THE ATTEMPTED SYNTHESIS OF

3-TRIFLUOROMETHYL-2,5-DIHYDROTHIOPHENE 1,1-DIOXIDE

by

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To my mother, wife and son

ACKNOWLEDGEMENTS

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INTRODUCTION

The original purpose of this investigation was to prepare and characterize the compound 3-trifluoromethyl-2, 5-dihydrothiophene 1,1-dioxide[1,2] (I). This compound was to be prepared by the modified Diels-Alder reaction of 2-trifluoromethyl-1,3 butadiene (II) with sulfur dioxide.

$$CH_2=CH-C=CH_2 + SO_2 \longrightarrow$$

(with CF$_3$ substituent on the butadiene carbon, yielding the cyclic product with CF$_3$ and SO$_2$)

(II)   (I)
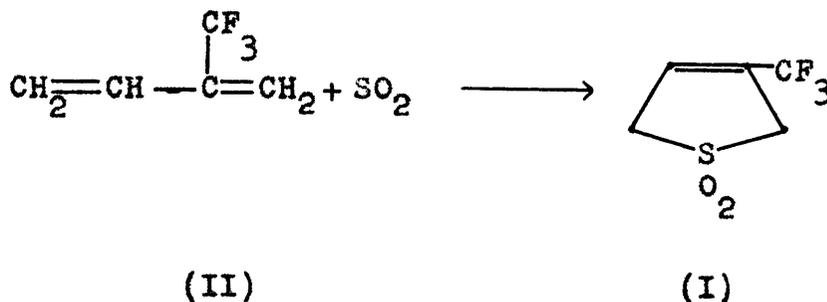
Difficulty was encountered in the preparation of the necessary fluorinated diene (II). Thus, only the preparation of I was accomplished.

A considerable amount of physical and infrared data has been obtained in recent investigations of dihydrothiophene 1,1-dioxides in this laboratory by Yen (1), Boswell (2),

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(1) In all structural formulas used, the hydrogen atoms required to complete the covalency of carbon are not shown unless special emphasis is intended.

(2) Capital Roman numerals will only be used to denote compounds specifically used in this research.

and Rigney (3). These data have been reviewed in an attempt to support the structure assigned to I.

Unsaturated cyclic sulfones have proven to be of great interest in recent years. Derivatives of these sulfones may be used as hypnotic drugs (6), plastics (14), insecticides (12) and antitubercular agents (9).

The reversibility of the Diels-Alder reaction gives rise to a most important use of sulfones; that is, the isolation and purification of conjugated diolefins from hydrocarbons (7, 8, 11).

The first method of preparing II, employed in this investigation, was that of Henne and Hinkamp (15). This method failed to yield the expected diene (II) and an entirely new synthesis was devised. The new synthesis, starting with vinylmagnesium chloride and 1,1,1-trifluoroacetone, was only partially completed when Richardson and Tarrant (18) published an identical procedure in late 1960. Work in progress in this laboratory was continued and the desired diene (II) was ultimately obtained.

The fluorinated diene was treated with sulfur dioxide and a colorless solid isolated. Evidence is presented to support the structure, 3-trifluoromethyl-2,5-dihydrothiophene 1,1-dioxide, assigned to this substance.

NOMENCLATURE

The nomenclature in this thesis is that recommended by E. J. Crane, past editor of Chemical Abstracts. The following table serves to illustrate various compounds and their accepted names.

Table I

Structural Formula	Systematic Name
	3-methyl-2,5-dihydrothiophene 1,1-dioxide
	4-methyl-2,3-dihydrothiophene 1,1-dioxide
	3-methyl-2,3-dihydrothiophene 1,1-dioxide
	3-trifluoromethyl-2,5-dihydrothiophene 1,1-dioxide (I)
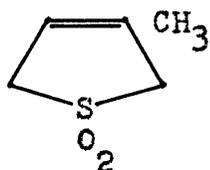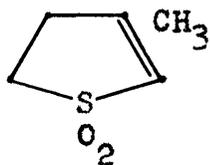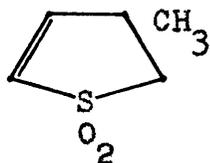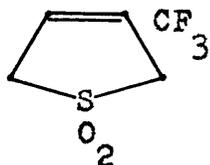
HISTORICAL BACKGROUND

The preparation of dihydrothiophene 1,1-dioxides was first achieved in 1914 when de Bruin (4) isolated pure 3-methyl-2,5-dihydrothiophene 1,1-dioxide from the reaction of 2-methyl-1,3-butadiene with sulfur dioxide as shown by the following equation:

$$CH_2=CH-\underset{\underset{CH_3}{|}}{C}=CH_2 + SO_2 \rightleftharpoons$$
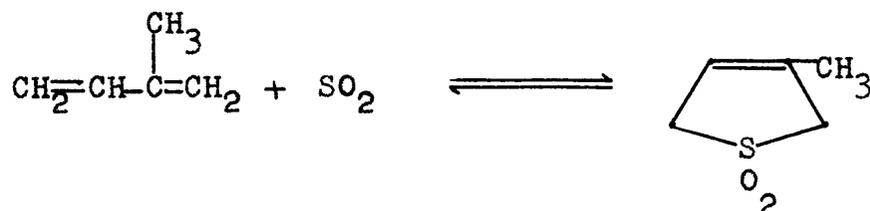
This modified Diels-Alder reaction has served as a most convenient route to the synthesis of unsaturated cyclic sulfones.

In recent years there have been extensive investigations into the preparation and study of the isomeric 3-methyl-di-hydrothiophene 1,1-dioxides. Yen (1) synthesized and studied the properties of 3-methyl-2,5-dihydrothiophene 1,1-dioxide, 3-bromomethyl-2,5-dihydrothiophene and 4-methyl-2,3-dihydro-thiophene 1,1-dioxide. Boswell (2) in 1960 synthesized and characterized 3-methyl-2,3-dihydrothiophene 1,1-dioxide, thus completing the series of isomeric 3-methyl-dihydrothiophene 1,1-dioxides.

The availability with which an unsaturated cyclic sul-

fone may be formed from the modified Diels-Alder reaction between a diene and sulfur dioxide is, in a sense, dependent upon the availability with which the desired diene may be prepared.

The first synthesis of a trifluoromethylated butadiene was reported in 1949. In that year, Hill and Towne (16) reported the preparation of 2-trifluoromethyl-1,3-butadiene (II). This preparation involved a series of reactions starting with the treatment of ethynylmagnesium bromide with 1,1,1-trifluoroacetone to yield 3-trifluoromethyl-1-butyne-3-ol. Catalytic reduction of the latter compound yielded 3-trifluoromethyl-1-butene-3-ol (III) which was dehydrated to yield II as shown by the following reactions:

$$HC{\equiv}CMgBr \; + \; CH_3COCF_3$$

$$\downarrow$$

$$\begin{array}{c} CF_3 \\ | \\ HC{\equiv}C-C-CH_3 \\ | \\ OH \end{array}$$

$$\downarrow \quad H_2, \; Pd$$

$$\begin{array}{c} CF_3 \\ | \\ H_2C{=}CH-C-CH_3 \\ | \\ OH \end{array} \quad (III)$$

$$\downarrow \quad -H_2O$$

$$\begin{array}{c} CF_3 \\ | \\ H_2C{=}CH-C{=}CH_2 \end{array} \quad (II)$$
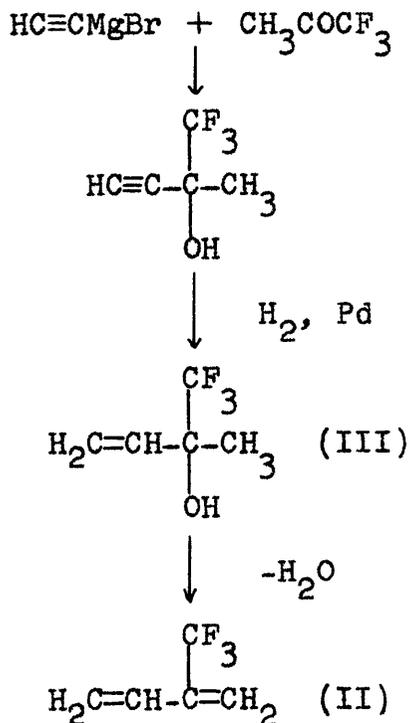
The dehydrating agents which were reported to be effective were anhydrous oxalic acid, anhydrous magnesium sulfate, succinic anhydride and sulfuric acid.

