



UNIVERSITÉ D'OTTAWA
UNIVERSITY OF OTTAWA

ORGANIC SULFUR CHEMISTRY:
CYCLIC SULFINATE ESTERS (SULTINES).

by

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To Vijay

I

ABSTRACT

Relatively few examples of cyclic sulfinates esters (sultines) have been described in the literature and the methods used to prepare these compounds are not applicable to the synthesis of sultines of different ring size bearing a variety of substituents. A general synthesis of sultines allowing variations in ring size and substitution pattern was developed during this work. The key step in this general synthesis involves the carbon-sulfur bond cleavage reaction of *t*-butyl alkyl sulfoxides upon treatment with positive halogen species. This reaction was successfully applied to the synthesis of five to eight membered ring sultines bearing alkyl and/or aryl substituents in various positions.

It was observed that β -sultines are thermally unstable, losing SO_2 very readily to give the corresponding olefins. This approach was successfully applied to the synthesis of a number of olefins starting with carbonyl compounds. The intermediacy of β -sultines in these reactions was indicated when a β -hydroxy sulfinates was isolated on addition of methanol during the course of the reaction.

During an attempt to isolate a β -sultine, a seven-membered sultine, 3,4,6,7-tetraphenyl-1,5-dioxo-2-thiepane-2-oxide, was isolated and its structure was established by

spectroscopic methods and by its chemical reactions.

The photolytic behaviour of γ -sultines was studied and it was noticed that γ -sultines with a phenyl group at position 5 (carbon α to oxygen) successfully led to the corresponding cyclopropanes in high yield. The mechanism of photolysis was briefly investigated.

Conformational aspects of δ -sultines were studied by the interpretation of proton and carbon-13 spectra. It was concluded that the sultines examined exist in the chair conformation with an axial sulfinyl oxygen.

Some of the physical and chemical properties of various sultines were briefly investigated. Mass spectral fragmentation pathways for the various sultines have been suggested. Attempted deoxygenation of two sultines with tri-phenylphosphine led to the formation of dichloro compounds.

Finally, halogenation of benzyl methyl sulfoxide was studied in various solvent systems. The results suggest that carbon-sulfur bond cleavage becomes more and more prominent as the polarity of the medium is increased.

ACKNOWLEDGEMENTS

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TABLE OF CONTENTS

	PAGE
ABSTRACT.....	I
ACKNOWLEDGEMENTS.....	III
TABLE OF CONTENTS.....	V
LIST OF TABLES.....	VII
LIST OF SCHEMES.....	VIII
LIST OF FIGURES.....	X
LIST OF ABBREVIATIONS.....	XI
LIST OF SULFUR NOMENCLATURE.....	XII
 CHAPTER 1: Introduction.....	 1
CHAPTER 2: Halogenation of Sulfoxides.....	21
CHAPTER 3: Synthesis of 5 to 8 membered sultines.....	38
a) General Introduction.....	38
b) Synthesis of unsubstituted sultines.....	41
c) Sultines bearing substitution α to sulfur.....	45
d) Sultines bearing substitution α to oxygen.....	50
e) Sultines bearing substitution β to oxygen or sulfur.....	60
f) Synthesis of benzfused sultines.....	64
CHAPTER 4: Conformational aspects of six membered sulfur heterocycles.....	73
a) Introduction.....	73
b) Thianes and their derivatives.....	73
c) Dithianes, Oxathianes and their derivatives.....	76
d) Conformational studies of cyclic sulfites.....	80

e) Conformational aspects of δ -sultines.....	84
CHAPTER 5: Reactions of Sultines.....	94
a) Introduction.....	94
b) Physical characteristics.....	94
c) Mass spectra of sultines.....	95
d) Thermal loss of SO_2 from 1,2-oxathietane- 2-oxides (β -sultines).....	113
e) Synthesis and characterization of 3,4,6, 7-tetraphenyl-1,5-dioxo-2-thiepane-2- oxide (Attempted isolation of 3,4-diphenyl -1,2-oxathietane-2-oxide).....	128
f) Photochemical extrusion of SO_2 (cyclopropane synthesis).....	139
g) Nucleophilic displacement on sulfur.....	144
h) Oxidation of sultines.....	149
i) Attempted deoxygenation of sultines.....	149
j) Solvolysis reactions (Isomerisations).....	154
EXPERIMENTAL.....	156
Chapter II (Experimental).....	158
Chapter III (Experimental).....	163
Chapter V (Experimental).....	210
REFERENCES.....	219
Claims to original research.....	230

LIST OF TABLES

TABLE

	<u>CHAPTER 2</u>	Page
I	Reaction of benzyl methyl sulfoxide with NCS.....	32
	<u>CHAPTER 3</u>	
I	Yields of unsubstituted sultines and their precursor hydroxy sulfoxides.....	43
II	Yields of C-5 substituted γ -sultines and their precursors.....	51
III	Spectroscopic properties of C-5 substituted γ sultines.....	59
	<u>CHAPTER 4</u>	
I	Carbon-13 n.m.r. chemical shifts for δ -sultines...	91
	<u>CHAPTER 5</u>	
I	Mass spectra of monomethyl γ -sultines.....	100
II	Mass spectra of substituted γ -sultines.....	103
III	Mass spectra of monomethyl δ -sultines.....	108
IV	Mass spectra of substituted δ -sultines.....	111
V	Yields of olefins and their precursor β -hydroxy sulfoxides.....	117
VI	Properties of sultines <u>48</u> and <u>51</u>	134

LIST OF SCHEMES

SCHEME

	<u>CHAPTER 2</u>	page
1.	Halogenation of phenyl hydroxy alkyl sulfoxides....	22
2.	Formation of chlorosulfones from hydroxy sulfoxides via alkoxyoxosulfonium salts.....	23
3.	Stereochemical course of C-S cleavage reaction.....	26
4.	Reaction of <i>t</i> -butyl methyl sulfoxide with NCS or SO ₂ Cl ₂	34
	<u>CHAPTER 3</u>	
1.	Mechanism of formation of sultines.....	40
2.	Synthesis of unsubstituted sultines.....	42
3.	Synthesis of sultines bearing substituents..... α to sulfur	45
4.	Attempted synthesis of 3-phenyl-1,2-oxathiolane-2-oxide.....	47
5.	Synthesis of C-5 substituted γ-sultines.....	51
6.	Synthesis of C-6 substituted δ-sultines.....	55
6a.	Synthesis of C-6 substituted δ-sultines from homoallylic alcohols.....	57
7.	Synthesis of 6-methyl-1,2-oxathiane-2-oxide.....	58
8.	Synthesis of 4-methyl-1,2-oxathiolane-2-oxide.....	61
9.	Synthesis of 4-methyl-1,2-oxathiane-2-oxide.....	62
10.	Synthesis of 5-methyl-1,2-oxathiane-2-oxide.....	63
11.	Synthesis of 3H-2,1-benzoxathiole-1-oxide.....	65
12.	Attempted synthesis of 3H-1,2-benzoxathiole-2-oxide.....	66

SCHEME

	page
13. Synthesis of 3,4-dihydro-1,2-benzoxathiin-2-oxide.....	71

CHAPTER 5

1. Mass spectral fragmentation of phenyl methyl sulfone and isomeric sulfinates.....	96
2. Fragmentation of 1,2-oxathiolane-2-oxide.....	99
3. Fragmentation of 1,2-oxathiane-2-oxide.....	107
4. Fragmentation of monomethyl δ -sultines.....	110
5. Synthesis of olefins from carbonyl compounds....	114
6. Interception of a β -sultine by nucleophilic reagent.....	120
7. Stereochemistry of the decomposition of β -sultines.....	121

X

LIST OF FIGURES

FIGURE

CHAPTER 3

page

1. N.M.R. spectrum of 5-methyl-1,2-oxathiolane-2-oxide.....52
2. N.M.R. spectrum of 6-methyl-1,2-oxathiane-2-oxide.....55
3. N.M.R. of the reaction product derived from 76 and SO_2Cl_2 68

CHAPTER 5.

1. Mass spectrum of 1,2-oxathiolane-2-oxide.....98
 2. Mass spectrum of 5-methyl-1,2-oxathiolane-2-oxide.....101
 3. Mass spectrum of 5-phenyl-1,2-oxathiolane-2-oxide.....104
 4. Mass spectrum of 1,2-oxathiane-2-oxide.....106
 5. Mass spectrum of 4-methyl-1,2-oxathiane-2-oxide..109
 6. Mass spectrum of 6-phenyl-1,2-oxathiane-2-oxide..112
- J

LIST OF ABBREVIATIONS

THF	-	Tetrahydrofuran
N.M.R.	-	Nuclear magnetic resonance
IR.	-	Infrared
u.v.	-	Ultra violet
M.S.	-	Mass spectrum
b.p.	-	boiling point
m.p.	-	melting point
eq.	-	equivalent
mcpba	-	<u>m</u> -chloro per. benzoic acid
Me	-	Methyl
Et	-	Ethyl
s	-	singlet
d	-	doublet
t	-	triplet
q	-	quartet
bs	-	broad singlet
m	-	multiplet
ax.	-	axial
eq.	-	equatorial
soln	-	solution
dil	-	dilute

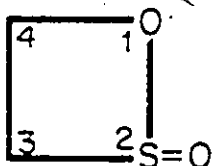
LIST OF SULFUR NOMENCLATURE

Sulfide	$R - S - R'$	Sulfoxide	$R - \overset{\overset{O}{\parallel}}{S} - R'$
Sulfone	$R - \overset{\overset{O}{\parallel}}{\underset{\underset{O}{\parallel}}{S}} - R'$	Sulfinic acid ester	$R - \overset{\overset{O}{\parallel}}{S} - OR'$
Sulfonate ester	$R - \overset{\overset{O}{\parallel}}{\underset{\underset{O}{\parallel}}{S}} - OR'$	Sulfinyl	$R - \overset{\overset{O}{\parallel}}{S} \cdot$
Sulfonyl	$R - \overset{\overset{O}{\parallel}}{\underset{\underset{O}{\parallel}}{S}} \cdot$	Sulfenium	$R - \overset{\oplus}{S} = CHR'$
Sulfonium	$R - \overset{\oplus}{S} - R' \begin{matrix} \\ R'' \end{matrix}$	Oxosulfenium	$R - \overset{\overset{O}{\parallel}}{\underset{\underset{\oplus}{\parallel}}{S}} = CHR'$
Oxosulfonium	$R - \overset{\overset{O}{\parallel}}{\underset{\underset{\oplus}{\parallel}}{S}} - R' \begin{matrix} \\ R'' \end{matrix}$	Alkoxyoxosulfonium	$R - \overset{\overset{O}{\parallel}}{\underset{\underset{\oplus}{\parallel}}{S}} - R' \begin{matrix} \\ OR'' \end{matrix}$
Sultone	$(CH_2)_n \begin{matrix} \text{SO} \\ \\ O \end{matrix}$	Sultone	$(CH_2)_n \begin{matrix} \text{SO}_2 \\ \\ O \end{matrix}$
Sultine	$(CH_2)_n \begin{matrix} \text{SO} \\ \\ O \end{matrix}$		

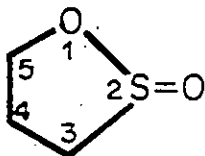
CHAPTER 1.

Introduction

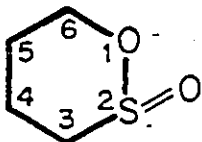
In contrast to the extensive literature on the preparation of cyclic sulfonate esters (sultones)¹ only a few cyclic sulfinic acid esters (sultines) have so far been reported. The name, "sultine", to describe a cyclic ester of sulfinic acid, was suggested by Dittmer². The word sultine is derived by replacing the "o" in sultone with an "i" to indicate that a sulfinic and not a sulfonic ester is involved. The I.U.P.A.C. nomenclature and numbering for these ring systems is as follows:



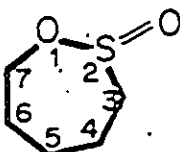
1, 2 - Oxathietane - 2 - oxide.



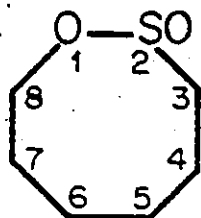
1, 2 - Oxathiolane - 2 - oxide.



1, 2 - Oxathiane - 2 - oxide.



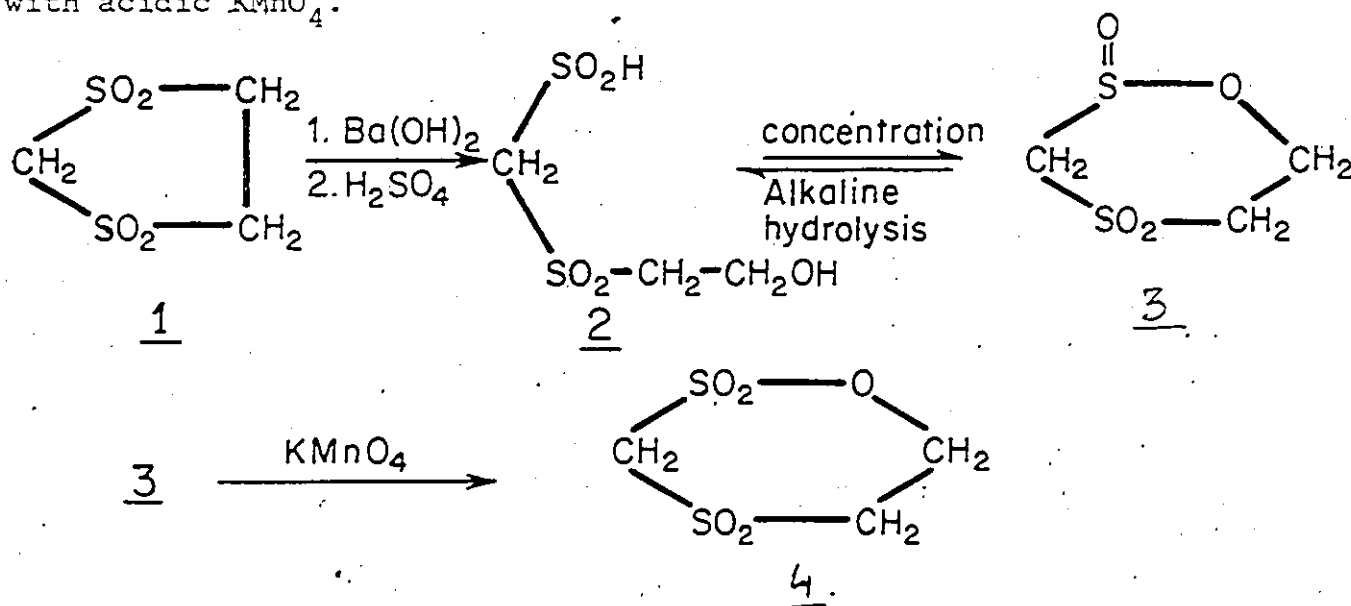
1, 2 - Oxathiepane - 2 - oxide.



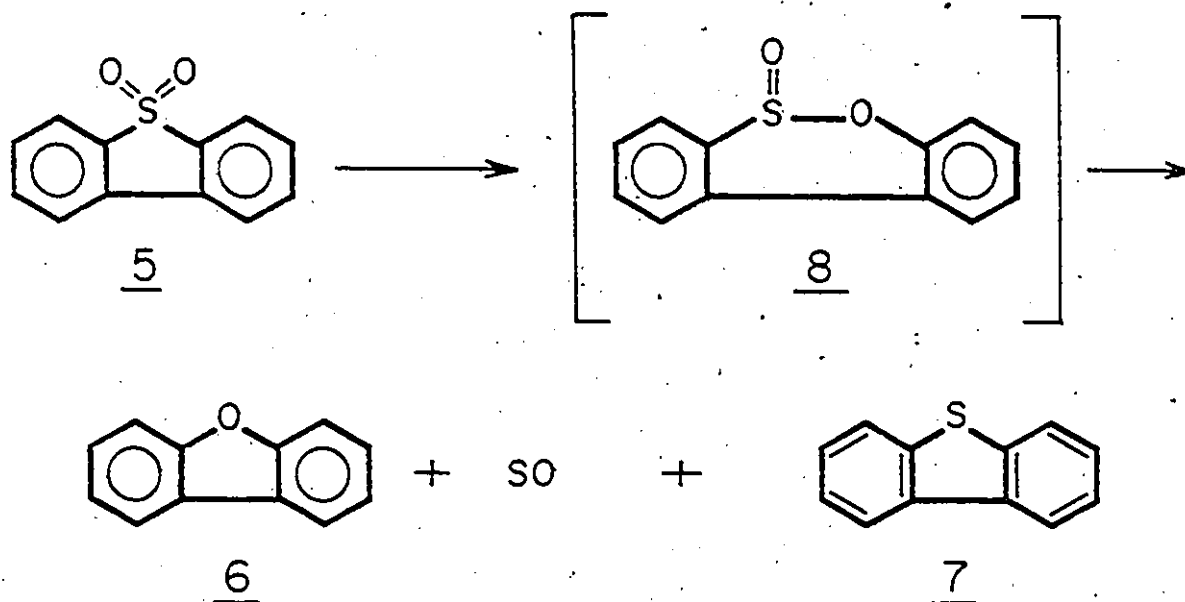
1,2-Oxathiocane -2-oxide.

Throughout the text the sultine and 1,2-oxathia-nomenclature are used interchangeably. For clarity, only the formal designation is generally used in the Experimental.

The earliest preparation of this type of compound was described by Baumann and Walter in 1893³. These authors reported the conversion of 1,3-dithiolane-1,1,3,3-tetraoxide, 1, into the hydroxysulfinic acid 2 by warming with barium hydroxide solution followed by acidification. Concentration of an aqueous solution of this hydroxysulfinic acid gave the cyclic sulfinate ester, 1,2,4-oxadithiane-2,4,4-trioxide, 3, as a crystalline solid, m.p. 164°C. The sultine 3 could be reconverted to the hydroxysulfinic acid 2 by alkaline hydrolysis or oxidized to the corresponding sultone, 1,2,4-oxadithiane-2,2,4,4-tetraoxide, 4, with acidic KMnO_4 .



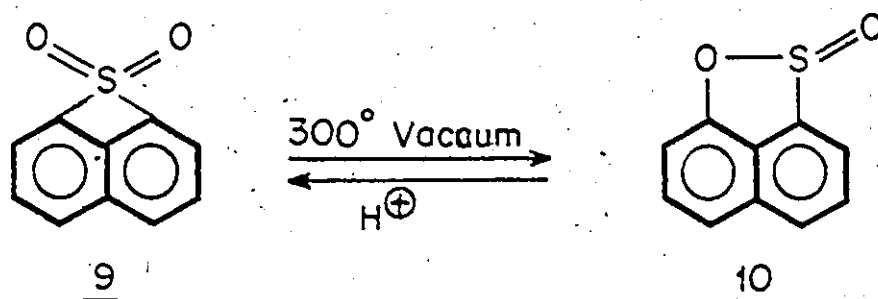
No further examples of sultines were reported until 1966. Fields and Meyerson⁴ reported that pyrolysis of dibenzothiophene-5,5-dioxide, 5, led only to dibenzofuran, 6, and dibenzothiophene, 7, but no biphenylene. The authors postulated the intermediacy of the cyclic sulfinates 8 to account for the formation of these products.



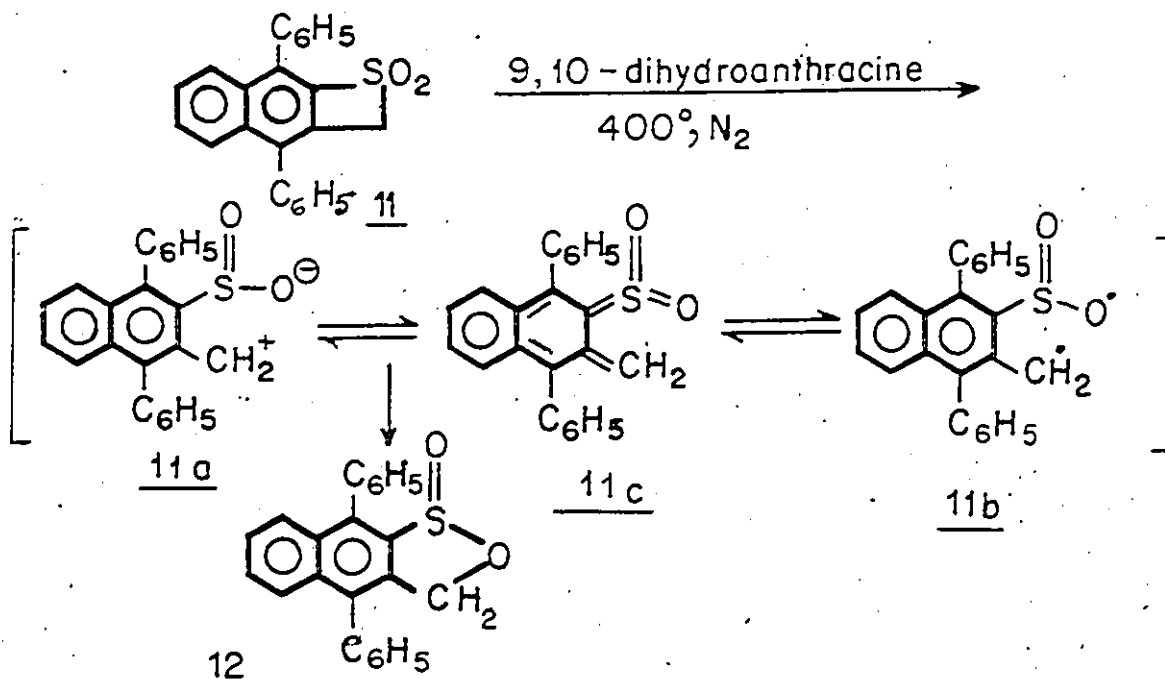
The mass spectrum of dibenzothiophene dioxide, 5, provided support for their postulate. The major primary decomposition processes were loss of SO and CO, both of which required prior formation of a C-O bond, a condition met by an initial isomerization of the sulfone to an internal sulfinates ester.

Shortly thereafter Hoffmann and Sieber⁵ reported the interconversion of naphtho (1,8-bc)thieten-1,1-dioxide, 9, to naphtho(1,8-cd) (1,2)oxathiol-S-oxide, 10. The sultine structure was inferred from the infrared spectrum of 10 which showed the

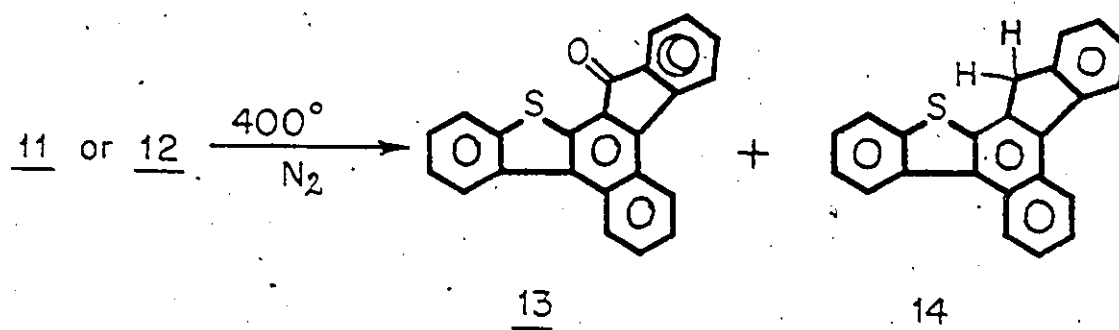
characteristic sulfinic ester absorption, at 1130 cm^{-1} and the absence of sulfone bands.



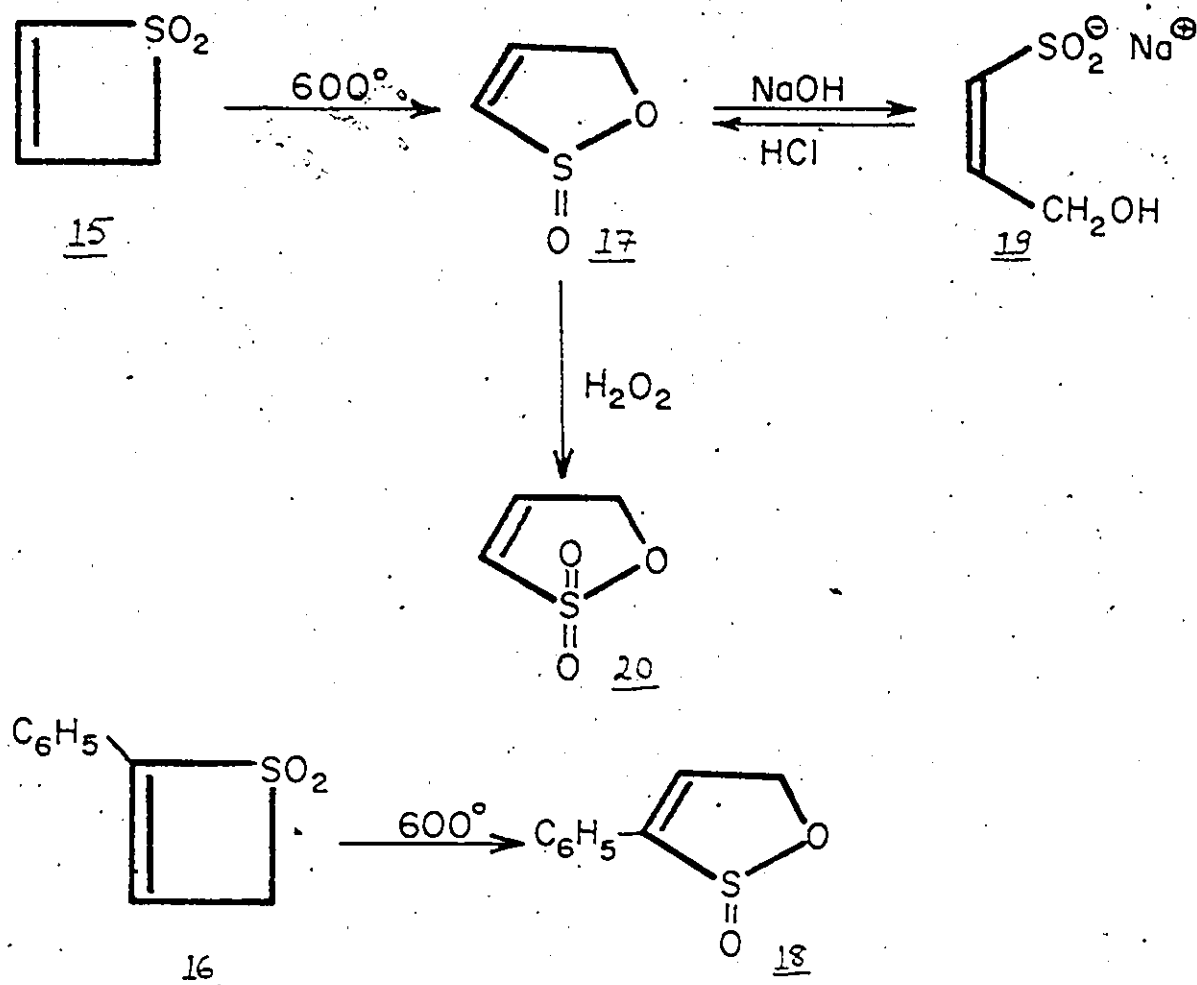
Dittmer, Henion and Takashina² found that pyrolysis of 3,8-diphenyl-2H-naphtho(2,3-b)-thiete-1,1-dioxide, 11, in the presence of a twofold excess of 9,10-dihydroanthracene at 400° led to the sultine, 4,9-diphenyl-3H-naphth(2,3-c)-2,1-oxothiole-1-oxide, 12, in 80% yield. Dittmer and coworkers could not decide the exact mechanism of the rearrangement of 11 to 12. It was suggested that pyrolysis of 11 involved initial scission of the methylene carbon-sulfur bond to give an intermediate (dipolar 11a, diradical 11b or sulfene 11c) which cyclized to the sultine 12 by formation of a carbon-oxygen bond.



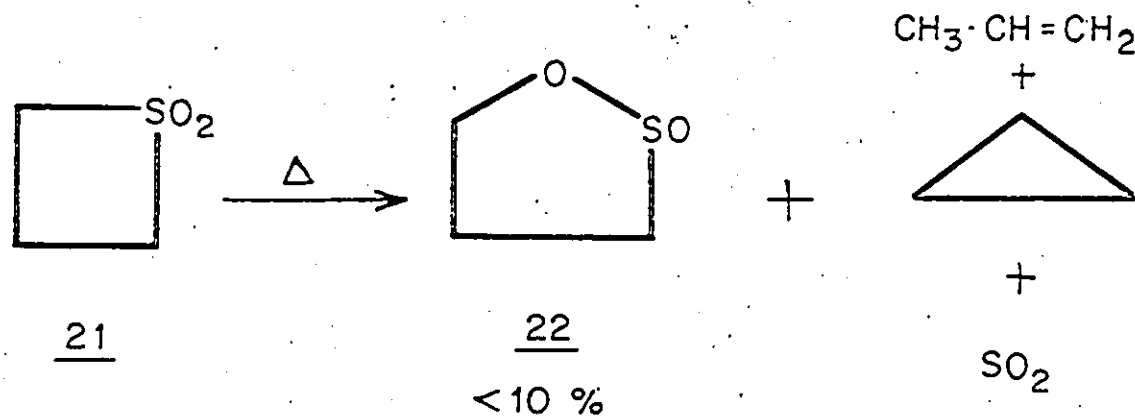
When the pyrolysis of the sulfone 11 was carried out at 400° in the absence of dihydroanthracene the polycyclic ring systems 13 and 14 were obtained. The effect of dihydroanthracene on the course of the pyrolysis is not obvious. Heating the sultine 12 under similar conditions also gave 13 and 14.



