spectrum and index of refraction of this authentic sample were in good agreement with those of the desulfurization products.

(b) Semimicro-scale Desulfurization. A 45.6 mg (2.6×10^{-4} mole) sample of 1.04:1 sulfide mixture composed of 29 and 30 respectively was dissolved in 3 ml of 95% ethyl alcohol in a 5" x 1/2" test tube. To this solution was added ca. 400 mg of No. 28 Raney nickel catalyst and the resulting mixture was placed in a water bath at 50°. Complete mixing of the reaction mixture was periodically effected simply by shaking the test tube. The catalyst was allowed to settle and a small portion of the clear solution was withdrawn for glpc analysis. This provided a convenient method for following the progress of the reaction. No sulfides were detected after 40 min and during this time, the unreacted sulfide mixture became considerably richer in 30. Sulfides 29 and 30 remaining after 35 min were present in a ratio of 1:1.60 respectively. A 5 μ l portion of p-cymene was added to each solution as an internal standard for further glpc analysis. These gas chromatograms (column D, 100°) showed the presence of hydrocarbons 27 and 28 in ratios ranging from 1:1.13 (after 5 min) to 1:1.44 (after 35

* This hydrocarbon was prepared from sec-butyl bromide, benzyl chloride, and sodium according to the procedure of J. W. E. Glattfeld and C. N. Cameron, J. Am. Chem. Soc., 49, 1043 (1927).

min) respectively.

Preparative-Scale Gas Chromatographic Separation of a Mixture Containing 29 and 30. The individual components of a 1.04:1 mixture of 29 and 30 were obtained in 100% purity using an Aerograph Autoprep model A-700 preparative gas chromatograph. A 20' x 3/8" Al 30% SE-30 on 45/60 Chromsorb P column was employed for this separation: column 225°; injector 300°; collector 265°; detector 340°; helium 100 ml/min. The neat sulfide mixture was injected onto the column in 20 µl samples. These conditions gave approximately an 80% separation of the two components. Therefore, to insure the complete purity of the samples collected, only the front half of peak I and the back half of peak II were collected. A total of 600 µl (630 mg) of mixture was injected onto the column and the individual components were trapped in small collection bottles containing isopentane at 0°. The contents of each collection bottle were transferred to a separate 5" x 1/2" test tube and a gentle stream of nitrogen was passed over each solution to evaporate the isopentane solvent. A 70.8 mg sample of 30 (collected as peak I) and a 45.8 mg sample of 29 (collected as peak II) were obtained. These individual isomers were 100% pure as shown by analytical glpc analysis (column B, 50-200° at 10°/min).

Desulfurization of 30. A 70.8 mg (3.9×10^{-4} mole) sample of 30

was desulfurized with ca. 600 mg of No. 28 Raney nickel catalyst in the manner previously described for these semimicro-scale reactions. The glpc analysis (column A, 145°) of the small samples withdrawn during the reaction showed the presence of one hydrocarbon and unreacted sulfide 30. A 5 μ l sample of p-cymene was added to each solution as an internal standard for further glpc analysis. These gas chromatograms (column D, 100°) showed the presence of the internal standard and only one other component, 1-phenyl-2-methylbutane (28).

Desulfurization of 29. A 45.8 mg (2.6×10^{-4} mole) sample of 29 was treated with ca. 400 mg of No. 28 Raney nickel catalyst as described previously. Small portions of clear solution were withdrawn at 5 min intervals for glpc analysis. The gas chromatogram (column A, 145°) of the sample withdrawn after a contact time of only 5 min showed the presence of unreacted sulfide 29 and a small percentage of sulfide 30. After 10 min, sulfides 29 and 30 were present in a ratio of 2.20:1 respectively. No sulfides were detected after 15 min. To these three samples was added 5 μ l of p-cymene as an internal standard for further glpc analysis. The gas chromatogram (column D, 100°) of each solution showed the presence of two components in addition to the internal standard. These were present in ratios ranging from 2.0:1 to 1.70:1 and were identified as 1-phenyl-3-methyl butane (27) and 1-phenyl-2-methylbutane (28) respectively.

Attempted Isomerization of a Mixture Containing 29 and 30. A 63.4 g (3.6×10^{-4} mole) sample of 1.04:1 sulfide mixture composed of 29 and 30 was treated with ca. 650 mg of powdered nickel in the manner described in the preceding desulfurization experiments. The powdered nickel was obtained by deactivating a portion of No. 28 Raney nickel catalyst. The active catalyst was placed in boiling ethyl alcohol for 24 hr and then baked in a vacuum oven at 180° for 24 hr. The course of this attempted isomerization reaction was also followed by periodic glpc analysis. The reaction was monitored for 8 hr and the gas chromatogram (column A, 145°) of each solution withdrawn during this time showed the relative percentage of each isomer to be unchanged.

2-n-Propyl-4-methyltetrahydrothiophene (31) and 2-n-Propyl-3-methyltetrahydrothiophene (32). In the apparatus previously described, a Grignard reagent was prepared from 73.8 g (0.60 mole) of n-propyl bromide and 14.6 g (0.60 g-atom) of magnesium turnings in 525 ml of tetrahydrofuran. The resulting mixture was refluxed for 3.5 hr and then cooled to room temperature. The exit line from the reaction vessel was connected to a trap equipped with a fritted glass dispersion tube. A solution of 25 ml of bromine in 100 ml of chloroform was placed in the trap and cooled in an ice bath. A solution of 17.7 g (0.15 mole) of 1 in 75 ml of tetrahydrofuran was then added during a 20 min period

to the rapidly stirred Grignard reagent. This mixture was stirred at room temperature for 20 hr, then cooled in an ice bath and carefully hydrolyzed with 30 g of concd sulfuric acid in 400 ml of ice water. The two phase mixture was separated and the aqueous layer was extracted with a single 100 ml portion of ethyl ether. The combined organic layers were washed with 50 ml of water and dried.

The contents of the trap containing the bromine solution was poured into 150 ml of water and solid sodium bisulfite was added to remove the excess bromine. The mixture was separated and the aqueous layer was extracted with a single 75 ml portion of ethyl ether. The organic layers were combined, dried, and concentrated. Distillation of the residue yielded 4.7 g (0.023 mole) of 1,2-dibromopropane: bp 129-132° (722 mm); n_D^{25} 1.5175 [lit⁶⁷ bp 141.6°, n_D^{20} 1.5203].

The dried organic phase from the original reaction was concentrated. Vacuum distillation of the residue yielded 7.4 g of colorless liquid: bp 50-87° (32 mm). Redistillation of this material afforded 3.8 g (25%) of clear liquid: bp 128-130°. This fraction was identified as 3-methyltetrahydrothiophene (16) by glpc analysis (column E, 102°) and comparison of the infrared spectrum with that of an authentic sample of 16. The original distillation also yielded 6.7 g (31%) of colorless liquid: bp 87-91° (32 mm); n_D^{25} 1.4815. The gas chromatogram (column B, 50-175° at 10°/min) showed this material to be a 7.34:1 mixture

composed of 31 and 32. A previous reaction yielded an analytical sample composed of 31 and 32 in a ratio of 4.26:1 respectively: bp 75.5-76.5° (15 mm); n_D^{25} 1.4803. The infrared spectrum of this mixture is shown in Figure 2b.

Anal. Calcd for $C_8H_{16}S$: C, 66.58; H, 11.20; S, 22.22.

Found: C, 66.57; H, 11.19; S, 22.29.

Desulfurization of a Mixture Containing 31 and 32. This reaction was carried out using both preparative-scale and semimicro-scale quantities of sulfide mixture.

(a) Preparative-scale Desulfurization. A solution containing 4.1 g (0.028 mole) of a 3:1 mixture composed of 31 and 32 respectively in 25 ml of 95% ethyl alcohol was added to a stirred suspension of ca. 20 g of No. 28 Raney nickel catalyst in 50 ml of 95% ethyl alcohol. This reaction and work-up were carried out as previously described for desulfurization of the mixture of 29 and 30. The present reaction yielded 2.3 g (71%) of a 1:1.44 mixture composed of 33 and 34 as shown by glpc analysis (column C, 45°). Distillation did not effect the composition of this mixture and 0.45 g of hydrocarbon mixture was obtained: bp 115°, n_D^{25} 1.3965. The infrared spectrum and index of refraction were in excellent agreement with those of an authentic sample of 33 and 34 prepared in a weight ratio of 1:1.44 respectively.

(b) Semimicro-scale Desulfurization. A 100 mg (6.9×10^{-4} mole) sample of a 5.24:1 mixture composed of 31 and 32 was treated with ca. 1 g of No. 28 Raney nickel catalyst in the manner previously described. Small samples of nickel free solution were withdrawn at 20 min intervals for glpc analysis (column A, 100°). No sulfides were detected after 60 min. A 5 μ l sample of n-heptane was then added to each solution for further glpc analysis. These gas chromatograms (column C, 45°) of each sample showed the presence of internal standard and two additional components present in an essentially constant ratio of 2.37:1. These were identified as hydrocarbons 33 and 34 respectively.

Preparative-Scale Gas Chromatographic Separation of a Mixture Containing 31 and 32. The individual components of a 5.25:1 mixture of 31 and 32 were obtained in 100% purity using the preparative gas chromatograph previously described. A 20' x 3/8" Al 30% SE-30 on 42/60 Chromsorb P column was employed for this separation: column 205° ; injector 250° ; collector 225° ; detector 300° ; helium 100 ml/min. The neat sulfide mixture was injected onto the column in 75 μ l samples. Under these conditions, the retention volume of 31 and 32 was 1,925 ml and 2,150 ml respectively. A total of 1,675 μ l of mixture was injected onto the column and the individual components were trapped in small collection bottles containing isopentane at 0° . The contents of each

collection bottle were transferred to a separate 5" x 1/2" test tube and a gentle stream of nitrogen was passed over each solution to evaporate the isopentane solvent. A 114.4 mg sample of 31 (collected as peak I) and a 5.0 mg sample of 32 (collected as peak II) were obtained. These individual isomers were 100% pure as shown by analytical glpc analysis (column B, 50-175° at 10°/min).

Desulfurization of 31. A 50 mg (3.5×10^{-4} mole) sample of 31 in 3 ml of 95% ethyl alcohol was treated with ca. 500 mg of No. 28 Raney nickel catalyst in the manner previously described. Small samples of nickel free solution were withdrawn at 5 min intervals for glpc analysis (column A, 100°). No sulfide was detected after 40 min and these gas chromatograms showed no evidence for the presence of sulfide 32 during the entire reaction. A 5 μ l sample of n-heptane was added to each sample as an internal standard for further glpc analysis. These gas chromatograms (column C, 45°) showed the presence of the internal standard and a mixture of 33 and 34. The ratio of hydrocarbons 33 and 34 in each sample was essentially constant at ca. 6:1.

Desulfurization of 32. A 5.0 mg (3×10^{-5} mole) sample of 32 in 3 ml of 95% ethyl alcohol was treated with ca. 50 mg of No. 28 Raney nickel catalyst in the manner previously described. Small samples of nickel free solution were withdrawn at 3 min intervals for glpc analysis.

No sulfide was detected after 40 min and the presence of sulfide 31 was undetected during the entire reaction. A 5μ l sample of n-heptane was added to each solution for further glpc analysis. These gas chromatograms showed the presence of the internal standard and a mixture of 33 and 34. The ratio of 33 and 34 in each sample was essentially constant at ca. 1:3.

Attempted Isomerization of a Mixture Containing 31 and 32. A 26.7 mg (1.9×10^{-4} mole) sample of 4.26:1 sulfide mixture composed of 31 and 32 respectively was treated with ca. 260 mg of powdered nickel in the manner previously described for the attempted isomerization of a mixture containing 29 and 30. The relative percentage of 31 and 32 was unchanged even after a contact time of 8 hr.