In 1954, Henne and Hinkamp (15) reported the preparation of II starting with the treatment of ethylmagnesium bromide with 1,1,1-trifluoroacetone.[1]

Tarrant and Taylor (17) reported two different syntheses of (II). These syntheses were investigated in hope of improving the yield over that reported by Henne and Hinkamp. The first of these preparations involves the treatment of hydrogen cyanide with 1,1,1-trifluoroacetone to give trifluoroacetone cyanohydrin. Treatment of the cyanohydrin with methylmagesnium bromide followed by reduction with lithium aluminum hydride yielded 2-trifluoromethyl-2,3-butanediol. This glycol gave 2-trifluoromethyl-1,3-butadiene in a 36.9% yield upon dehydration with phosphoric anhydride.

The better of the methods involved the condensation of malonic acid with 1,1,1-trifluoroacetone to yield β-hydroxy-β-trifluoromethylbutyric acid. This acid was dehydrated to β-trifluoromethylcrotonic acid with sulfuric acid. The unsaturated acid was then reduced to 2-trifluoromethyl-2-butene-4-ol by use of lithium aluminum hydride. Dehydration

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(1) This preparation will be discussed at greater length under the discussion portion of this thesis.

of this carbinol with phosphoric anhydride gave II in a 60%
yield. This synthesis is shown by the following equations:

$$CF_3COCH_3 \; + \; HO_2CCH_2CO_2OH$$

$$\underset{OH}{\overset{CF_3}{CH_3-C-CH_2-CO_2H}}$$

$$\overset{CF_3}{CH_3-C=CH-CO_2H}$$

$$LiAlH_4$$

$$\overset{CF_3}{CH_3-C=CH-CH_2OH}$$

$$P_2O_5$$

$$\overset{CF_3}{CH_2=C-CH=CH_2} \quad (II)$$
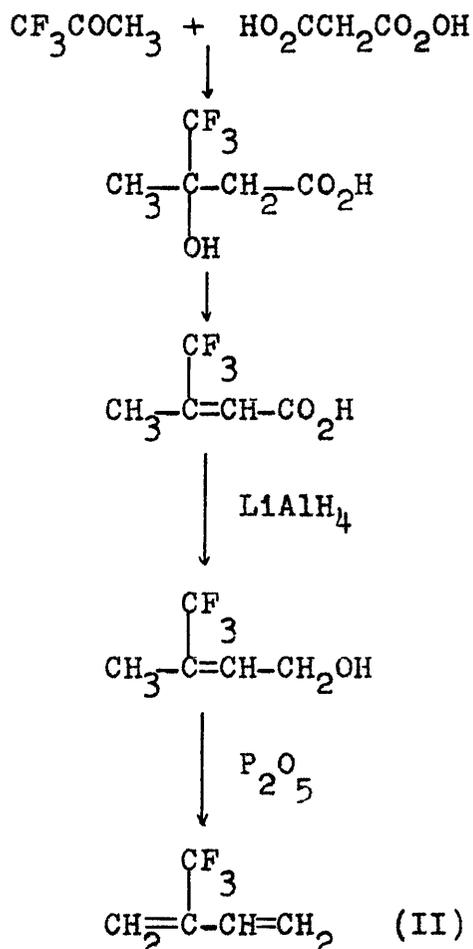
The improvement in yield of each of the methods reported by
Tarrant and Taylor was attributed to the removal of the
hydroxyl group from a carbon atom which did not have a tri-
fluoromethyl group attached to it.

In late 1960, Richardson and Tarrant (18) reported a
synthesis of II starting with vinylmagnesium chloride and
1,1,1-trifuoroacetone.[1]

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(1) The same procedure was being carried out by the author at
that time and, therefore, this method will be covered in
detail in the discussion section of this thesis.

Addition reactions of trifluoromethylated halides
have received considerable attention in the past few years.
Very little work has been done using trifluoromethyl bromide
and trifluoromethyl chloride since it appears that the C-Br
and the C-Cl bonds show little, if any, tendency to cleave
and form free radicals (20).   On the other hand, trifluoro-
methyl iodide has been used extensively. Most of the known
reactions have been shown to involve a free radical mechanism
(20) as illustrated by the following reactions:

$$CF_3I \xrightarrow{hr} CF_3\cdot \quad I\cdot$$

$$I\cdot + CF_3\cdot + HC\equiv CH \longrightarrow CF_3CH\!=\!CHI$$
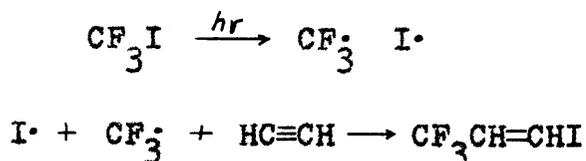
Another example of the free radical addition of trifluoro-
methyl iodide is that reported by Haszeldine (23). Hexa-
fluorocyclobutane and trifluoromethyl iodide were irradiated
with ultraviolet light for twenty-five days in a sealed tube
to give 1-iodo-2-trifluoromethylhexafluorocyclobutane in good
yield.

An analogous reaction is that of Kharasch, Freiman,
and Urry (24). It was found that trichloromethyl bromide
would react with 2,5-dihydrothiophene 1,1-dioxide by means
of a free radical mechanism to give a 40% yield of 3-trichloro-
methyl-4-bromo-2,5-dihydrothiophene 1,1-dioxide as shown in
the following equations:

$$Br\text{-}CCl_3 \xrightarrow{h\nu} Br\cdot \ + \ \cdot CCl_3$$

$$Br\cdot + \cdot CCl_3 \longrightarrow$$
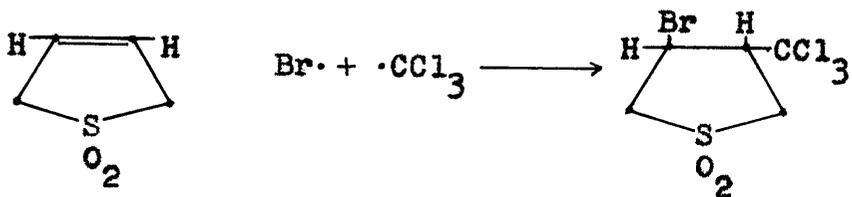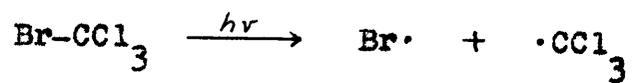
DISCUSSION

I.   Preparation of 2 Trifluoromethyl-1,3-butadiene (II)

A.   Ethylmagnesium Bromide and 1,1,1 Trifluoroacetone.

Of the two methods available for the preparation of
2 trifluoromethyl 1,3-butadiene (II), the one which seemed
the more feasible was that of Henne and Hinkamp (15). The
major drawback was that a very low yield was reported.

The first intermediate, 2 trifluoromethyl-2-butanol
(IV), was conveniently prepared by use of the Grignard reagent.
Ethylmagnesium bromide was treated with 1,1,1-trifluoro-
acetone to give IV in a 49% yield and 2-trifluoromethyl-2
propanol in a 40% yield. The yields obtained were only in
slight disagreement with that reported in the literature, 51%
and 31% respectively (15).

Introduction of the first unsaturated linkage into IV
presented some difficulties. The presence of the trifluoro-
methyl group attached to the same carbon atom to which the
hydroxyl group is attached would cause dehydration to be
difficult. The strong inductive effect would make the C-O
bond difficult to break. Therefore, rather than attempt such
a dehydration, the author resorted to pyrolysis of the acetate
from IV.

Several methods are available for the preparation of

an acetate from a tertiary carbinol. Since Henne and Hinkamp
did not specify which method was employed, both the acetyl
chloride and acetic anhydride method were investigated. The
acetic anhydride proved to give better yields. Thus the
second intermediate, 2-trifluoromethyl-2-acetoxybutane (V)
was obtained in a 79.8% yield.