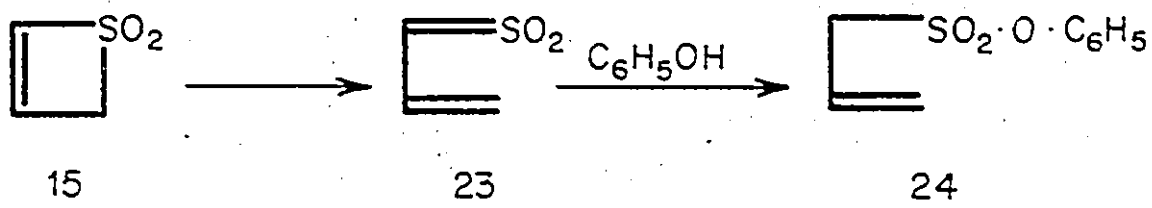
The thermolysis of 4-membered ring sulfones, both saturated and unsaturated, has been studied in some detail by King and deMayo⁶, utilizing the flash thermolysis technique. In this method a substance is volatilized and passed through a hot (600-1100°) quartz tube under high vacuum and the product collected in a cold trap. Because of the short contact time surprisingly clean reaction products are generally obtained, despite the very high temperatures. Thus the thiete-1,1-dioxides 15 and 16 rearranged to the corresponding sultines at 600° in the yields of 85% and 27% respectively.



In contrast, flash thermolysis of the cyclic sulfone 21 gave only a small amount of the saturated sultine 22, the major products being propylene, cyclopropane and sulfur dioxide.

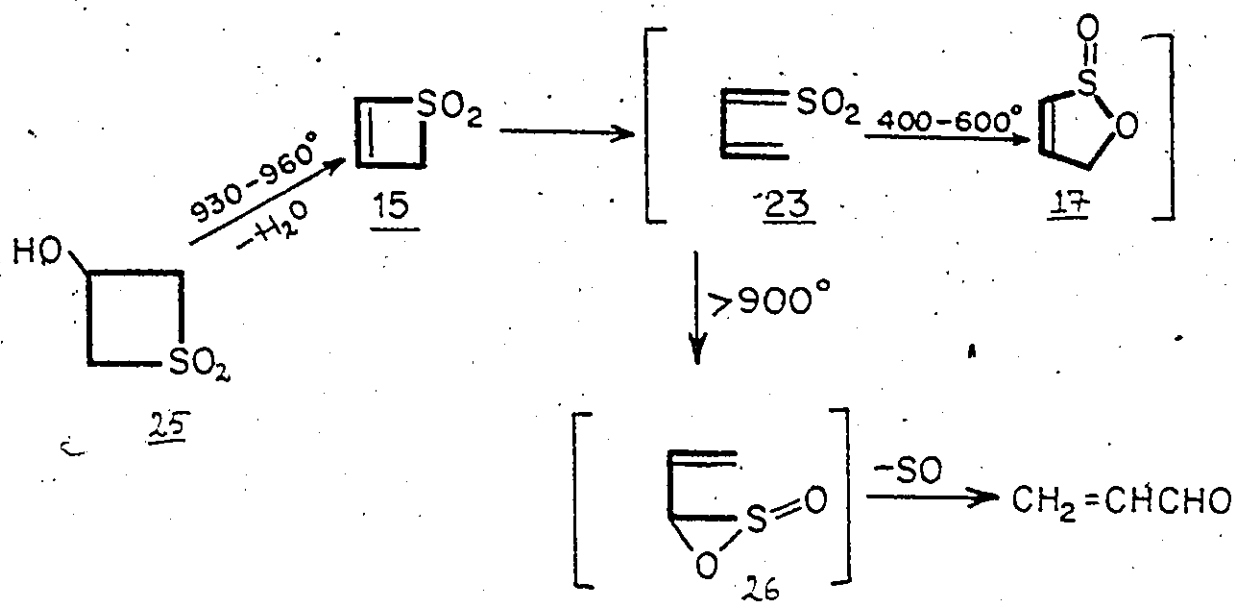


Strong evidence was presented to suggest that the rearrangement of 15 to 17 and 16 to 18 involves the intermediacy of a vinyl sulfene (rather than ionic or diradical intermediate) which undergoes "abnormal" (nucleophilic attack on the sulfonyl oxygen) addition of the double bond to the sulfene. A pyrolysis of 15 carried out in the presence of phenol gave phenyl-2-propenesulfonate, 24, presumably via the sulfene 23.

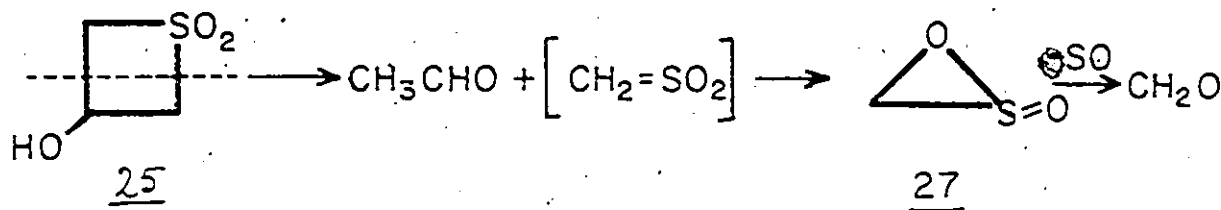


The difference in behaviour between 15 and 21 under thermolytic conditions was also considered to be consistent with ring opening to sulfene intermediate by 15 and a diradical by 21.

Thermolysis of 3-hydroxythietane-1,1-dioxide, 25, at $930-960^\circ$ gave a series of aldehydes and ketones whose formation was again explained in terms of sulfene intermediates.

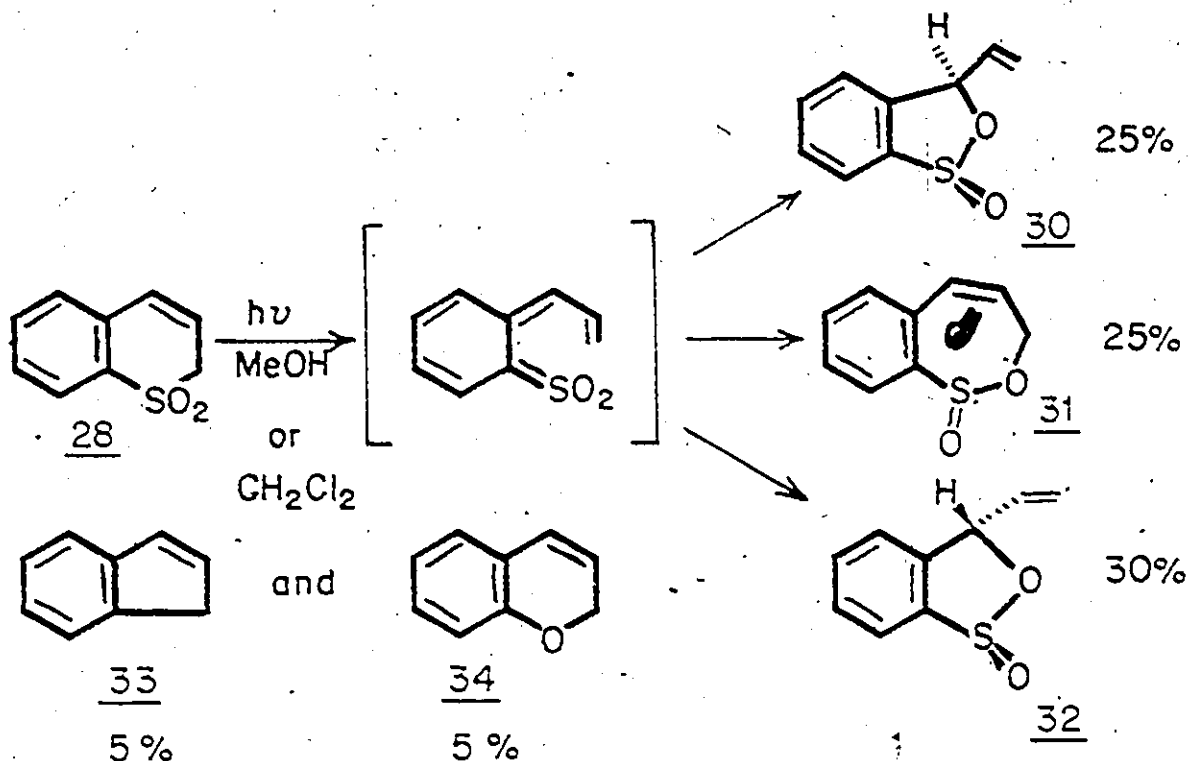


The intermediate α -sultine 26, which does not form below 600° , is proposed to form at temperatures greater than 900° . Loss of sulfurmonoxide from 26 would give acrolein, one of the observed products⁷. Formaldehyde obtained may be produced from vinyl sulfene via the intermediate sultine 27.

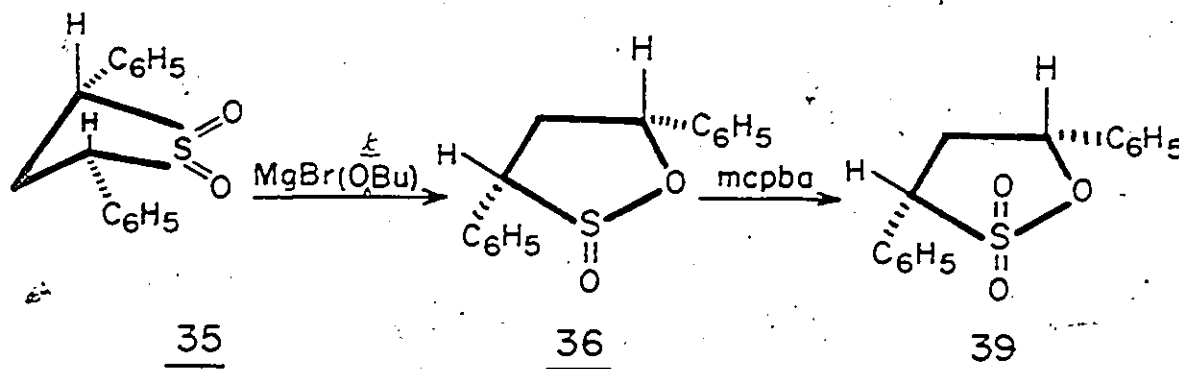


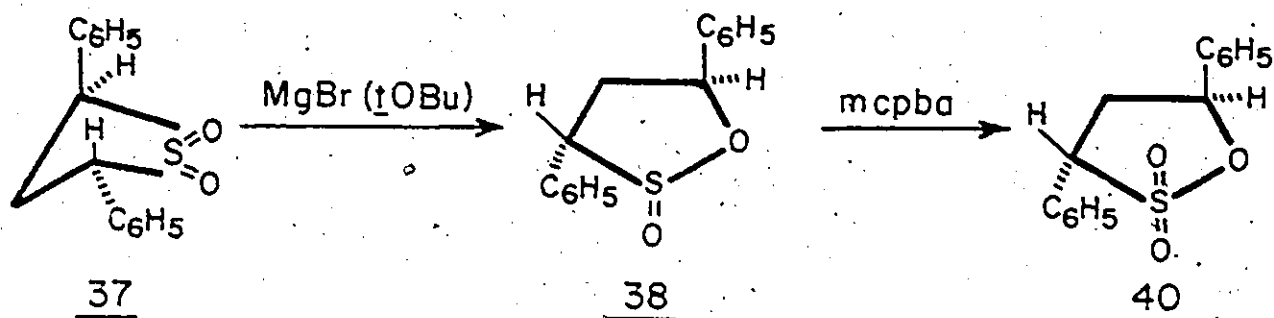
Very recently Hall and Smith¹⁰ have reported the results of the photolysis of 2H-1-benzothiopyran-1,1-dioxide, 28, in dichloromethane or methanol with light of 254 nm wavelength. When the photolysis was carried out in methylene chloride a mixture of sultines 30, 31 and 32 together with smaller amounts of indene, 33, and 2H-1-benzopyran, 34, were obtained. The formation of these products could be explained by assuming

initial ring opening to a sulfene.

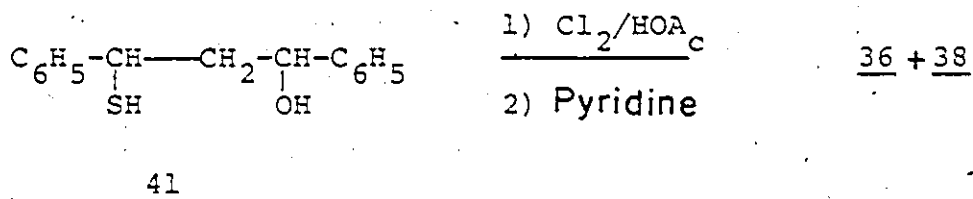


A base-catalysed rearrangement of a cyclic sulfone to the isomeric cyclic sulfinates has been described by Dodson's group^{11,12}. These workers were able to achieve a stereospecific rearrangement of the four-membered cyclic sulfones 35 and 37 into the isomeric five-membered cyclic sulfinates 36 and 38.



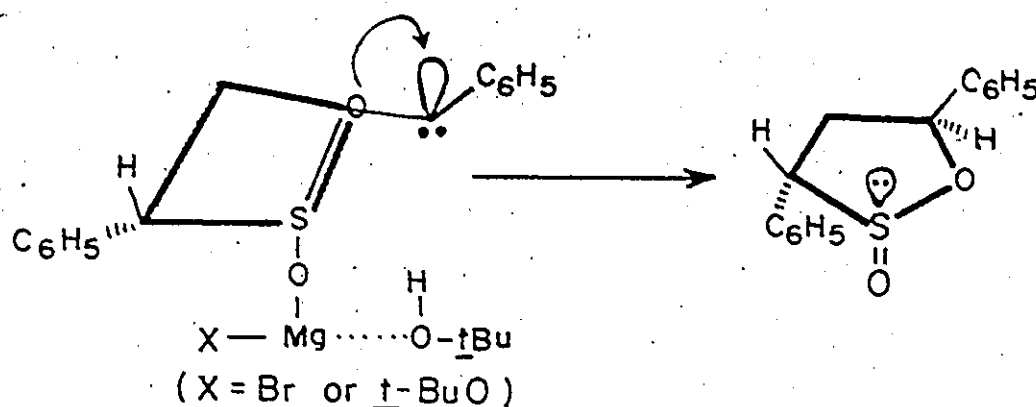


The structures of 36 and 38 were confirmed by independent syntheses from 1,3-diphenyl-3-hydroxypropane thiol, 41, via controlled oxidation with chlorine in glacial acetic acid and by the oxidation of 36 and 38 with *m*-chloroperbenzoic acid to the corresponding diphenyl sultones 39 and 40. Since distinctly different sultones 39 and 40 respectively, were obtained

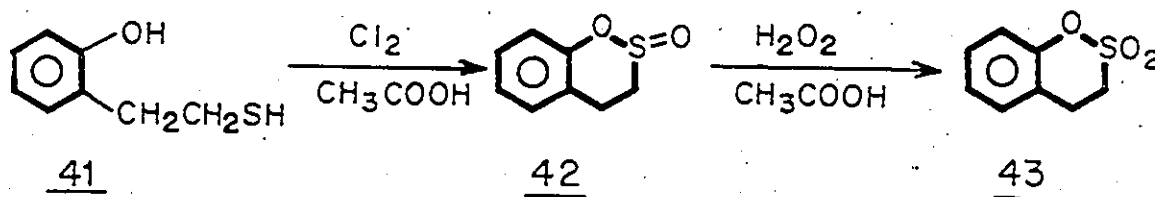


it was concluded that the difference between 36 and 38 was not due to the S=O geometry, but rather that one of these must have the phenyl group cis while in the other they must be trans.

The rearrangement was found to be specific for *t*-butoxymagnesiumbromide. Other closely related bases such as ethyl magnesium bromide or potassium *t*-butoxide in DMF did not initiate the rearrangement of these sulfones to sultines. Dodson tentatively suggested this rearrangement to occur via a carbene formed by base abstraction of a benzylic proton and α -elimination of a benzyl sulfinyl group by cleavage of the C-S bond¹².

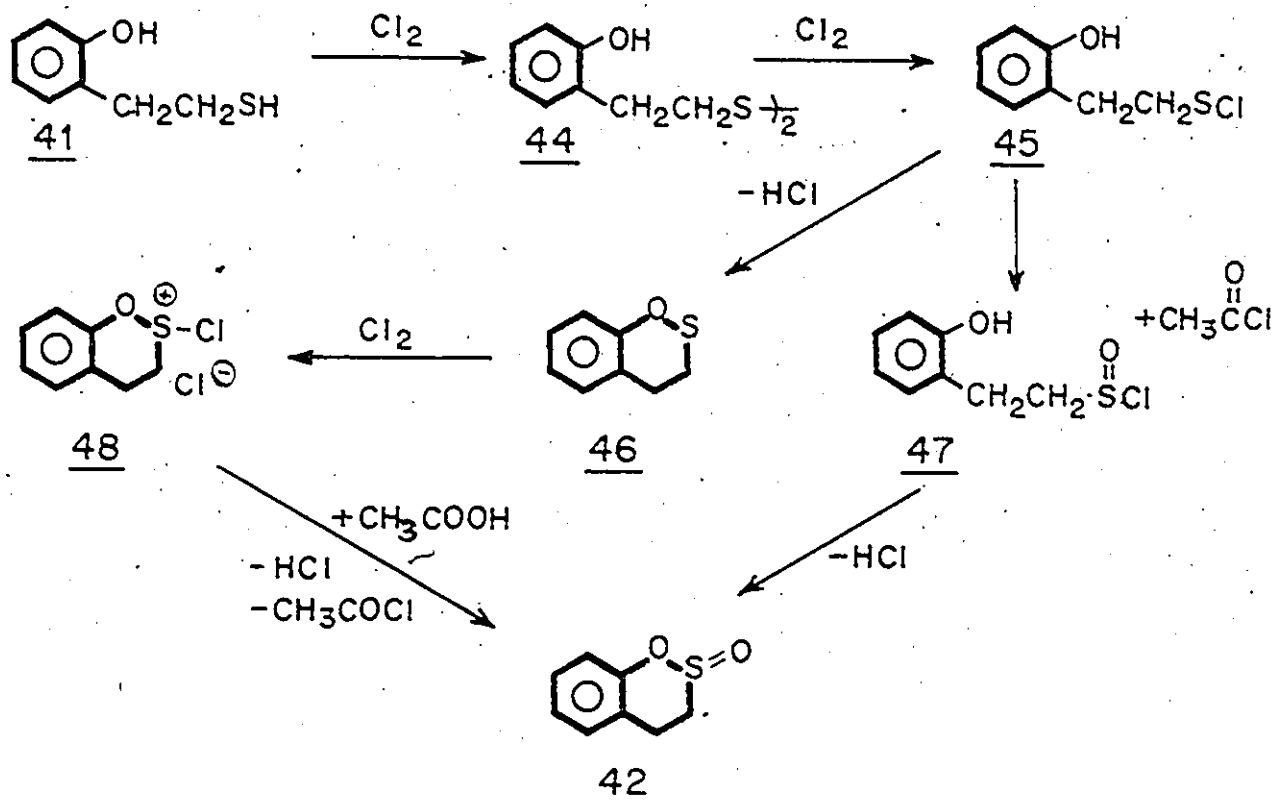


The method of the controlled oxidation of a hydroxythiol with chlorine in acetic acid was first applied by Givens and Hamilton¹³ to the synthesis of benz-fused cyclic sulfinate 1,2-benzoxathian-2-oxide, 42, from the phenolic thiol 41. Structural proof for the sultine 42 was provided by oxidation to the known sultone 43 with hydrogen peroxide in acetic acid.

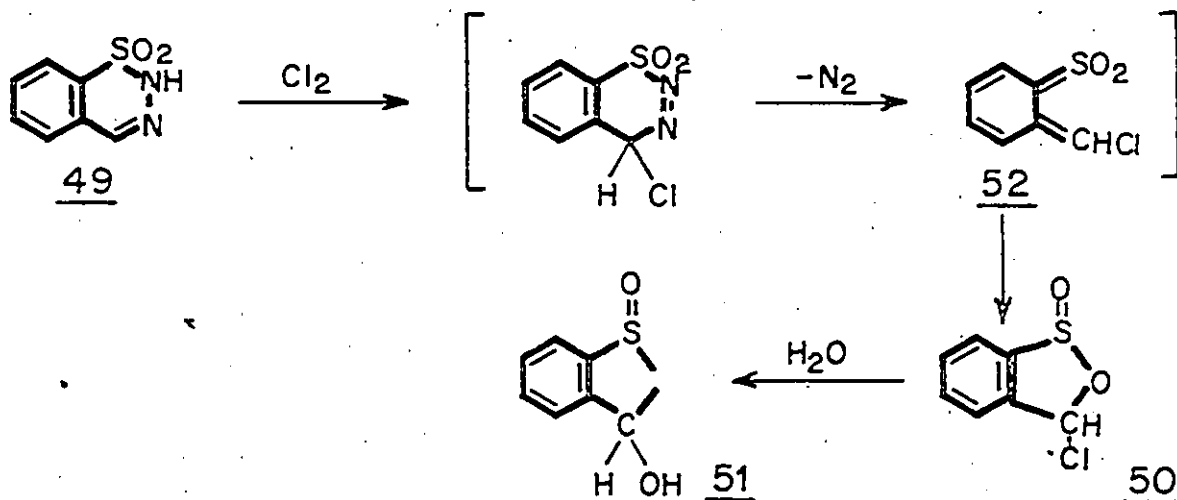


The formation of 42 was proposed to proceed via the cyclic sulfenate ester 46. In principle, displacement of the chloride ion from 48 with acetate, followed by loss of acetyl chloride would lead to the sultine 42. However, in view of our recent experiments, hydroxy sulfenyl chlorides do not seem to cyclize very readily to the cyclic sulfenates. Thus, it seems more likely that in this reaction the phenolic sulfenyl chloride

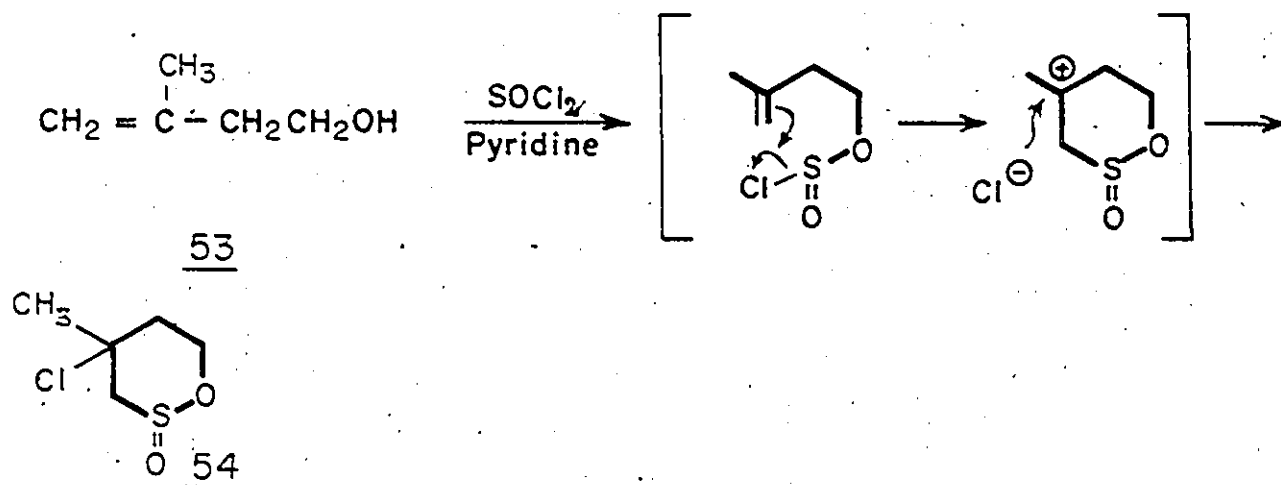
is oxidized to the corresponding sulfinyl chloride followed by cyclization to the sultine.



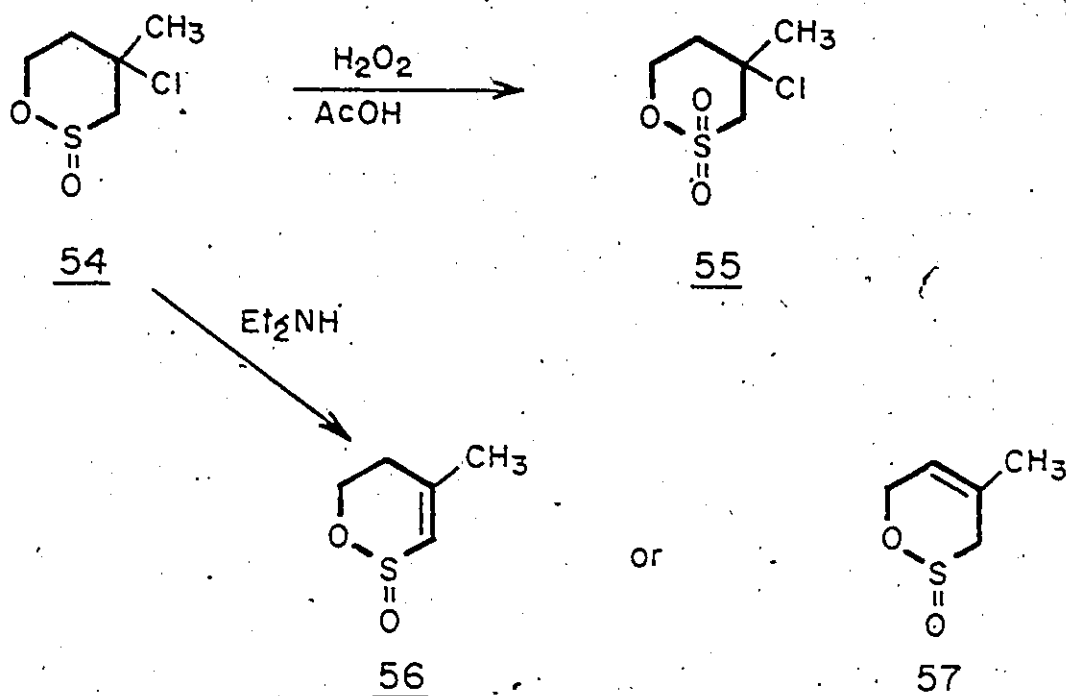
Chlorination of 2H-1,2,3-benzothiadiazine-1,1-dioxide, 49, with chlorine in dry methylene chloride afforded, probably via the sulfene 52, the sultine 50 as an unstable product^{8,9}. Treatment of 50 with water converted it to the pseudoacid 51.



Several sultines have been prepared by the reaction of thionyl chloride with unsaturated alcohols. This novel reaction was first encountered by Dhami^{14a}. Reaction of 2-methyl but-1-en-4-ol, 53, with thionyl chloride in the presence of pyridine at ice bath temperature afforded a 50% yield of the chlorosultine 54.

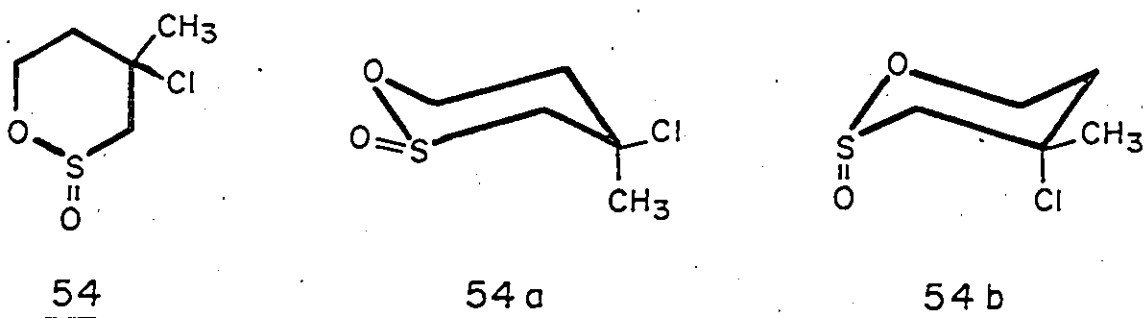


The chlorosultine was oxidized to the chlorosultone 55 with H_2O_2 in acetic acid. When heated with diethylamine in benzene an unsaturated sultine was obtained which was assigned the structure 56. In view of the recent work reported from this laboratory¹⁵, structure 57 does not seem likely to represent a stable sultine since 3,6-dihydro-1,2-oxathiin-2-oxides were found to fragment very rapidly to sulfur dioxide and 1,3-dienes at temperature below 0° . The alternate structure 56 is mechanistically more reasonable and in much better agreement with the given n.m.r. data.

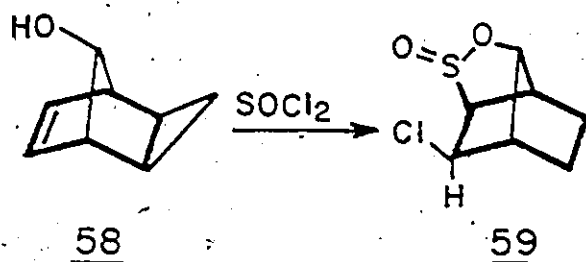


Dhami also prepared some more sultines by varying substituents on the carbon α to oxygen in the alcohol 53. However the yield of the desired sultine was relatively low in every case due to the side reactions such as chloride and sulfite formation.