2-(2,2-Dimethylpropyl)-4-methyltetrahydrothiophene (35) and 2-(2,2-Dimethylpropyl)-3-methyltetrahydrothiophene (36). In the apparatus previously described, a Grignard reagent was prepared from 25.0 g (0.235 mole) of 1-chloro-2,2-dimethylpropane and 5.64 g (0.235 g-atom) of magnesium turnings in 190 ml of tetrahydrofuran. The Grignard reagent formed very slowly and 1.0 ml of ethyl bromide was added to initiate the sluggish reaction. Most of the magnesium was consumed after a 12 hr reflux period. The dark reagent was cooled to room temperature and 11.8 g (0.10 mole) of 1 in 60 ml of tetrahydrofuran was

added during a 30 min period. The resulting reaction mixture was stirred at 25° for 24 hr, then cooled in an ice bath and carefully hydrolyzed with 12.5 g of concd sulfuric acid in 200 ml of ice water. The two phase mixture was separated and the aqueous layer was extracted with two 60 ml portions of ethyl ether. The combined organic layers were dried and concentrated. Vacuum distillation of the residue yielded 7.5 g of clear liquid: bp 65-70° (3.5 mm). Redistillation of this material afforded 5.0 g (29%) of colorless liquid: bp 67-69° (3.4 mm); n_D^{25} 1.4745; d_4^{25} 0.8988. The gas chromatogram (column A, 154°) showed this material to be a 8.09:1 mixture composed of 35 and 36 respectively. The infrared spectrum of this mixture is shown in Figure 3a.

Anal. Calcd for $C_{10}H_{20}S$: C, 69.70; H, 11.69; S, 18.60.

Found: C, 69.33; H, 11.90; S, 18.35.

Desulfurization of a Mixture Containing 35 and 36. A 29.0 mg (1.7×10^{-4} mole) sample of 8.09:1 sulfide mixture composed of 35 and 36 was treated with ca. 300 mg of No. 28 Raney nickel catalyst in the manner previously described. Small samples of nickel free solution were withdrawn at 3 min intervals for glpc analysis (column A, 145°). No sulfides were detected after 15 min and during this time, essentially no change in the ratio of unreacted sulfides was detected. A 5 μ l sample of 3-methylheptane was added to each solution as an internal standard for further glpc analysis. These gas chromatograms (column

C, 34°) showed, in addition to the internal standard, the presence of two components in a ratio of 5.25:1. The major component was identified as 2, 2, 6-trimethylheptane (37) by comparing the retention volume of the experimental chromatogram with that of an authentic sample of 37.

2, 2, 6-Trimethylheptane (37). A solution of 42.6 g (0.40 mole) of 1-chloro-2, 2-dimethylpropane and 63.9 g (0.60 mole) of 1-chloro-3-methylbutane in 20 ml of dry benzene was slowly added to 22.9 g (1.0 mole) of sodium which had been cut into small pieces about 0.5 cm on a side. The exothermic reaction was periodically cooled during the three hr period required for complete addition of the halides. The resulting deep blue mixture was heated at reflux for 7 days. During this time, small portions of dry benzene were added to maintain a stirrable mixture. The mixture was cooled and treated with 50 ml of methyl alcohol followed by 70 ml of aqueous 50% methyl alcohol. After stirring for 1.5 hr, the mixture was filtered and the solid was washed with two portions of ethyl ether. The filtrate was washed with two 50 ml portions of water, two 50 ml portions of 25% sulfuric acid, and finally with 50 ml of water. The solution was dried and concentrated. Distillation of the residue yielded 18.5 g (13%) of colorless material: bp 130-165°. The gas chromatogram (column A, 50-175° at 10°/min) of this material showed the presence of three major components. This material was

washed with cold concd sulfuric acid and fractionated using a GE-196 Wheeler spinning band column (Precision Distillation Apparatus Co., Woodland Hills, California). A 5 g sample of colorless 37 was collected: bp 144-146°; n_D^{25} 1.4069 [lit⁶⁸ bp 148.2°, n_D^{20} 1.4059].

Identification of the Minor Component of the 5.25:1 Hydrocarbon Mixture Obtained from the Desulfurization of an 8.09:1 Mixture of 35 and 36. A ternary hydrocarbon mixture composed of 2, 2, 5, 5-tetramethylhexane (bp 137.5°), 2, 2, 5-trimethylheptane (38) (bp 148.2°), and 3, 6-dimethyloctane (bp 160°)⁶⁸ was separated on the basis of boiling point by analytical glpc analysis (column A, 125°). The retention volume of the "middle boiling" component 38, relative to an internal standard 3-methylheptane, (column C, 34°) was exactly the same as that of the minor product detected in the desulfurization of the 8.09:1 mixture of 35 and 36.

F. The Reaction of 3-Methyl-2, 5-dihydrothiophene 1-Oxide with Grignard Reagents

Purification of Starting Materials. The 3-methyl-2, 5-dihydrothiophene 1-oxide was distilled from powdered calcium hydride before use. All other materials were purified as described in Section IV E.

1-n-Propyl-2-methyl-1, 3-butadiene (48). In the apparatus previously described, a Grignard reagent was prepared from 49.2 g (0.40 mole) of 1-bromopropane and 9.7 g (0.40 g-atom) of magnesium turnings in 325 ml of tetrahydrofuran. The mixture was refluxed for 2 hr after complete addition of the halide and then cooled to 0° in an ice bath. The exit line from the reaction vessel was connected, as previously described, to a trap containing 25 ml of bromine in 100 ml of chloroform. A solution of 11.6 g (0.10 mole) of 2 in 75 ml of tetrahydrofuran was added to the well-stirred Grignard reagent. The reaction mixture was stirred for 1 hr at 0°, then allowed to warm naturally and stirred for 15 hr at 25°. The mixture was again cooled in ice and carefully hydrolyzed with an ice cold solution of 10.7 g of ammonium chloride in 15 ml of water. After warming to room temperature, the mixture was separated and the aqueous layer was extracted with two 100 ml portions of ethyl ether. The combined organic layers were washed with a single 50 ml portion of water, dried, and concentrated.

Vacuum distillation of the residue yielded 8.2 g of liquid: bp 75-78° (18 mm). Redistillation of this material afforded 6.9 g (49%) of colorless 48: bp 85° (20 mm); n_D^{25} 1.5233; d_4^{25} 0.8993; ultraviolet maximum (95% ethanol) at 281 m μ . The gas chromatogram (column B, 50-175° at 10°/min) of this material showed the presence of only one component. The infrared and nmr spectra of 48 are shown in Figures 5a and 13 respectively.

Anal. Calcd for C₈H₁₄S: C, 67.55; H, 9.91; S, 22.54.

Found: C, 67.70; H, 9.80; S, 22.30.

1-n-Propylthio-2-methylbutane (50). This compound was obtained by catalytic hydrogenation of 48 and was also prepared by an independent synthesis.

(a) Catalytic Reduction of 48. A mixture of 35 g of 10% palladium on carbon catalyst in 100 ml of 95% ethyl alcohol was placed in a Parr Hydrogenation Apparatus (Parr Instrument Co., Moline, Ill., Model No. 3911). This mixture was shaken at 41 psig until no further sorption of hydrogen was noted. A solution of 5.4 g (0.038 mole) of 48 in 80 ml of 95% ethyl alcohol was added to the activated catalyst. This mixture was shaken at 36 psig for 1 hr (final pressure 30.5 psig) and filtered through Celite. The collected catalyst was washed with 100 ml of boiling ethyl alcohol. The filtrate was concentrated to about 60 ml by flash evapora-

tion and diluted with 60 ml of ethyl ether. The ether solution was washed with 30 ml of 10% sodium hydroxide, two 25 ml portions of water, dried, and concentrated. Distillation of the residue afforded 1.3 g (23%) of colorless 50: bp 170° (710 mm); n_D^{25} 1.4490. The gas chromatogram (column C, 120°) of this material showed the presence of only one component. The infrared and nmr spectra of 50 are shown in Figures 5b and 14 respectively.

(b) Synthesis of 50. A solution of 4.0 g (0.10 mole) of sodium hydroxide in 75 ml of water was placed in a 250 ml flask equipped with a reflux condenser, a magnetic stirrer, and a dropping funnel. To this stirred solution was slowly added 7.62 g (0.10 mole) of n-propyl mercaptan. The resulting solution was warmed to 50° and carefully treated with 15.1 g (0.10 mole) of optically active 1-bromo-2-methylbutane*. This mixture was vigorously stirred for 6 hr at 80-90°. The mixture was cooled and diluted with 70 ml of ethyl ether. The organic layer was separated, washed with a 40 ml portion of 10% sodium hydroxide and two 50 ml portions of water, dried, and concentrated. Distillation of the residue afforded 6.1 g (42%) of colorless 50: bp 174° (712 mm). Redistillation of this material yielded an analytical sample of 50: bp 178°

* This alkyl halide was prepared in moderate yield from active-amyl alcohol according to the procedure of H. O. Jones, J. Chem. Soc., 138 (1905).

(713 mm); n_D^{25} 1.4512; d_4^{25} 0.8422; principal infrared absorptions at 2907, 2857, 1575, 1418, 1379, 1335, 1294, 1279 and 1233 cm^{-1} ; nmr peaks (neat) at 7.72 (4 H multiplet), 8.65 (8 H multiplet, major peaks separated by 7 cps) and 9.22 τ (6 H multiplet).

Anal. Calcd for $\text{C}_8\text{H}_{18}\text{S}$: C, 65.69; H, 12.39; S, 21.92.

Found: C, 65.62; H, 12.16; S, 22.15.

1-n-Propyl-3-methylbutane (51). This compound was prepared in the manner described for the synthesis of 50. The halide employed in the present synthesis, however, was 1-bromo-3-methylbutane. Reaction, work-up, and distillation afforded 5.7 g (39%) of colorless 51: bp 173° (712 mm); n_D^{25} 1.4483 [lit⁶⁹ bp 179-181° (740 mm), n_D^{20} 1.4495]. The infrared and nmr spectra of this material are shown in Figures 6 and 15 respectively.

1-Phenylthio-2-methyl-1,3-butadiene (44). In the apparatus previously described, a Grignard reagent was prepared from 62.8 g (0.40 mole) of bromobenzene and 9.7 g (0.40 mole) of magnesium turnings in 325 ml of tetrahydrofuran. After complete addition of the halide, the mixture was refluxed for 1.5 hr and then cooled to 0° in an ice bath. A solution of 11.6 g (0.10 mole) of 2 in 75 ml of tetrahydrofuran was added to the well-stirred Grignard reagent during a 30 min period. The reaction mixture was stirred at 0° for 1 hr and after warming to room

temperature was stirred for 20 hr at 25°. The mixture was again cooled in ice and carefully hydrolyzed with 19.6 g of concd sulfuric acid in 325 ml of ice water. The mixture was separated and the aqueous layer was extracted with two 100 ml portions of ethyl ether. The combined organic layers were washed with a single 50 ml portion of water, dried, and concentrated. Distillation of the residual oil yielded 13.4 g of pale yellow liquid: bp 77-79° (0.15 mm). Redistillation of this material afforded 12.3 g (70%) of colorless 44: bp 77° (0.15 mm); n_D^{25} 1.6192; d_4^{25} 1.0329; ultraviolet maximum (95% ethanol) at 288 m μ . The gas chromatogram (column B, 100-225° at 10°/min) of this material showed the presence of only one component. The infrared and nmr spectra of 44 are shown in Figures 3b and 10 respectively.

Anal. Calcd for C₁₁H₁₂S: C, 74.94; H, 6.88; S, 18.19.

Found: C, 74.90; H, 6.97; S, 17.97.

1-Phenylthio-2-methylbutane (46). This compound was obtained by catalytic hydrogenation of 44 and was also prepared by an independent synthesis.

(a) Catalytic Reduction of 44. A mixture of 32.0 g of 10% palladium on carbon catalyst in 100 ml of 95% ethyl alcohol was placed in a Parr Hydrogenation Apparatus and shaken at 39 psig until no further sorption of hydrogen was detected. A solution of 7.0 g (0.18 mole) of

44 in 100 ml of 95% ethyl alcohol was carefully added to the activated catalyst. This mixture was shaken at 47 psig for 4 hr (final pressure 42.5 psig). The solution was filtered through Celite and the collected catalyst was washed with 100 ml of boiling ethyl alcohol. The filtrate was concentrated to about 60 ml by flash evaporation and diluted with 60 ml of ethyl ether. The ether solution was washed with 30 ml of 10% sodium hydroxide and two 25 ml portions of water, dried, and concentrated. Vacuum distillation of the residue afforded 4.2 g (13%) of colorless 46: bp 125° (17 mm); n_D^{25} 1.5362 [lit⁷⁰ bp 99-101° (4.5 mm), n_D^{20} 1.5408]. The gas chromatogram (column B, 100-225° at 10°/min) of this material showed the presence of only one component. The infrared and nmr spectra of this material are shown in Figures 4a and 11 respectively.