The usual method for the conversion of an acetate to
an olefin is thermal decomposition. Bailey and co-workers
have shown that the Hofmann rule for eliminations applies in
the vast majority of simple aliphatic and alicyclic esters
(25, 26). It is known that pyrolytic decomposition of esters
proceeds through a six-membered cyclic intermediate as shown
below (27):
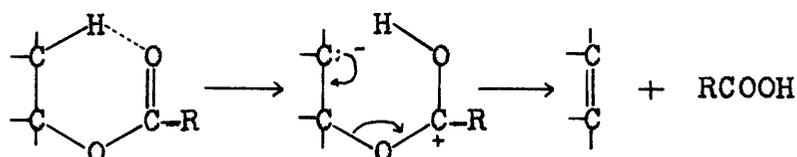
Experiment showed that a mixture of olefins, 2-trifluoro-
methyl-1-butene and 2-trifluoromethyl-2-butene (VI), was
formed by thermal decomposition of V. A six-membered cyclic
intermediate may be postulated for the formation of both of
these olefins. In the application of the Hofmann rule a
preference is usually shown for reaction with a methyl hydro-
gen over a methylene hydrogen. It is possible that the
electronegative trifluoromethyl group causes the methylene
hydrogen to become more readily available. The second ole-
finic linkage was to be introduced by allylic bromination

followed by dehydrohalogenation. The allylic bromination proceeded smoothly, but the dehydrohalogenation step which was reported to give II in a 20% yield failed in the two attempts made in this investigation. As a result of these failures to duplicate Henne's and Hinkamp's work, this method of preparation was terminated due to insufficient material.

B.   Vinylmagnesium chloride and 1,1,1-Trifluoroacetone

As a result of the failure of the previous method for preparing II, an entirely new synthesis was undertaken. Ramsden and co-workers (5) in 1957 reported the use of vinyl-magnesium chloride in the preparation of 2-methyl-1,3-buta-diene. It was thought that if acetone could be treated with vinylmagnesium chloride to yield dimethylvinyl carbinol, then 1,1,1-trifluoroacetone could be treated in an analagous manner to yield III. Since dimethylvinyl carbinol can be dehydrated to 2-methyl-1,3-butadiene, it seemed possible that III could also be dehydrated to give II. It may be noted that all previous preparations of II have involved at least five steps. It was the hope that a two-step synthesis could be accomplished by paralleling this work. However, the reaction of vinylmagnesium chloride and 1,1,1-trifluoro-acetone presented much difficulty. The reaction of the Grignard reagent with the trifluoroacetone resulted invariably in an impure product and a large amount of residue. A study of the infrared spectrum of impure III and the consideration of possible contaminants led to the conclusion that the impurity was tetrahydrofuran, which had been employed as a solvent in the reaction.

Interpretation of the vapor phase chromatogram led to the conclusion that the carbinol was contaminated with about 30% tetrahydrofuran. Richardson and Tarrant (18), who published the same synthesis in late 1960, also reported difficulty in obtaining a pure sample by distillation. Steam distillation, followed by distillation using a 25 cm. column packed with protuded nickel packing, yielded III contaminated with approximately 20% tetrahydrofuran. The purification of III, as well as its conversion to II, will be covered in detail in later sections.

C.   Attempted Dehydration of Impure 3-Trifluoromethyl-1-
     butene-3-ol (III)

Even though III was contaminated, it was decided that
dehydration would be attempted. As discussed previously,
the greatest deterrent to dehydration is the fact that the
trifluoromethyl group is attached to the same carbon atom
bearing the hydroxyl group and the inductive effect hinders
the removal of the hydroxyl group. It may be noted in general
that tertiary alcohols are more easily dehydrated than
secondary and primary alcohols.

Activated alumina is one of the common reagents for
the vapor phase dehydration of alcohols. Taylor and Shenk
(10) reported the dehydration of dimethylvinylcarbinol over
activated alumina at 300° to give 2-methyl-1,3-butadiene in
good yield. Campbell and co-workers (19) reported that
1,1,1-trifluoro-2-octanol and 1,1,1-trifluoro-2-pentanol re-
sisted attempted dehydration with alumina at 350°. Three
attempts to dehydrate III in this investigation using acti-
vated alumina over a temperature range of 250 - 360° failed.

Hill and Towne (16) reported the use of anhydrous
oxalic acid to dehydrate III. However, the use of anhydrous
oxalic acid in this investigation failed.

The use of p-toluenesulfonic acid and phenyl isocy-
anate, both of which are known to cause dehydration of
tertiary alcohols also failed.

Iodine has also been shown to cause dehydration of

olefinic tertiary alcohols (13). Distillation of III from a crystal of iodine produced no evidence of dehydration.

Fieser and Wiegnard (29) successfully dehydrated an olefinic tertiary alcohol using potassium acid sulfate. Campbell and co-workers (19) failed in their attempts to dehydrate 1,1,1-trifluoro-2-octanol and 1,1,1-trifluoro-2-pentanol using this reagent. Heating III for one hour with potassium acid sulfate failed to cause dehydration.

The use of sulfuric acid was investigated and all attempts at dehydration were unsuccessful. The secondary alcohols, 1,1,1-trifluoro-2-octanol and 1,1,1-trifluoro-2-pentanol, also resisted dehydration using concentrated sulfuric acid (19). Hill and Towne (16) did report the dehydration of III using sulfuric acid.

Several attempts to dehydrate III were made with phosphoric anhydride. One of these attempts produced a small amount of low boiling material which was never identified. Richardson and Tarrant (18) were also unsuccessful in their attempt to dehydrate III by the use of phosphoric anhydride. Campbell and co-workers (19) were unable to dehydrate the secondary alcohols, 1,1,1-trifluoro-2-octanol and 1,1,1-trifluoro-2-pentanol, using phosphoric anhydride.

It may be noted that impure III was employed in all of the methods of attempted dehydration in this investigation.

D.   Purification of 2-Trifluoromethyl-1-butene-3-ol (III)

As previously noted, all attempts to purify III by distillation failed. Richardson and Tarrant (18) successfully purified this carbinol for analytical purposes by use of vapor phase chromatography. However, this information was not known until purification had been completed in the present investigation.

The first attempt to purify III consisted of heating with a dilute sodium hydroxide solution. This procedure improved the quantitative analysis for carbon and hydrogen only by a negligible amount. On the assumption that the impurity was tetrahydrofuran, impure III was heated to reflux with constant boiling hydrochloric acid since this reagent is known to cleave the tetrahydrofuran ring. No significant change was observed in the physical properties of the carbinol and thus another method was sought. As previously stated, vapor phase chromatography gave fairly conclusive evidence that the impurity was tetrahydrofuran. This method would have been ideal for purification, but since the equipment available was limited to the detection of components of a mixture, it could not be used. After determining that tetra-hydrofuran was soluble in 85% phosphoric acid, it was decided that this method might work. Significant changes in the physical properties of III, the infrared spectrum, and the vapor phase chromatogram all seemed to indicate that success

had been obtained. Quantitative analysis of the reaction
product showed that this assumption was true. Table II lists
some of the properties of III.

Table II

Physical Constants of the Carbinol III

Property	Description
State (25°)	Colorless liquid
Boiling Point	86-87°/atmos. press.
Solubility	Soluble: benzene, pyridine, dioxane, methanol, acetone and tetrahydrofuran. Insoluble: water
Infrared Spectrum[1]	See Figure I

The major absorption maxima and their assignments are
given in Table III:

Table III

Infrared Absorption of the Carbinol III

Wavelength (μ)	Assignment
2.85	OH stretching
6.10	C=C stretching
7.29	C-O stretching
7.75	CF stretching
9.05-9.25	CF stretching
10.15	CH out of plane deformation (Vinyl)

(1) All infrared spectra reported in this thesis were
obtained with a Beckman IR-5 Infrared Spectrophotometer.