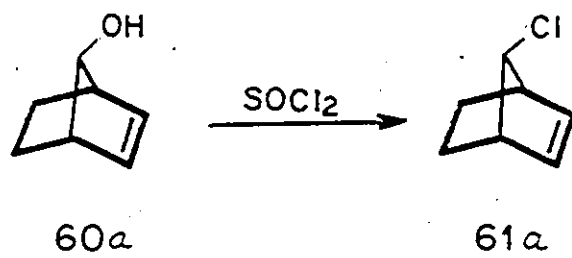
Very recently Dhami has reported the n.m.r. and ir studies on sultine 54 and its derivatives and proposed that 54 exists in a single conformation with both the chlorine and $\text{S}=\text{O}$ groupings in the axial configuration 54^{14b}.



The above route to sultines has been used very recently by the Australian workers, Henrick and Johnson¹⁶, who obtained a γ -sultine 59 from thionyl chloride and exo-tricyclo (3,2,1,0^{2,4}) oct-6-en anti-8-ol, 58.



The electrophilic exo cis addition to the double bond in a (2,2,1) system is somewhat unusual and surprisingly bicyclo (2,2,1)hept-2-en syn-7-ol, 60a, and thionyl chloride did not lead to a sultine but only to the replacement of the OH by Cl that is 60a $\rightarrow$ 61a.

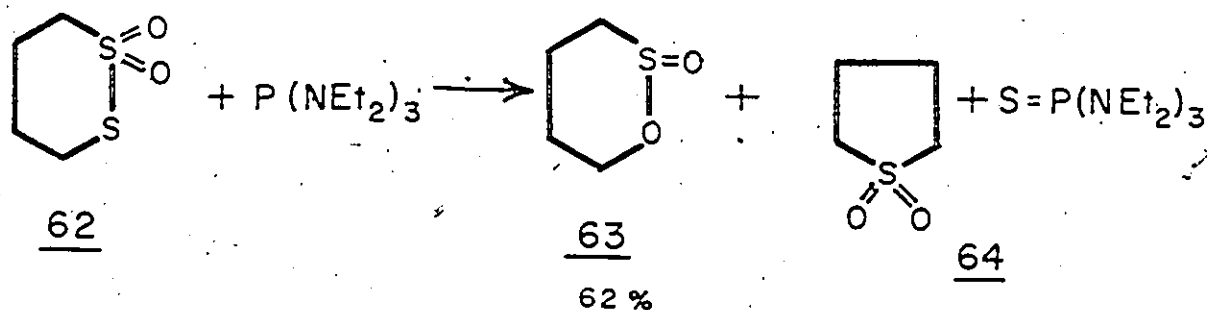
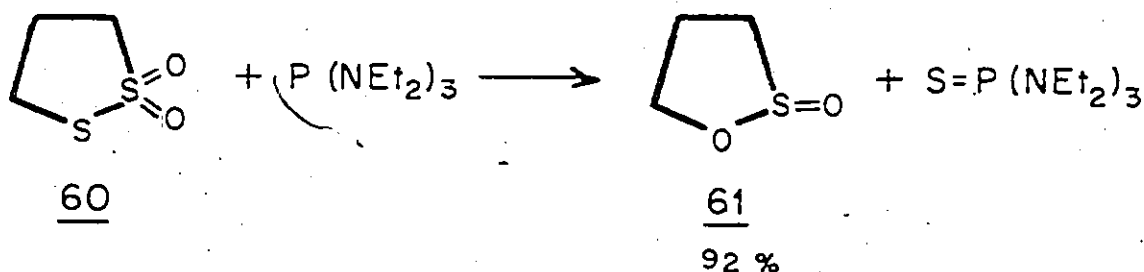


The authors, on the basis of these findings, suggested that in cyclic $\Delta^{3,4}$ unsaturated alcohols, both a fixed geometric syn relationship and an optimal distance between the hydroxyl group and the double bond are required before the sulfinate ester formation occurs.

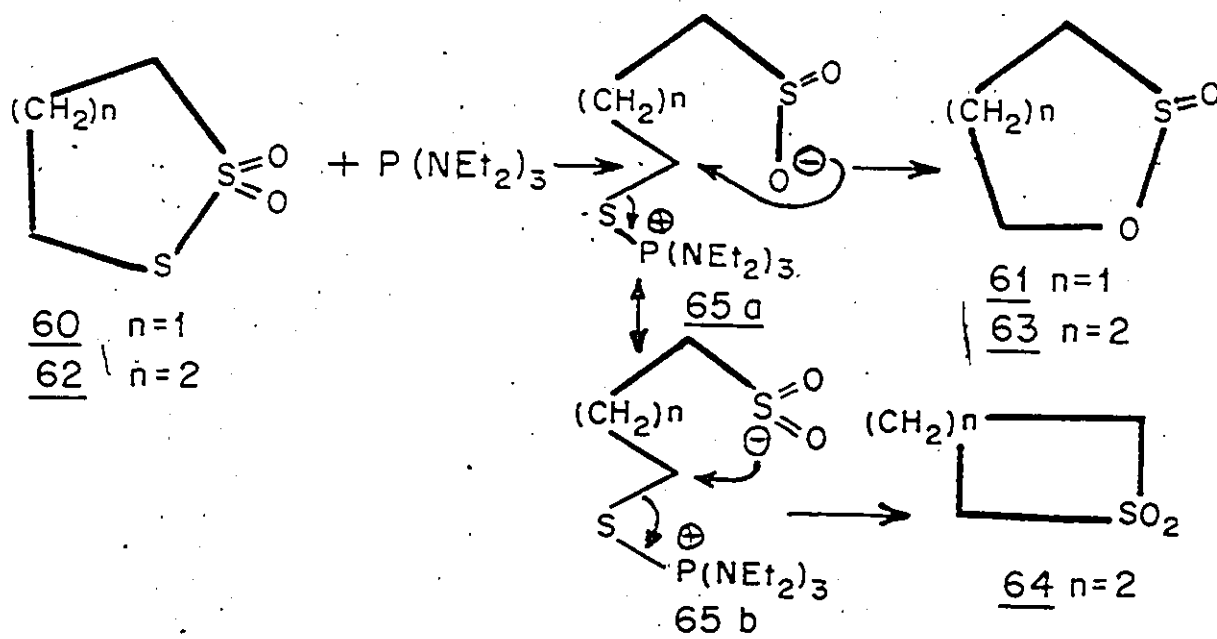
It is however more reasonable to suggest that the key feature necessary for sulfone formation is the nucleophilicity of the π bond. In 58 the intermediate produced by the interaction of the π system with the chlorosulfite group can be stabilized by the cyclopropane.

Such interactions would not be available for 60. In addition the cyclopropane interaction could explain the cis exo addition by preventing attack from the endo side.

Harpp and his co-workers¹⁷ have used an altogether different approach involving the reductive desulfurization of thiosulfonates with tris (diethylamino) phosphine. Thus the parent compound in the five-membered ring system, 1,2-oxathiolane-2-oxide, 61, was prepared in 92% yield by the reduction of 1,2-dithiolane-1,1-dioxide, 60, whereas 1,2-dithian-1,1-dioxide, 62, afforded a 62% yield of 1,2-oxathian-2-oxide, 63; tetrahydrothiophene-1,1-dioxide, 64, was a significant biproduct in the latter reaction.

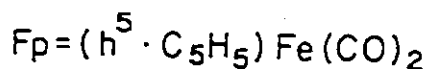
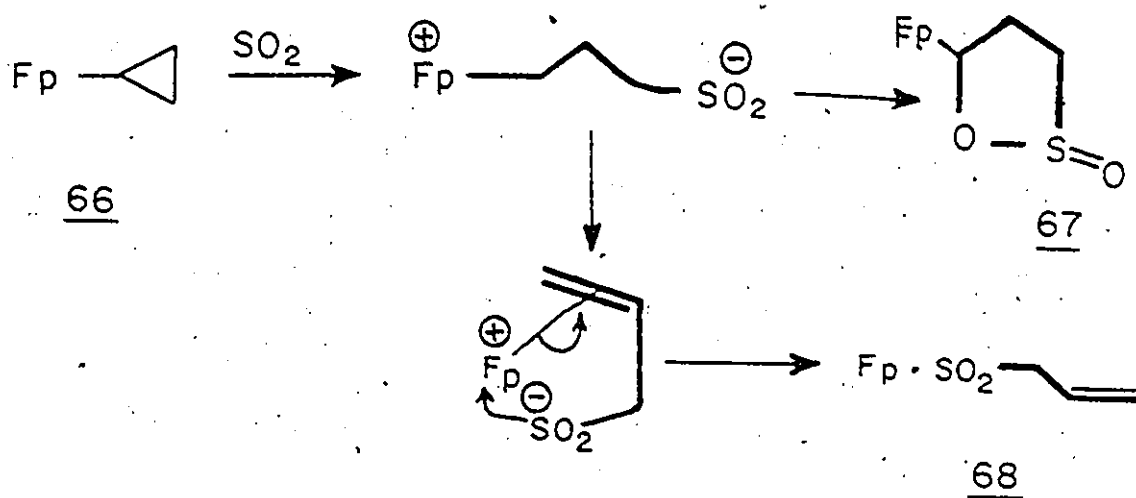


In each case the sultine was characterized by its spectroscopic data and the ready oxidation to the corresponding sultone. The authors proposed that the desulfurization reaction proceeded via an ionic intermediate of the type 65 which cyclized through either sulfur or oxygen (due to the ambident nature of the sulfinate anion) thus leading either to a sulfone or a sultine. Presumably 60 did not form a cyclic sulfone because of the difficulty in cyclizing to a four-membered ring.



Harpp et al also studied the conformational aspects of 1,2-oxathiane-2-oxide, 63, by analyzing the n.m.r. spectrum over a wide range of temperature¹⁸. The spectrum was interpretable only in terms of a single conformational isomer. A strong preference for the axial $S=O$ configuration was indicated.

Very recently a new synthesis of a metal complexed sultine has been reported¹⁹ based upon the reaction of δ -bonded cyclopropyl iron complex 66 with SO_2 . The sultine 67 and the metal allyl sulfone 68 were obtained as the major and minor products respectively.

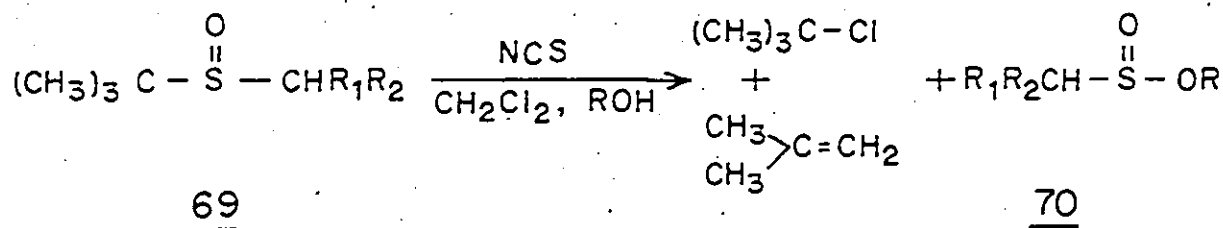


The routes to sultines discussed above are for the most part applicable to the synthesis of a limited number of sultines. For example, the thermolysis apparently is not suitable for the preparation of saturated sultines and has not been applied to the preparation of δ -sultines. Mixtures may result in the thermolysis of unsymmetrical sulfones. The route from unsaturated alcohols to sultines suffers from generally low yields due to the competing side reactions and severe structural requirements of the unsaturated alcohol. Thus only a

limited number of substitution patterns are accessible. Obviously the double bond in the unsaturated alcohol must be relatively nucleophilic in order to attack the chlorosulfite intermediate.

In the reductive desulfurization of thiosulfonates only two examples have so far been reported. Although the yields in these two specific cases are quite acceptable the success of the approach would seem to depend on the ease with which specifically substituted starting materials can be prepared. Furthermore, the method though probably quite useful for γ -sultines is less so for δ -sultines; seven-membered sultines would probably be obtained only in very low yields (if at all) due to the ease of formation of the isomeric sulfones.

From this laboratory it was reported²⁰ that t-butyl alkyl or aryl sulfoxides undergo carbon-sulfur bond cleavage upon treatment with positive halogen species such as N-bromo or N-chlorosuccinimide. When the cleavage reactions were carried out in the presence of alcohols, the products were sulfinate esters and products derived from the t-butyl carbocation.



It was therefore felt that if a hydroxyl group were part of R_1 or R_2 in 69 the sulfur containing product should be

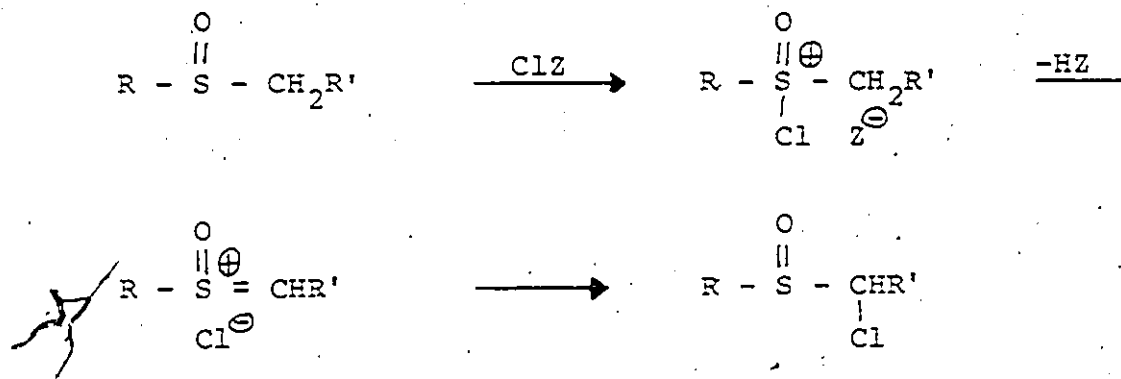
a cyclic sulfinic ester. Thus t -butyl γ -hydroxyalkyl sulfoxides should lead to γ -sultines; t -butyl δ -hydroxyalkyl sulfoxide could be precursors to δ -sultines and so on. An initial exploratory reaction by Dr. F. Jung gave an acceptable yield of 5-phenyl-1,2-oxathiolane-2-oxide from the appropriate precursor and N -chlorosuccinimide. The present study was undertaken to determine whether the above was generally applicable and would allow a synthesis of various sultines differing in ring size and the substitution pattern.

These synthetic goals, their achievements together with the stereochemical aspects and several new reactions of sultines will be described in the subsequent chapters.

CHAPTER II

Halogenation of Sulfoxides

α -Chlorination of sulfoxides with sulfuryl chloride in methylene chloride was described by Tin and Durst¹ in 1970. This was an example of a number of facile α -chlorinations of sulfoxides with positive halogen species (such as *p*-toluenesulfonyl chloride², nitrosyl chloride³, iodobenzene dichloride⁴, *t*-butyl hypochlorite⁵, N-chlorobenzotriazole⁶, N-chlorosuccinimide⁷, molecular chlorine⁸) reported during the years 1968-73. The mechanism of the reaction has been studied by a number of workers⁹⁻¹¹. Although there still remains some disagreement,¹² the more commonly accepted mechanism is as shown below:

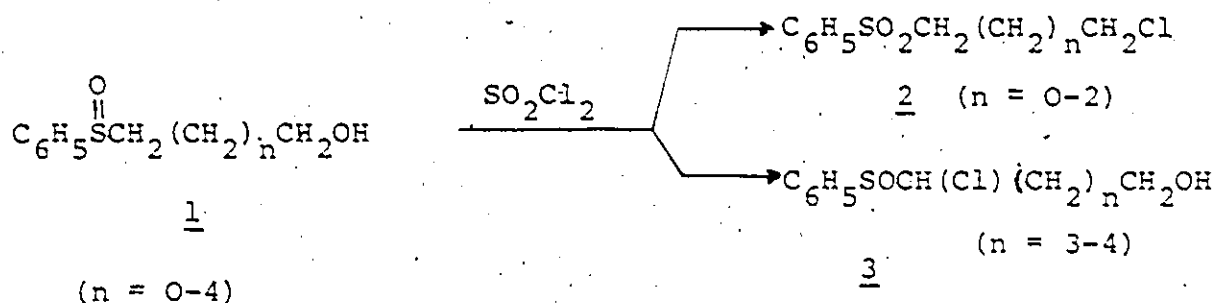


Durst and coworkers have attempted to gain information regarding the mechanism by studying the chlorination of a number of phenyl hydroxy-alkyl sulfoxides^{13,14}. It was found that hydroxysulfoxides bearing the OH group in the β , γ or δ position were converted in high yield to the corresponding

chlorosulfones. In contrast, those having the OH at a more remote position gave only α -chloro- ω -hydroxysulfoxides (Scheme 1)

SCHEME 1

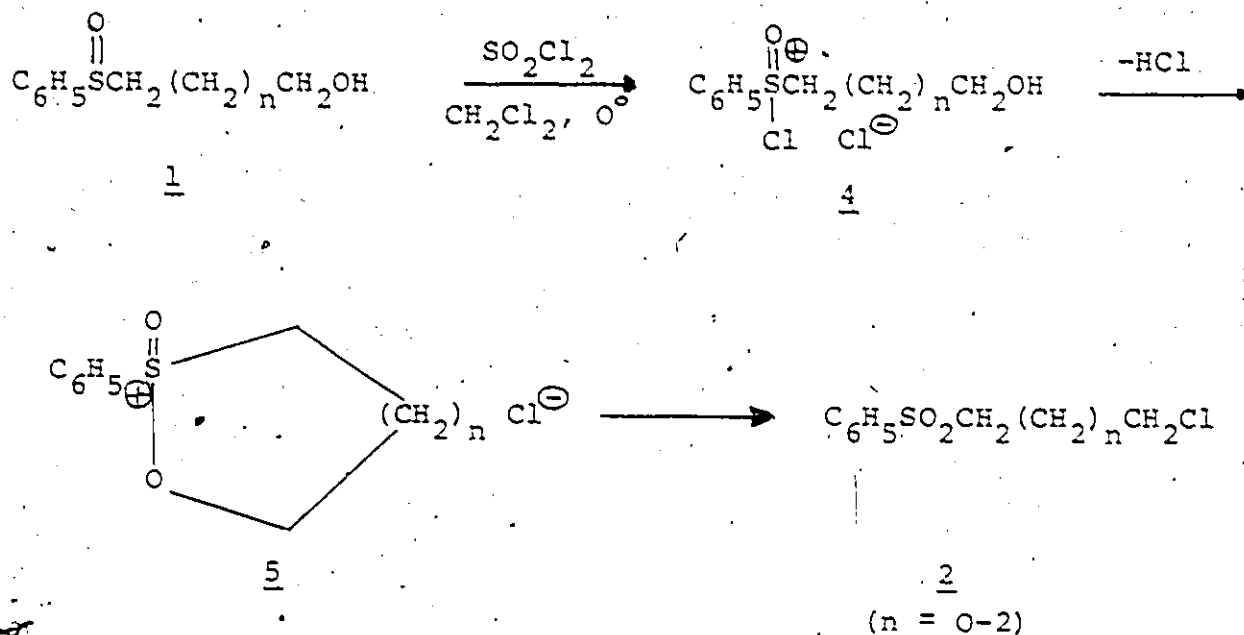
Halogenation of phenyl hydroxy alkyl sulfoxides



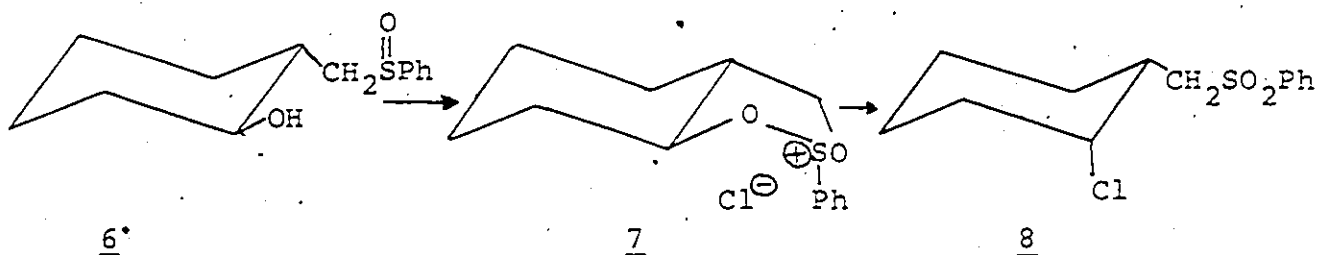
It was proposed that cyclic alkoxyoxosulfonium salts, e.g. 4, formed by intramolecular nucleophilic displacement of chloride from sulfur by the terminal hydroxyl group were intermediates in the conversion of these hydroxysulfoxides to chlorosulfones. (Scheme 2)

SCHEME 2

Formation of chlorosulfones from hydroxysulfoxides
via alkoxyoxosulfonium salts

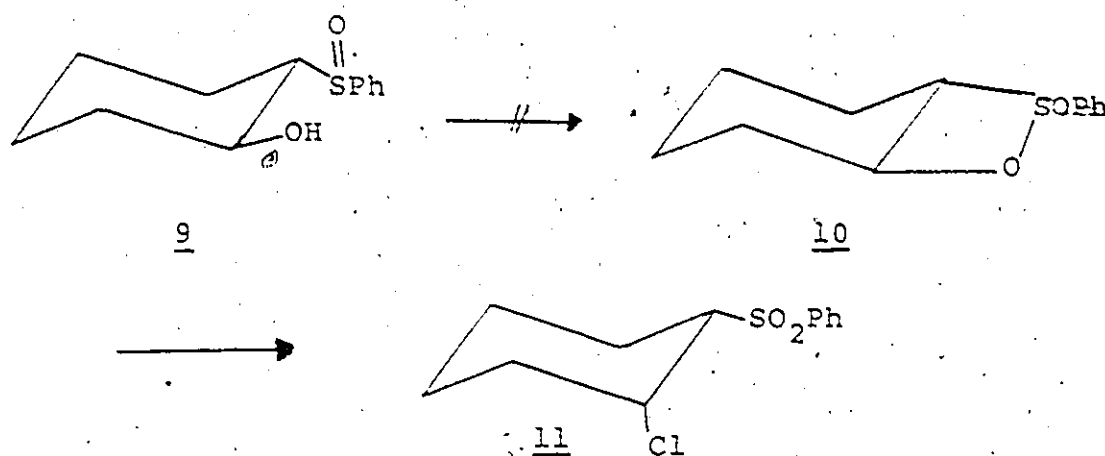


This mechanism was supported by the formation of the cis-chlorosulfone 8 from the trans-hydroxysulfoxide 6, a reaction which showed the required inversion of configuration at the carbon originally bearing the hydroxyl group.



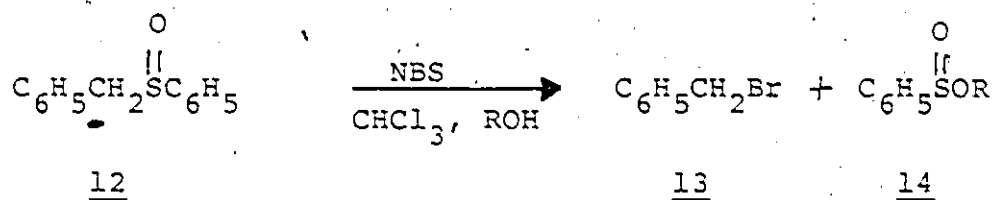
In contrast to 6 chlorination of the trans sulfoxide 9 resulted in a complicated mixture of products containing

little, if any, of the cis-chlorosulfone 11. This was rationalized in terms of the required intermediacy of 10, a highly strained trans-6,4 ring system and thus not readily formed.



The following feature of the above reactions is noteworthy and pertinent to the mechanism of sulfone formation. The displacement of chloride ion from chloro-oxosulfonium salts occurs with great ease. Simple sulfoxides such as phenyl ethyl sulfoxide can be converted in excellent yield to α -chloro-derivatives within five minutes at -78° or 0° upon exposure to sulfuryl chloride.¹⁶ However the replacement of a β -hydrogen by a hydroxyl group can completely suppress the rapid chlorination reaction by intercepting the chloro-oxosulfonium ion intermediate, despite the fact that such a reaction leads to the formation of a 4-membered ring intermediate. Indeed, chloro-oxosulfonium ions can be effectively intercepted by external nucleophiles such as water or methanol.¹⁶

In 1973, Jung and Durst observed that whereas α -bromination and α -chlorination of phenyl ethyl sulfoxide proceeded normally to the corresponding α -halosulfoxide, α -chlorination and especially α -bromination of benzyl phenyl sulfoxide, 12, led to considerable amounts of carbon-sulfur bond cleavage.¹⁷ For example, when the bromination was carried out in the presence of an alcohol alkylphenyl sulfinates, 14, and benzyl bromide, 13, were isolated as the major products.



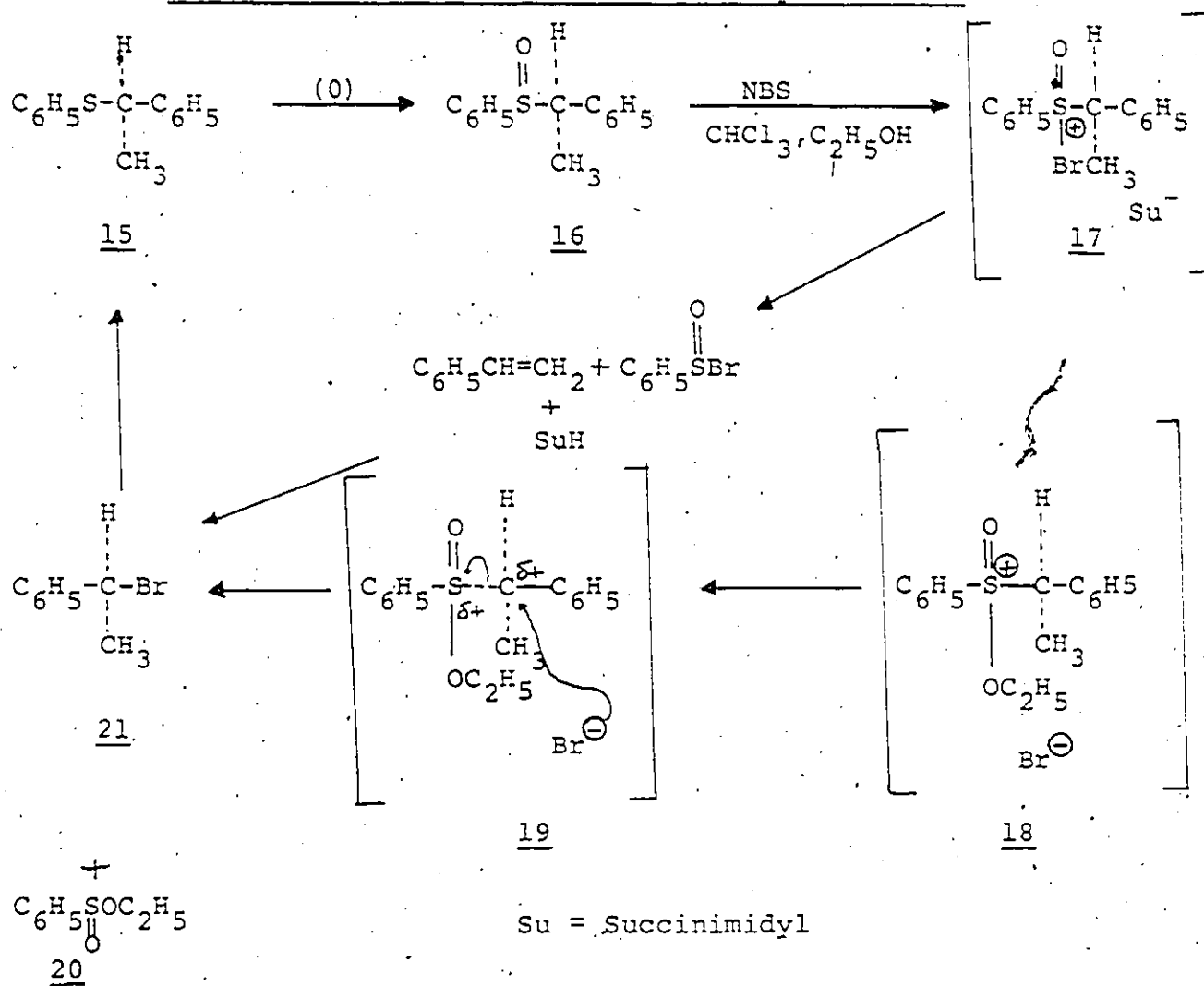
Jung and Durst investigated the mechanism of the fragmentation by studying the stereochemical course of the cleavage reaction using the optically active sulfoxide 16 prepared by the oxidation of R- α -methyl benzyl phenyl sulfide, 15. When 16 was treated with N-bromosuccinimide in CHCl_3 containing 1% $\text{C}_2\text{H}_5\text{OH}$ at 0° for 90 minutes a mixture of α -phenethyl bromide, 21, and ethyl benzene sulfinates, 20, was obtained in quantitative yield. The bromide was converted into the sulfide 15 by treatment with potassium thiophenolate in methanol, a reaction known to give complete inversion of configuration at the benzylic carbon. The optical activity of the product 15

was only 6% and the sign of the rotation same as that of the starting sulfide.