(b) Synthesis of 46. In the reaction vessel previously described for the synthesis of 50, a solution of 8.4 g (0.15 mole) of potassium hydroxide and 16.5 g (0.15 mole) of thiophenol in 50 ml of 95% ethyl alcohol was treated with 22.6 g (0.15 mole) of optically active 1-bromo-2-methylbutane during a 30 min period. Precipitation of potassium hydroxide occurred immediately and vigorous stirring was employed. After refluxing for 5 hr, the solution was cooled, diluted with 100 ml of water, and extracted with three 50 ml portions of ethyl ether. The combined ether layers were washed with a single 50 ml portion of 5%

sodium hydroxide and two 50 ml portions of water, dried, and concentrated. Vacuum distillation of the residue afforded 11.5 g (43%) of 46: bp 135-136.5° (22 mm); n_D^{25} 1.5369; principal infrared absorptions at 3077, 2950, 2874, 1587, 1481, 1462, 1441, 1379, 1300, 1279, 1235, 1093, 1070, 1029, 727 and 690 cm^{-1} ; nmr peaks (neat) at 3.15 (5 H multiplet), 7.55 (2 H multiplet), 8.80 (3 H multiplet) and 9.42 τ (6 H triplet).

1-Phenylthio-3-methylbutane (47). This compound was prepared in the manner described for the synthesis of 46. The halide used in this synthesis, however, was 1-bromo-3-methylbutane. Reaction, work-up, and distillation yielded 19.0 g (70%) of 47: bp 132-133.5° (25 mm); n_D^{25} 1.5351 [lit⁷⁰ bp 100-100.5° (6 mm), n_D^{20} 1.5380]. The infrared and nmr spectra of this compound are shown in Figures 4b and 12 respectively.

V. SUMMARY

1. The synthesis and characterization of the previously unknown 3-methyltetrahydrothiophene 1-oxide (1) and 3-methyl-2, 5-dihydrothiophene 1-oxide (2) has been accomplished. Nuclear magnetic resonance studies have provided significant information concerning the stereochemistry of these unsymmetrical cyclic molecules.

2. Hydriodic acid rapidly and cleanly reduced 2 to the corresponding sulfide.

3. The partial base catalyzed isomerization of 2 to 3-methyl-4, 5-dihydrothiophene 1-oxide (13) was carried out and detected by gas chromatographic analysis of the reduced products. A mechanism, consistent with the data, has been proposed for this reaction.

4. The reaction of 1 with Grignard reagents has been studied. In all cases, a binary mixture of substituted 3-methyltetrahydrothiophenes was obtained. Predominant reaction occurred at position-5 of 1. A plausible mechanism has been proposed.

5. The partial isomerization of some substituted 3-methyltetrahydrothiophenes was observed during desulfurization reactions.

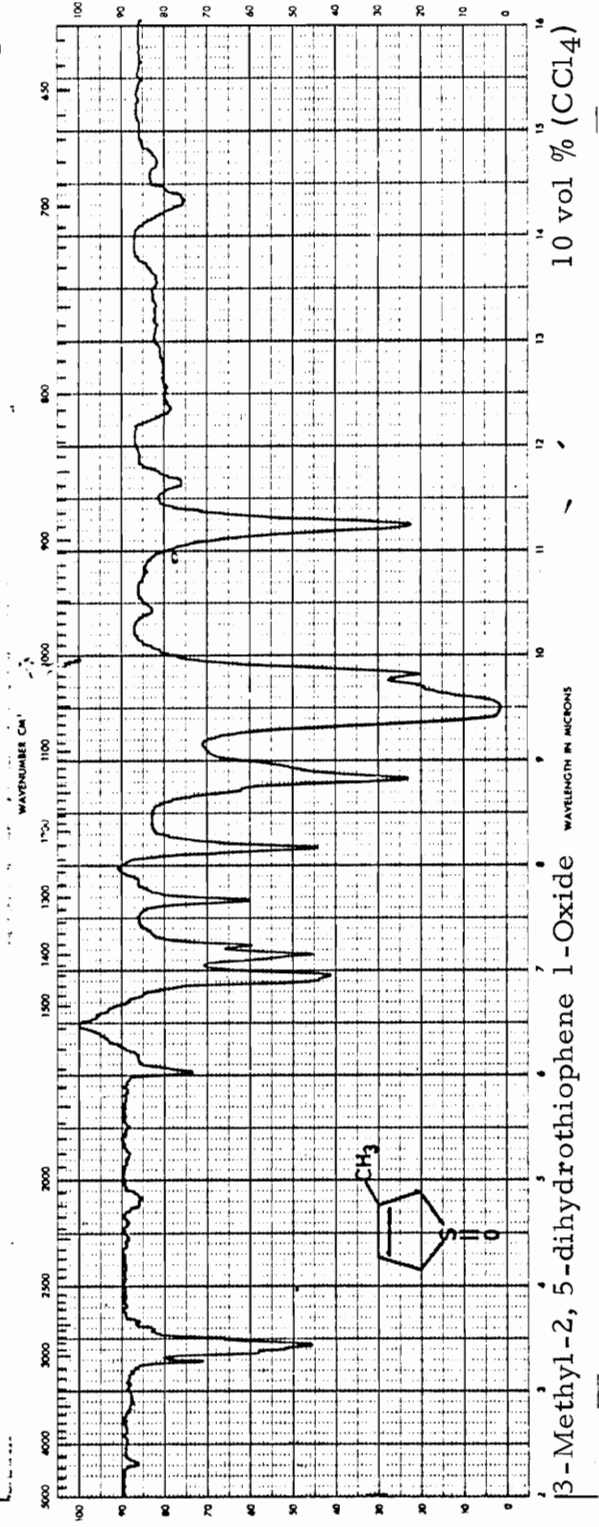
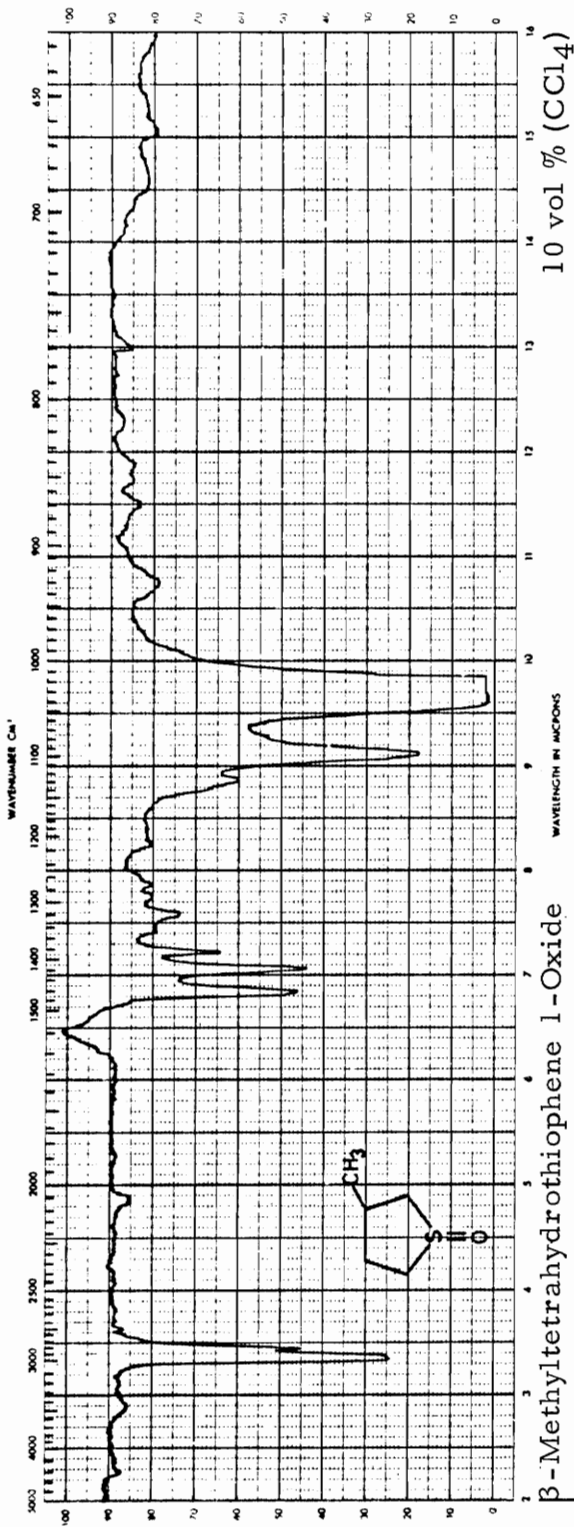
6. The reaction of 2 with Grignard reagents was investigated and

shown to yield single dienyl sulfides. A mechanism for this stereospecific reaction has been proposed.

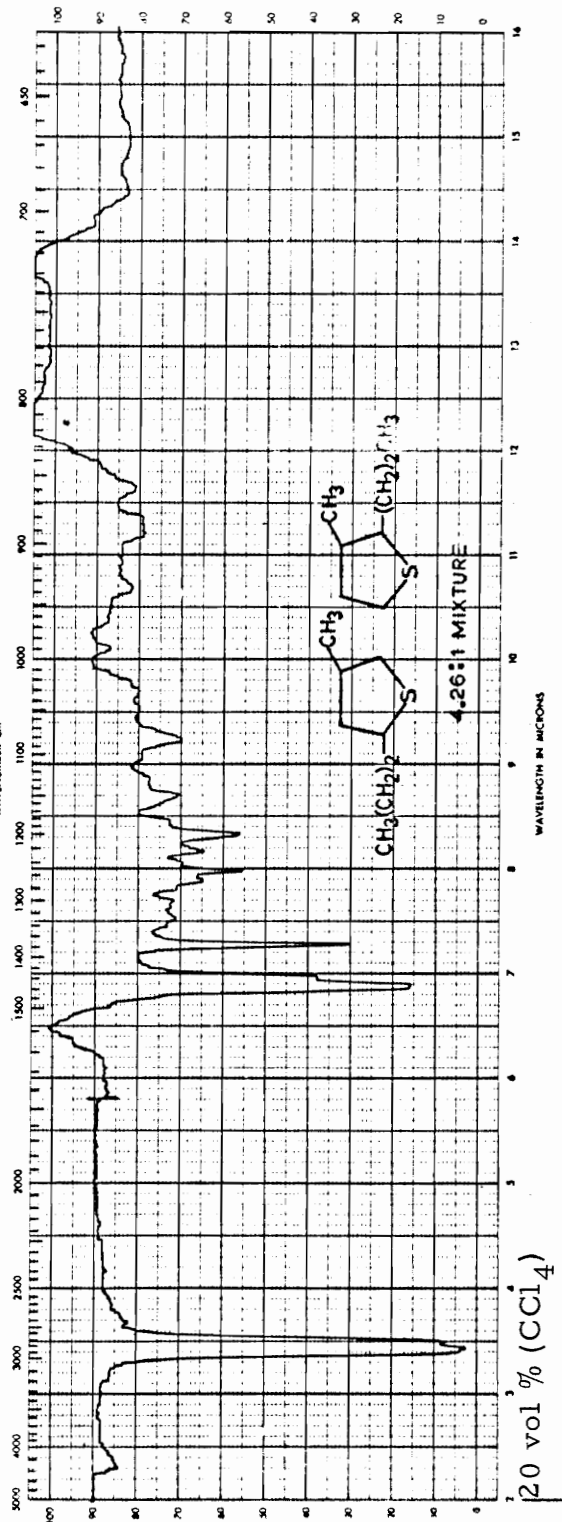
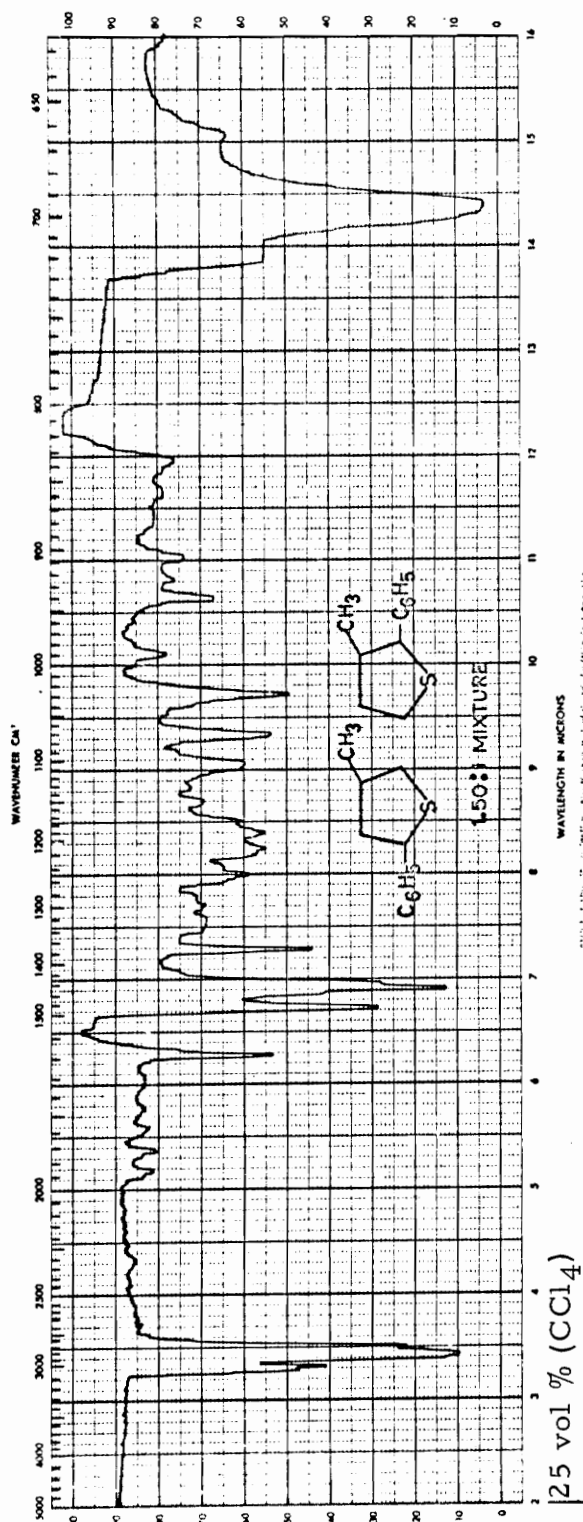
7. The preparation and characterization of the previously unreported 1-n-propylthio-2-methylbutane has been accomplished.