FIGURE I

10% in C_6H_6
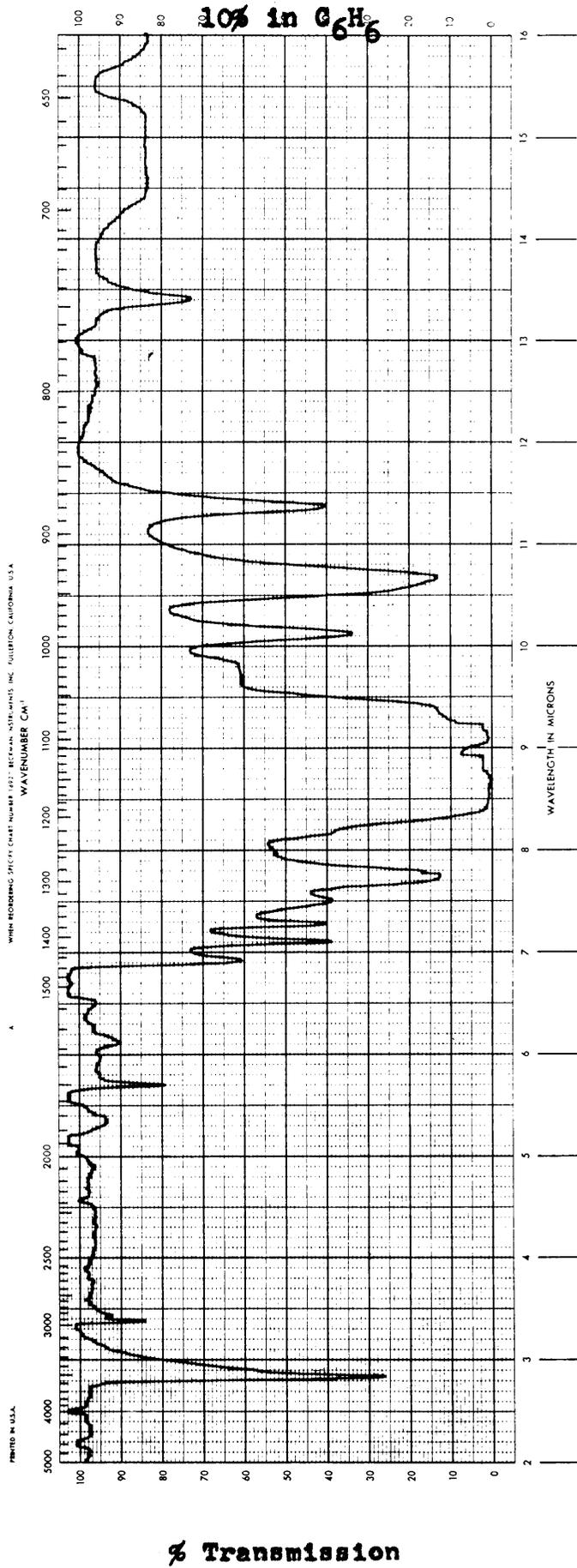
3-Trifluoromethyl-1-butene-3-ol

% Transmission

E.   Attempted Preparation of Derivatives from 2-Trifluoro-
      methyl-1-butene-3-ol (III)

The bromine adduct from III, 3,4-dibromo-2-trifluoro-
methyl-2-butanol (VIII), was originally intended as a
possible method of purification and as supporting evidence
for the structure assigned to III. If bromine could be added,
it would be verification of the presence of a carbon-carbon
double bond in III. Bromine was added, without difficulty,
yielding an adduct, which proved to be the one expected.
Table IV lists some of the physical properties of VIII.

Table IV

Physical Constants of the Dibromide VIII

Property	Description
State (25°)	Colorless liquid
Boiling point	66-65°/3 mm.
Solubility	Soluble: benzene, ethyl ether, acetone
	Insoluble: water
Infrared Spectrum	See Figures II and III

The major absorption maxima and their assignments are
given in Table V:

Table V

Infrared Absorption of the Dibromide VIII

Wavelength (μ)	Assignment
2.79	OH stretching
3.32	CH_3, CH stretching
6.58	CH deformation
7.20	CH deformation; CO stretching
7.75	CF stretching
8.30-8.70	CF stretching; OH deformation
9.78	CF stretching

FIGURE II

8% in C$_6$H$_6$
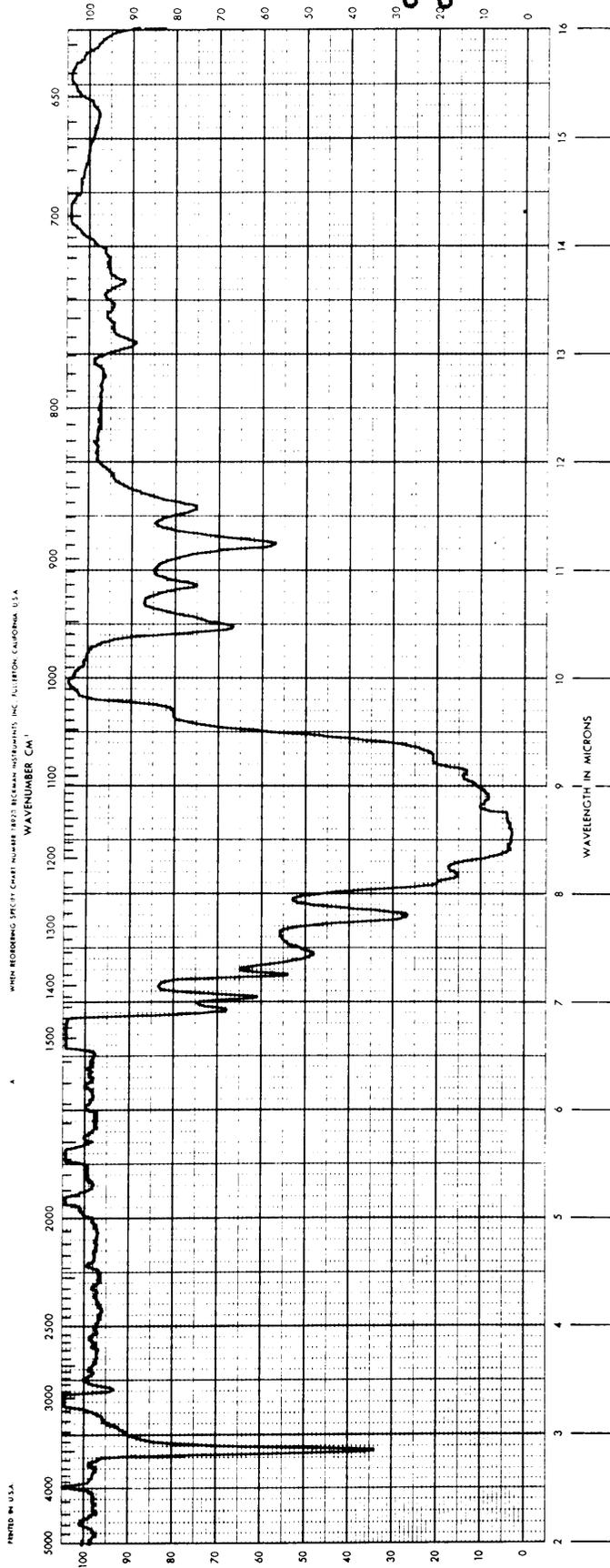
3,4-Dibromo-2-Trifluoromethyl-
2-butanol

FIGURE III

10% in C₆H₆
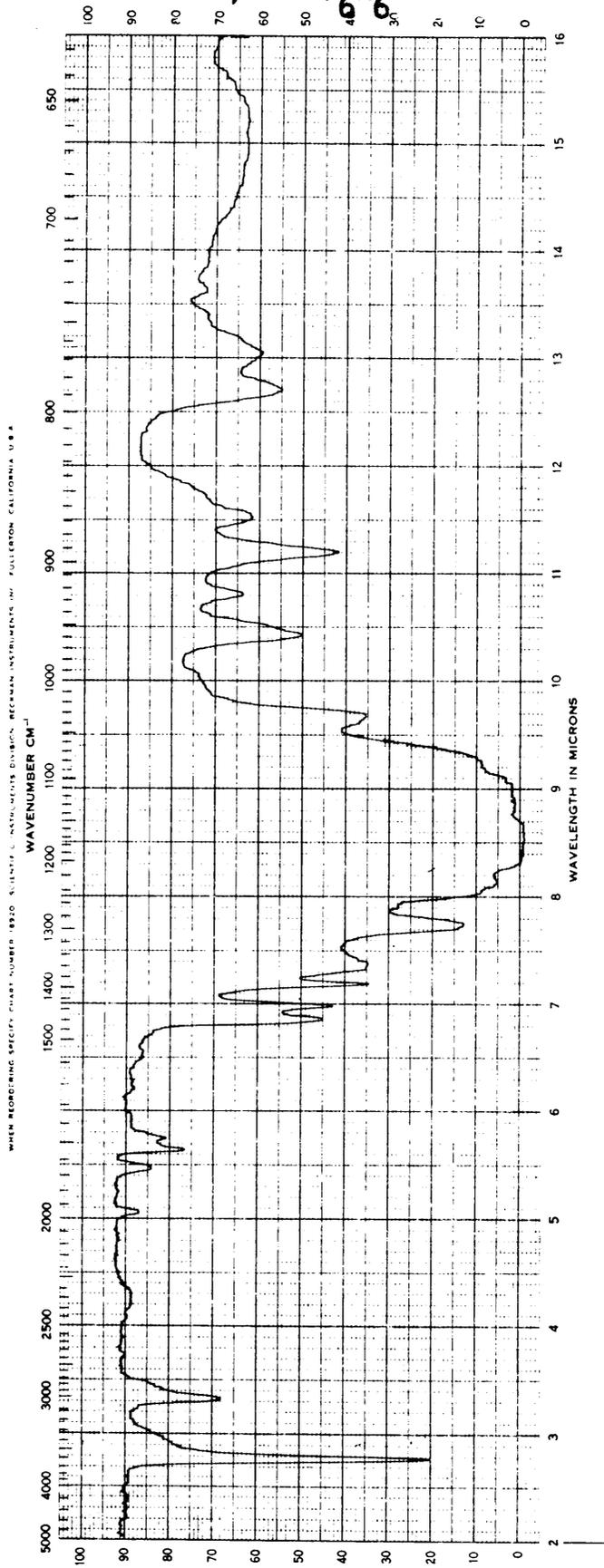
3,4-Dibromo-2-Trifluoromethyl-2-butanol