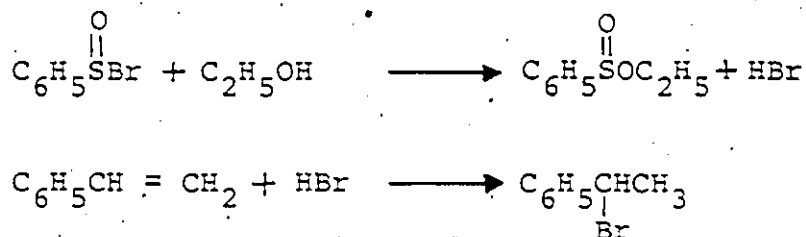
Thus the fragmentation must have occurred with net inversion of configuration at the benzylic carbon. The low optical purity of 15 is consistent with a transition state for the cleavage reaction having considerable S_N1 Character. (Scheme 3)¹⁷

SCHEME 3

Stereochemical course of C-S cleavage reaction

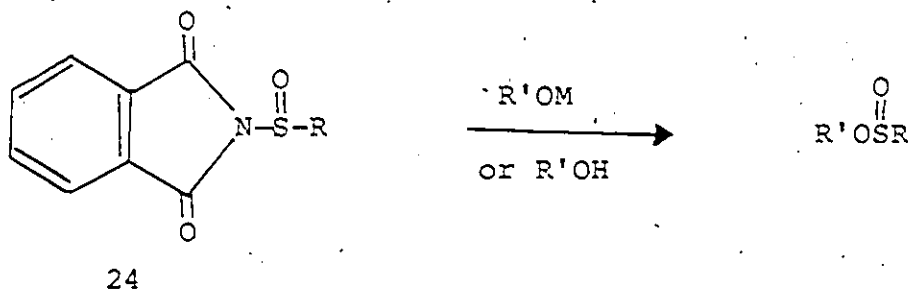
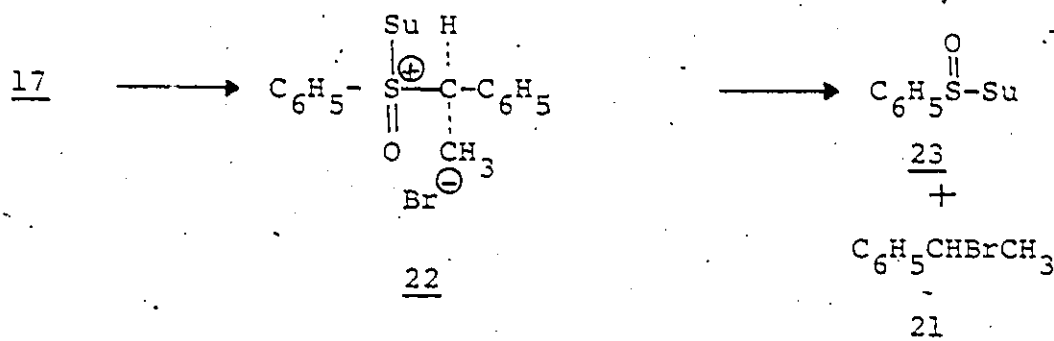


Carbon-sulfur bond cleavage is possible at several different stages in Scheme 3. For example, cleavage could take place in the bromo-oxosulfonium ion 17 to give phenyl sulfinyl bromide, styrene (by deprotonation of $\text{C}_6\text{H}_5\text{CHCH}_3^\oplus$), and succinimide. These products could be converted into those observed by the reactions shown below. The observation that the α -phenethyl-bromide obtained from the optically active sulfoxide 16 has some residual rotation rules out the above as the sole pathway. Nevertheless cleavage at this stage is feasible as shown by the fact that chlorination of benzyl methyl sulfoxide with SO_2Cl_2 in CH_2Cl_2 leads to considerable carbon-sulfur bond cleavage. (ref. 16 and below)



In view of the great ease of displacement of halide ion from halo-oxosulfonium ions by suitably placed internal hydroxyl groups (e.g. the formation of 7) a similar intermolecular displacement to form the alkoxy-oxosulfonium bromide. 18 was considered highly probable. Fragmentation of this species via a transition state such as indicated (structure 19) would yield the reaction products directly. Net inversion of configuration at the benzylic carbon would be expected on the basis of the above scheme in agreement with the experimental results.

Finally it is conceivable that the succinimide anion could displace the bromide in 17 to form the intermediate 22, cleavage of which would, in a manner analogous to 19, give the sulfinamide 23 and α -phenethyl bromide. Harpp and coworkers have shown that the analogous phthalimide derivatives 24 transfer the sulfinyl group to alcohols under basic and neutral conditions.



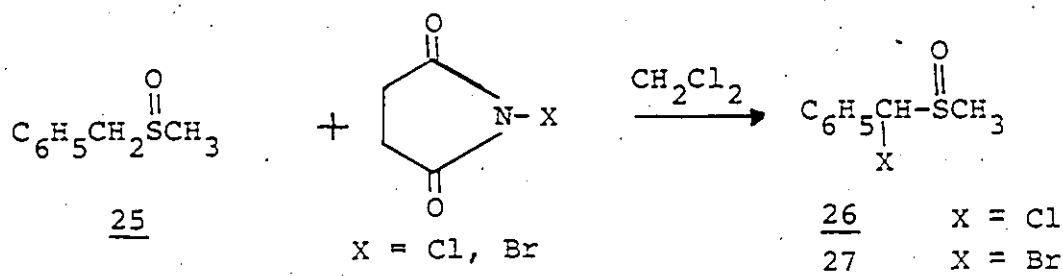
Most of the results cannot be clearly explained by any one of the above routes. Probably the best point of view is that the first two are the most probable, the predominance of one or the other being dependent on the reaction conditions. From the point of view of the major synthetic goal of this thesis - the preparation of cyclic sulfinate esters - the distinction is not of critical importance. Nevertheless some further experiments were conducted on the halogenation of benzylic sulfoxides in the hope of gaining further insight into

this reaction. These results are discussed in the following pages.

Halogenation of benzylic sulfoxides:

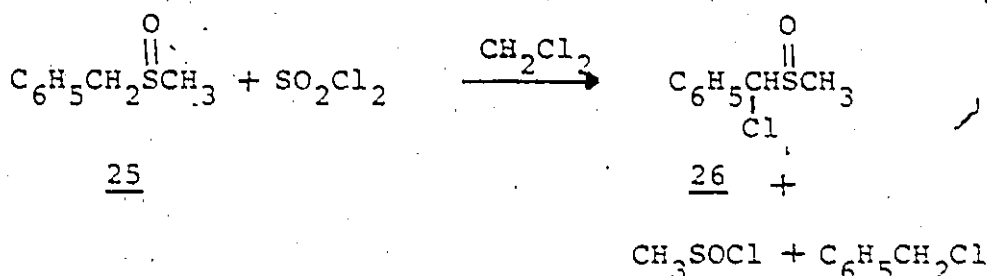
When benzyl methyl sulfoxide, 25, was treated with N-chlorosuccinimide in methylenechloride at room temperature for thirty minutes the starting material completely disappeared and the reaction mixture, after removal of succinimide and solvent, furnished α -chlorobenzyl methyl sulfoxide, 26, as 4:1 diastereomeric mixture in 91% yield. The n.m.r. of the product showed singlets at 2.2, 2.6, 5.6 and 7.3 δ . The two high field singlets, present in a 4:1 ratio, were ascribed to methyl protons in the two diastereomers. The singlet at 5.6 δ is due to the remaining benzylic proton. The aromatic protons exhibited resonance at 7.3 δ .^{1,16}

Bromination with NBS under these conditions gave the α -bromosulfoxide 27 as the major product.¹⁵



In sharp contrast, the use of sulfuryl chloride instead of N-chlorosuccinimide resulted in the formation of a complex mixture. The n.m.r. of the crude material indicated the presence of benzyl chloride and methane sulfinyl chloride in addition to α -chlorobenzyl methyl sulfoxide. The latter product was isolated

in 20% yield by column chromatography, a result in agreement with the data reported by Tin^{1,16}



When the reaction of 25 with N-chlorosuccinimide was conducted in CH_2Cl_2 : CH_3OH mixtures a complex mixture of products resulted. It was observed that the yield of α -chlorosulfoxide 26 decreased as the percentage of methanol in the solution was increased (see Table I). Other products formed in the reaction and identified by n.m.r. peak matching and analytical T.L.C. behaviour were: benzylchloride, benzyl methyl ether, benzaldehyde and benzyl methyl sulfide. A number of other peaks could be seen in the n.m.r. spectra of the total crudes but the structures which they represent have not been identified. The above compounds represent the major components in most of the spectra. Contrary to the report by Tin¹⁶, we were not able to see any significant amounts of benzyl methyl sulfone. The formation of methyl methanesulfinic acid, an expected cleavage product could not be verified possibly due to its volatility. Qualitatively the yield of benzaldehyde appeared to decrease slightly while that of benzyl methyl ether increased substantially in going from 5 to 50 to 100% methanol. Very little benzyl methyl ether was formed

when the methanol concentration was low. The peaks due to benzyl methyl sulfide were absent or weak if the n.m.r. spectra were taken immediately after evaporation of the solvents. They increased significantly over a period of a few hours. When the crude products were directly chromatographed on silica, significant amounts of the sulfide were obtained.

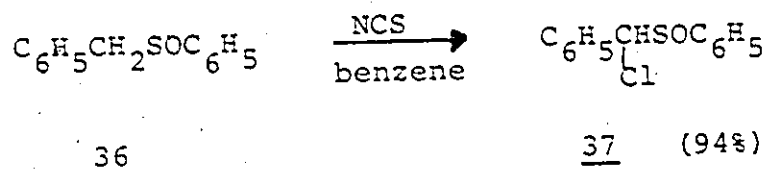
TABLE I

Reaction of benzyl methyl sulfoxide with NCS^a

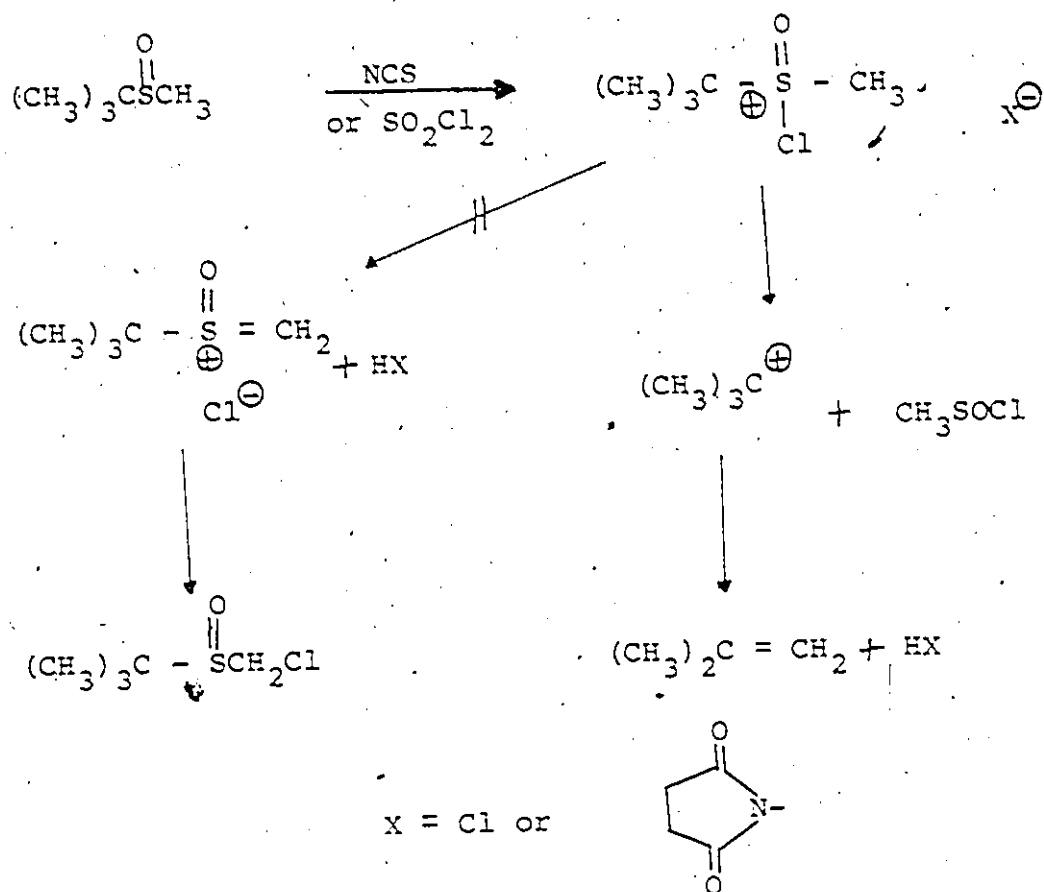
Solvent system	α -chloro sulfoxide	yields ^a of various products			
		benzaldehyde	benzylchloride	benzylmethyl ether	benzylmethyl sulfide
1. Methylene chloride	91	-	-	-	-
2. Methylene Chloride: methanol (95:5)	60	15	9	-	5
3. Methylene chloride: methanol (50:50)	50	10	5	12	8
4. Methanol	10	6	6	33	18

a. Yields are approximate, based on the isolated yield of α -chlorosulfoxide and estimation of the relative yields of other compounds from the n.m.r. of crude reaction mixture. For the entry no. 4 the yields were verified by VPC.

When benzyl phenyl sulfoxide, 36, was used as substrate the reaction was very slow in refluxing methylene chloride, about 50% of starting material was recovered after refluxing for a period of 48 hours; the α -chlorosulfoxide 37 was isolated in 40% yield. However with benzene as the solvent the reaction was complete in one hour and 37 was isolated in 94% yield. In benzene-methanol mixture the reaction did not proceed to completion presumably because of decomposition of the N-chlorosuccinimide in a competing reaction with methanol. Cleavage products, among them PhCHO and PhCH₂OCH₃ were identifiable from the n.m.r. of the crude product.



Finally t-butyl methyl sulfoxide when treated with either N-chlorosuccinimide or sulfurylchloride in methylene chloride gave no α -chlorination products. Presumably only C-S bond fragmentation occurred in both cases. (Scheme 4)

SCHEME 4Reaction of t-butyl methyl sulfoxide with NCSor SO₂Cl₂

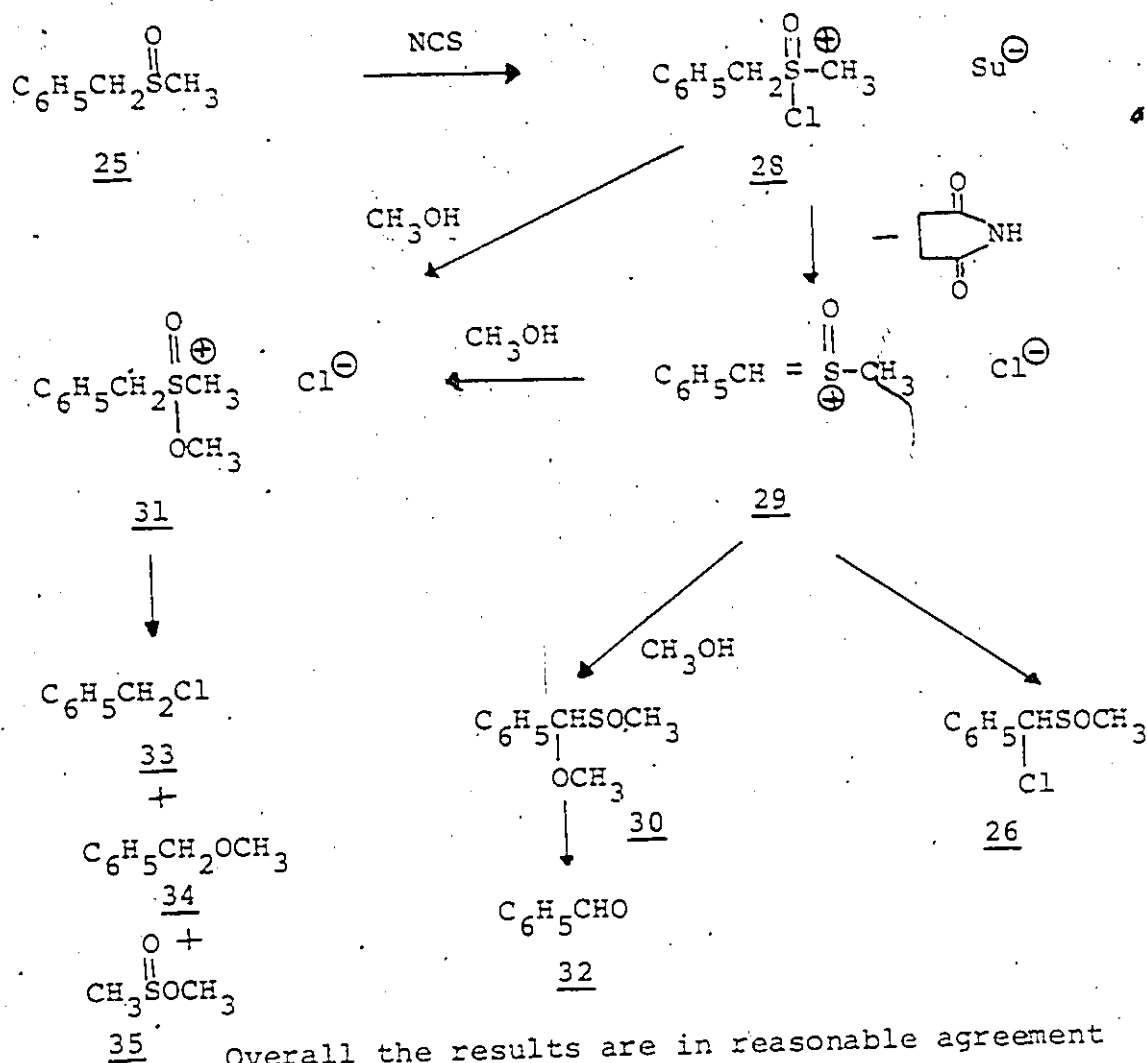
The chlorination of benzyl methyl sulfoxide in pure methylene chloride allows a comparison of the reaction pathways when X^- is changed from chloride to succinimide anion. The succinimide ion is relatively non-nucleophilic and presumably more basic than the chloride ion (pKa of succinimide = 9.6, that of HCl = -7, although in aqueous systems) and thus when it is the counter ion the chloro-oxosulfonium ion is rapidly converted to the oxo-sulfenium ion and hence to α -chlorosulfoxide 26. When halide ion is present as the counter ion the elimination of HCl to the oxo-sulfenium ion is slower thereby allowing the cleavage reaction to be dominant. Furthermore chloride ion can act as a nucleophile toward the benzylic carbon thus giving rise to the cleavage via S_N2 like processes.

The addition of methanol allows alkoxy oxo sulfonium ion formation to compete with the above two processes. The presence of methanol also changes the ionic strength of the medium thereby facilitating the C-S bond cleavage reaction (carbonium ion formation). Methanol also competes effectively with chloride ion in trapping the oxo-sulfenium ion as judged by the benzaldehyde formation. This oxidation reaction is thought to proceed via the intermediacy of α -methoxy benzyl methyl sulfoxide. A similar decomp. of α -alkoxy sulfoxides to aldehydes has been observed by Hanessian and coworkers¹⁹. Benzyl methyl ether can be formed either as cleavage product of the initial chloro-oxosulfonium salt 28 or the alkoxyoxosulfonium salt 30.

Another possible route which could account for some of the ether formation is methanolysis of benzyl chloride. The routes to these products are summarized in Scheme 5.

SCHEME 5

Reaction of benzyl methyl sulfoxide with NCS



Overall the results are in reasonable agreement with the mechanism for the α -halogenation outlined above. It is evident that the fate of the initially formed chloro-oxosulfonium ion 28 depends substantially on the reaction

conditions. The highest yields of α -chlorination are obtained in the presence of basic reagents NCS or a positive halogen species such as NCS^7 , $\text{SO}_2\text{Cl}_2^{16}$ or iodobenzene dichloride⁴ (in the presence of pyridine). Products derived from carbon-sulfur bond cleavage become the major products when either the structure of the sulfoxide or the nature of the solvent are such that carbocation formation is favoured. The formation of benzaldehyde presumably via α -alkoxy sulfoxide apparently represents, one of the few examples¹⁹, of the trapping of an oxo-sulfenium ion by an ion other than chloride or bromide.

The formation of benzyl methyl sulfide from benzyl methyl sulfoxide in the presence of an oxidizing agent is novel, to say the least. The formation of this unusual product was proved by comparison of its n.m.r. and T.L.C. behaviour with that of the commercial product and by its oxidation to benzyl methyl sulfone. Its mode of formation is an unsolved problem at this time. Presumably the isolation of some of the minor products of the reaction will shed some light on the situation.

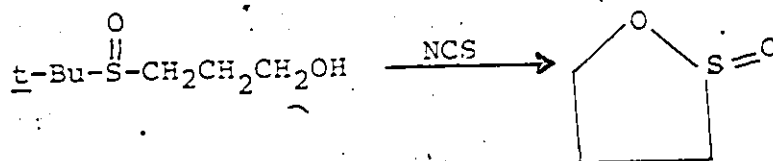
CHAPTER III

Synthesis of 5 to 8 membered sultines:a) General Introduction.

As has already been mentioned in the Chapter I (Introduction), the syntheses of only a few cyclic sulfinic acid esters (sultines) had been reported prior to the commencement of this work. No general method for preparing sultines having different ring size and substitution pattern was available.

In Chapter II (Halogenation of sulfoxides) we have seen that NCS or SO_2Cl_2 treatment of *t*-butyl alkyl sulfoxides in the presence of an alcohol led to the formation of sulfinic acid esters. It was therefore reasonable to believe that if a hydroxyl group was part of the *t*-butyl sulfoxide, the cleavage products would be cyclic sulfinic acid esters (sultines).

Jung and Durst demonstrated that this hypothesis was correct by showing that the cleavage reaction of 3-*t*-butylsulfinyl-1-propanol with N-chlorosuccinimide in methylene chloride led to the formation of 1,2-oxathiolane-2-oxide in good yield.



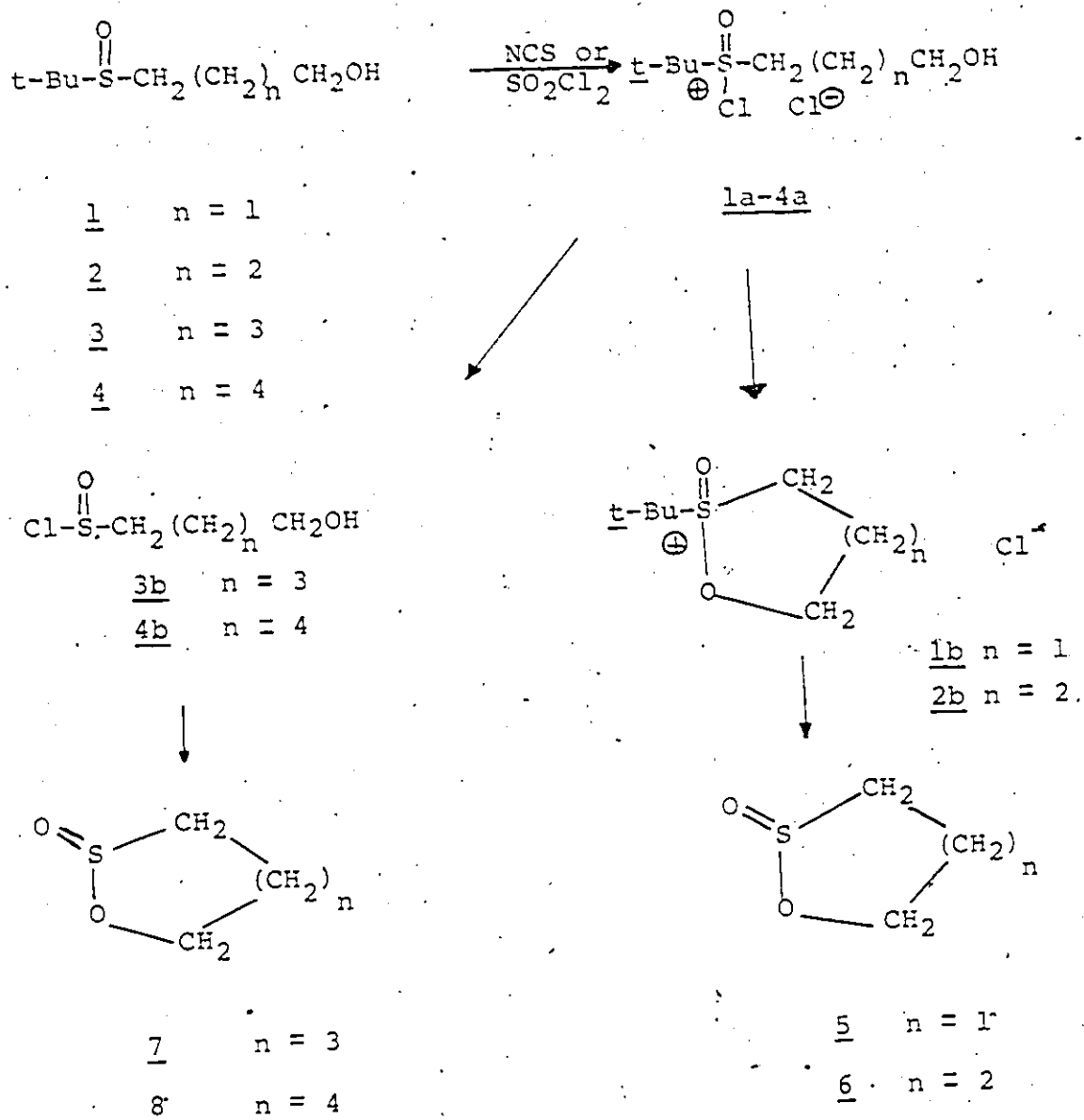
Sultines varying in ring size and bearing a variety of substituents should thus be accessible by this route.

The mechanism of the sultine formation from t-butyl hydroxyalkyl sulfoxides should be similar to that of the acyclic sulfinates discussed in the previous chapter. The initially formed chloro-oxosulfonium ions(1a - 4a) could be transformed into the observed products via one of the two following routes:

a) Intramolecular cyclization to the cyclic alkoxy-oxosulfonium chloride (1b , 2b) followed by cleavage to the sultine (3 , 4) and products derived from the t-butyl carbocation (t-butyl chloride, isobutylene, HCl), or,

b) carbon-sulfur bond cleavage at the chloro-oxosulfonium chloride stage, (3a , 4a) to the hydroxy sulfinyl chloride (3b , 4b) followed by intramolecular cyclization.

SCHEME 1

Mechanism of Formation of Sultines

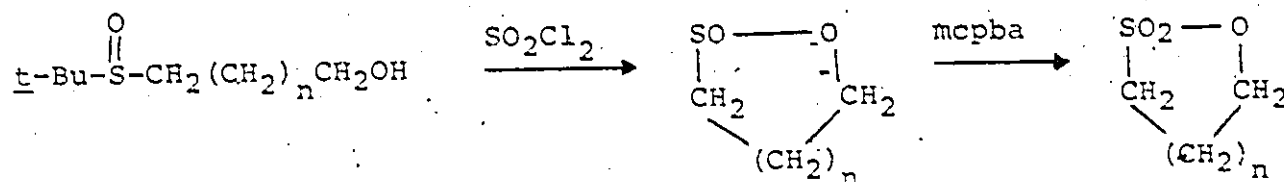
Based on the results obtained by Durst and coworkers² it is highly probable that for 5 and 6 (formation of five and six membered rings) route (a) is predominant, while for the larger membered rings, route (b) is in all likelihood the correct pathway.

A number of groups exist which stabilize the carbocations as well, or better than t-butyl, and thus could have been used as "cleaving groups". The t-butyl was chosen as the most useful because of the availability of the thiol necessary for the synthesis of the required sulfoxides, the possibility for the introduction of substituents α to the sulfur via carbanion reactions and the ease of separation of the desired products from the byproducts derived from the t-butyl carbocation. Occasionally throughout the thesis other "cleaving" groups such as benzyl and α -phenethyl were successfully employed.

b) Synthesis of unsubstituted sultines:

According to scheme 2 shown below, the unsubstituted t-butyl α -hydroxyalkyl sulfoxides 1 - 4 should yield the parent five to eight membered ring sultines 5 - 8 respectively.

SCHEME 2

Synthesis of unsubstituted sultines1, n = 15, n = 19, n = 12, n = 26, n = 210, n = 23, n = 37, n = 311, n = 34, n = 48, n = 412, n = 4

These precursors necessary to prove the generality of the sultine synthesis were readily available by the reaction of potassium t-butyl thiolate with the appropriate halohydrins in methanol, followed by oxidation with t-butyl hypochlorite³. The hydroxysulfoxides thus obtained were nondistillable, hygroscopic oils. The structure assignments were based on the straight forward method of synthesis and were in agreement with their n.m.r. and ir. spectra. (See Experimental section)

Reaction of the hydroxysulfoxides 1 - 4 with sulfonyl chloride in methylene chloride at room temperature for approximately 30 minutes led to the disappearance of the starting material and formation of the sultines 5 - 8. As expected, the

yields of sultines, though good for the five and six membered ring compounds, decreased somewhat in going to the seven and eight membered ring homologs. The yields of the sultines, together with those of the required intermediates, are summarized in Table I.