8. Experimental data obtained in the reactions of 1 and 2 has been compared, when possible, with previous experiments employing acyclic and cyclic sulfoxides and sulfones.

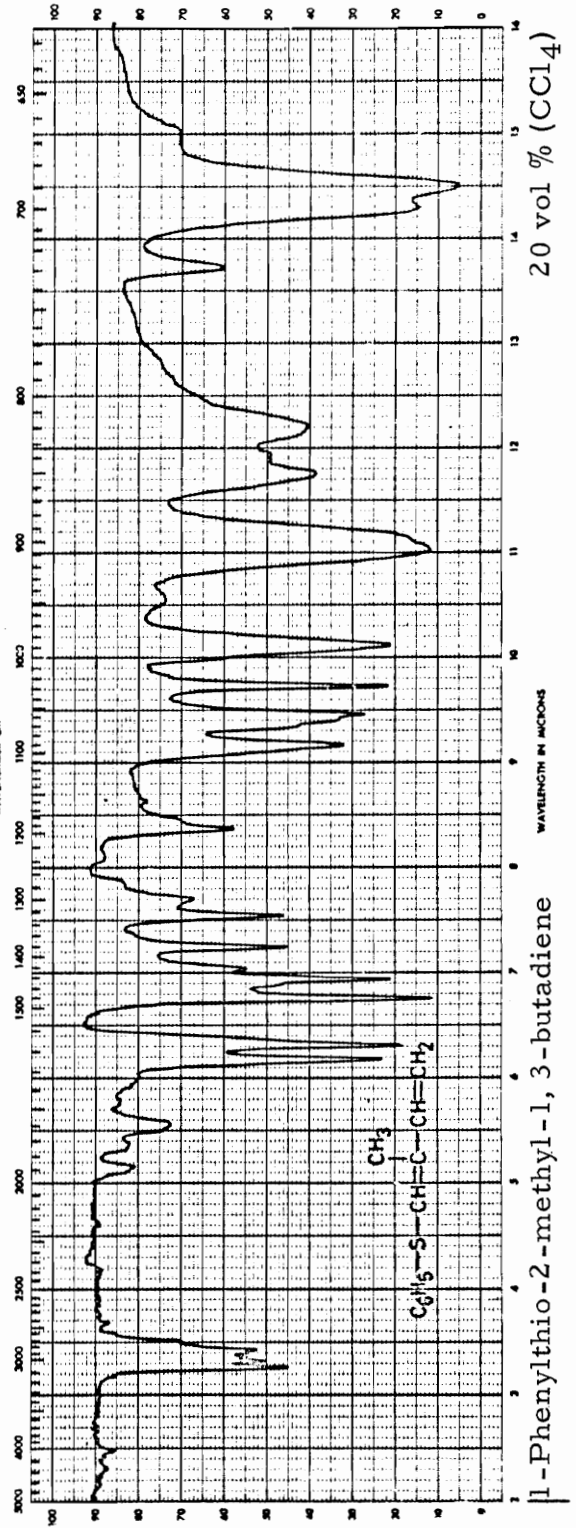
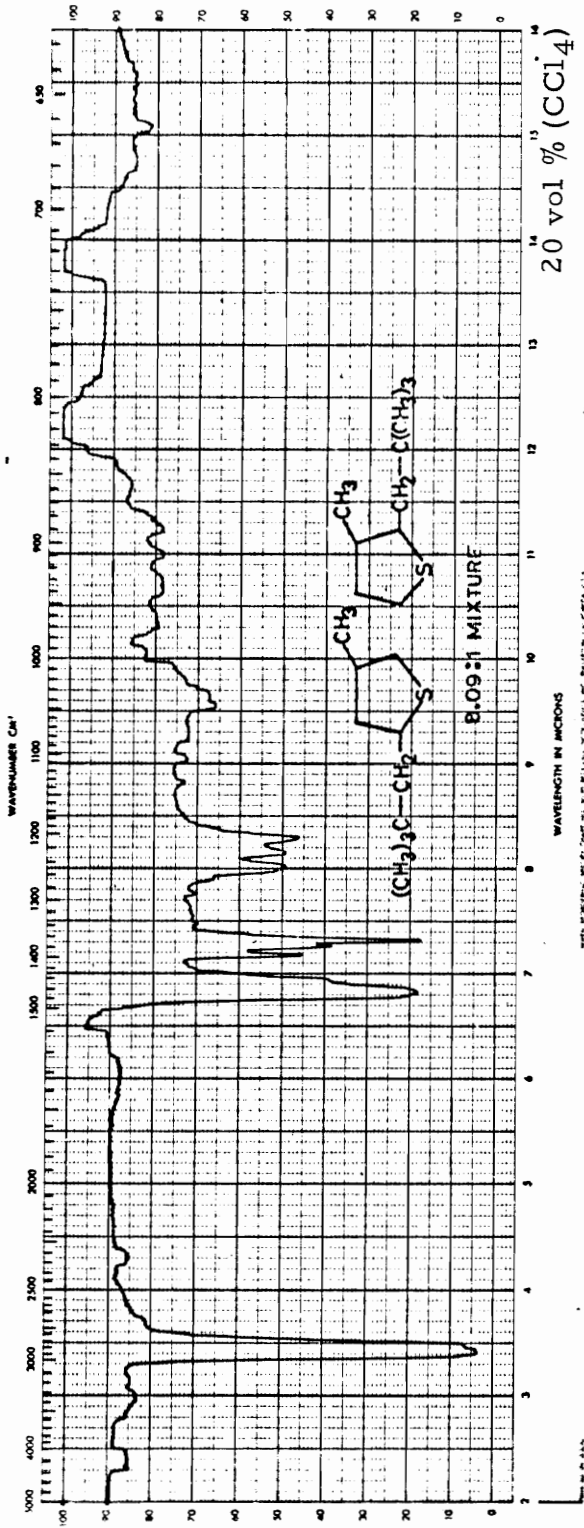
VI. APPENDIX



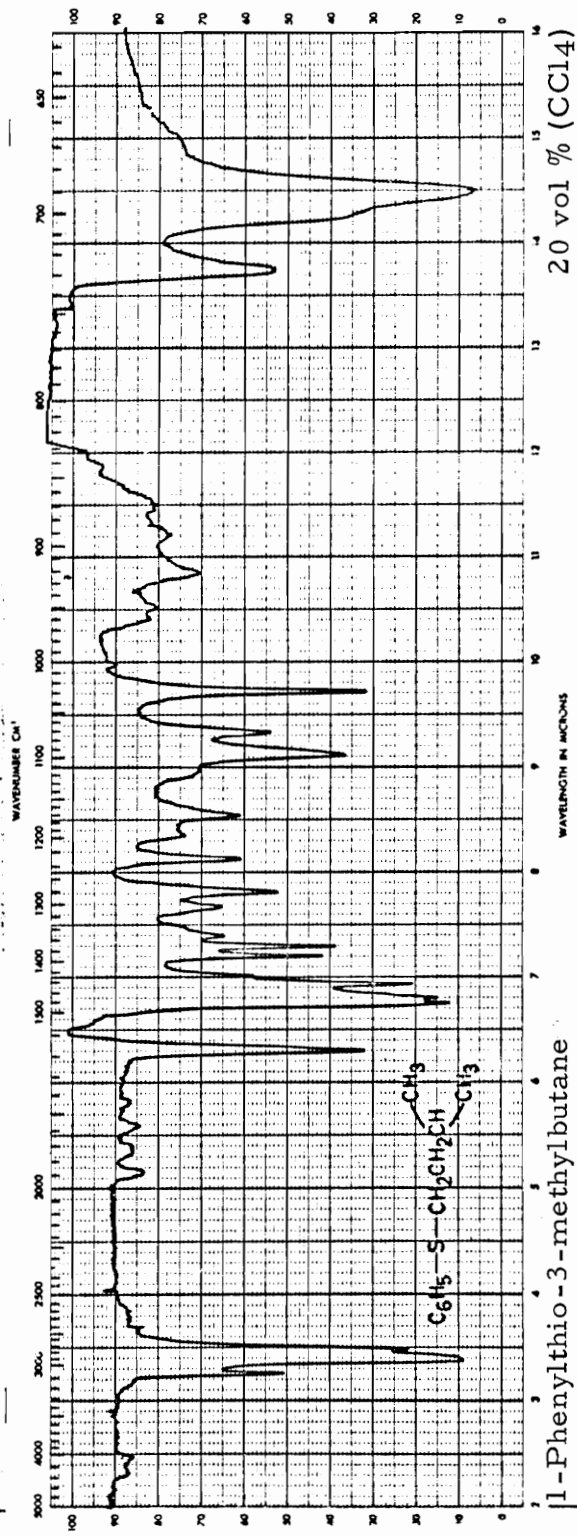
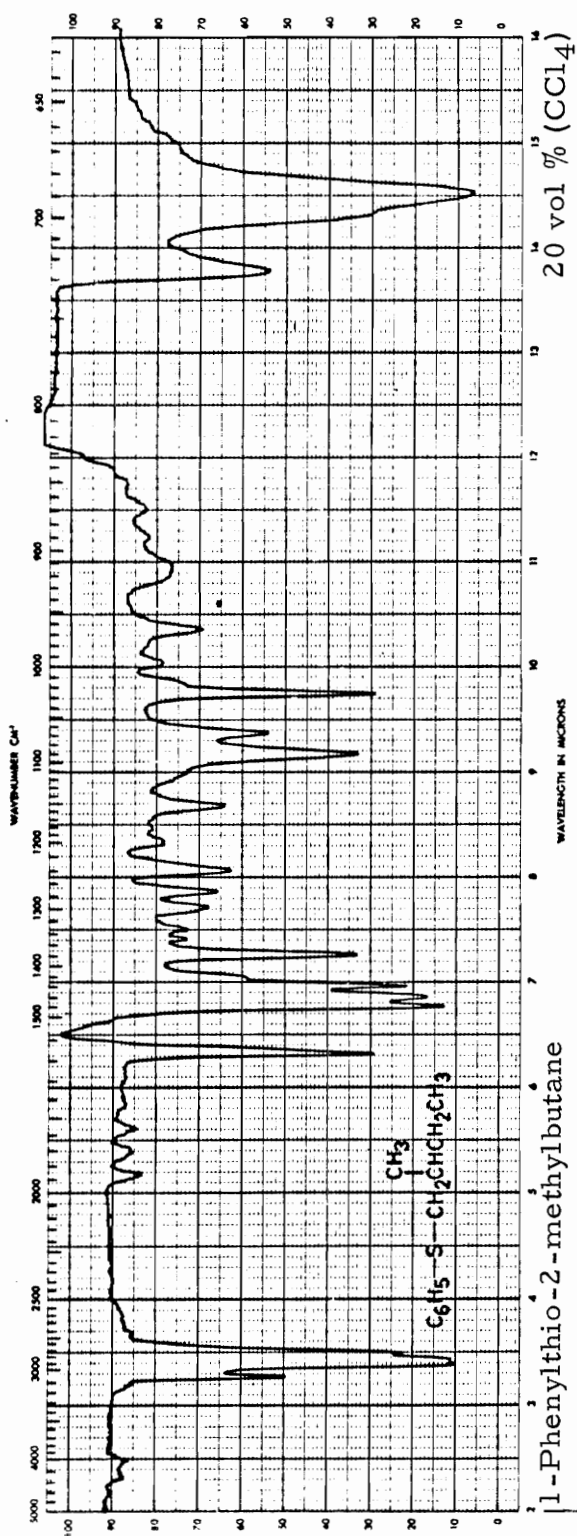
Figures 1a and 1b. - Infrared Spectra