An attempt to prepare the benzoate from pure III by
a modification of the method of Shriner and Fuson (21) was
made in order to obtain a solid derivative. Heating III
in pyridine with benzoyl chloride for five hours failed to
produce the expected ester. As mentioned before, the
inductive effect of the trifluoromethyl group would render
the C-O bond difficult to break. By the same reasoning the
inductive effect would tend to render the O-H bond more
easily broken. There seems to be no logical explanation for
the failure of the benzoate to form. This same reasoning
may be applied to the attempted preparation of the tosylate,
where the introduction of sodium hydroxide would tend to
aid in the breaking of the O-H bond. Tiers, et al, (22)
reported that this procedure for preparing the tosylate of
phenols worked quite well with several fluorine-containing
alcohols. Again there seems to be no logical reason for its
failure.

Although the acetate (IX) from III is an intermediate
in the preparation of the diene, it may be also used as
supporting evidence for the existence of the hydroxyl group
in III. The procedure of Richardson and Tarrant (18) was
followed without difficulty. For the infrared spectrum of
IX, see Figure IV. The major absorption maxima and their
assignments are given in Table VI.

FIGURE IV

10% in C$_6$H$_6$
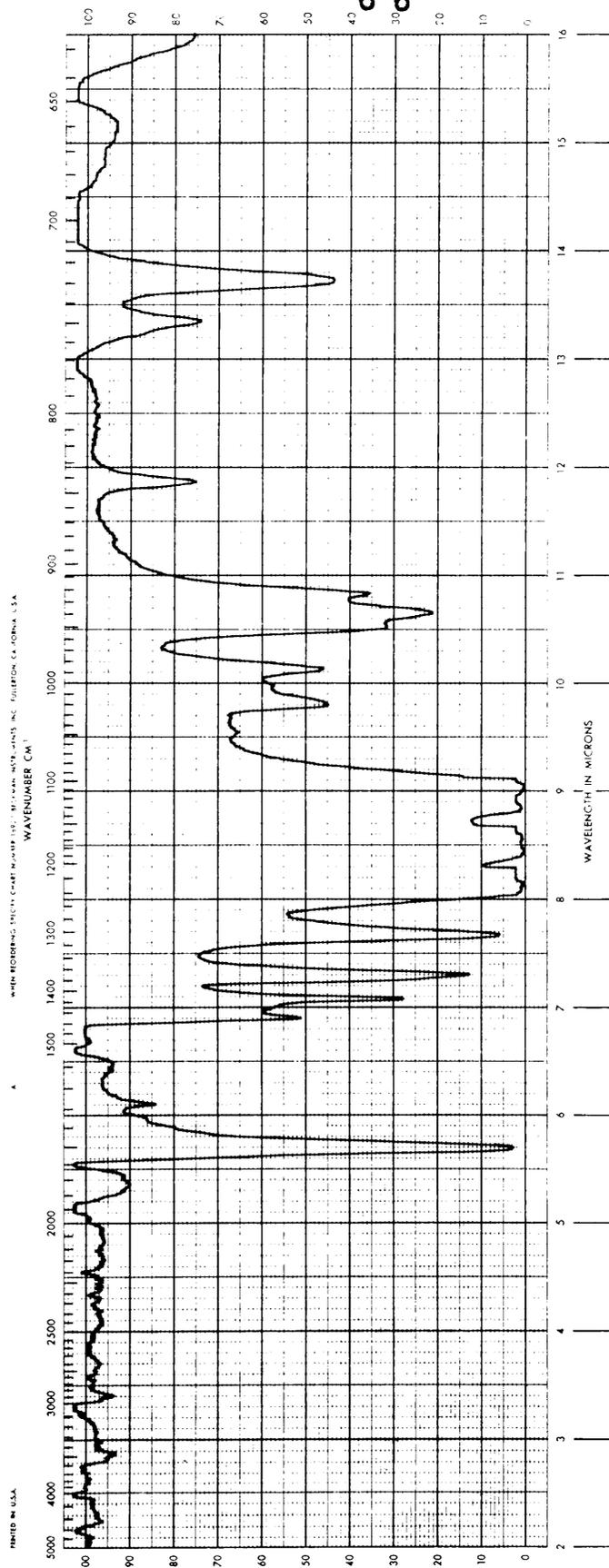

3-Trifluoromethyl-3-acetoxybutene-1

% Transmission

Table VI

Infrared Absorption of the Acetate (IX)

Wavelength (μ)	Assignment
3.40	CH_3, CH stretching
5.70	C-O stretching
6.10	C=C stretching
7.30	C-O stretching
7.68	CF stretching
8.40-8.28	CF stretching
10.15	CH out of plane deformation (Vinyl)

F.   Pyrolysis of 3-Trifluoromethyl-3-acetoxy-1-butene (IX)

The familiar route to dienes through the pyrolytic decomposition of an unsaturated ester was used. Richardson and Tarrant (18) reported successful pyrolysis of IX at 500-550°. In this investigation, the pyrolysis was accomplished at a temperature of 545-550°. The 2-trifluoro-methyl-1,3-butadiene was not isolated, but was distilled directly into the pressure vessel for reaction with sulfur dioxide.

II. Attempted Preparation of 3-Trifluoromethyl-2,5-
     Dihydrothiophene 1,1-dioxide (I)

A. 2-Trifluoromethyl-1,3-butadiene and Sulfur Dioxide

A convenient preparation of the title compound is
the modified Diels-Alder combination of 2-trifluoromethyl-
1,3-butadiene and sulfur dioxide. The procedure developed
by Rigney (28) was employed.

$$CH_2=CH-\underset{\underset{CF_3}{|}}{C}=CH_2 \quad + \quad SO_2 \quad \longrightarrow$$

(I)
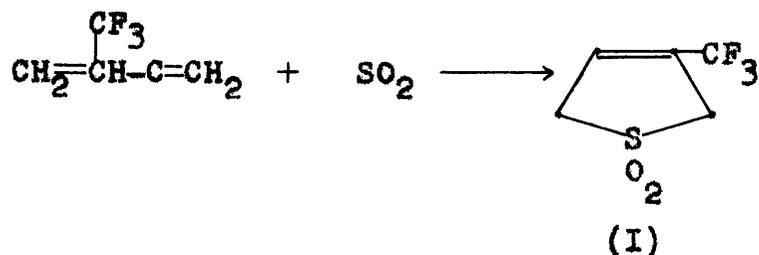
An ionic mechanism (30, 32) has been suggested for
the Diels-Alder reaction and it seems plausible that this
mechanism may apply to the reaction of a diene and sulfur
dioxide.

$$CH_2=CH-CH=CH_2 \quad + \quad :S \quad \longrightarrow$$
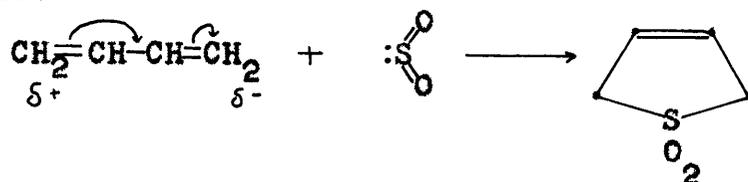
Introduction of an electron attracting group, such as
chlorine, in the case of 2-chloro-1,3-butadiene, would have
a pronounced effect on the reaction. In this particular
case, the I effect and the M effect would be in opposition
to each other and the overall effect would be intermediate,
thus giving poor yields (1).
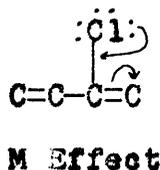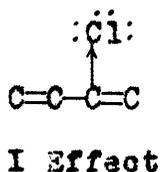
I Effect   M Effect

Substitution of a 2-trifluoromethyl group on 1,3-butadiene would impose an I effect which would cause an unfavorable electron distribution in the molecule.

$$\begin{matrix} & & \overset{\displaystyle CF_3}{\underset{\displaystyle |}{}} & \\ C{=}C & {-} & C{=}C & \end{matrix}$$
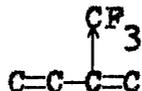
However, Henne and Hinkamp (15) reported the successful formation of a maleic anhydride adduct from II in 76% yields. Thus it would appear that the trifluoromethyl group does not inhibit the Diels-Alder reaction.