TABLE I

<u>Hydroxysulfoxide</u>	<u>Yield %</u> *	<u>Sultine</u>	<u>Yield %</u>
<u>1</u>	75	<u>5</u>	83
<u>2</u>	75	<u>6</u>	75
<u>3</u>	72	<u>7</u>	58
<u>4</u>	70	<u>8</u>	45

* Based upon hydroxysulfide as starting material.

All of the sultines were distillable colorless oils which gave correct elemental analyses. They were found to be stable at room temperature but deteriorated to brown colored liquids upon exposure to the atmosphere for several weeks. No decomposition was observed when the samples were stored in the dark at -5° for periods of more than one year.

The structures of the sultines were based on their spectroscopic properties, mass spectral and analytical data. In particular, the infrared spectrum of each sultine showed a strong absorption in the $1100-1120\text{ cm}^{-1}$ range, which was assigned to the S=O stretching frequency⁴. There appears to be less variation in the frequency of the S=O absorption in

going from the five to six membered ring sultines than there is in the change in the C=O frequency of the corresponding lactones. The small variations noted appeared to be related to the substitution pattern.

The mass spectra of the unsubstituted sultines 5 - 8 showed small parent molecular ions. Major fragmentation pathways were the loss of SO₂ (M-64) and SO₂H (M-65). A more detailed discussion of the mass spectra of the sultines is presented in Chapter V.

The n.m.r. spectrum of compound 5 showed multiplets from 1.7 - 3.2 δ (4H) and 4.0 - 4.7 δ (2H) in agreement with the data obtained by Harpp and coworkers.⁶ In addition, 5 was oxidized with excess m-chloroperbenzoic acid to the known propane 1,3-sultone, 9.⁵

The δ sultine 6 also gave an n.m.r. spectrum which was essentially identical to that reported by the Harpp group⁶. Again oxidation resulted in the formation of the known 1,4-butane sultone, 10.⁵

The n.m.r. of sultine 7 showed multiplets at δ 1.2 - 2.2 (6H), 2.6 - 2.8 (2H) and 3.8 - 4.2 (2H) which is in agreement with its structure. The two protons in the low field region (3.8 - 4.2 δ) can be ascribed to the hydrogens on the carbon α to oxygen, while those attached to the carbon α to sulfur resonated at 2.6 - 2.8 δ . The sultine structure was supported by the strong infrared absorption at 1100 cm⁻¹. The isomeric sulfone structure, thiane-S,S-dioxide,

was ruled out due to the lack of the sulfone bands around 1150 and 1300 cm^{-1} . Finally the structure was confirmed by its oxidation to 1,5-pentane sultone, 11, which showed strong infrared absorptions at 1338, 1150 and 895 cm^{-1} .^{7a}

Sultine 8 was similarly prepared from the hydroxy-sulfoxide 4. Its structure was established along the same lines as for 7. The infrared spectrum showed the characteristic absorption at 1110 cm^{-1} , while the n.m.r. spectrum showed multiplets at 1.2 - 2.2 (8H), 2.5 - 3.0 (2H) and 3.8 - 4.2 (2H). Again oxidation resulted in the formation of 1,6-hexane sultone, 12,^{7b} which showed strong infrared absorptions at 1340, 1150 and 900 cm^{-1} .

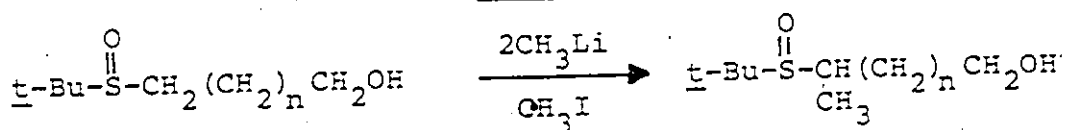
c) Sultines bearing substitution α to sulfur:

Sultines bearing alkyl substituents only α to sulfur were prepared as shown in Scheme 3.

SCHEME 3

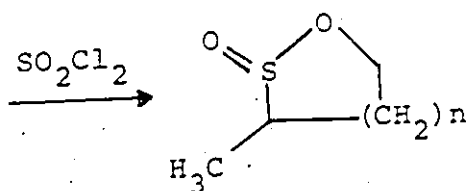
Synthesis of sultines bearing substituents

α to sulfur

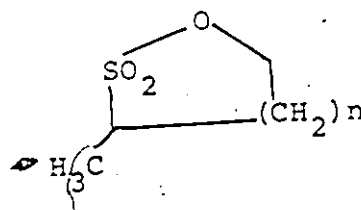


1 $n = 1$
2 $n = 2$

13 $n = 1$
14 $n = 2$



mcpba



15 $n = 1$
16 $n = 2$

17 $n = 1$

Thus the unsubstituted sulfoxides 1 and 2 were converted to their dilithio salts upon reaction with two equivalents of CH_3Li in THF at 0°C . Subsequent reaction with methyl iodide furnished the C-alkylated products 13 and 14 in 82 and 80% yields respectively. No O-alkylation was detected under these conditions despite the fact that the alkylating agent was used in excess.

When 13 was reacted with sulfuryl chloride in methylene chloride it gave 3-methyl-1,2-oxathiolane-2-oxide, 15, in 72% yield. Similarly δ -sultine 16 was obtained from 14 in 78% yield.

Sultine 15 showed infrared absorption at 1100 cm^{-1} and n.m.r. peaks at 1.22 & 1.38, (d, $J = 7\text{Hz}$, 3H), 1.7 - 3.5 (m, 5H) and 4.2 - 4.9 (m, 2H). It was oxidized with *m*-chloroperbenzoic acid to the sultone 17, characterized by infrared absorptions at 1325, 1130 and 880 cm^{-1} . The n.m.r. of the sultone displayed a doublet at 1.46 δ ($J = 7\text{Hz}$, $\text{O-SO}_2\text{-CH}$) and
 CH_3
 multiplets at 2.0 - 2.9 (2H), 3.2 - 3.6 (1H) and 4.2 - 4.6 (2H). These were identical with those available in this laboratory.¹⁰

Sultine 16 showed infrared absorption at 1120 cm^{-1} and n.m.r. peaks at 1.08 (d, $J = 6\text{Hz}$, 3H), 1.1-3.0 (m, 5H), 3.3 - 3.8 (m, 1H) and 4.0 - 4.6 (m, 1H).

It is noteworthy that the sultine 15 was obtained as a diastereomeric mixture. In general γ -sultines were

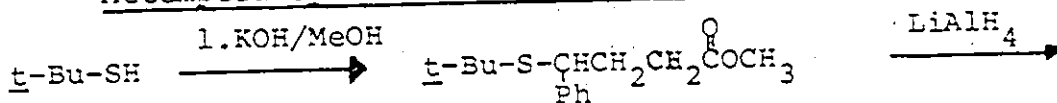
obtained as nonseparable diastereomeric mixtures while in the case of δ -sultines only the most stable isomer was isolated. (See figures 1 and 2).

Although only two examples of this sequence were actually carried out it is quite obvious that the scheme is applicable to the preparation of a wide variety of 3-substituted sultines. Alkyl or aryl substituents in other positions are compatible with this route.

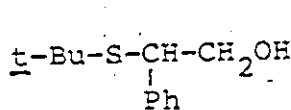
It is obvious that a phenyl group cannot be introduced in this manner. An attempt was made to synthesize 3-phenyl-1,2-oxathiolane-2-oxide, 21, according to the reaction sequence depicted in Scheme 4.

SCHEME 4

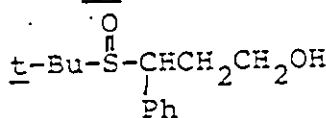
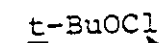
Attempted synthesis of 3-phenyl-1,2-oxathiolane-2-oxide



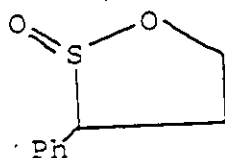
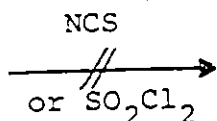
2. $\text{PhCH} = \text{CHCOOCH}_3$



19



20



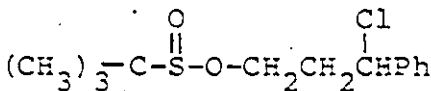
21

Michael addition of t-butyl mercaptan to methyl cinnamate gave the sulfide ester 18 in 50% yield. This compound was successively reduced with LiAlH_4 (100%) to 19 and then oxidized with t-butyl hypochlorite to the hydroxy-sulfoxide 20, m.p. $94 - 96^\circ$, (50%). The n.m.r. spectrum of 20 showed peaks at 1.03 (s, 9H), 1.9 - 2.6 (m, 3H), 3.3 - 4.2 (m, 3H) and 7.2 - 7.5 (m, 5H).

Attempted cyclization of the above hydroxysulfoxide with SO_2Cl_2 in the usual manner yielded none of the sulfone 21. The n.m.r. spectrum of the crude product showed a prominent signal at $\delta = 1.33$ assigned to a t-butyl group. Most of the remaining peaks could be fitted to the open chain ester 22. Attempted purification of the supposed 22 via column chromatography led only to further decomposition products.

In a subsequent experiment SO_2Cl_2 was replaced by NCS. Again no pure substance was isolable by chromatography of the crude reaction mixture.

These results are not altogether surprising. The sulfoxide group of 20 is flanked on one side by t-butyl group and on the other by a substituted benzyl group. Because of the greater stability of the carbocation derived from the latter group, cleavage of the C^{*}-S bond in 20b would be expected to predominate.



$(\text{CH}_3)_3\text{C}-\text{S}(=\text{O})-\text{CH}_2\text{Ph}$
 $\xrightarrow[2. \text{CH}_2=\text{CH}_2]{1. \text{CH}_3\text{Li}}$
 $(\text{CH}_3)_3\text{C}-\text{S}(=\text{O})-\underset{\text{Ph}}{\text{CH}}\text{CH}_2\text{CH}_2\text{OH}$

20

This is based on a sequence developed for the syntheses of γ -sultines substituted α to oxygen discussed

in the next section.

d) Sultines bearing substitution α to oxygen:

Hydroxysulfoxides needed as precursors for γ -sultines bearing substitution α to oxygen were synthesized starting with a variety of *t*-butyl alkyl sulfoxides and epoxides. The sulfoxide was metalated by treatment with one equivalent of methylolithium in tetrahydrofuran at 0 °C under nitrogen and subsequently reacted with the appropriate epoxide for several hours at room temperature. These reactions afforded the desired hydroxysulfoxides in excellent yields. With unsymmetrical epoxides essentially complete regioselectivity was observed in the epoxide ring opening; attack of the α -lithio-salts occurred, as expected, at the least hindered position.

Cyclization of the hydroxysulfoxides afforded sultines bearing substitution at C-5. The method proved to be very versatile for the preparation of γ sultines and a number of them were prepared according to the reaction sequence shown in Scheme 5. The yields of hydroxysulfoxides and the sultines are recorded in Table II. The spectroscopic properties (ir. and n.m.r.) of these sultines are been presented in Table III, those of the intermediates are given in the Experimental Section of this thesis.

SCHEME 5

Synthesis of C-5 substituted γ -sultines:

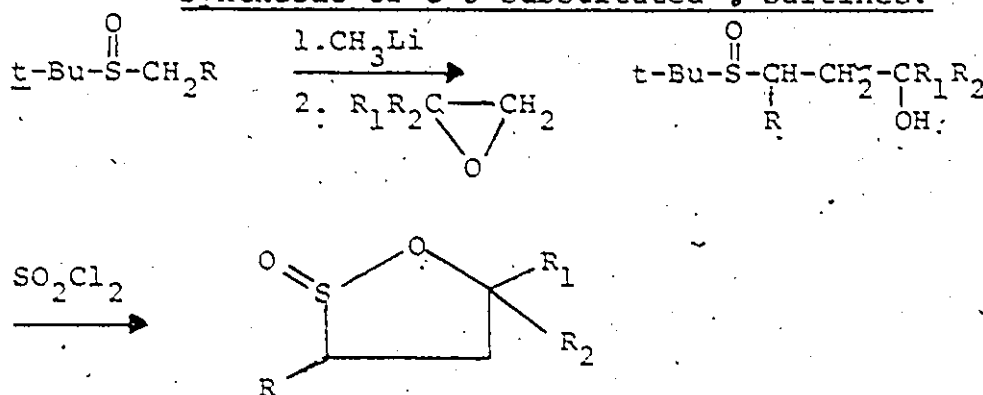


TABLE II

Yields of C-5 substituted γ -sultines and their precursors:

R	R ₁	R ₂	Hydroxy Sulfoxide	Yield %	Sultine	Yield %
H	H	CH ₃	<u>22</u>	88	<u>23</u>	80
H	H	Ph	<u>24</u>	85	<u>25</u>	96
CH ₃	H	Ph	<u>26</u>	88	<u>27</u>	96
CH ₃	H	CH ₃	<u>28</u>	90	<u>29</u>	90
H			<u>30</u>	60	<u>31</u>	88

Figure 1. N.M.R. spectrum of
5-methyl-1,2-oxathiolane-2-oxide

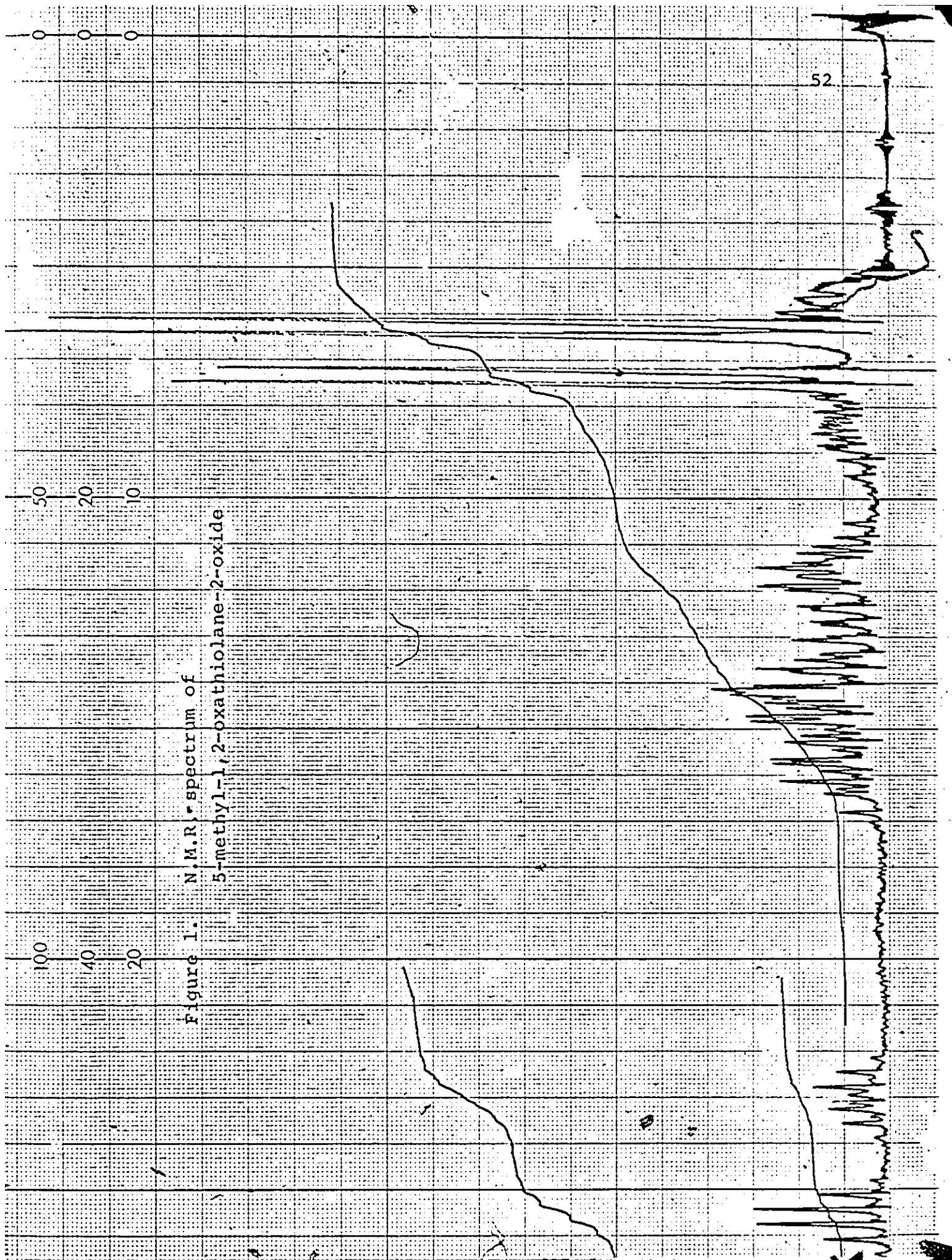
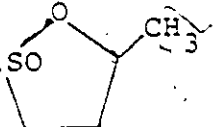
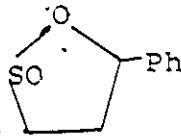
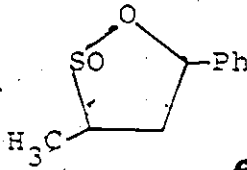
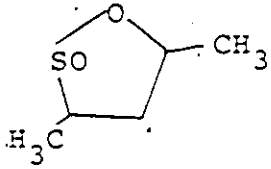
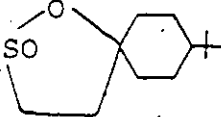


TABLE III
Spectroscopic properties of C-5 substituted
 γ -sultines

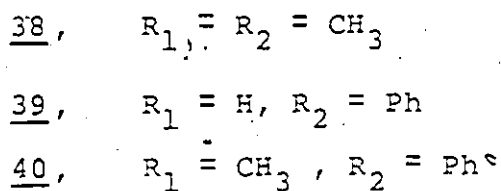
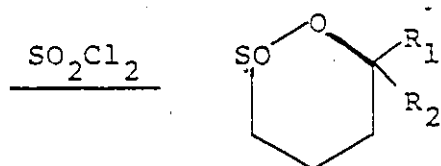
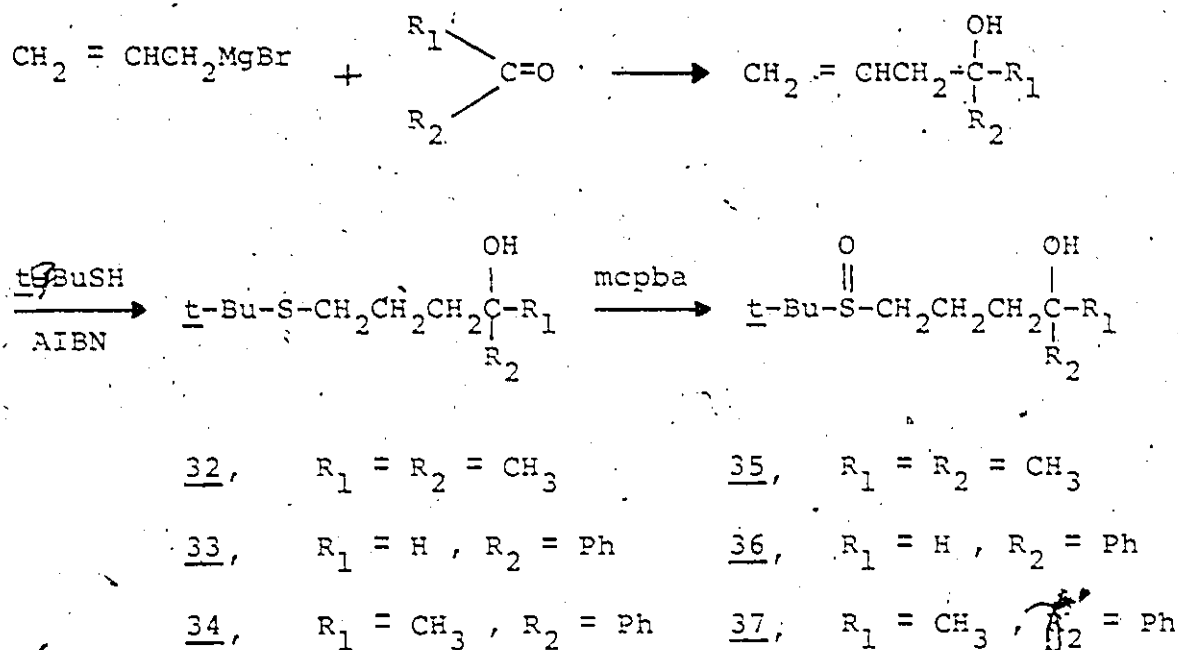
<u>Sultine</u>	<u>Structure</u>	<u>ir</u> <u>(cm⁻¹)</u>	<u>n.m.r. (ppm)</u>
<u>23</u>		1120	1.39 & 1.59 (d, J= 6H ₂ , 3H); 2.2 - 3.4 (m, 3H); 4.7 - 5.2 (m, 1H).
<u>25</u>		1110	2.5 - 3.5 (m, 4H); 5.5 and 6.0 (m, 1H); 7.2 - 7.5 (m, 5H).
<u>27</u>		1105	1.25 and 1.31 (d, J= 6H ₂ , 3H); 2.0 - 3.0 (m, 2H); 3.3 - 3.6 (m, 1H); 5.4 - 6.0 (m, 1H); 7.1 - 7.4 (m, 5H).
<u>29</u>		1105	1.1 - 1.6 (4 ds, 6H); 1.7 - 2.7 (m, 2H); 2.8 - 3.5 (m, 1H); 4.5 - 5.3 (m, 1H).
<u>31</u>		1110.	0.86 (s, 9H); 1.3 - 2.5 (m, 11H); 3.0 - 3.2 (m, 2H).

Unfortunately this approach cannot be readily extended to the synthesis of δ sultines. In principle the reaction of α -lithio t-butyl alkyl sulfoxides with oxetanes

would give the required δ -hydroxysulfoxides. Since suitably substituted oxetanes are not readily available the generality of the approach was considered too limited to warrant investigation.

Use was therefore made of the radical addition of ⁸
~~t~~-butyl thiol to unsaturated alcohols. Addition of thiols ⁹
to carbon-carbon double bonds is well known and a variety of unsaturated homoallylic alcohols are either commercially available or can be readily synthesized from allylic Grignard reagents and carbonyl compounds. Thus the synthesis of the appropriate δ -hydroxy t-butyl alkyl sulfides was readily achieved. These were oxidized to the corresponding hydroxysulfoxides and subsequently cyclized to the desired sultines. (Scheme 6).

SCHEME 6

Synthesis of C-6 substituted δ -sultines

As an example the synthesis of 6,6-dimethyl-1,2-oxathiane-2-oxide, 38, a compound of interest from a conformational point of view (see Chapter IV) will be discussed in some detail. Thus addition of acetone to a solution of allylmagnesium bromide in ether afforded 4-pentene-2-ol in 60% yield.

This alcohol, when refluxed with one equivalent of t-butyl thiol in the presence of AIBN was converted into the sulfide 32 (80%). None of the isomeric (Markownikoff addition) product could be detected in the n.m.r. of the crude product. Oxidation of 32 with m-chloroperbenzoic acid (70%) followed by cyclization with sulfur chloride (70%) completed the synthesis of 38.

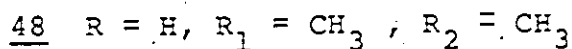
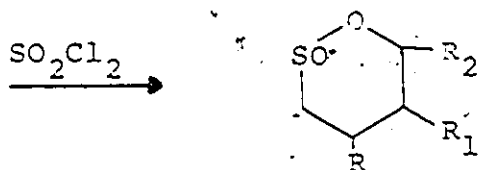
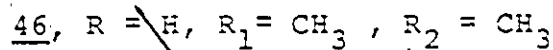
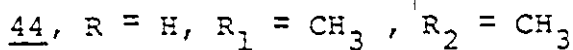
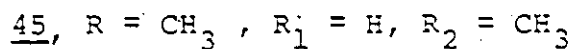
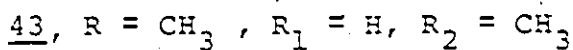
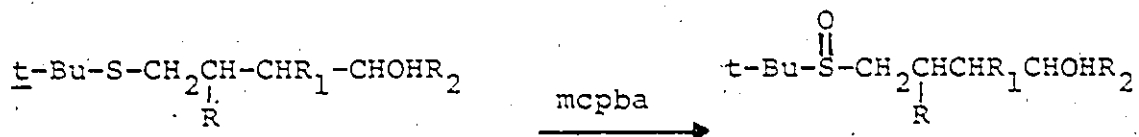
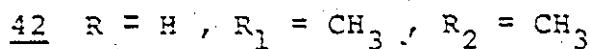
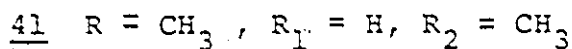
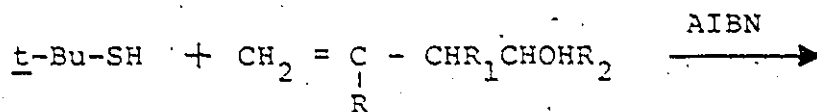
The 6-phenyl isomer 39 was prepared in the analogous manner in 45% overall yield from allylmagnesium bromide and benzaldehyde.

Similarly allylmagnesium bromide and acetophenone served as the starting materials for the preparation of 6-phenyl-6-methyl-1,2-oxathiane-2-oxide. The overall yield was 45%.

4,6-Dimethyl-1,2-oxathiane-2-oxide, 47, and 5,6-dimethyl-1,2-oxathiane-2-oxide, 48, required for the conformational studies of 6 sultines, were prepared as in Scheme 6a starting with the commercially available alcohols 41 and 42 respectively (see Experimental).

SCHEME 6a

Synthesis of C-6 substituted δ sultines
from homoallylic alcohols

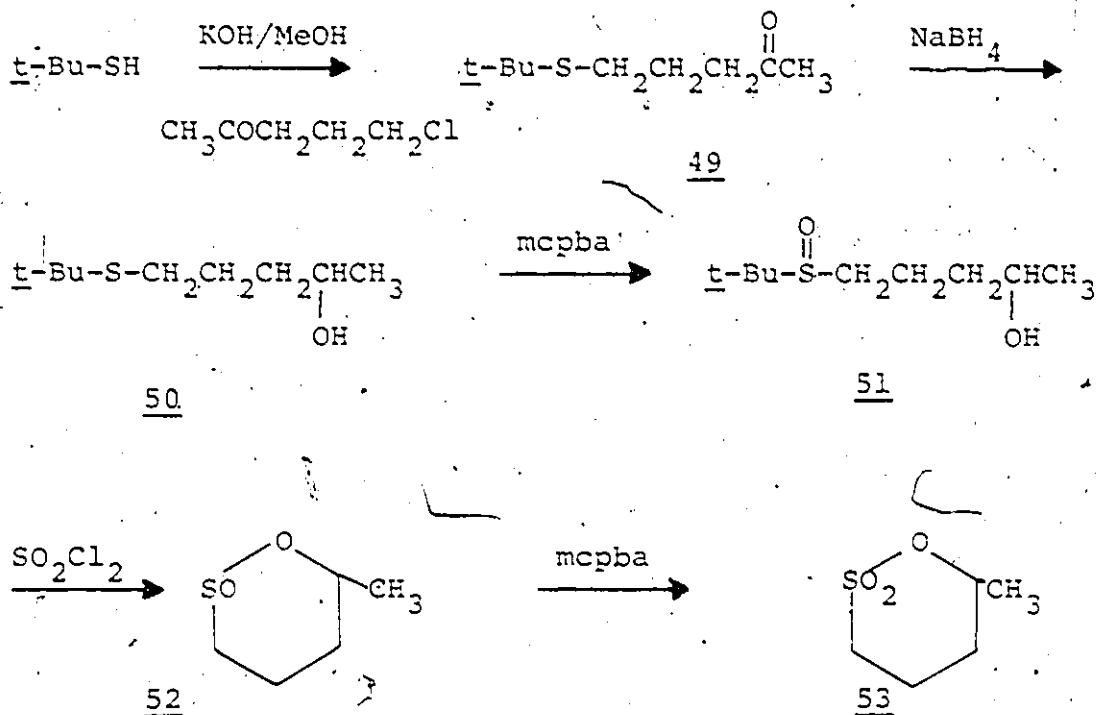


6-Methyl-1,2-oxathiane-2-oxide, 52, although obviously accessible via Scheme 6, using allylmagnesium bromide and acetaldehyde as starting materials, was, in fact, prepared

by the alternate route outlined in Scheme 7.