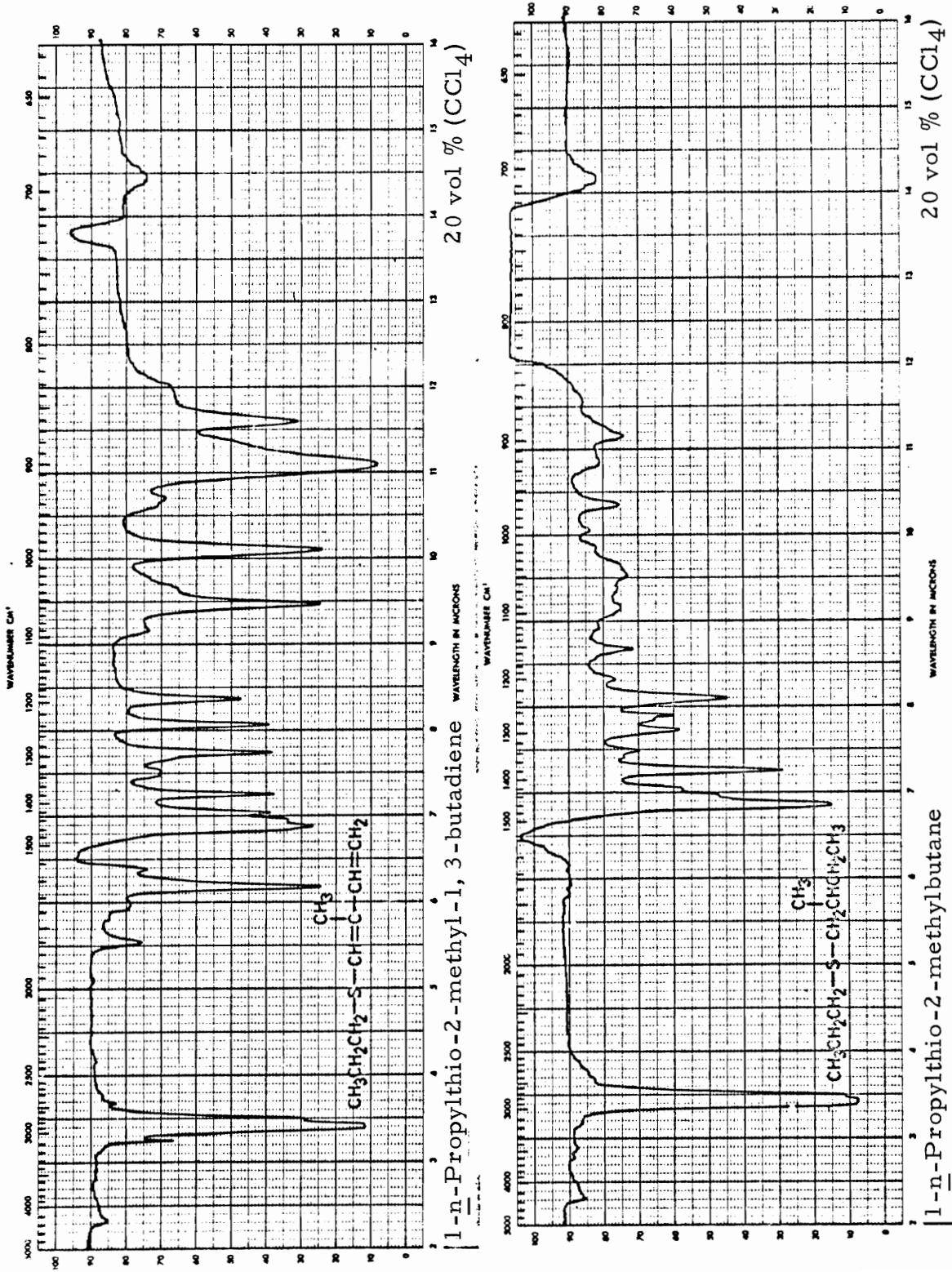
Figures 2a and 2b. - Infrared Spectra



Figures 3a and 3b. - Infrared Spectra



Figures 4a and 4b. - Infrared Spectra



Figures 5a and 5b. - Infrared Spectra

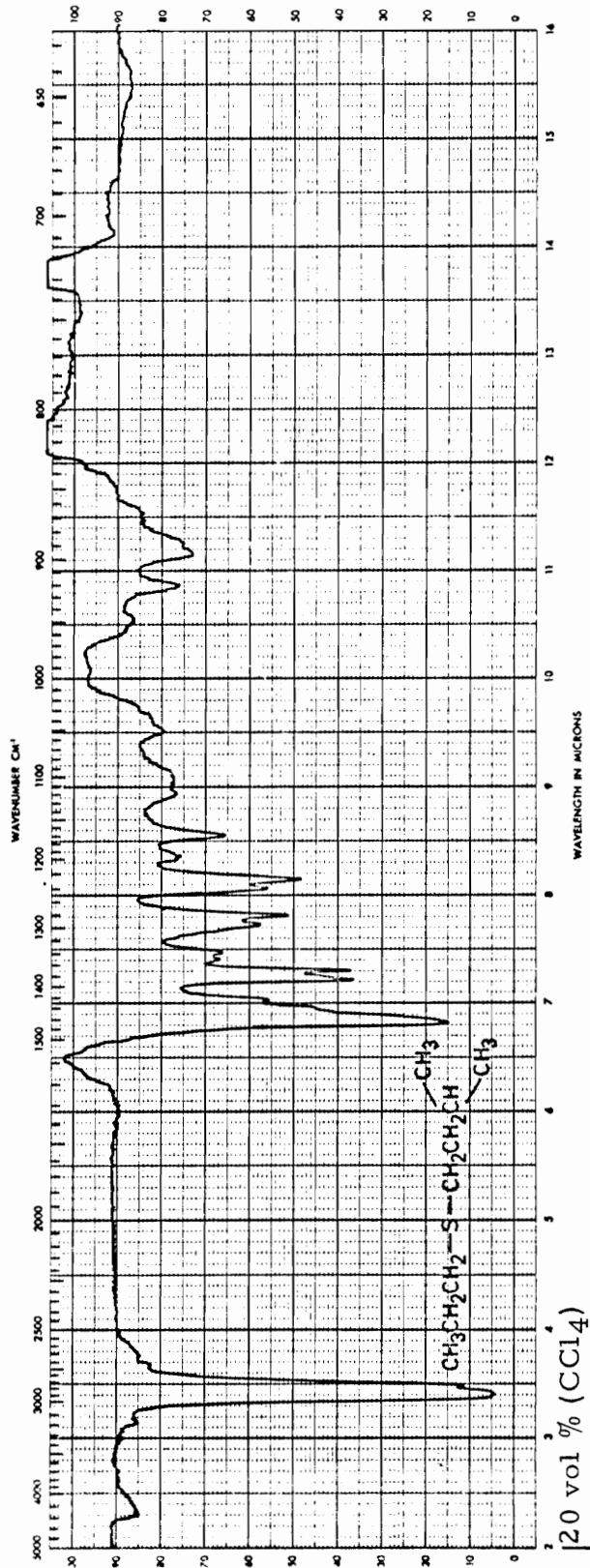
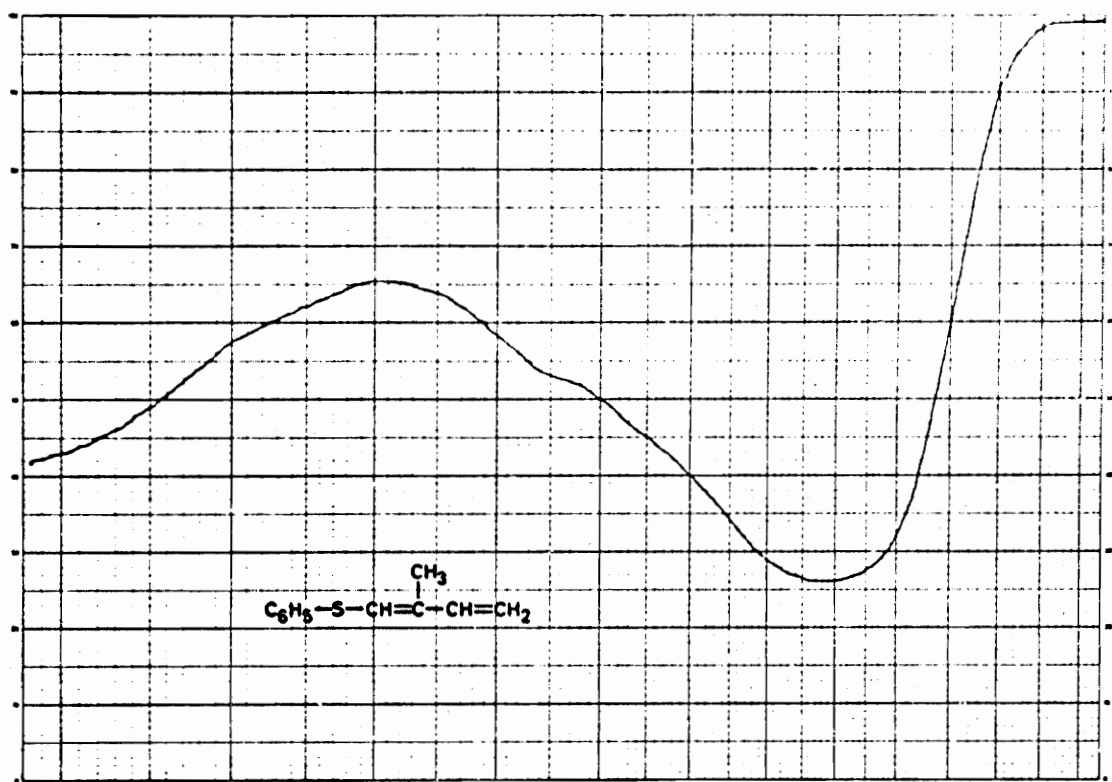
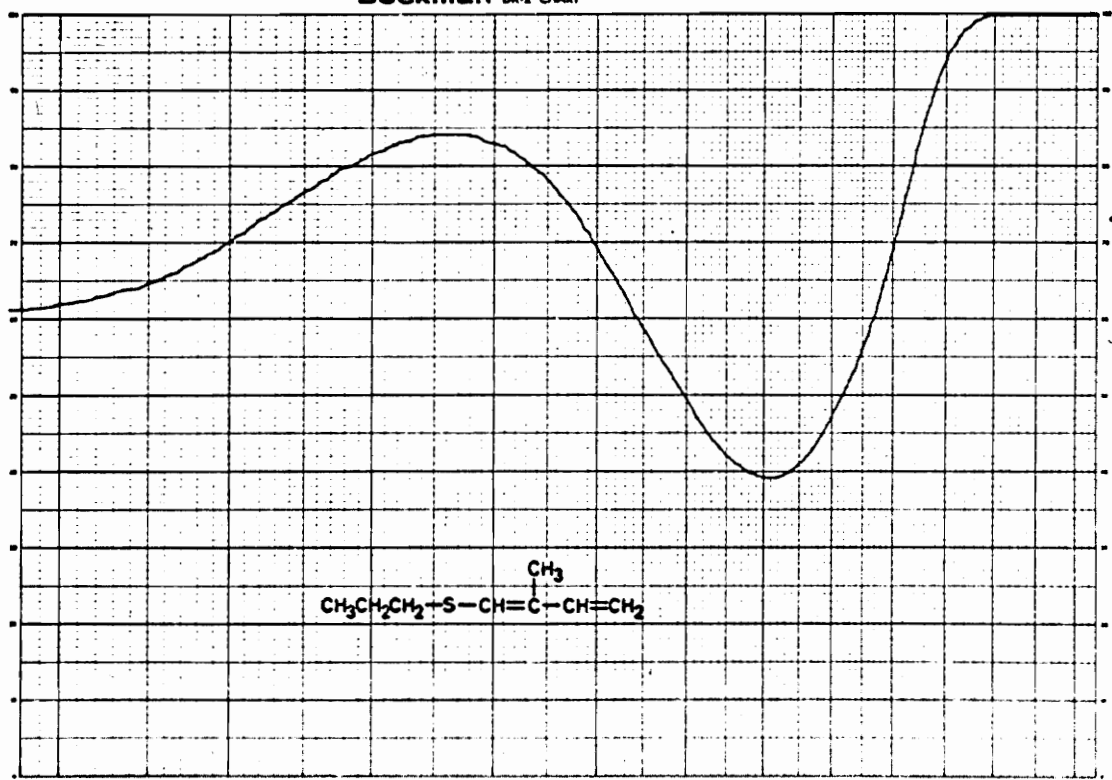