The physical properties of I, other than the melting point and the infrared spectrum, were not determined due to the lack of material. For the infrared spectrum, see Figure V.

FIGURE V

0.50% in KBr
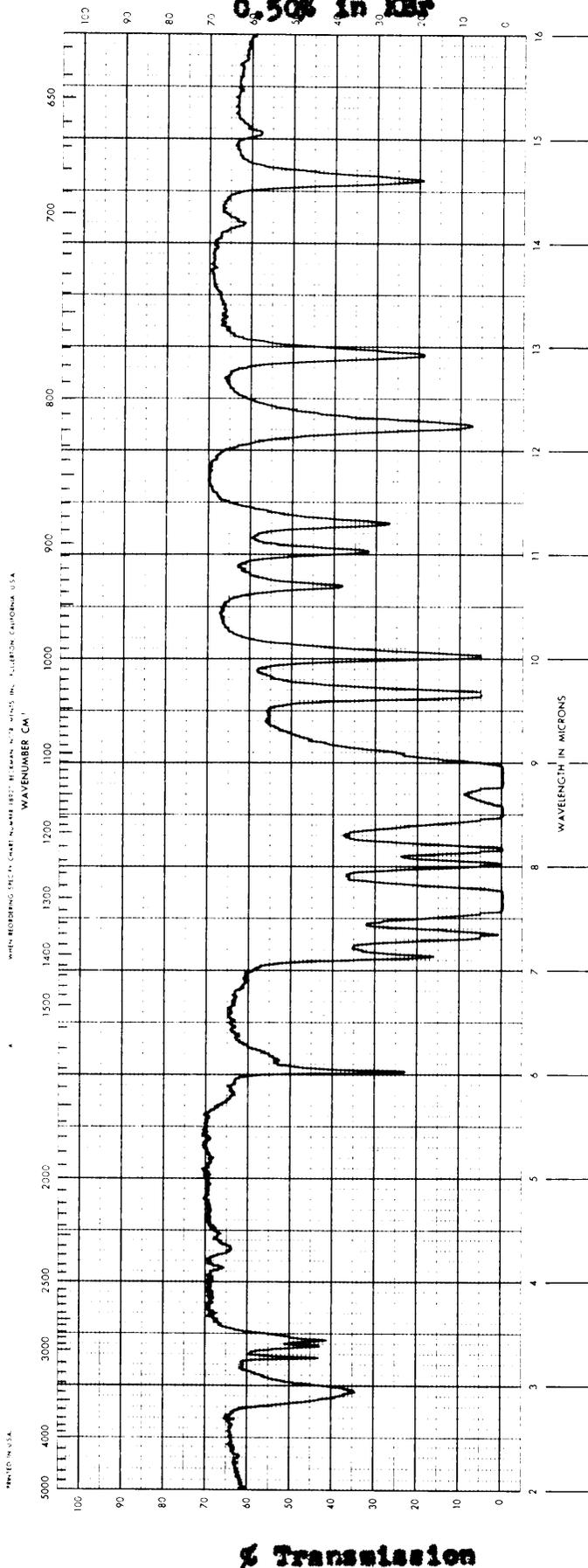
% Transmission

3-Trifluoromethyl-2,5-dihydrothiophene 1,1-dioxide

B.   Trifluoromethyl Bromide and 2,5-Dihydrothiophene
      1,1-Dioxide

All attempts to react trifluoromethyl bromide with
2,5-dihydrothiophene 1,1-dioxide were unsuccessful. As pre-
viously discussed, the C-Br bond is difficult to break due
to the inductive effect. In addition, the 2,5-dihydrothio-
phene 1,1-dioxide cannot be heated very strongly due to its
dissociation. Only the starting materials and a resinous
material were isolated.

EXPERIMENTAL[1]

I. Preparation of 2-Trifluoromethyl-1,3-butadiene (II)

A. Ethylmagnesium Bromide and 1,1,1-Trifluoroacetone

2-Trifluoromethyl-2-butanol (IV)

Into a 5000 ml. flask equipped with a mechanical stirrer, a reflux condenser and a dropping funnel was placed 134.4 g. (5.52 moles) of magnesium turnings in 2.25 liters of anhydrous ethyl ether. To the rapidly stirred mixture was added 623.5 g. (5.72 moles) of ethyl bromide at such a rate as to permit gentle reflux. Upon completion of the addition, the reaction mixture was stirred for one hour. A dry ice-methanol cooled condenser was inserted into the top of the water cooled condenser and a scintered glass diffusion tube was inserted into the reaction flask in place of the dropping funnel. To the rapidly stirred solution was added 471.5 g. (4.32 moles) of gaseous 1,1,1-trifluoroacetone at such a rate as to maintain gentle reflux. After standing overnight, the reaction mixture was hydrolyzed with 5N sulfuric acid. The ethereal layer was separated, treated with a 10% sodium bicarbonate solution, and subsequently, washed with water until neutral to litmus. The ethereal solution was then dried over anhydrous magnesium sulfate, filtered,

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(1) All melting points and boiling points are in degrees centigrade and uncorrected. The quantitative analyses were performed by Galbraith Microanalytical Laboratories, Knoxville, Tennessee.

and fractionated using a 26 inch vacuum-jacketed column
packed with glass helices to yield 291.6 g. (49%) of IV as
a colorless liquid, b.p. 94-97° [Lit. (15) 96-97°].

2-Trifluoromethyl-2-acetoxybutane (V)

A solution of 461.8 g. (3.24 moles) of IV in 335 g.
(3.28 moles) of freshly distilled acetic anhydride and 0.5 g.
of anhydrous zinc chloride were placed in a 1000 ml. flask
equipped with a reflux condenser. The mixture was shaken
thoroughly and heated to reflux for two hours. Upon dis-
tillation the fraction boiling below 125° was collected,
treated with 10% sodium bicarbonate and subsequently washed
with water until neutral to litmus. After drying over
anhydrous magnesium sulfate, the organic layer was filtered
and fractionated to yield 414.7 g. (79.8%) of V as a color-
less liquid, b.p. 110-117° [Lit. (15) 112°].

2-Trifluoromethyl-1-butene and 2-Trifluoromethyl-2-butene
(VI)

A solution of 328 g. (1.78 moles) of V in 328 ml. of
benzene was added at a rate of 25 drops per minute under a
constant flow of nitrogen to a vertically mounted column,
packed with six inches of pyrex wool and two inches of
pyrex beads. The temperature in the column was maintained
at 420-430°. The pyrolysate was collected in a dry ice-
methanol cooled trap. It was necessary to recycle unreacted
V twice. The pyrolysate was treated with a 10% sodium
bicarbonate solution and subsequently washed with water

until neutral to litmus. Fractionation yielded 123 g.
(56%) of VI b.p. 38-50° [Lit. (15) 38-40°].

2-Trifluoromethyl-3-bromo-1-butene and 3-Trifluoromethyl-4-bromo-2-butene (VII)

A solution of 16.1 g. (0.13 mole) of VI in 195 ml. of
freshly distilled carbon tetrachloride was placed in a
500 ml. flask equipped with a mechanical stirrer and a
reflux condenser. To the solution was added 23.2 g.
(0.13 mole) of N-bromosuccinimide and the resulting mixture
was heated to reflux and irradiated with ultraviolet light
for eight hours. Filtration of the reaction mixture yielded
10 g. (79%) of succinimide. Upon distillation, no unreacted
VI was recovered. The residue boiling above 78° was held
for dehydrohalogenation.

2-Trifluoromethyl-1,3-butadiene (II)

The above residue was added to 50 ml. of triethyl-
amine causing an immediate precipitation. The reaction
mixture was heated but; however, none of the desired product
was obtained. [Lit. (15) 20%, 34-35°].

B.   Vinylmagnesium Chloride and 1,1,1-Trifluoroacetone

Vinylmagnesium Chloride

Into a 3000 ml. flask equipped with a mechanical
stirrer, a thermometer, a dropping funnel, and a dry ice-
methanol cooled condenser was placed 71.9 g. (2.95 moles) of
magnesium turnings. A solution of 4 ml. of ethyl bromide
in 15 ml. of a vinyl chloride-tetrahydrofuran solution was
added to initiate the reaction. The remainder of the vinyl
chloride-tetrahydrofuran solution originally prepared by
absorbing 202.3 g. (3.25 moles) of vinyl chloride in 701.6 g.
(9.73 moles) of tetrahydrofuran, was added dropwise to the
flask at such a rate as to maintain the reaction temperature
below 50°. Upon completion of the addition, the mixture
was stirred at 50° for one hour. A nitrogen atmosphere was
maintained during the entire reaction.