SCHEME 7

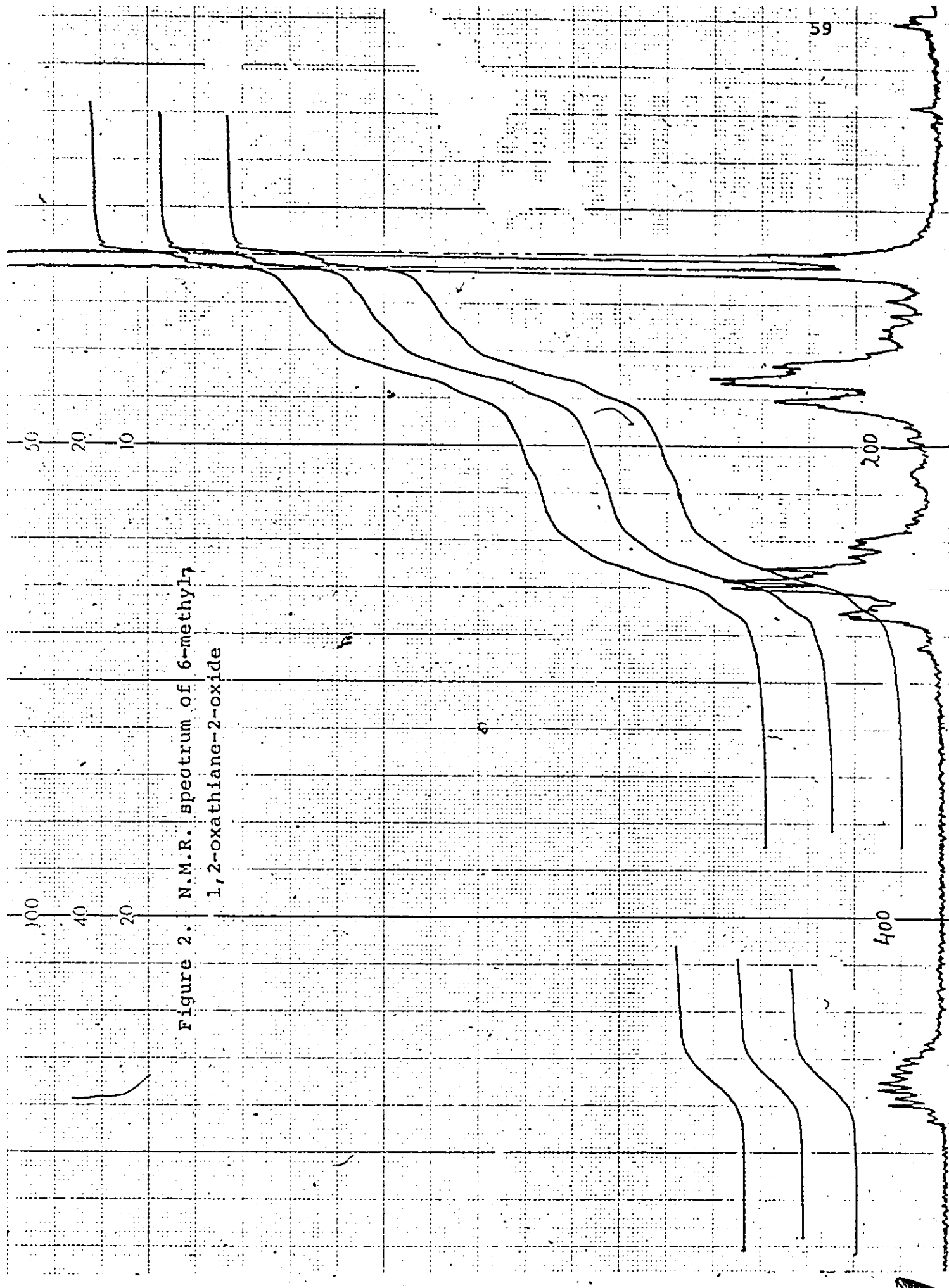
Synthesis of 6-methyl-1,2-oxathiane-2-oxide



Reaction of t-butyl thiolate with 5-chloro-2-pentanone in methanol afforded 5-t-butylthio-2-pentanone in 45% yield. This substance was reduced with sodium borohydride (95%), and the resulting hydroxysulfide oxidized with m-chloroperbenzoic acid to yield 5-t-butylsulfinyl-2-pentanol, 51, (80%).

Compound 51 showed infrared absorption at 3360 and 1005 cm^{-1} . In the n.m.r. spectrum there were peaks at 1.20 and 1.26 (d, $J = 6\text{Hz}$, 3H); 1.25 (s, 9H); 1.4 - 2.2 (m, 4H); 2.3 - 2.9 (m, 2H) and 3.2 - 4.0 (m, 2H). Cyclization of 51 in the

Figure 2. N.M.R. spectrum of 6-methyl,
1,2-oxathiane-2-oxide



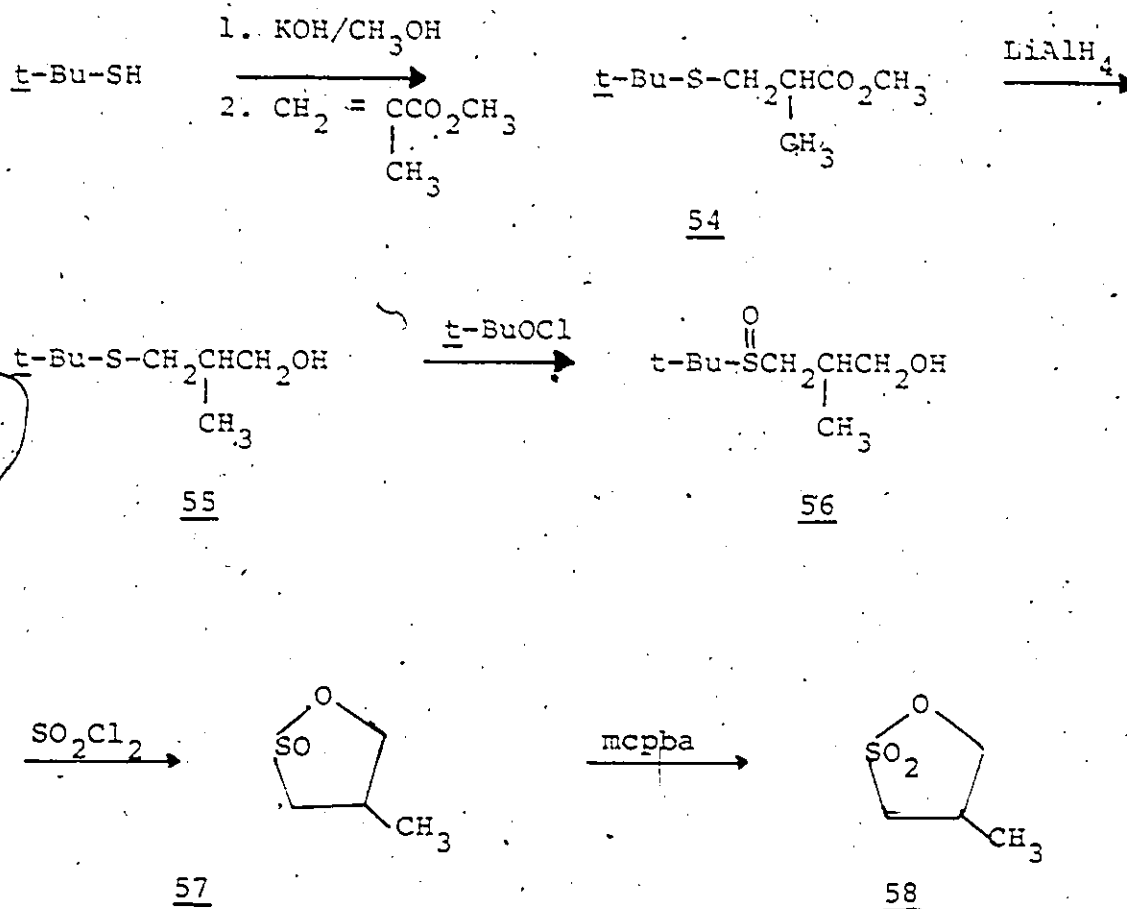
usual manner furnished 6-methyl-1,2-oxathiane-2-oxide, 52, in 85% yield. It was characterized by its ir, n.m.r. and mass spectra and by oxidation to the known 6-methyl-1,2-oxathiane-2,2-dioxide, 53.⁵

e) Sultines bearing substituents β to oxygen or sulfur:

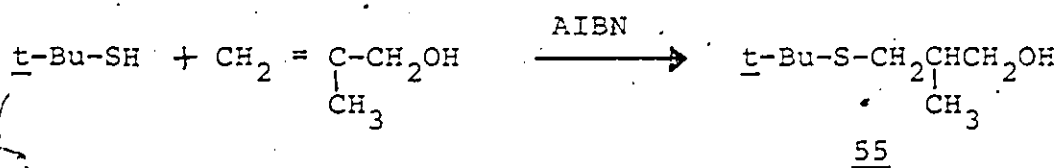
Substitution was more difficult to achieve at these positions than in the positions discussed earlier. In the case of γ sultines the problem was solved by employing a Michael addition reaction of t-butylthiolate to α, β -unsaturated carbonyl compounds. Thus t-butylthiolate was added to methyl methacrylate and the sulfide ester 54 thus obtained in 90% yield was reduced quantitatively with lithium aluminium hydride to the hydroxysulfide 55. Oxidation of 55 with t-butyl hypochlorite afforded 2-methyl-3-t-butylsulfinyl-propanol, 56, in 70% yield. Cyclization of 56 with sulfur chloride in methylene chloride gave 4-methyl-1,2-oxathiolane-2-oxide, 57, in 75% yield. Thus the overall yield of sultine 57 employing this route was 47%. (Scheme 8).

Sultine 57 showed the characteristic S=O infrared absorption at 1110 cm^{-1} and n.m.r. peaks at 1.07 & 1.18 (d, $J = 7\text{ Hz}$, 3H); 2.2 - 4.9 (m, 5H). It was oxidized with m-chloroperbenzoic acid to the sultone 58.

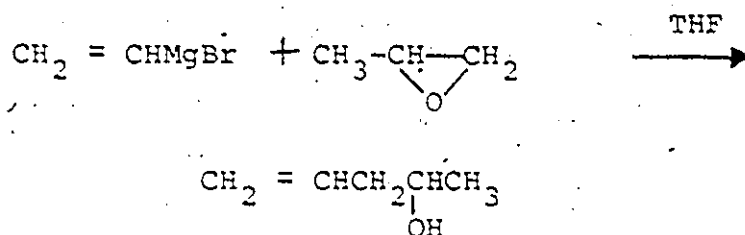
SCHEME 8

Synthesis of 4-methyl-1,2-oxathiolane-2-oxide

During the later part of this work it was realized that the hydroxysulfide 55 could be prepared more conveniently and in higher yield by the radical addition of t-butyl thiol to methallyl alcohol (yield 92%). Thus 57 is available in three simple steps from methallyl alcohol.



of 4-pentene-2-ol could be obtained from this reaction.

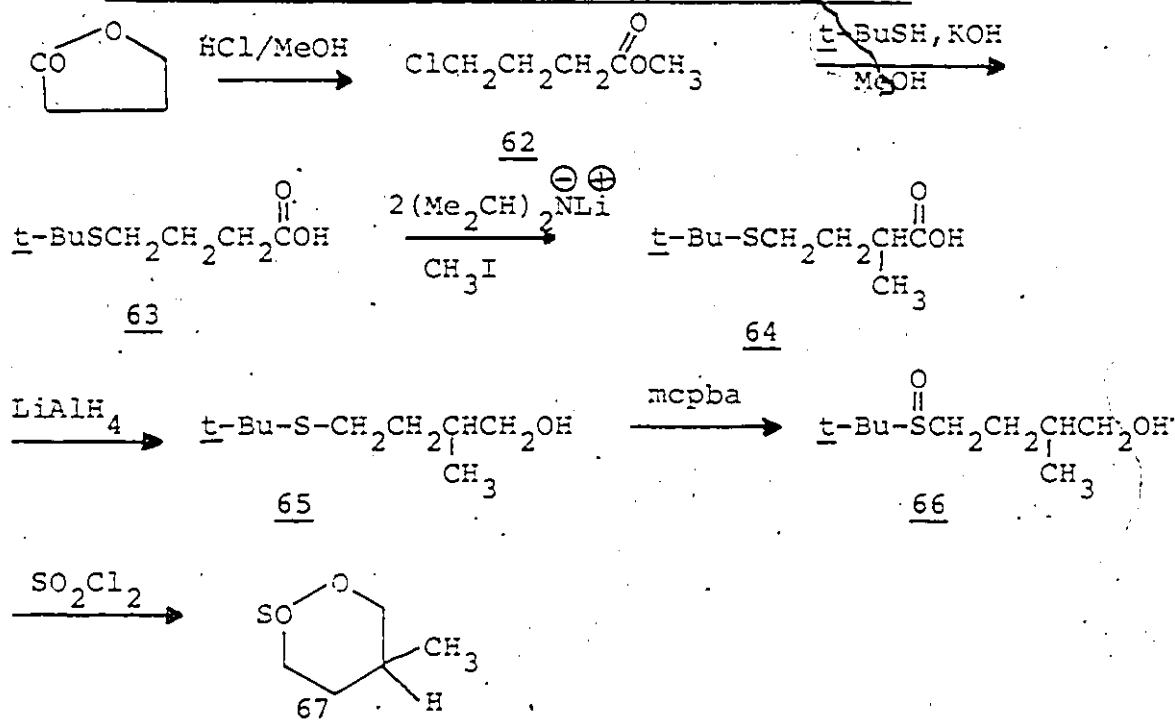


This route to 5-methyl-1,2-oxathiane-2-oxide was therefore abandoned.

The sultine 67 was successfully synthesized according to ~~the~~ Scheme 10.

SCHEME 10

Synthesis of 5-methyl-1,2-oxathiane-2-oxide

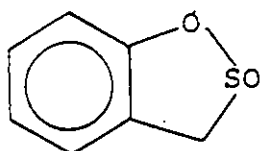


γ -Butyrolactone was converted to methyl 4-chlorobutanoate, 62, by bubbling HCl gas through a solution of the lactone in methanol (90%). 4-t-Butylthiobutanoic acid, 63, was obtained from 62 in 40% yield, by treatment of 62 with t-butyl thiol in methanolic KOH. The acid 63 was converted to its dianion by treatment with two equivalents of lithium¹² di-isopropylamide in THF.

This dianion underwent C-alkylation upon quenching with methyl iodide to afford 64. From here the synthesis required only reduction with lithium aluminium hydride and oxidation with m-chloroperbenzoic acid to obtain the required oxidation states of 66. This hydroxysulfoxide showed infrared absorption at 3340 and 1000 cm^{-1} . The n.m.r. spectrum of 66 had peaks at 0.94 & 0.95 (2d, each with $J = 6\text{Hz}$, 3H; 1.25 (s, 9H; 1.6 - 1.9 (m, 3H); 2.0 - 2.4 (m, 3H); 3.2 (d, 5Hz, 2H). Cyclization of 66 with sulfuryl chloride gave 67 in 65% yield. Sultine 67 was characterized by its infrared absorption at 1105 cm^{-1} and the n.m.r. peaks at 0.87 (d, $J = 6\text{Hz}$, 3H); 1.3-3.0 (m, 5H); 3.3 - 4.5 (m, 2H).

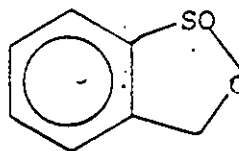
f) Synthesis of Benz-fused sultines:

Two unsubstituted benz-fused γ -sultines are possible.



68

and



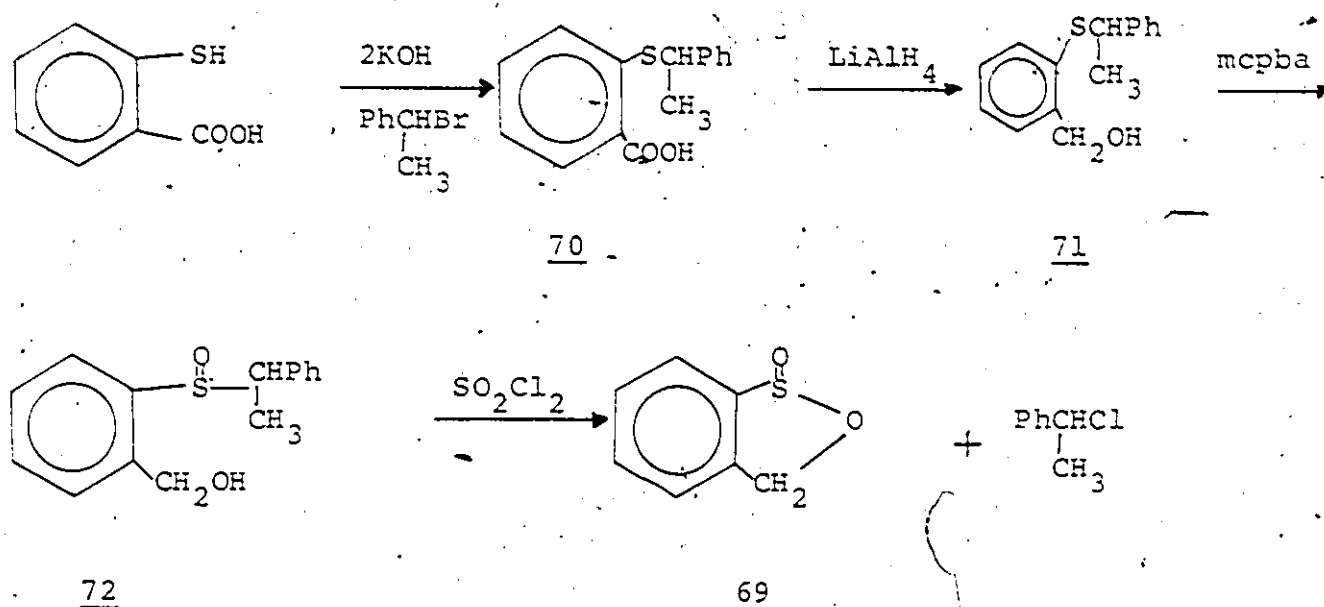
69

The synthesis of 69 has been described by King¹³ and coworkers but that of 68 has not been reported to the best of this author's knowledge.

As part of this work 69 was synthesized as outlined in Scheme 11.

SCHEME 11

Synthesis of 3H-2,1-benzoxathiole-1-oxide



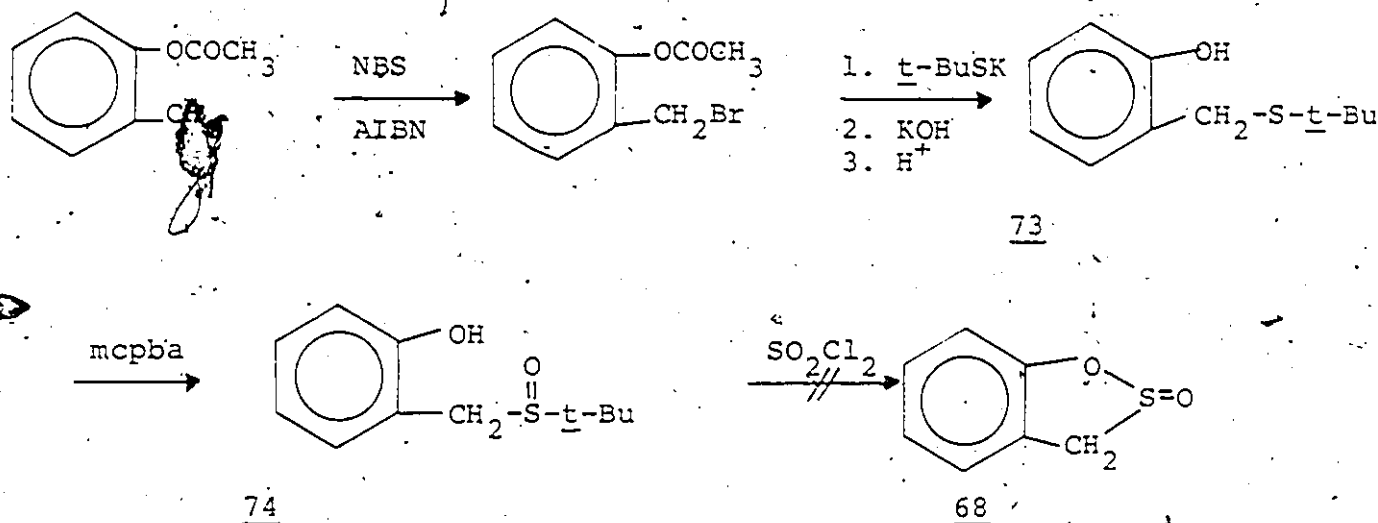
The dianion of *o*-mercaptobenzoic acid was alkylated with α -phenethyl bromide to give 70 in 85% yield. The acid 70 was reduced with lithium aluminium hydride to the sulfide alcohol 71 (92%) which in turn was oxidized with *m*-chloroperbenzoic acid to the sulfoxide 72 (85%). This hydroxysulfoxide on treatment with sulfuryl chloride gave the sultine 69 in 60% yield together with α -phenethyl chloride (60%).

The sultine 69 (m.p. 39-40°, literature m.p. 39-40)¹³ showed the characteristic S=O infrared absorption at 1120 cm⁻¹. The n.m.r. spectrum showed an AB quartet ($\delta_A = 5.42$, $\delta_B = 5.78$, $J_{AB} = 13.5$ Hz) and the aromatic protons in 1:2 ratio.

The synthesis of 68 was attempted according to Scheme 12. α -Bromo-*o*-cresyl acetate, prepared by the bromination of *o*-cresyl acetate with NBS, was converted with *t*-butyl thiol in alkaline medium to the phenolic sulfide 73 (92%). Oxidation of 73 gave the required sulfoxide 74 in 80% yield. However when the phenolic sulfoxide 74 was treated with sulfuryl chloride none of the desired sultine could be obtained.

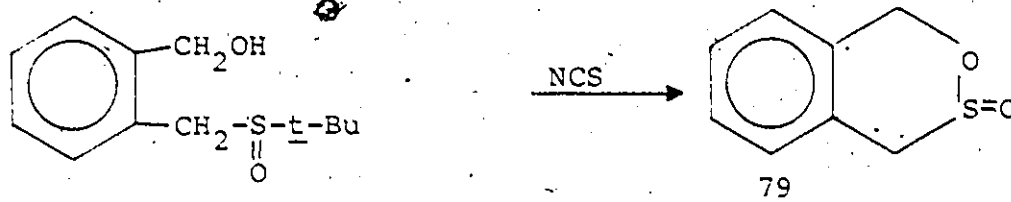
SCHEME 12

Attempted synthesis of 3H.- 1,2-benzoxathiole-2-oxide



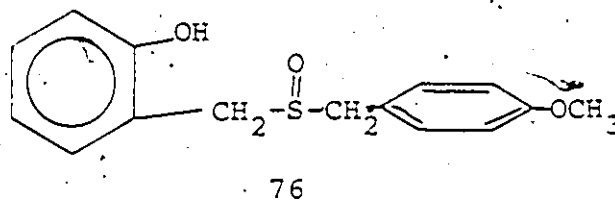
Again it appears that carbon-sulfur bond cleavage took place preferentially at the benzylic carbon-sulfur rather than at the desired S-C(CH₃)₃ bond.

16
Jung et al have reported the synthesis of sultine 79 from the precursor hydroxysulfoxide in good yield.



Thus the preferential cleavage at the benzylic carbon-sulfur bond in the reaction of 74 can be attributed to the resonance stabilization of thus formed benzyl cation by the phenolic hydroxyl group of 74.

It was therefore decided to replace the t-Bu group in 74 by a p-methoxy benzyl group with the hope that this might lead to cleavage in the desired direction.



Reaction of the phenolic sulfoxide 76 synthesized in the same manner as 74, with SO_2Cl_2 gave a crude product whose n.m.r. was interpreted in terms of an equimolar mixture of 68 and p-methoxy benzyl chloride. The spectrum (reproduced in figure 3) showed peaks at δ 3.90 (s) and 4.66 (s) in a 3:2 ratio attributed to the $-\text{OCH}_3$ and $-\text{CH}_2\text{Cl}$ groups of p-methoxybenzylchloride. The highfield portion of the AA'BB'

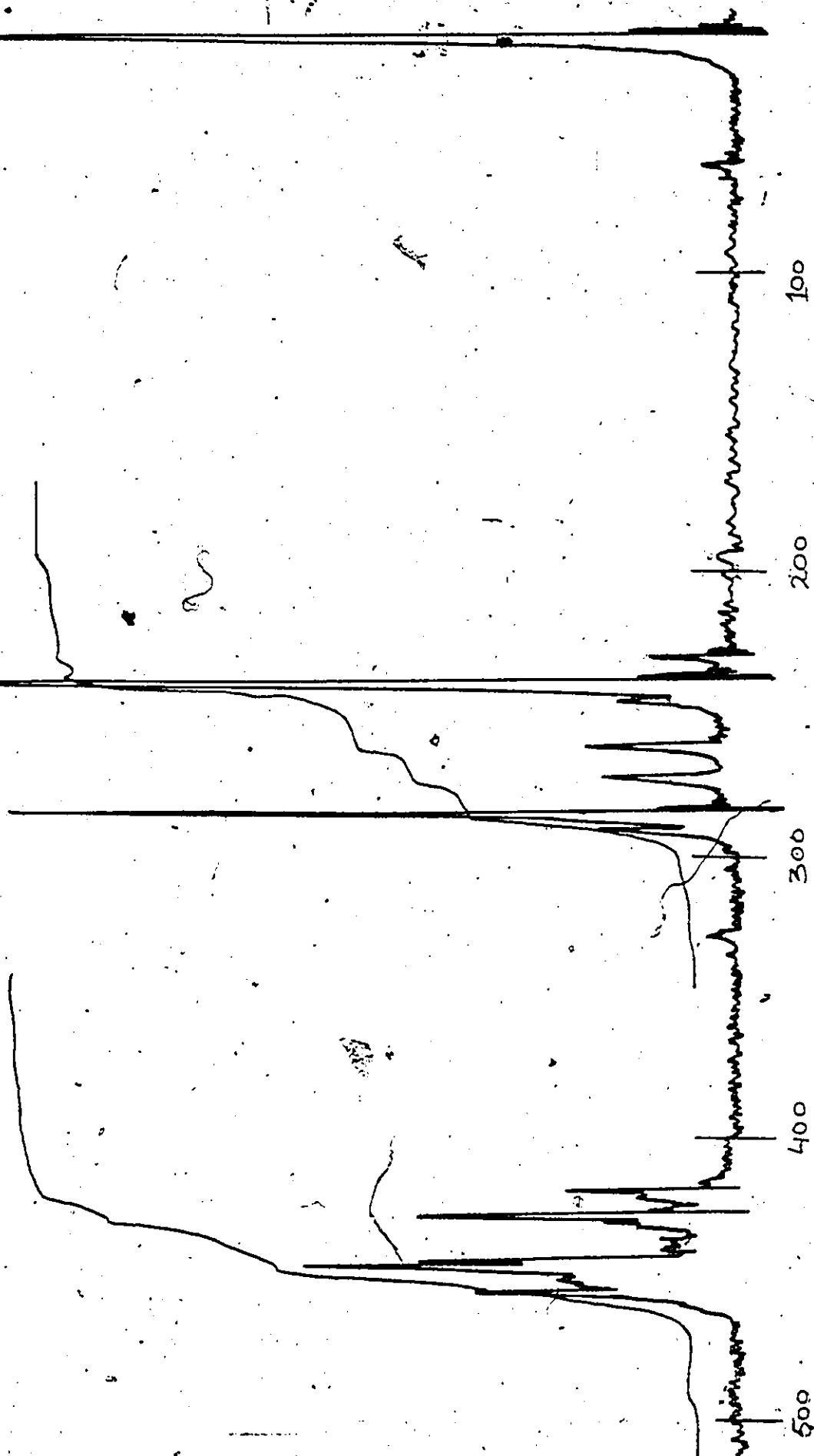
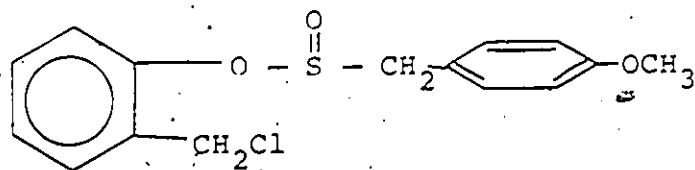


Figure 3: N.M.R. of the reaction product derived from $\overline{76}$ and SO_2Cl_2 .

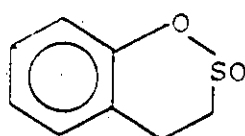
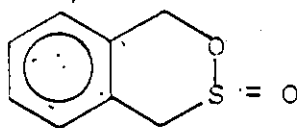
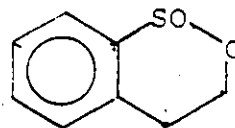
pattern expected for the aromatic protons of this substance was also visible at $\delta = 7.0$. The remaining part of the n.m.r. spectrum showed an AB quartet ($\delta_A = 4.16$, $\delta_B = 4.56$, $J = 16\text{Hz}$) together with a multiplet centred at 7.4. These data are in agreement with the sultine structure. Unfortunately, despite considerable attempts, the isolation of the sultine was not successful. Chromatography of the crude reaction product on silica gel gave a number of fractions which contained peaks not found in the crude thus indicating decomposition of the initial products. In one fraction there appeared to be an enrichment of the sultine portion as judged by a change in relative size of the peaks ascribed to the sultine vs the *p*-methoxy benzyl chloride (*p*-methoxy benzyl alcohol). The only pure substance which was isolated from the column was *p*-methoxy benzyl alcohol (identified by its n.m.r. spectrum)¹⁴. This compound was presumably formed upon hydrolysis of the chloride.

The crude spectrum could also be accounted for by the ester 77 formed by cleavage in the undesired direction. The observation that *p*-methoxy benzyl alcohol is formed on column chromatography is however inconsistent with such a hypothesis since ester hydrolysis of 77 would be expected to give *o*-hydroxy benzyl chloride and eventually *o*-hydroxy benzyl alcohol.