Figure 6. - Infrared Spectrum of 1-n-Propylthio-3-methylbutane



1-Phenylthio-2-methyl-1,3-butadiene .006 g/liter

Beckman DK-2 CHART



1-n-Propylthio-2-methyl-1,3-butadiene .005 g/liter

Figures 7a and 7b. - Ultraviolet Spectra

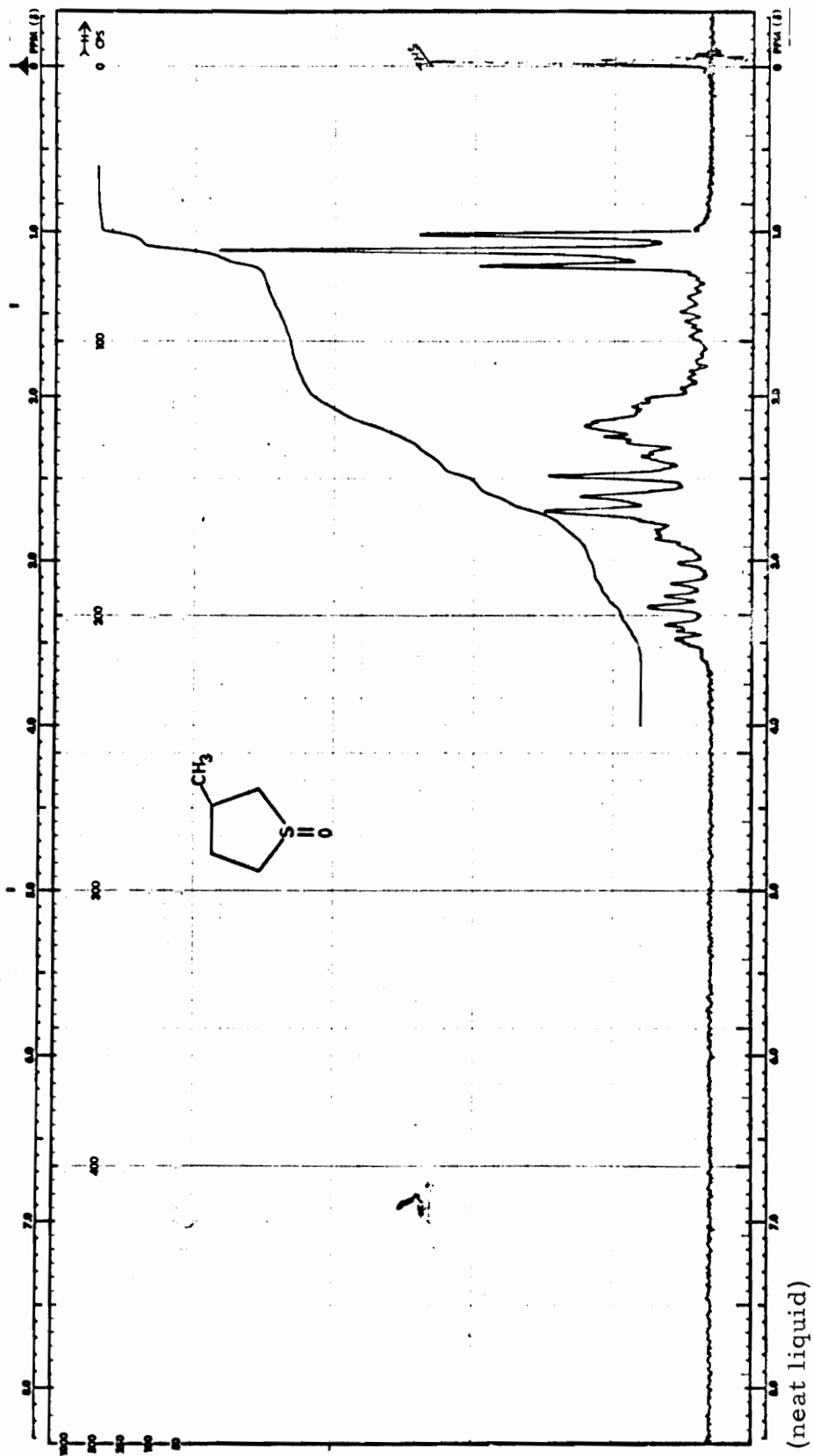


Figure 8. - N. m. r. Spectrum of 3-Methyltetrahydrothiophene 1-Oxide

(neat liquid)

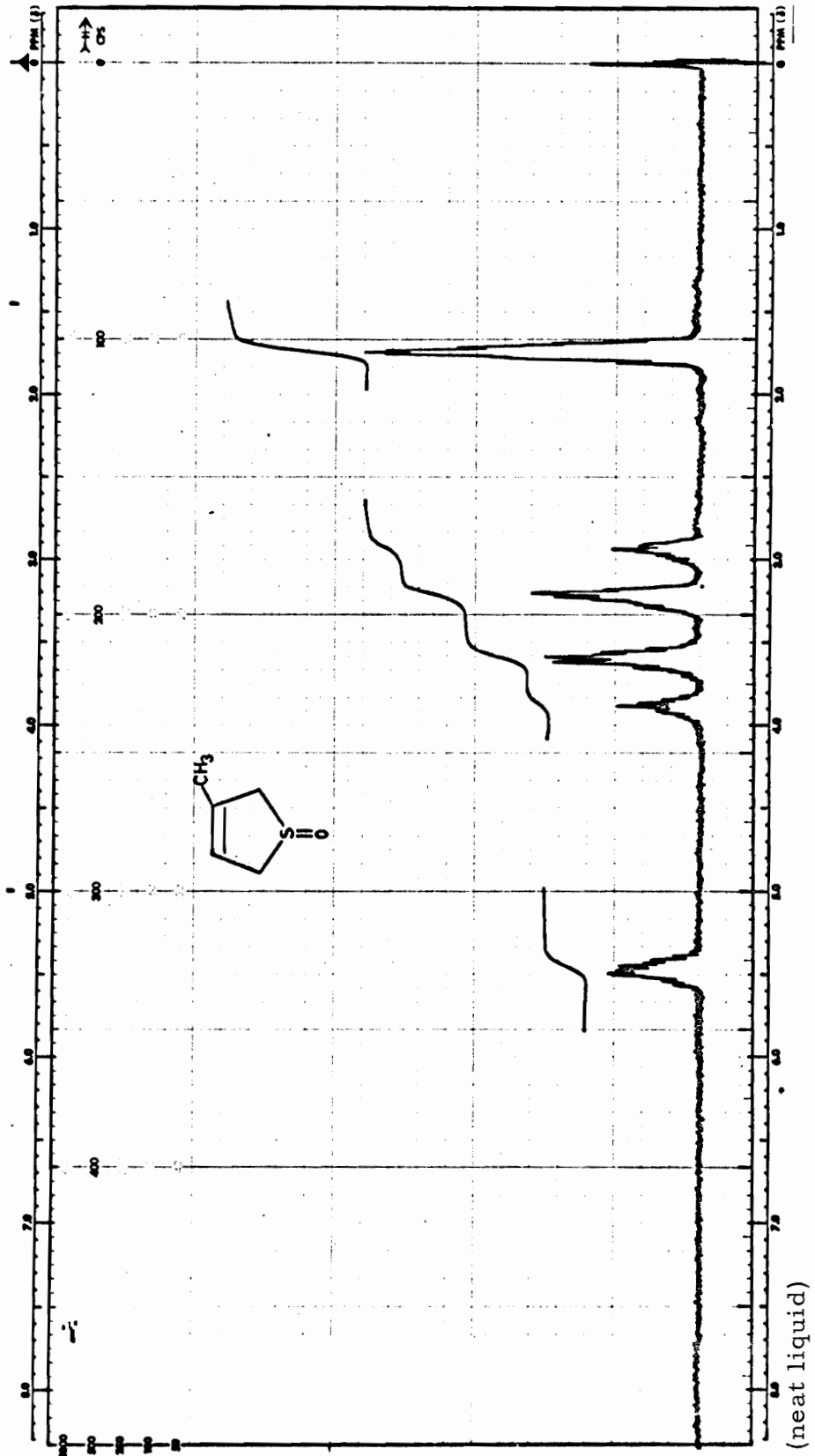


Figure 9. - N. m. r. Spectrum of 3-Methyl-2, 5-dihydrothiophene 1-Oxide

(neat liquid)