3-Trifluoromethyl-1-butene-3-ol (III)

To the previously prepared vinylmagnesium chloride
was added 165.8 g. (1.51 moles) of 1,1,1-trifluoroacetone
(amount based on dehydration of 192.5 g. of the monohydrate)
at such a rate as to permit gentle reflux. An atmosphere
of nitrogen was maintained during the addition. Upon com-
pletion of the addition, the reaction mixture was stirred
for one hour and then hydrolyzed with 250 ml. of 12N
hydrochloric acid in 750 ml. of water. The organic layer
was washed with a 10% sodium bicarbonate solution and with

water until neutral to litmus. After drying over phosphoric anhydride, fractionation, using a 26 inch vacuum-jacketed column packed with glass helices, yielded 70.9 g. of III; b.p. 89-94°, n_D^{25} 1.3710, d_4^{25} 1.1065, M_{r_D} 26.58 calds; 28.71 obsd.

Anal. Calcd. for $C_5H_7F_3O$: C, 42.86; H, 5.04. Found: C, 48.08; H, 6.54.

Due to the incorrect analysis, some qualitative work was undertaken. The use of zirconium-alizarin test paper showed that the compound contained fluorine. Interpretation of the infrared spectrum of the impure material indicated that the proper functional groups were present. Of the possible contaminants, the most likely seemed to be tetrahydrofuran, which was employed as the solvent in the Grignard reaction.

Purification of III will be covered later under section D.

C.   Attempted Dehydration of Impure 2-Trifluoromethyl-1-
      butene-3-ol (III)

1)   Using Activated Alumina

To a vertically mounted pyrex tube, packed with 8
inches of 8 mesh alumina and 2 inches of pyrex beads, was
added 50.0 g. of impure III at a rate of 25 drops per minute.
The temperature within the column during the addition was
maintained at 350-360° with a continuous flow of dry nitrogen.
The products were collected in a test tube cooled in an ice-
salt bath, treated with a 10% sodium bicarbonate solution and
subsequently washed with water until neutral to litmus. After
drying, by freezing out the water at -80°, distillation yielded
15 g. of III, b.p. 90-94°. No other substances were isolated.

2)   Using Anhydrous Oxalic Acid

To a 50 ml. flask, equipped with a reflux condenser
and a drying tube, was added 20 g. of impure III and 15 g.
of anhydrous oxalic acid. The reaction mixture was refluxed
for 8 hours. Distillation of the reaction mixture yielded
10 g. of III, b.p. 90-94°.

3)   Using p-Toluenesulfonic Acid

To a 50 ml. flask, equipped with a reflux condenser
and a drying tube, was added 11 g. of impure VI and 11 g.
of p-toluenesulfonic acid. The reaction mixture was heated
to reflux for 3 hours at 95-100°. Distillation of the
reaction mixture yielded 5 g. of III, b.p. 90-94°.

4)   Using Phenyl Isocyanate

To a 20 ml. flask, equipped with a reflux condenser
and drying tube was added 4.5 g. of impure III and 2 ml.
phenyl isocyanate. The reaction mixture was heated at
90-95° for 1 hour. The reaction mixture was neutralized
with a dilute solution of sodium bicarbonate and subsequently
washed with water until neutral to litmus. The organic
layer was dried over anhydrous magnesium sulfate and dis-
tilled to yield 2.0 g. of III, b.p. 90-94°.

5)   Using Iodine

To a 10 ml. flask, equipped with a Vigreux column
and distilling head, was added 4 g. of impure III and a
crystal of iodine. Distillation of the reaction mixture
yielded 2.3 g. of III, b.p. 90-94°.

6)   Using Potassium Acid Sulfate

To a 10 ml. flask, equipped with a reflux condenser
and a cold trap, was added 4.0 g. of impure III and 4 g. of
potassium acid sulfate. The reaction mixture was refluxed
for 1 hour at 100°. There was no evidence of dehydration.
Distillation of the reaction mixture yielded 2.9 g. of III,
b.p. 90-94°.

7)   Using Sulfuric Acid

To a 50 ml. flask, equipped with a dropping funnel
and a distilling head, was added 25 ml. of 50% sulfuric
acid. To the sulfuric acid, at room temperature, was added

dropwise 4.0 g. of impure III. There was no evidence of dehydration. The reaction mixture was heated to 110° and no material boiling in the range of the expected product was isolated. Considerable charring occurred and no un-reacted III was recovered.

8) Using Phosphoric Anhydride

a) Into a small flask containing 50 g. of phosphoric anhydride heated to 130° was added dropwise 30.5 g. of impure III. After the addition was completed, the tempera-ture was maintained at 130° for 90 minutes. During this time, 11 g. of material was collected in an ice-salt cooled trap. Distillation of the isolated material yielded 4 g. of material, b.p. 35-41°. This material was expended in an unsuccessful effort to prepare a maleic anhydride adduct (15).

b) Into a flask containing 30 g. of phosphoric anhydride and 30 g. of sand was added 10.5 g. of impure III, with external cooling. The temperature was raised rapidly to 130° with constant agitation. The temperature was maintained for 30 minutes. During this time 4.0 g. of material was collected in an ice-salt cooled trap. Distillation of the isolated material yielded 3.5 g. of III, b.p. 90-94°.

D.   Purification of 2-Trifluoromethyl-1-butene-3-ol (III)

1)   Using Sodium Hydroxide

To a small flask, equipped with a reflux condenser, was added 11.1 g. of impure III and 15 ml. of a 10% sodium hydroxide solution. The mixture was heated to reflux for 90 minutes. The aqueous layer acquired a light brown color during this time. The organic layer was washed with water until neutral to litmus, dried over anhydrous magnesium sulfate, filtered and distilled to yield 2.1 g. of impure III, b.p. 94-95°.

2)   Using Constant Boiling Hydrochloric Acid

To a small flask, equipped with a reflux condenser, was added 11.1 g. of impure III and 25 ml. of constant boiling hydrochloric acid. The mixture was heated to reflux for 4 hours. The organic layer was washed with 10% sodium bicarbonate and subsequently with water until neutral to litmus. After being dried over anhydrous magnesium sulfate, distillation of the organic layer yielded 5.8 g. of material, b.p. 87-96.5°, n_D^{25} 1.3690, d_4^{25} 1.1197, M_{r_D} 26.582 calcd., 28.237 obsd.

3)   Vapor Phase Chromatography

As previously discussed, the most likely contaminant in III would be tetrahydrofuran. Interpretation of the infrared spectrum of impure III and comparison with the infrared spectrum of tetrahydrofuran gave further support

to this conclusion. Several vapor phase chromatograms were made by Dr. J. W. Murray using impure III and pure tetrahydrofuran as a control. Interpretation of these chromatograms led to the final conclusion that III was contaminated with approximately 30% tetrahydrofuran.

The vapor phase chromatograph employed was constructed by Dr. Murray of this department. The chromatograms were obtained by use of a Varian recorder attached to the chromatograph. The packing used was ADSORBENT 3X (Burrell Corporation) and the liquid phase was dinonyl phthalate. The temperature of the column was maintained at 110°. Helium was employed as the carrier gas.

4)   Using 85% Phosphoric Acid

Based on the previous work which showed that tetrahydrofuran was the contaminant, it was decided that 85% phosphoric acid, in which tetrahydrofuran is soluble, would be employed.

a)   Into a small separatory funnel was introduced 7.9 g. of impure III and 20 ml. of 85% phosphoric acid. The mixture was shaken thoroughly and refrigerated overnight. After separation, the organic layer was washed with distilled water, dried over phosphoric anhydride, filtered and distilled to yield 2.7 g. of III, b.p. 86-87°. A vapor phase chromatogram, made using this material, showed that the sample was approximately 99% pure.

b)   Based on the evidence obtained above, 10.9 g. of impure III was mixed with 30 ml. of 85% phosphoric acid in a small separatory funnel and refrigerated overnight. After separation, the organic layer was again treated with 30 ml. of 85% phosphoric acid, and refrigerated for several hours. The organic layer was separated, washed with water, dried over phosphoric anhydride, and filtered. Distillation of the dried organic layer yielded 3.0 g. of pure III, b.p. 86-87°, n_D^{25} 1.358, d_4^{25} 1.1709, M_{r_D} 26.582 calcd., 26.512 obsd. For the infrared spectrum see Figure I.