77

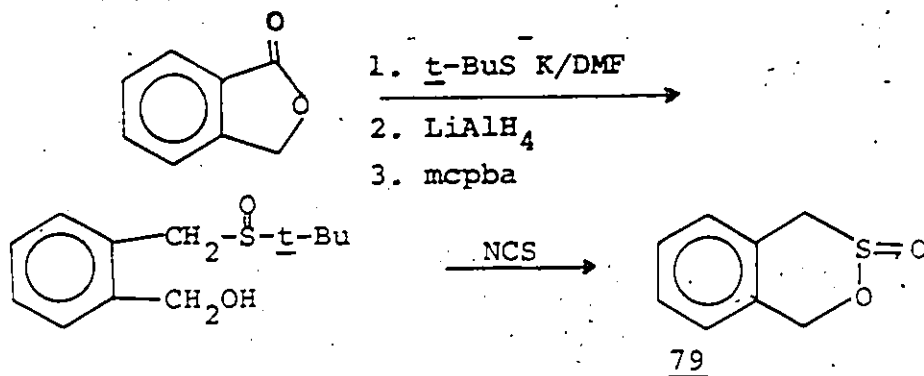
The instability of 68 compared to 69 is not at all surprising. Sultines generally undergo ring opening in the presence of nucleophiles by cleavage of the S-O bond. In sultine 68 such a cleavage results in the formation of the relatively stable phenolic anion, compared to an alkoxide anion in the cleavage of the 69. Givens and Hamilton¹⁵ have reported that sultine 78 completely decomposed, when stored overnight at room temperature.

Three benzofused δ -sultines can be envisaged.

787980

The sultine 78, 3,4-dihydro-1,2-benzoxathiin-2-oxide has been prepared by Givens and Hamilton¹⁵ via controlled chlorination of β -(*o*-hydroxyphenyl)-ethyl mercaptan in acetic acid.

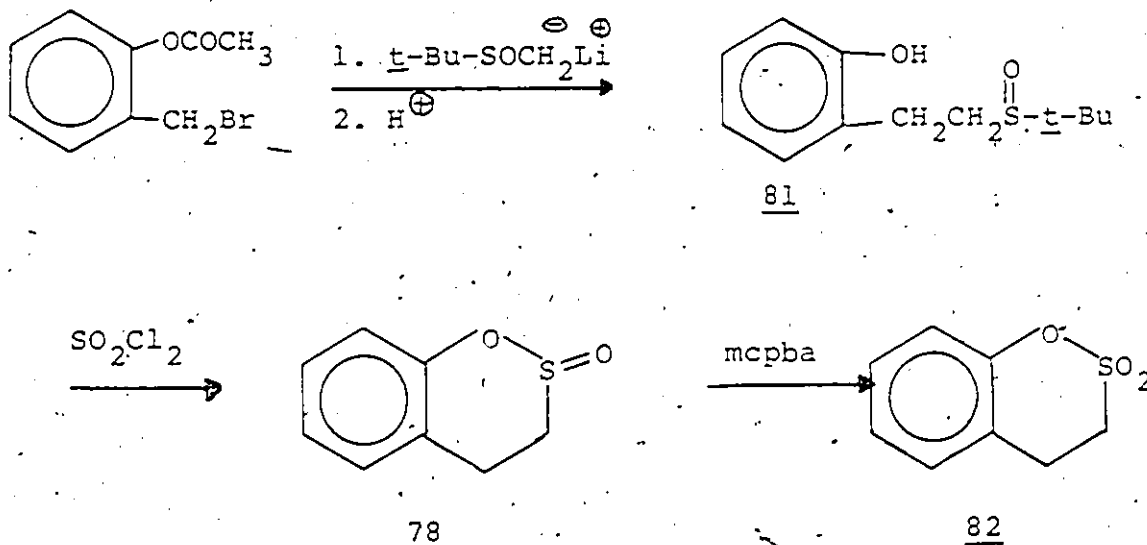
The synthesis of 79, 1,4-dihydro-2,3-benzoxathiin-3-oxide and several of its methyl and phenyl derivatives has been described by Jung and coworkers¹⁶ utilizing the sulfoxide cleavage route as shown below.



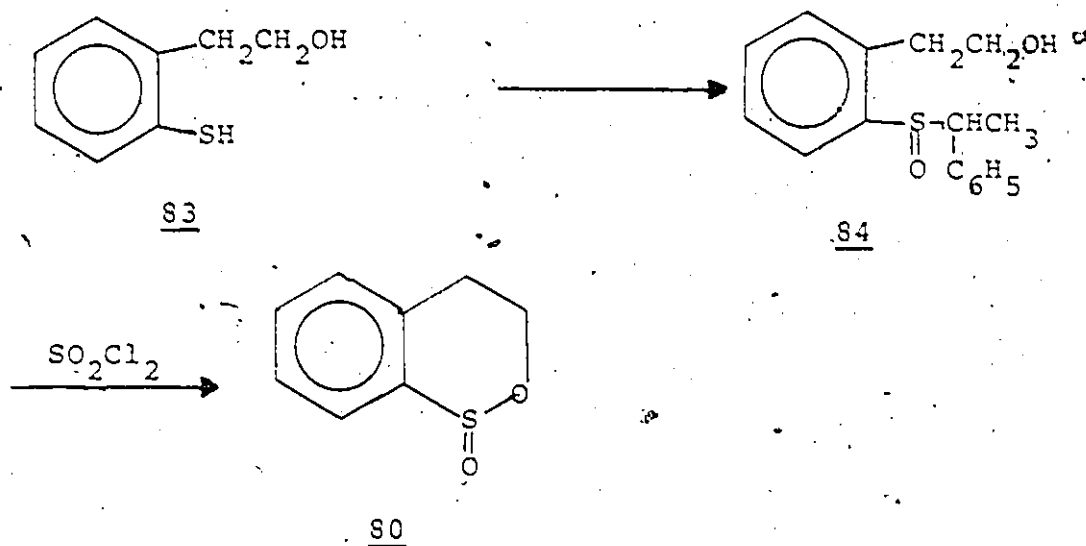
An alternate synthesis of 78 based on the sulfoxide cleavage route was developed. Reaction of α -lithiomethyl *t*-butyl sulfoxide with α -bromo-*o*-cresylacetate gave directly the hydroxysulfoxide 81 in 70% yield. The hydroxysulfoxide 81 showed infrared absorption at 3360 and 1010 cm^{-1} . Its n.m.r. showed peaks at 1.25 (s, 9H); 1.6 - 2.2 (m, 4H) and 6.9 - 7.3 (m, 5H). When 81 was reacted with SO_2Cl_2 , the sultone 78 was formed in a crude yield of >95%. The n.m.r. spectrum showed multiplets at 2.3 - 3.5 (4H) and 6.8 - 7.4 (4H). In agreement with the observation by Givens and Hamilton¹⁵ 78 was found to be unstable. The crude product was therefore directly oxidized to the sultone 82 (75% conversion). The spectral properties of the sultone were in agreement with those reported in the literature.¹⁵ (Scheme 13)

SCHEME 13

Synthesis of 3,4-dihydro-1,2-benzoxathiin -2-oxide



The isomer 80 has not been prepared. A synthesis via the cyclization of 84, (prepared from the known hydroxy-¹⁷thiol 83), with sulfonyl chloride can be easily envisaged:



CHAPTER IV

Conformational aspects of six membered sulfur heterocycles.

a) Introduction:

Conformational equilibria in the alicyclic molecules particularly the substituted cyclohexanes have been studied in great detail.¹ In contrast to the wealth of information in the cyclohexane area less is known regarding the conformational consequences of introducing one or more heteroatoms into a ring. The conformational analysis of ring systems containing sulfur is of interest because these heterocycles provide an interesting contrast to the carbocyclic systems. In addition a study of these systems is of considerable value in the understanding of the conformational behaviour of related heterocycles such as tetrahydropyrans, piperidines and the six membered ring phosphorus heterocycles.

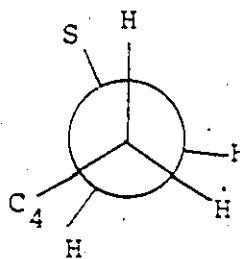
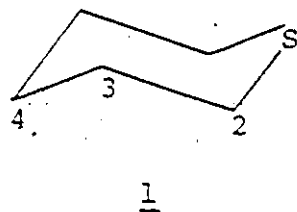
Because of the relationship with the sulfones which constitute the substance of this thesis, this review will consider in detail only the work on six membered rings containing the S=O function.

b) Thianes and their derivatives:

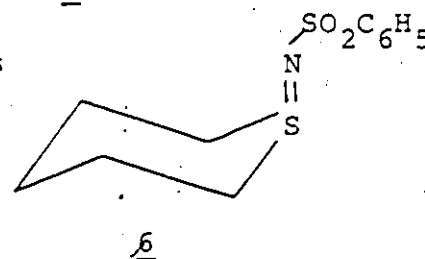
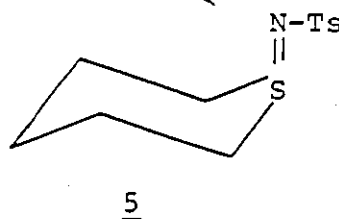
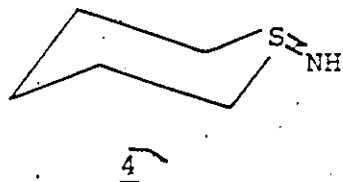
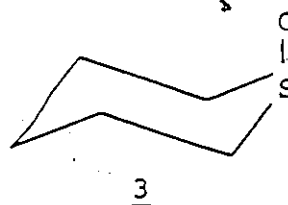
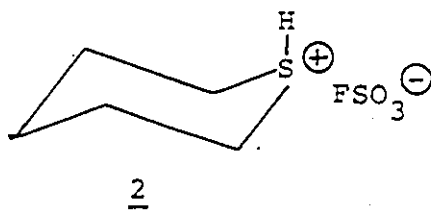
2,3

Lambert and coworkers^{2,3} on the basis of the vicinal n.m.r. coupling constants between the hydrogens of C₂ and C₃ deduced that whereas piperidine and tetrahydropyran possess conformation close to that of a "perfect chair", thiacyclo-

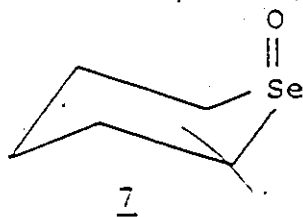
hexane,1, as well as selenacyclohexane and telluracyclohexane are slightly distorted in such a manner that the equatorial protons are pushed more closely together.



In protonated thiacyclohexane,2, the acidic hydrogen prefers the axial position (>1500 cal/mole at -30°). Lambert and coworkers have shown by low temperature n.m.r. that in the thiane-1-oxide,3, the axial oxide is favoured at -90° by 175 cal/mole (62/38).^{4,5,6} However the isoelectronic thiane-1-imide,4, was found to have a slight excess (55/45 at -85°)⁷ of the imide functionality in the equatorial position. The same workers observed that the N-tosyl,5, and N-benzenesulfonyl,6, derivatives of thiane-1-imide favor the axial imide conformation (145 cal/mole at -89°).

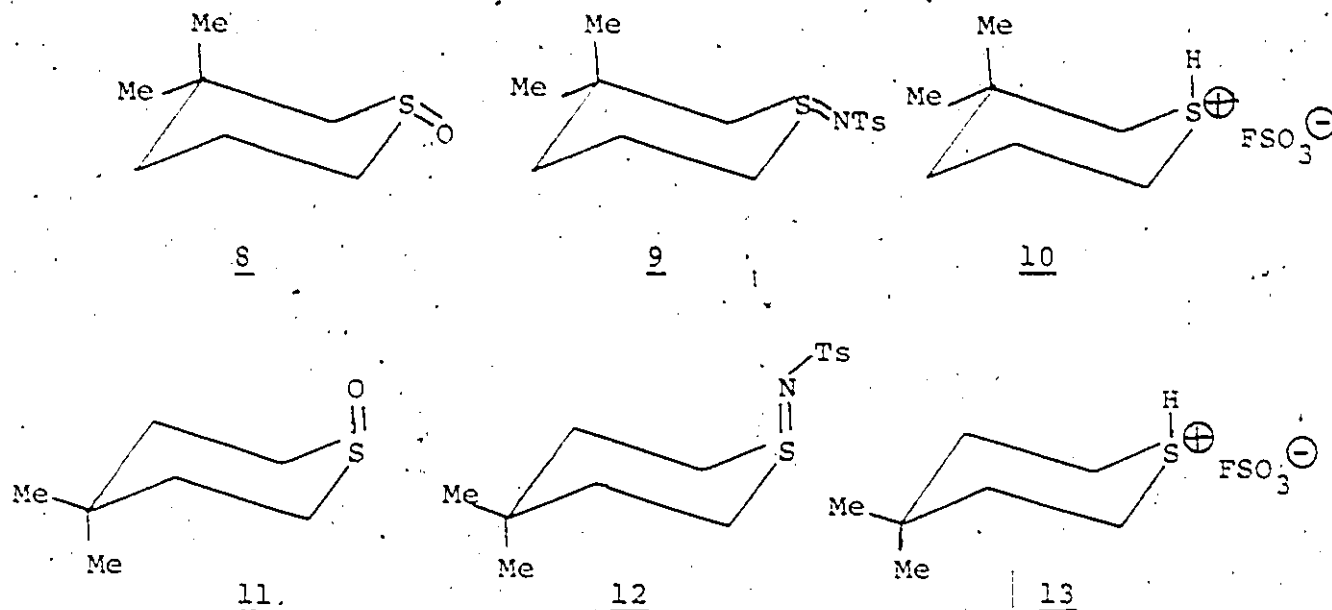


Several explanations of this "unusal" axial preference for the case of thiane-1-oxide have been offered. Allinger and coworkers⁸ attributed this preference to an attractive interaction between the 1-substituent and the 3,5 axial protons. In cyclohexane this interaction is a repulsive one. Apparently the increase in the C-S bond length compared to C-C moves the distance between 1,3-diaxial substituents from the repulsive to the attractive region of the potential energy well. The observation that in selenane-1-oxide,⁷ the axial oxygen preference is even higher (84/16 at -102°) than in thiane-S-oxide (62/38 at -85°) suggests that the minimum in the attractive region had not been reached in the six membered ring sulfoxide.



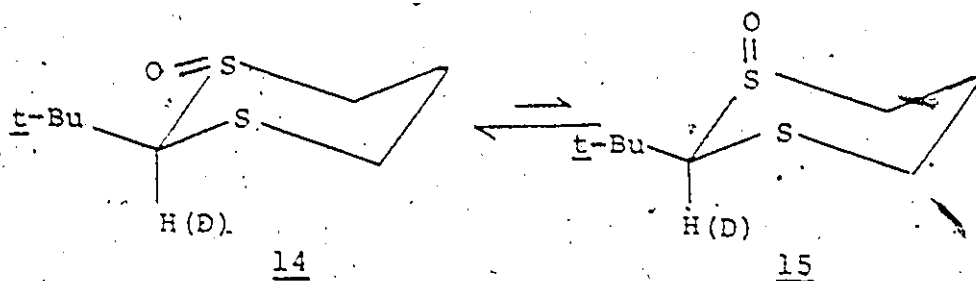
Based on the above explanation, replacement of a 3-axial proton by a methyl group should make the 1,3 interaction repulsive (or less attractive) and decrease the proportion of the 1-axial isomer. To test this, Lambert and coworkers prepared the 3,3-dimethyl derivative of thiane-1-oxide,⁸ thiane-1-(N-tosyl)-imide,⁹ and protonated thiane,¹⁰ and noted that the oxide and imide become predominantly equatorial ($>95\%$) while the protonated compound still remains in the axial conformation. The corresponding 4,4-dimethyl derivatives

(11, 12 and 13) maintain the predominance of 1-axial isomer thereby supporting the idea of an attractive interaction between the oxygen and the 3,5 axial protons.^{9,10}

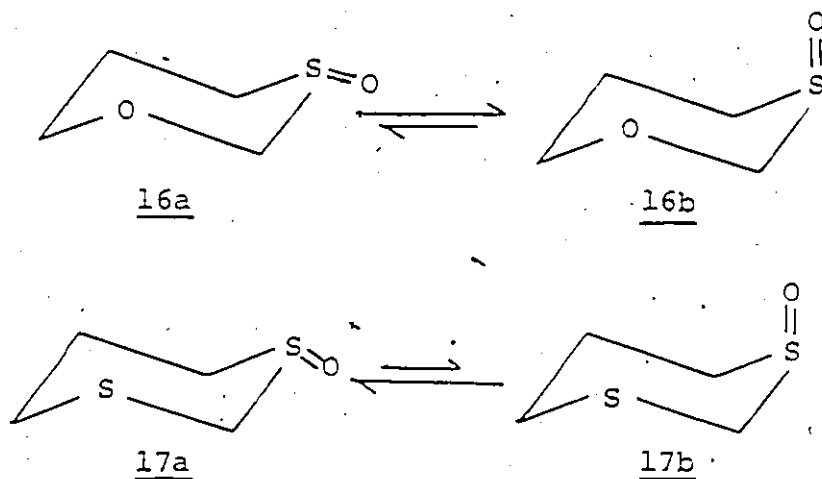


c) Dithianes, Oxathianes and their derivatives:

Conformational equilibria in some 1,3-dithiane-1-¹¹oxides were recently examined by Cook and Tong who observed that the "normal" axial preference of the sulfinyl oxygen is reversed in this system. Using the acidity of the hydrogen on C₂ the conformational equilibrium 14 ⇌ 15 was examined. Thus 14 and 15 were each treated with NaOD/DMSO at 84° for eighteen hours, whereby both the structures underwent H-D exchange at the 2-position and yielded mixtures of similar ratio. The isomer 14 was converted into a 68/32 mixture of 14 and 15 while 15 gave a 69/31 mixture ($-\Delta G_{84}^\circ = 0.5$ kcal/mole).

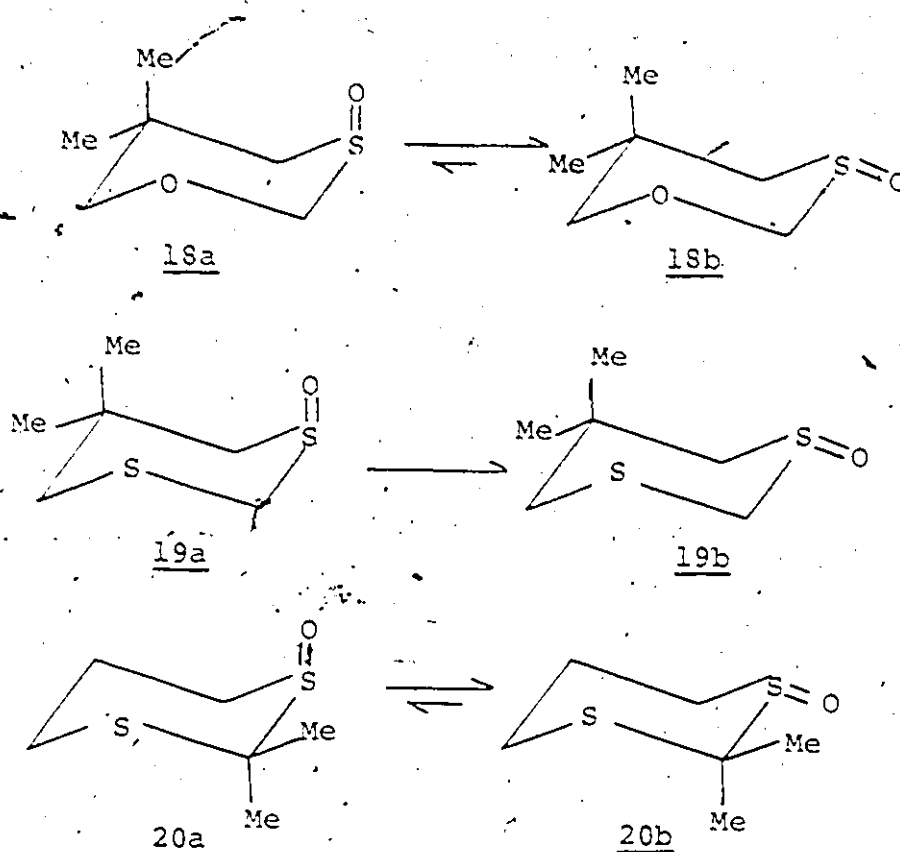


In contrast, 1,3-oxathiane-3-oxide, 16, was found to possess an axial S=O preference (84% at -98° , $-\Delta G^\circ = 570$ cal/mole) whereas 1,3-dithiane-1-oxide, 17, contained only 15% of the axial form in agreement with the results obtained by Cook and Tong.^{11,12} These results have recently been verified by Khan et al.¹³



5,5-Dimethyl-1,3-oxathiane-3-oxide, 18, showed a decrease in the proportion of the 1-axial isomer (10% at -102° , $-\Delta G^\circ = 730$ cal/mole). The S=O bond in 5,5-dimethyl-1,3-dithiane-1-oxide, 19, is exclusively equatorial which is significantly more than the 80% observed for 2,2-dimethyl-1,3-dithiane-1-

oxide, 20. From the equilibration data for 16 and 18 the "axial-SO-disfavoring effect" of a syn-axial methyl group was estimated to be 1.3 kcal/mole.¹²



It is fairly difficult to rationalize these observations. The state of affairs can perhaps best be illustrated by the following quote:¹²

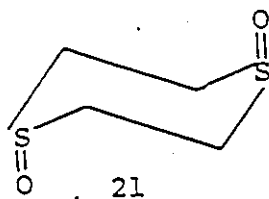
"Rationalization of the above observations may probably be found in terms of 'a balance between attractive and repulsive interactions' with a dynamic concept of the SO bond as basis (1,10); that means that it is able to adapt its stereoelectronic features to those of the very molecule".

(1) L. Van Acker in "Some aspects of the stereochemical investigation of sulfoxides" (a review in Dutch), Belg. Chem. Ind. (in press).

(10) a) S. Wolfe, A. Rauk, L.M. Tel, I.G. Csizmadia; J. Chem. Soc. B., 136 (1971).

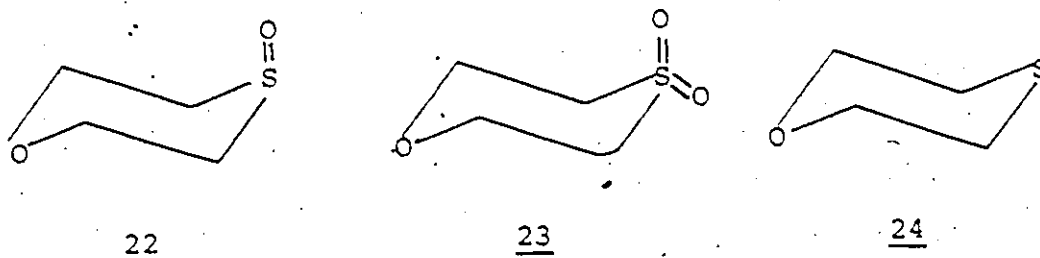
b) S. Wolfe, Accts. Chem. Res., 5, 102 (1972).

The oxide function in trans-1,4-dithiane-1,4-dioxide, 21, has recently been shown to be axial.



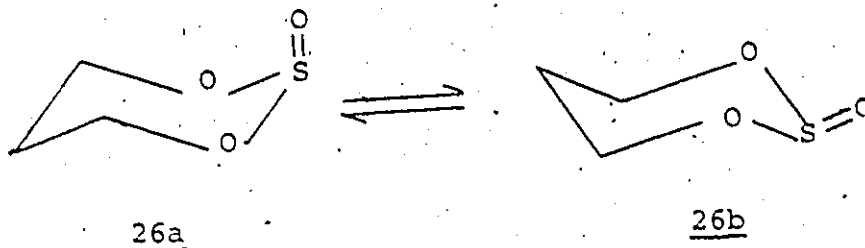
¹⁴
Szarek and coworkers have studied proton and carbon-¹³ n.m.r. spectra of 1,4-oxathiane derivatives including 1,4-oxathiane-4-oxide, 22, and showed that 22 exists in the conformation with axial S=O oxygen. It was observed that, in both the sulfoxide 22 and the sulfone 23, C-2 and C-6 are shielded (9.5 and 2.5 ppm respectively) as compared to the corresponding carbons in 1,4-oxathiane, 24. In 22, the axial S=O bond seemed to have a very large influence on the shieldings of C-2 and C-6 which was attributed to the γ -steric

effect. A somewhat lower shielding was observed in 23 which according to the authors is due to the diminished anisotropy of the axial S=O bond in the sulfone 23 versus the S=O anisotropy in the sulfoxide 22.



d) Conformational studies of cyclic sulfites:

Conformational studies of the cyclic sulfites have drawn the attention of many workers and considerable controversy existed until recently regarding the preferred shape¹⁵ of these compounds. For example, de la Mare and coworkers¹⁵ in 1956, using infrared techniques, came to the conclusion that trimethylene sulfite, 26, and its derivatives are chair-shaped with an equatorially oriented S=O group. However, Arbuzov¹⁶ in 1960 observed that the dipole moment of trimethylene sulfite, 26, is 3.60 and suggested that it exists in solution as a mixture of the two possible chair forms 26a and 26b, having calculated dipole moments equal to 1.8 and 4.9 respectively.



17

In 1963, it was observed by Hellier and coworkers that the dipole moment of 26 remains unchanged in a variety of solvents and that in the infrared, the number of bands, their positions and relative intensities remain unaltered in widely different solvents including the pure liquid.

The n.m.r. spectrum of 26 at room temperature showed multiplets in four regions centred at δ 1.76, 2.50, 3.99 and 4.92. These were assigned, from the magnitude of the couplings, to the equatorial hydrogen at C_5 , the axial hydrogen at C_5 , two equivalent equatorial hydrogens at C_4 and C_6 , and the two equivalent axial hydrogens at C_4 and C_6 respectively.

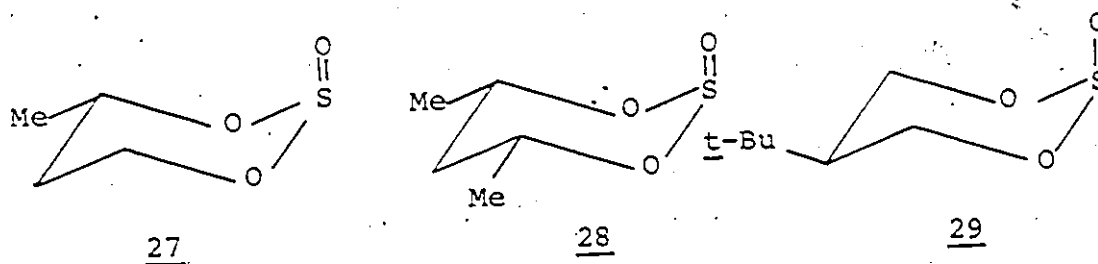
It was strongly suggested that this molecule exists exclusively as the conformer 26a, which is a rigid chair form having the $S=O$ group in the axial position.

The situation in a number of substituted sulfites is less clear. The bulk of the published data comes from dipole moment measurements, i.r. spectroscopy, and ultrasonic relaxation studies.

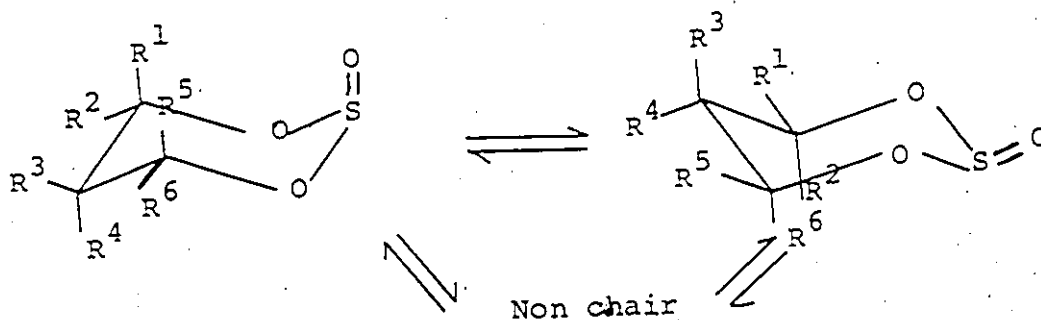
Detailed proton and carbon-13 magnetic resonance studies by Buchanan, Stothers and Wood on a variety of

alkyl substituted trimethylene sulfites have led to the conclusion that both the chair and the nonchair conformations are possible for these compounds depending upon the nature of the substitution pattern. The results supported a large free energy difference between the two chair forms and lower free energy differences between the favored chair and the boat conformations. The high preference for the axial S=O orientation was evident from the various deshielding parameters in the proton spectra as well as the observed Eu (dpm)₃ shifts.

It was concluded that trimethylene sulfite, 26, and derivatives such as 27, 28 and 29 should be regarded as chair forms with axial S=O conformations.

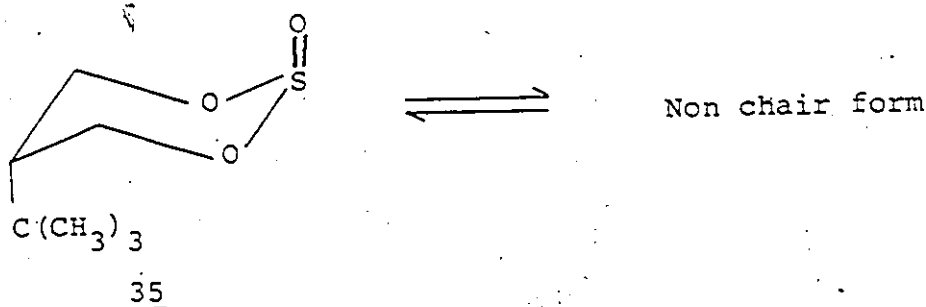


With the increased steric interaction between the syn-axial methyl groups and the exocyclic oxygen atom, non-chair forms become more prominent as in 30, 31, 32, 33 and 34.