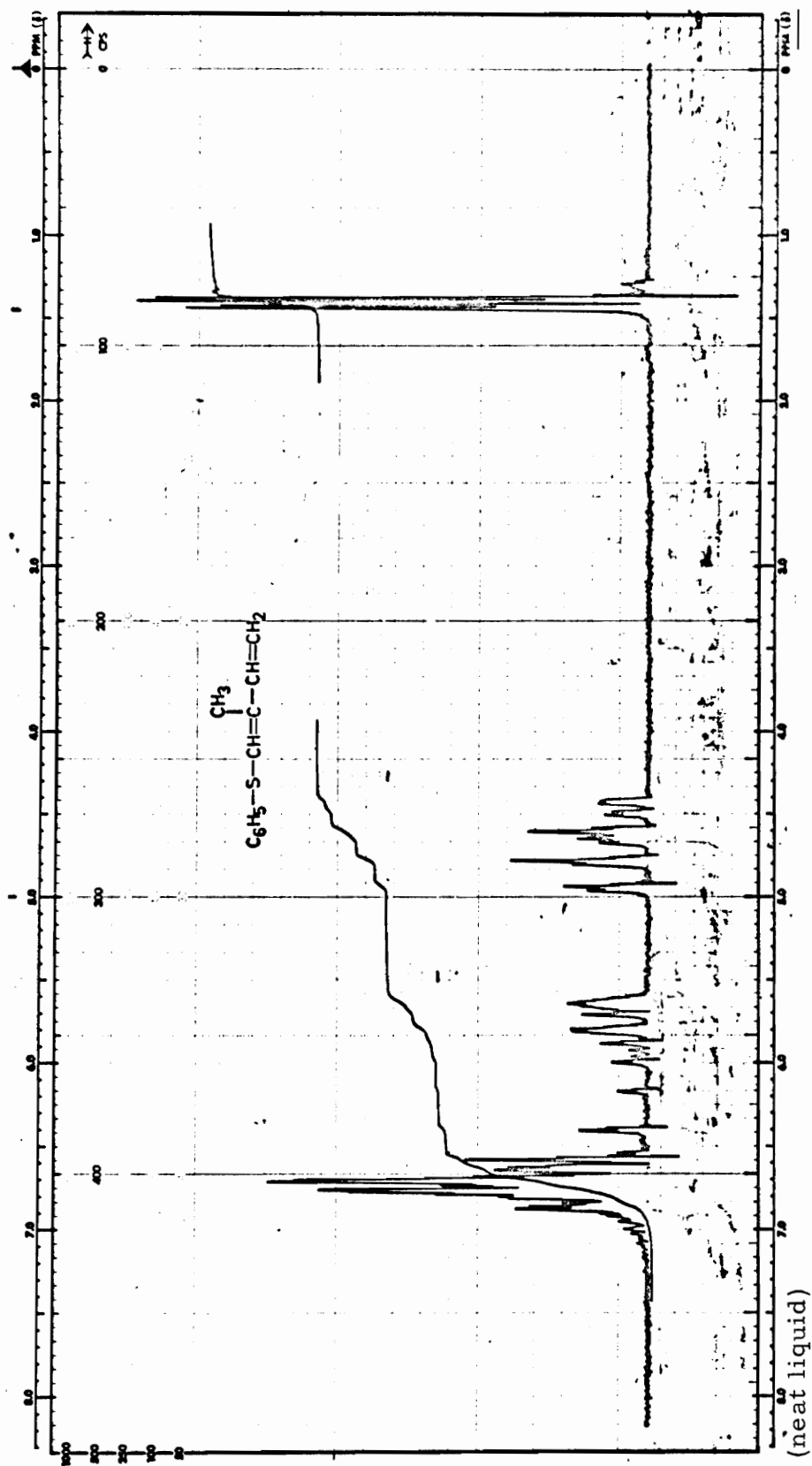


Figure 10. - N. m. r. Spectrum of 1-Phenylthio-2-methyl-1, 3-butadiene

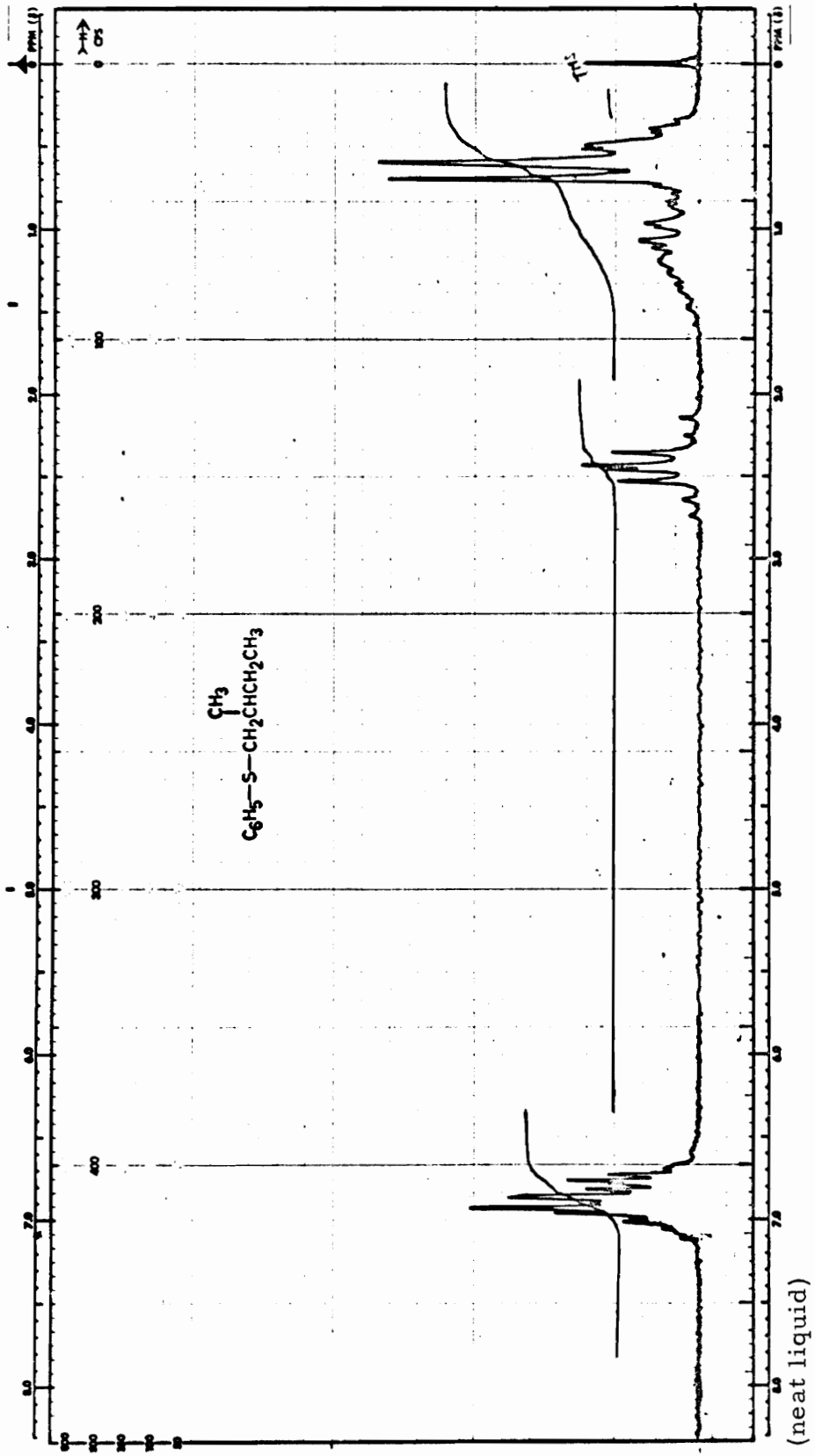


Figure 11. - N. m. r. Spectrum of 1-Phenylthio-2-methylbutane

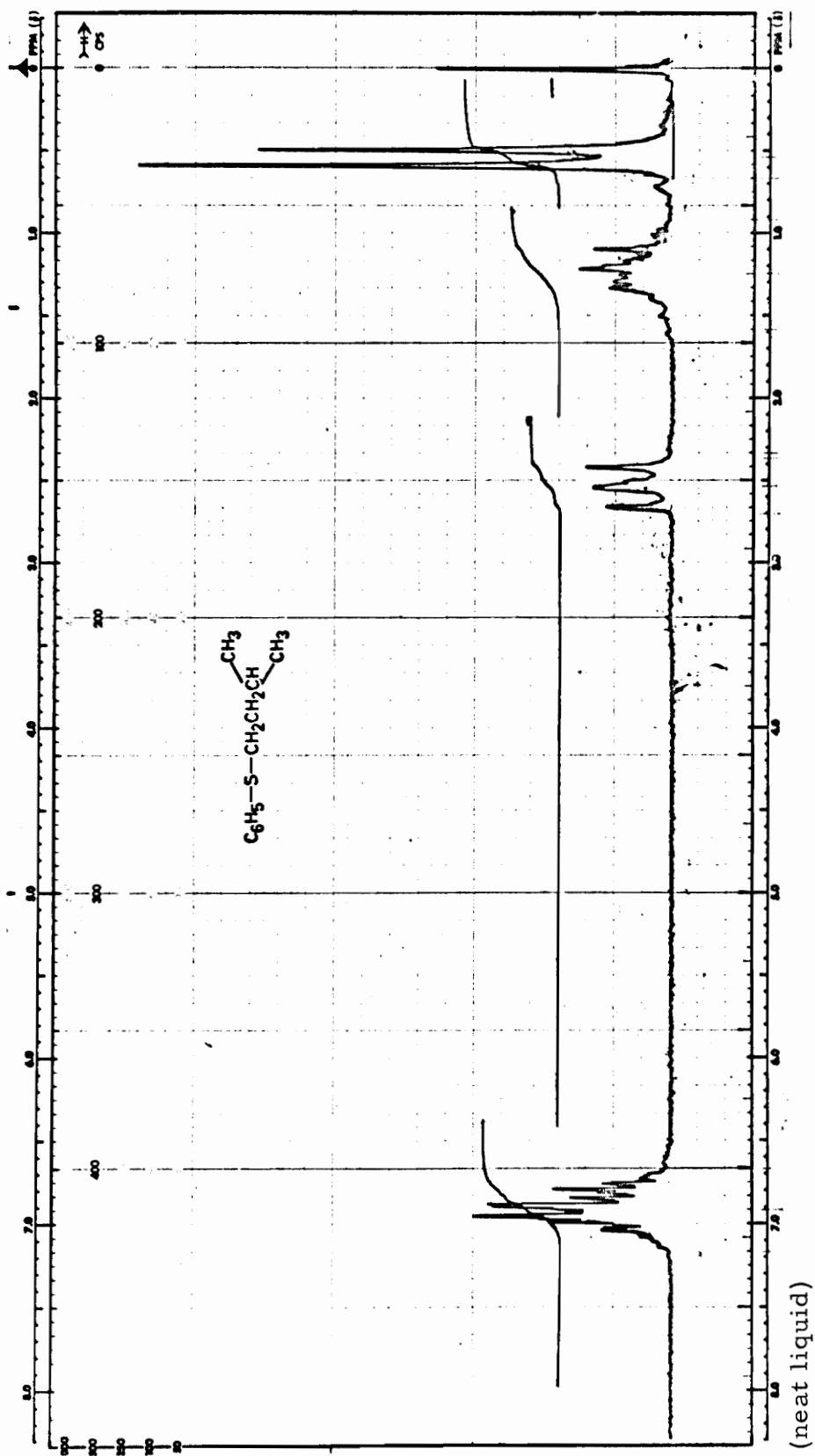


Figure 12. - N. m. r. Spectrum of 1-Phenylthio-3-methylbutane

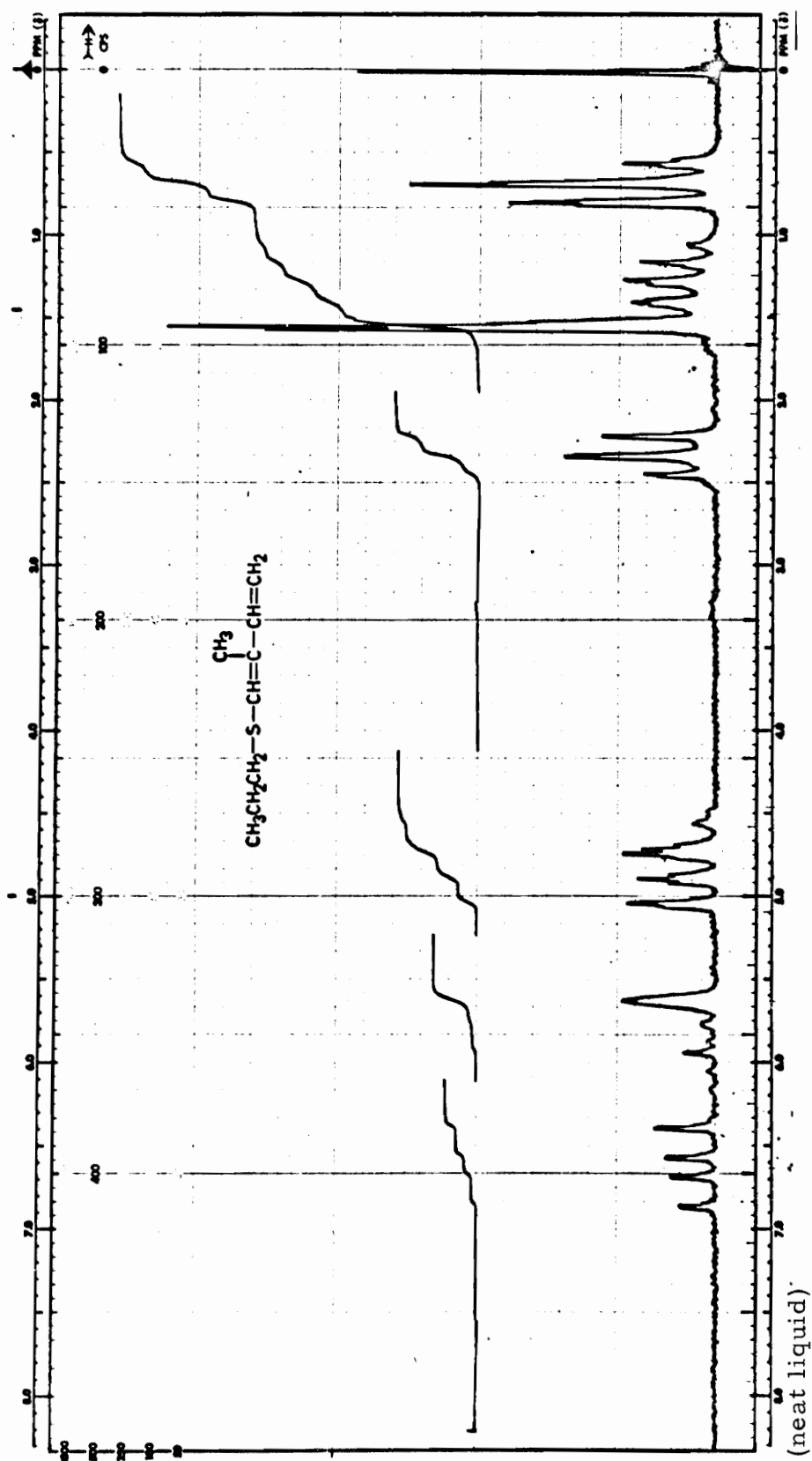


Figure 13. - N. m. r. Spectrum of 1-n-Propylthio-2-methyl-1,3-butadiene

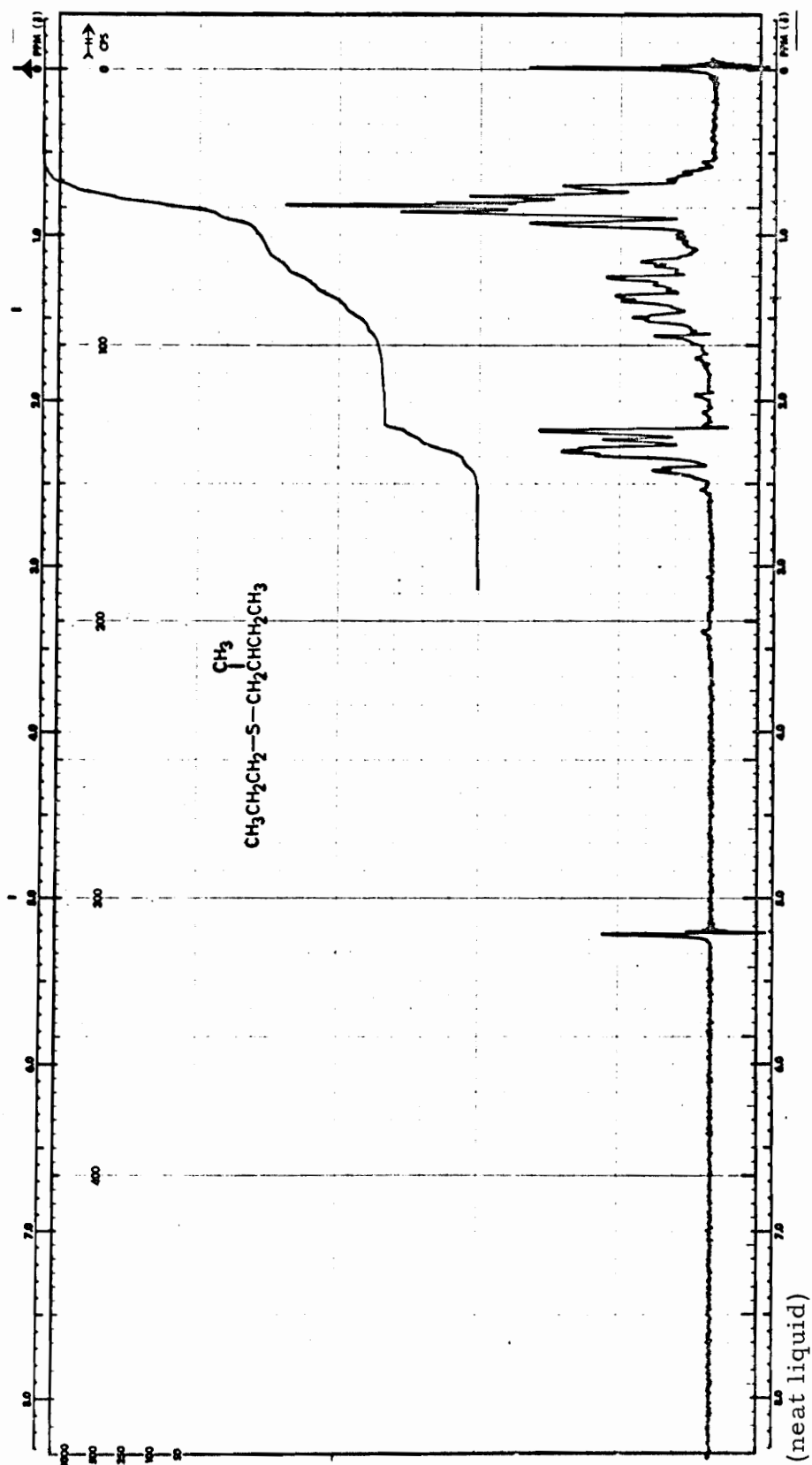


Figure 14. - N.m.r. Spectrum of 1-n-Propylthio-2-methylbutane

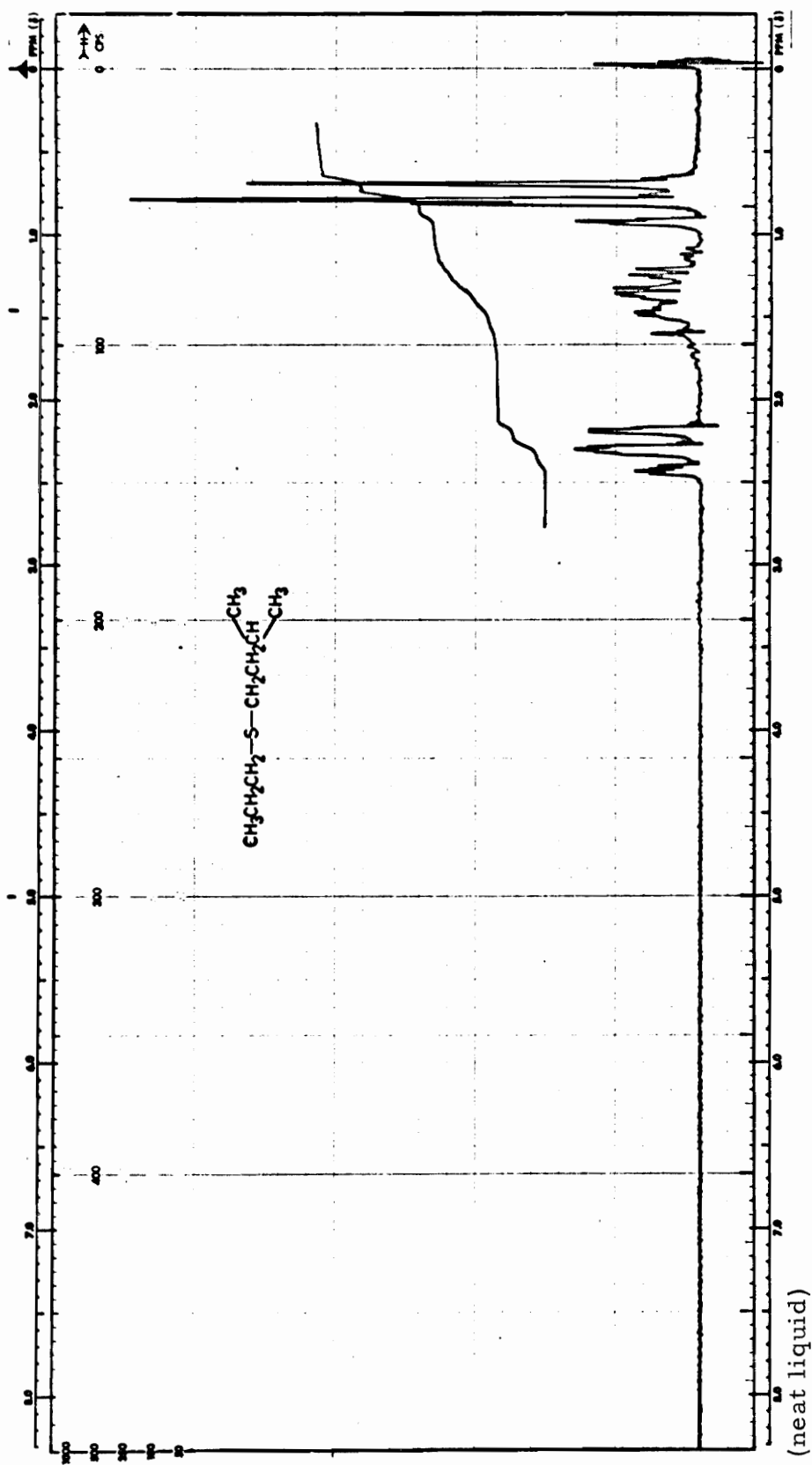


Figure 15. - N. m. r. Spectrum of 1-n-Propylthio-3-methylbutane

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ABSTRACT

The previously unreported 3-methyltetrahydrothiophene 1-oxide (1) and 3-methyl-2, 5-dihydrothiophene 1-oxide (2) have been prepared by oxidation of the corresponding sulfides. The structure of these unsymmetric sulfoxides was established by chemical and physical methods. Nuclear magnetic resonance analyses have provided significant information concerning some stereochemical aspects of these molecules. In the case of 1, which has four possible configurations, both cis and trans isomers were shown to exist in the synthetic material. A study on the temperature dependence of the nuclear magnetic resonance spectrum of 2 between -34° and 100° , suggested little or no association of a dimeric nature between molecules of this unsaturated sulfoxide.

The rapid and clean reduction of 2 to the corresponding sulfide was carried out using hydriodic acid and detected by gas chromatographic analysis.

The partial base catalyzed isomerization of 2 to 3-methyl-4, 5-dihydrothiophene 1-oxide (13) was carried out in sodium hydroxide solution and detected by gas chromatographic analysis of the reduced products. Maximum isomerization occurred after 96 hours when 2 and 13 were present in a ratio of 1.78:1 respectively. This finding is similar to the previously observed isomerization of the corresponding sulfone, but is