Anal. Calcd. for $C_5H_7F_3O$: C, 42.86; H, 5.04.
Found: C, 42.98; H, 5.45.

E.   Attempted Preparation of Derivatives From 2-Trifluoro-
      methyl-1-butene-3-ol (III)

1)   3,4-Dibromo-2-Trifluoromethylbutanol-2 (VIII)

Into a small flask equipped with a reflux condenser
and a magnetic stirrer was added 8.6 g. of impure III. The
flask was immersed in an ice water bath and 10.0 g. of
bromine was dropped slowly into the rapidly stirred solution.
Upon completion of the addition, the flask was removed
from the ice water bath and stirring was continued for 3
hours at room temperature. A dilute solution of sodium
bisulfite was added to the reaction mixture until the bro-
mine color disappeared. The organic layer was separated,
washed with water until neutral to litmus, dried over
anhydrous magnesium sulfate and distilled to yield 6.4 g.
of VIII, b.p. 65-66°/3mm, n_D^{25} 1.4685, D_4^{25} 1.9803, M_{r_D}
42.579 calcd; 42.143 obsd. For infrared spectrum see
Figures II and III.

Anal. Calcd. for $C_5H_7Br_2F_3O$: C, 20.02; H, 2.35;
Br, 53.28. Found: 20.29; H, 2.74; Br, 53.05.

2)   Using Benzoyl Chloride

The procedure used for the preparation of the benzoate
was a modification of the method of Shriner and Fuson (21).
A solution of 1.0 g. (.007 mole) of pure III in 3 ml. of
anhydrous pyridine was introduced into a small flask
equipped with a reflux condenser. The solution was heated
to reflux for five hours. The reaction mixture was poured,

with vigorous stirring, into 10 ml. of water. No precipitate formed at this point, Upon standing, crystals of benzoic acid were obtained and identified by a mixed melting point. No other material was isolated.

3) Using p-Toluenesulfonyl Chloride

The procedure of Tiers, et al, (22) was used. A solution of 0.5 g. (.0035 mole) of pure III, 0.7 g. (.0040 mole) of p-toluenesulfonyl chloride and 1.2 ml. of water were placed in a large test tube and heated to 50°. Into the warm mixture was dropped a solution containing 0.16 g. (.004 mole) of sodium hydroxide and 0.64 ml. of water. The temperature was maintained below 65° during the addition. The mixture was cooled and extracted with petroleum ether, which was then washed with 25 ml. of concentrated aqueous ammonia and subsequently with water. Evaporation of the solvent and recrystallization from petroleum ether yielded only 0.3 g. (29%) of p-toluenesulfonyl chloride, m.p. $68-69^{\circ}$.

4) 3-Trifluoromethyl-3-acetoxybutene-1 (IX)

The procedure of Richardson and Tarrant (18) was used. A solution of 11.2 g. (.079 mole) of pure III and 11.2 g. (.148 mole) of freshly distilled acetyl chloride was placed in a small flask equipped with a reflux condenser. The solution was heated to reflux for 5 hours, cooled, and poured into 30 ml. of ice water. The organic layer was separated, washed with a 10% sodium bicarbonate and subsequently washed with water until neutral to litmus.

After drying over anhydrous magnesium sulfate, distillation
of the organic layer yielded 6.7 g. of IX, b.p. 116-117.5°
(45.9%), n_D^{26} 1.3698 $\left[\text{Lit. (18) } 119^{\circ}; n_D^{24} 1.3685 \right]$. For
the infrared spectrum see Figure IV.

F.   Pyrolysis of 3-Trifluoromethyl-3-acetoxybutene-1 (IX)

2-Trifluoromethyl-1,3-butadiene (II)

The procedure of Richardson and Tarrant (18) was
used. Into a vertically mounted tube, packed with six
inches of pyrex wool and one inch of pyrex beads, was
introduced 6.7 g. (.036 mole) of IX at a rate of 30 g. per
hour. The temperature in the column was maintained at
545-550° under a continuous flow of nitrogen. The pyrolysate
was collected in a dry ice-methanol cooled trap. The desired
diene was not isolated as such.

II.   Attempted Preparation of 3-Trifluoromethyl-2,5-
      Dihydrothiophene 1,1-Dioxide (I)

A.   2-Trifluoromethyl-1,3-Butadiene and Sulfur Dioxide

      The procedure developed by Rigney (28) was used.
Into a small glass bottle was introduced .037 g. of hydro-
quinone. The bottle was cooled to -80° and II was intro-
duced by direct distillation from the pyrolysate. Into the
cooled bottle was introduced approximately 30 ml. of
liquid sulfur dioxide. The glass bottle was then placed
in a 400 ml. stainless steel bomb, which had previously
been cooled to -80°. Approximately 30 ml. more of liquid
sulfur dioxide was added to the bomb. The bomb was sealed
and placed in a water bath at 80-85° for 3 hours. After
cooling to -80°, the reaction vessel was opened and the
sulfur dioxide allowed to evaporate. The residue was
taken up in methyl alcohol and the volume reduced to 5 ml.
Upon refrigeration of the solution, colorless crystals
formed. Recrystallization yielded 0.7 g. of I, m.p. 119.5-
120°. For infrared spectrum see Figure V.

      Anal.[1] Calcd. for $C_5H_5F_3O_2S$: C, 32.26; H, 2.71;
S, 17.22. Found: C, 32.81; H, 3.17; S, 17.98.

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(1) The differences between the calculated and experimental
values in this analysis are not within the commonly accepted
limits.

B.   Trifluoromethyl Bromide and 2,5-Dihydrothiophene
1,1-Dioxide

To a 200 ml. test tube equipped with a thermometer,
a gas diffusion tube and an outlet tube attached to a
series of dry ice-methanol cooled traps was added 25.0 g.
(.21 mole) of butadiene sulfone and 2.0 g. of benzoyl
peroxide. The reaction mixture was heated until it
became molten and 76 g. (.51 mole) of trifluoromethyl bro-
mide was introduced into the solution through the gas
diffusion tube. The traps were so arranged that the gas
was passed back and forth through the solution for a total
of fifty-six times. The total reaction time was twenty-
four hours and eleven minutes. During the entire time
the reaction mixture was irradiated with ultraviolet light.
The temperature range was 60-87°. Extraction of the reac-
tion mixture with petroleum ether yielded .25 g. of benzoyl
peroxide. Extraction of the remaining reaction mixture
yielded 14.2 g. (56.7%) of starting material. The residue,
after extraction, was a dark brown resinous material
which weighed 6.3 g. and gave a positive test for sulfur
and a negative test for bromine and fluorine. This residue
was not further characterized.

SUMMARY

Evidence has been given for the structure assigned
to the title compound, 3-trifluoromethyl-2,5-dihydrothio-
phene 1,1-dioxide, which was obtained by the reaction of
2-trifluoromethyl-1,3-butadiene with sulfur dioxide.

Two methods for the preparation of 2-trifluoro-
methyl-1,3-butadiene have been investigated. One of these
methods was devised in this laboratory but was published
by other workers before this investigation had been com-
pleted.

A study of possible methods for the dehydration of
3-trifluoromethyl-1-butene-3-ol was undertaken. All of
the methods attempted in this investigation were unsuccess-
ful.

Possible methods for the purification of 3-trifluoro-
methyl-1-butene-3-ol were investigated. A successful
method, using 85% phosphoric acid was devised. As a result
of the purification studies, a new compound, 3,4-dibromo-
2-trifluoromethyl-2-butanol was obtained.

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ABSTRACT

The preparation of 3-trifluoromethyl-2,5-dihydrothiophene 1,1-dioxide (I) was attempted by means of a modified Diels-Alder reaction of 2-trifluoromethyl-1,3-butadiene (II) and sulfur dioxide. Evidence is given to support the structure of the product of the Diels-Alder reaction as that assigned to I. The reaction of vinylmagnesium chloride with 1,1,1-trifluoroacetone gave impure 3-trifluoromethyl-1-butene-3-ol (III). Treatment of impure III, which was contaminated with tetrahydrofuran, with 85% phosphoric acid yielded pure III. The attempted dehydration of III using various dehydrating agents was unsuccessful. Treatment of III with bromine gave 3,4-dibromo-2-trifluoromethyl-2-butanol (VIII). Treatment of III with acetyl chloride yielded 3-trifluoromethyl-3-acetoxybutene-1 (IX). Thermal decomposition of IX yielded II.