in contrast to the lack of isomerization of the olefinic bond of the related 2,5-dihydrothiophene 1-oxide. A plausible mechanism has been proposed for this interesting isomerization of 2.

Sulfoxide 1 was reacted with various Grignard reagents and shown to undergo a substitution reaction at the α -carbon atoms. Predominant reaction occurred at position-5 of 1 and binary sulfide mixtures composed of 2-substituted-4-methyl- and 2-substituted-3-methyltetrahydrothiophenes were obtained in yields ranging from 17-31%. The ratio of isomeric sulfides ranged from 1.50:1, in the case of phenylmagnesium bromide, to 8.09:1 when using neopentylmagnesium chloride. The binary sulfide mixtures were desulfurized and the hydrocarbon products were identified. In this manner, the structure and composition of the components of the sulfide mixtures was established. Preparative-scale gas chromatography was used to separate two binary sulfide mixtures. Desulfurization of the individual sulfides led to the discovery of isomerization reactions which occurred during desulfurization. By-products of the Grignard reaction were identified as 3-methyltetrahydrothiophene, 3-methyl-2,3- and 3-methyl-4,5-dihydrothiophene, and, in some cases the alkene and alcohol derived from the Grignard reagent. A reaction pathway, by which these products and by-products may conceivably be formed has been proposed.

Results of the reaction of the unsaturated sulfoxide 2 with Grignard

reagents were quite different than with sulfoxide 1. Sulfoxide 2 underwent reaction at the sulfur atom with a subsequent cleavage of the ring yielding single dienyl sulfides. These novel compounds were formed by a stereospecific ring cleavage of 2, a reaction similar to that previously observed with the corresponding sulfone. The dienyl sulfides, 1-phenylthio- and 1-n-propylthio-2-methyl-1,3-butadiene, were isolated in good yield and characterized by their spectral properties and by conversion to known compounds. The only detectable by-product of this reaction was a trace amount of 3-methyltetrahydrothiophene. A mechanism, consistent with the data obtained, has been suggested.