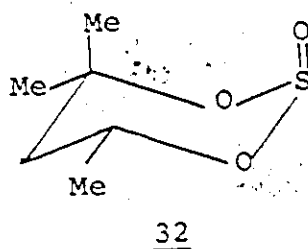
Compound	Substituents
<u>30</u>	$R^1 = CH_3$
<u>31</u>	$R^2 = R^5 = CH_3$
<u>32</u>	$R^1 = R^2 = R^6 = CH_3$
<u>33</u>	$R^1 = R^2 = R^5 = CH_3$
<u>34</u>	$R^1 = R^2 = R^5 = R^6 = CH_3$

For the t-butyl derivative 35 the molecule was suggested to exist as a mixture of a diaxial chair and a nonchair conformation rather than a diequatorial chair.



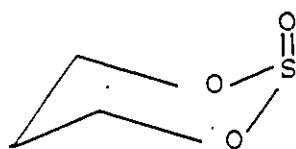
The barrier in 5,5-dimethyl trimethylene sulfate is 8.3 kcal/mole and in 5,5-dimethyl-1,3,2-dioxathiane is 12.5 kcal/mole. Accordingly, the chair⇌chair barrier for the sulfites is likely in the accessible n.m.r. range and the lack of observed coalescence phenomena for compounds thought to be chairs with axial S=O functions was attributed to the low population of the higher energy form with equatorial S=O ($-\Delta G_{S=O}^\circ = 2.1 \pm 0.5$ kcal/mole).

In general the results obtained in the proton n.m.r. study were verified by the carbon-13 n.m.r. study results (See also section e of this chapter) with the exception that for 32 the chair conformation having the S=O bond axial was now suggested to predominate in contrast to the conclusions based on ^1H n.m.r. and dipole studies.

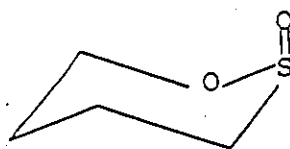


e) Conformational aspects of δ -sultines:

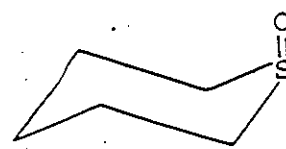
1,2-Oxathiane-2-oxides (δ -sultines) fall between the cyclic sulfites and cyclic sulfoxides and it thus seemed worthwhile to study the conformational aspects of these compounds using the spectroscopic techniques employed for the sulfites and sulfoxides.



Sulfite



Sultine

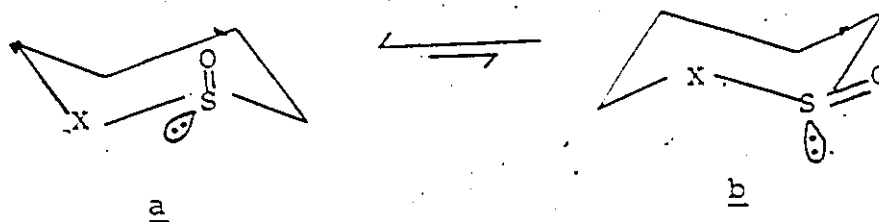


Sulfoxide

Harpp and Gleason have reported a detailed analysis of the 100 MHz n.m.r. spectrum of 1,2-oxathiane-2-oxides, 36, and found it interpretable in terms of a single conformational

isomer having axial S=O function. The n.m.r. spectrum was unchanged over a wide range of temperatures (-90° to 150°) thereby indicating its conformational purity. The energy difference between the two chair conformations was estimated to be in excess of 2000 cal/mole.

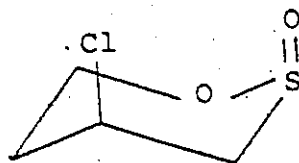
This strong preference for an axial S=O conformation was attributed to a dipolar interaction analogous to the anomeric effect observed in carbohydrates.



36 X = O
37 X = S

The configuration of S=O bond could not be assigned definitively in the analogous 1,2-dithiane-2-oxide,37. However it was noted by the authors that this ring was not undergoing interconversion.

Very recently n.m.r. and infrared studies on 4-chloro-4-methyl-1,2-oxathiane-2-oxide,38 and some of its derivatives have been reported by Dhami.²⁷ Again the results are consistent with a single conformation having the S=O group in the axial configuration.

38

Since we had available the 1,2-oxathiane-2-oxide, 36, and several of its monomethyl and dimethyl derivatives (for the synthesis see Chapter III) it was decided to examine the proton and carbon-13 n.m.r. spectra of these compounds in detail with the hope to gain insight into the conformational behaviour of these heterocycles, especially the extent of the axial preference by the sulfinyl oxygen.

The proton n.m.r. shielding for 1,2-oxathiane-2-oxide, 36, its four possible monomethyl derivatives 39-42 and the 6,6-dimethyl derivative 43 are recorded with the structures on page 92a and 93a.

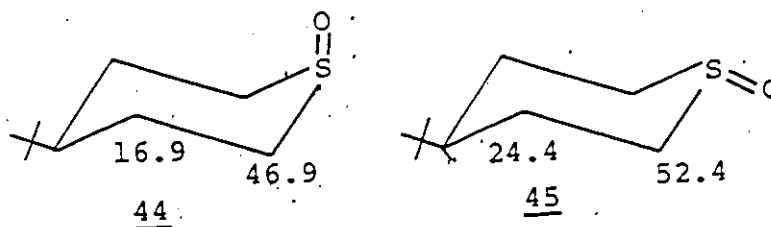
The n.m.r. spectrum of 36 is in complete agreement with that reported by Harpp and Gleason. The multiplet at $\delta 4.42$ is assigned to the axial proton attached to C_6 and that centred at $\delta 3.72$ to the corresponding equatorial hydrogen. Similarly the multiplet at $\delta 2.87$ is assigned to the axial proton attached to C_3 . It is seen that the axial protons at C_3 and C_6 are deshielded by about 0.8 ppm compared to their equatorial counterparts. This is in contrast to the carbocyclic systems in which the axial protons are displaced to high field relative to the equatorial protons. The deshielding

influence of the axial S=O group on 1,3-diaxial protons in various cyclic systems (sulfites, sulfoxides etc) is well documented.^{24,28,29}

The above assignments were supported by Eu (fod)₃ shift studies. Many reports, including those dealing with sulfoxides³⁰ and sulfites,²⁴ of the application of lanthanide reagents to spread out and simplify the proton spectra can be seen in the literature.³¹ The origin of the induced shift is believed to be due to a pseudo-contact interaction. Accordingly, the observed shifts in fixed systems are found to be proportional to $1/\gamma_i^3$ where γ_i is the lanthanide-proton distance.

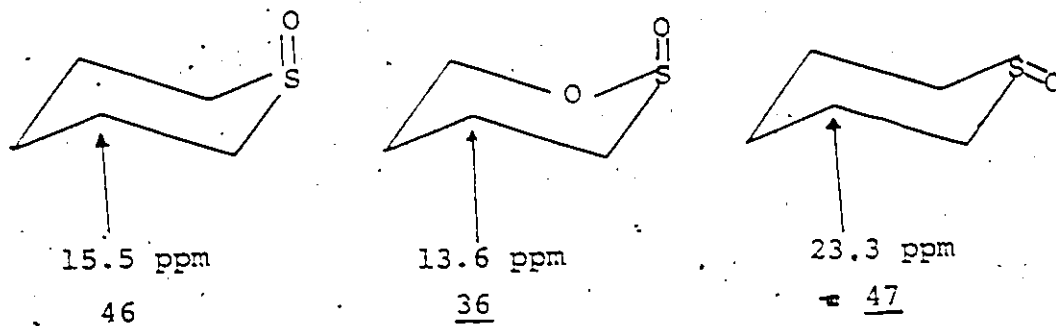
Incremental addition of Eu(fod)₃ up to ca 0.5 equivalent caused a downfield shift of the order of 8 ppm for the axial proton at C₆ in the sultine 36. The corresponding axial proton at C₄ was also deshielded by a similar amount thus indicating that H_{4a} and H_{6a} are closest to the lanthanide atom. This observation is similar to the results obtained for sulfites and supports a chair structure for the sultine in which the S=O group is in the axial configuration.

Further support regarding the shape of the heterocycle comes from carbon-13 n.m.r. shieldings of 36 which are given in Table I. As model compounds, chemical shifts for cis and trans 4-t-butyl thiane-1-oxide 44 and 45 are shown below.³²



A 7.5 ppm shielding at $C_{3,5}$ of 44 relative to 45³³ has been interpreted in terms of the "gauche γ " steric shift since $C_{3,5}$ of 44 are gauche to the exocyclic oxygen whereas in 45 they are anti. Accounting for the β -effect of t-butyl group in 44, the C_4 resonance of 36 at 13.6 ppm clearly suggest that the sulfinyl oxygen in this compound is in axial configuration.

Comparison of the C_4 resonance parameters in the sulfoxides 46 and 47³² and the sultine 36 further supports the idea of axial sulfinyl oxygen in 36.

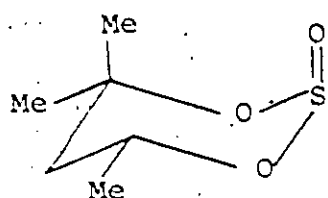


In tetrahydropyran γ -effect of the oxygen has been found to be -2.7 ppm.³⁴ If a similar effect is assumed to be operative in the sultine 36 versus the sulfoxide 46, the resonance value of C_4 would be expected to be 12.8 ppm which is in excellent agreement with the observed value.

C_6 of 36 resonates at 58.5 ppm which is again in agreement with the observed 57.1 ppm for C_6 of trimethylene sulfite,26.

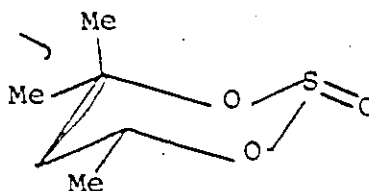
The proton n.m.r. spectrum of the dimethyl derivative 43 can also be reconciled satisfactorily in terms of a single conformer with the axial S=O function. Two methyl

groups absorb (at δ 1.25 and 1.57 assigned to the equatorial and axial methyls (at C₆) respectively. In the model compounds, sulfites 32 and 33, the resonance parameters for such methyl groups are as shown.

32

$$6\text{-CH}_3(\text{a}) = 1.70\delta$$

$$6\text{-CH}_3(\text{e}) = 1.28\delta$$

33

$$6\text{-CH}_3(\text{a}) = 1.50\delta$$

$$6\text{-CH}_3(\text{e}) = 1.45\delta$$

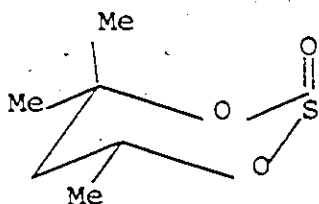
It can be seen that in the isomer 33, in which the sulfinyl oxygen is mainly in the equatorial position, the axial methyl resonates at a lower field as compared to its equatorial counterpart, the shift difference being 0.05 ppm. In the isomer 32 (axial sulfinyl oxygen) the corresponding shift difference is 0.42 ppm.

Comparison of these data with those for the sultine 43 (the axial methyl resonating lower field with a shift difference of 0.32 ppm) indicates that the sulfinyl oxygen in the sultine 43 is mainly in the axial configuration.

Addition of ca. 0.3 equivalents of Eu (fod)₃ caused shifts of 3.0 and 1.5 ppm for CH₃ groups originally at δ 1.57 and 1.25 respectively. This confirms that the methyl group

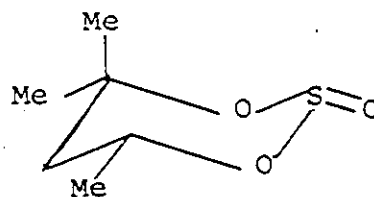
at δ 1.57 is closer to the lanthanide atom and thus further supports the idea of axial configuration of the sulfinyl oxygen.

In the carbon-13 n.m.r. spectrum, the axial and equatorial methyl groups resonate at 31.8 and 28.4 ppm respectively. These assignments were confirmed by selective proton decoupling. Again a comparison with the closest available models, sulfites 32 and 33 supports the assigned conformation in the case of 43.

32

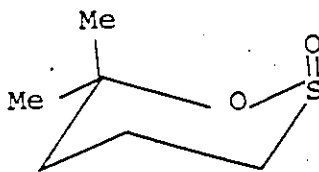
$$6\text{-CH}_3(\text{a}) = 32.2 \text{ ppm}$$

$$6\text{-CH}_3(\text{e}) = 28.8 \text{ ppm}$$

33

$$6\text{-CH}_3(\text{a}) = 31.5 \text{ ppm}$$

$$6\text{-CH}_3(\text{e}) = 26.4 \text{ ppm}$$

43

$$6\text{-CH}_3(\text{a}) = 31.8 \text{ ppm}$$

$$6\text{-CH}_3(\text{e}) = 28.4 \text{ ppm}$$

TABLE I

Carbon-13 n.m.r. chemical shifts for δ -sultines

Compound	Structure	δ_c (0.1 ppm from TMS)				
		C-3	C-4	C-5	C-6	CH ₃ 'S
<u>36</u>		49.5	13.6	-24.5	58.5	-
<u>39</u>		53.1	20.8	24.9	58.6	15.1
<u>40</u>		56.4	20.1	33.1	59.1	21.9
<u>41</u>		50.0	17.6	29.8	63.7	21.8
<u>42</u>		48.7	14.3	32.0	65.2	21.5
<u>43</u>		49.6	11.4	36.0	81.3	28.4 (e) 31.8 (a)

For the four monomethyl isomers 39 - 42 only the most stable isomer could be isolated in each case. In general the proton n.m.r. spectra support the conformations with axial oxygen as evidenced by the deshielding of axial protons at C_6 and C_4 relative to their equatorial counterparts.

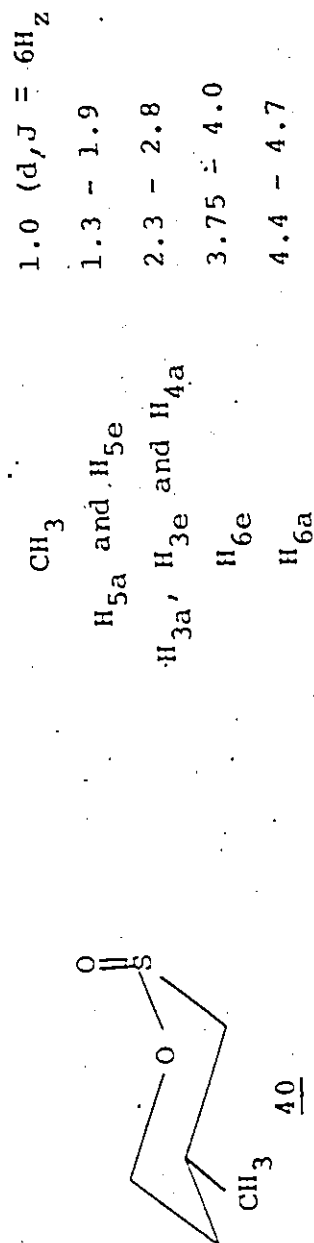
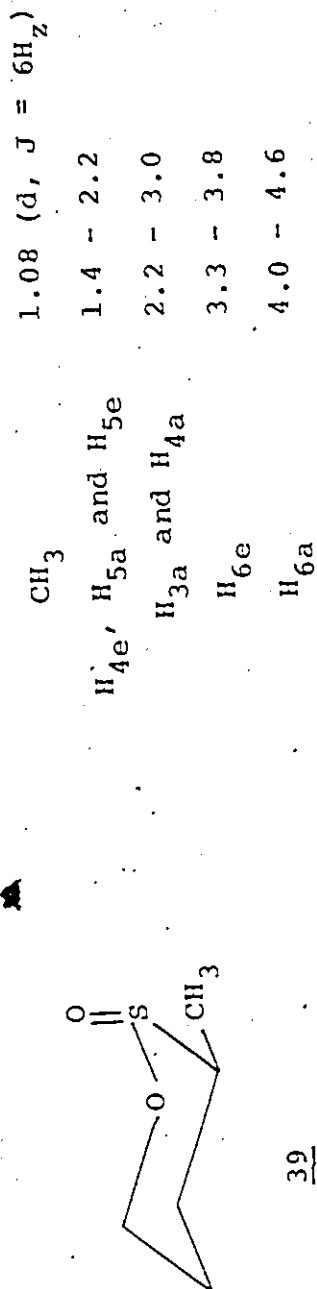
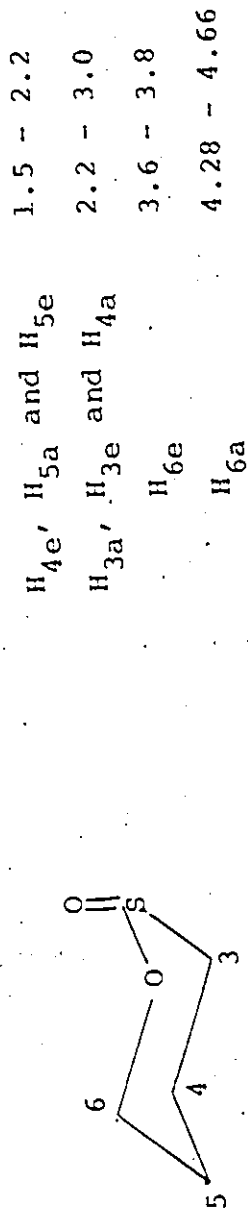
Further support comes from the carbon-13 spectra. The methyl carbon of the isomer 39 resonates at 15.1 ppm. Comparison of this value with those observed in the other isomers indicates that it is shielded by ca. 6.6 ppm suggesting thereby that C-CH₃ bond is gauche to the S=O bond. Shielding values for C_5 and C_6 are within 0.5 ppm of those for the corresponding carbons in 36.

In the 4-methyl isomer 40 the shielding for C_6 is 59.1 ppm which is again in agreement with the idea of a conformation with axial S=O oxygen.

In the 5-methyl isomer C_4 and C_6 cannot be compared with the corresponding carbons in 36 because of β effect of the methyl group. However in the 6-methyl isomer 42 the shielding value for C_4 (14.3 ppm) is in reasonable agreement with the value for corresponding carbon in 36 (13.6 ppm).

Thus it appears that in general the six sultines represented in Table 1 exist at least predominantly (if not exclusively) in the chair conformation with the S=O bond in the axial position. It is somewhat unfortunate that not enough model compounds are available for comparison. Our recent encouraging results in effecting the epimerization at sulfinyl

The proton n.m.r. shieldings for Σ -sultines



0.87 (d, J = 6H₂)

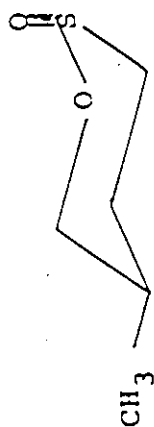
1.6 - 2.4

2.6 - 3.0

3.6 - 3.8

4.0 - 4.5

CH₃
 H_{4e} and H_{5a}
 H_{3a}, H_{3e} and H_{4a}
 H_{6e}
 H_{6a}

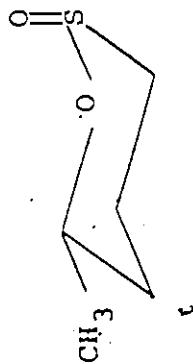
1.22 (d, J = 6H₂)

1.45 - 2.0

2.3 - 2.8

4.5 - 4.9

CH₃
 H_{4e}, H_{5a} and H_{5e}
 H_{4a}, H_{3a}, and H_{3e}
 H_{6a}



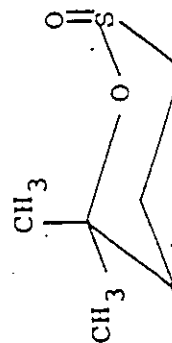
1.25

1.57

1.6 - 1.9

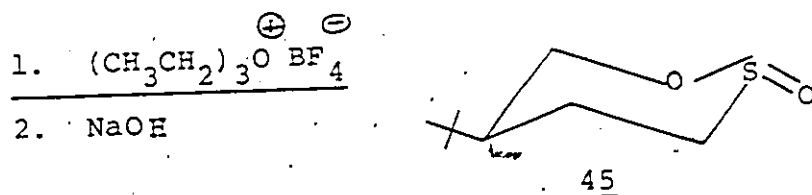
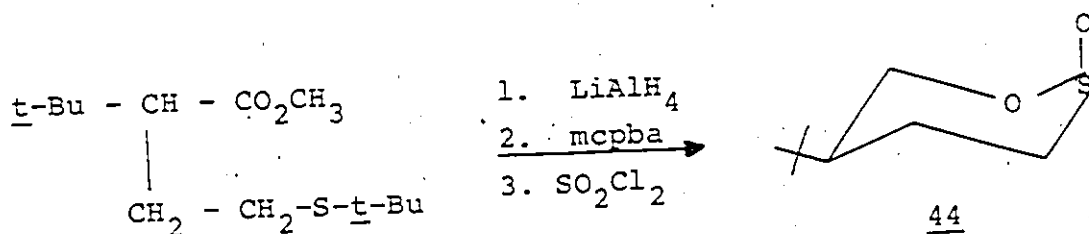
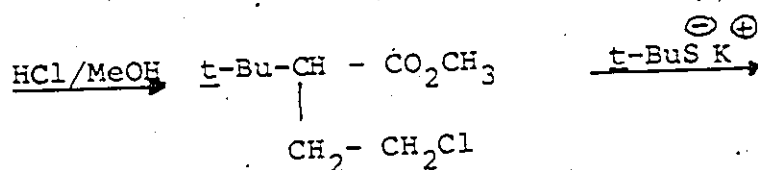
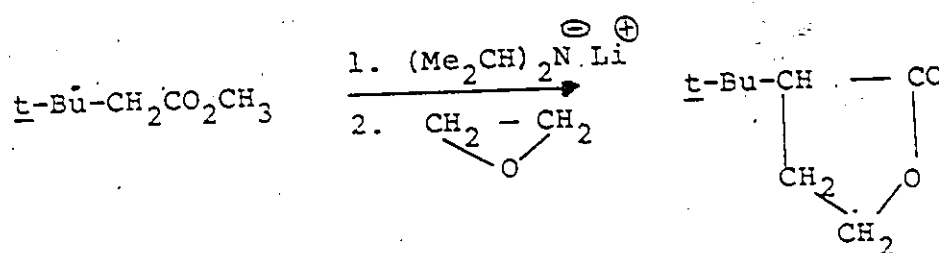
2.35 - 2.75

CH₃ (e)
 CH₃ (a)
 H_{4e}, H_{5a} and H_{5e}
 H_{4a}, H_{3a} and H_{3e}



sulfur by using triethyloxonium tetrafluoroborate (see chapter V) should allow the isolation of the less stable epimers of 39 - 42 and thus throw more light on the conformational aspects of these compounds.

Cis and trans 4-t-butyl-1,2-oxathiane-2-oxides 44 and 45 appear to be suitable model compounds for comparing the n.m.r. shifts in various sulfoxides. A simple and convenient synthesis of these isomers has been envisaged and is shown below.



CHAPTER V

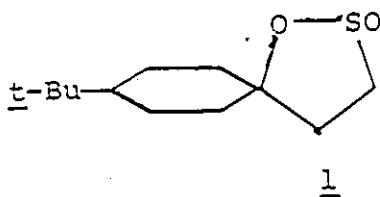
Reactions of Sultines

a) Introduction:

Since not many sultines were known prior to the commencement of this work, the properties (physical and chemical) of this class of compounds have not been adequately described. Several useful reactions of possible interest from a synthetic point of view, particularly the thermal and photochemical extrusion of SO_2 leading to the olefins¹ or cyclopropanes², were explored during the course of this work. A description of these follows in the subsequent pages.

b) Physical Characteristics:

All the new sultines, except 1 (m.p. 114-116^o C), prepared during this work, were found to be colorless distillable liquids. They were stable at room temperature for a few days but gradually deteriorated to yellow or brown materials.



In chloroform solutions the 5 - and 6 - membered sultines showed S=O band in the 1100-1120 range.^{3a} The band is somewhat broad in character and is the most intense in the whole spectrum and thus somewhat difficult to position precisely under normal conditions. Some tentative correlations can

however be suggested from the limited data.

Generally speaking it appears that the S=O absorption in the 5-membered species occurs at the lower end of the 1100-1120 range and in the δ -sultines toward the higher range. Harpp, Gleason and Ash^{3b} report 1105 and 1125 for the parent γ and δ sultines respectively. This trend is opposite to that observed for the analogous lactones⁴; γ -lactones generally absorb at 1750-1760 cm^{-1} while for δ -lactones the range is 1735-1740 cm^{-1} .

The data also suggest that in the γ -series, substitution at C₃ (α - to S=O) causes a slight lowering of the S=O frequency. In the six membered ring series the results are too scattered to make even tentative correlations.

The chloroform spectra all showed significant OH bands in the 3400-3500 cm^{-1} region suggesting that the sultines are significantly hygroscopic.

c) Mass spectra of sultines:

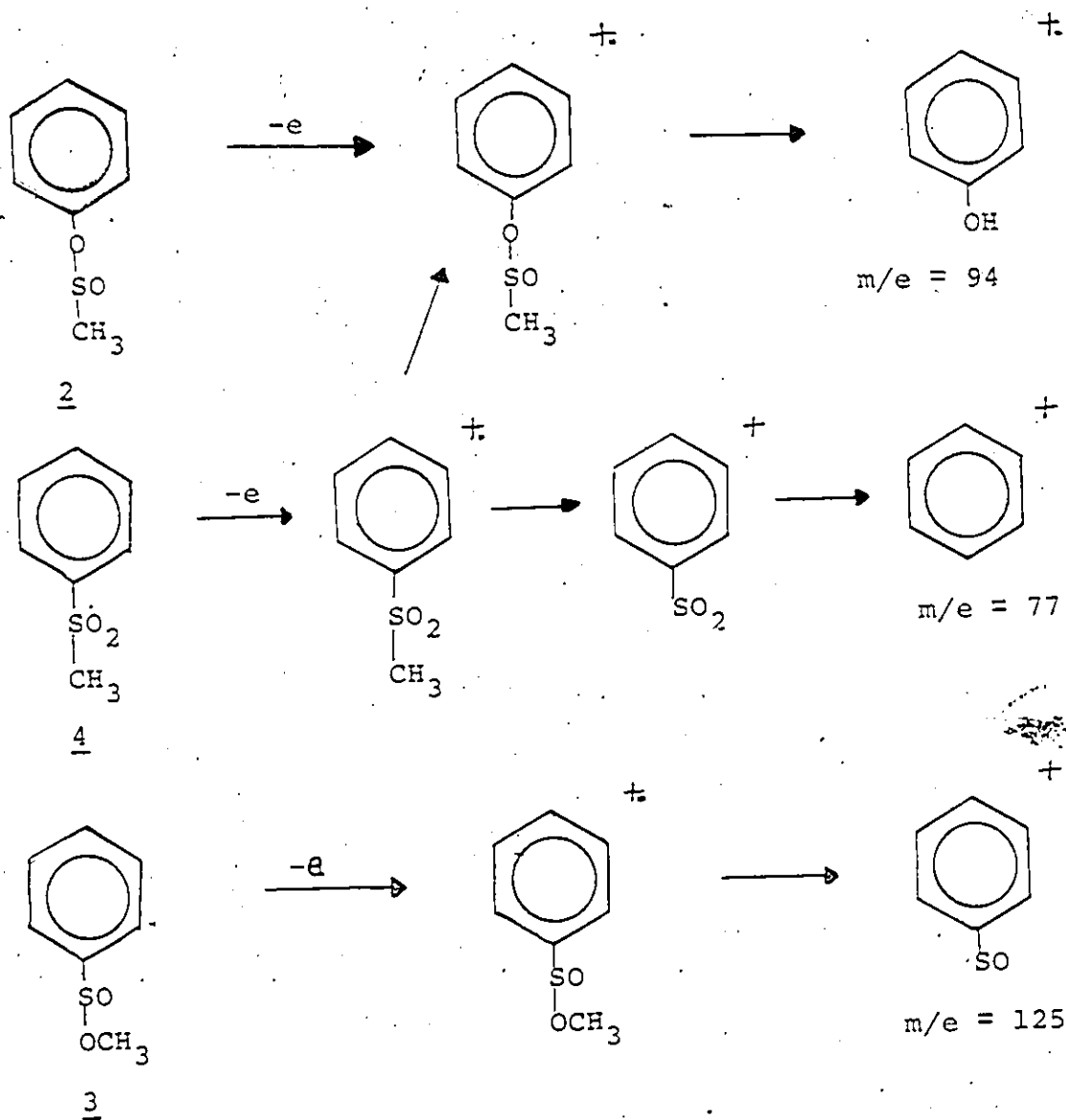
Baarschers and Krupay⁵ have recently reported what appears to be the first mass spectral study of the sulfinates esters. It was observed that the mass spectra of alkyl arene sulfinates were distinctly different from the spectra of the isomeric aryl alkane sulfinates. Both classes of compounds in turn could easily be distinguished mass spectroscopically from the sulfones with which they are isomeric.

For example in phenyl methane sulfinat_e,₂, the predominant peak was due to the loss of CH_2SO from the parent

molecular ion. In methyl phenyl sulfinates, 3, the loss of OCH_3 gave rise to the base peak while in phenyl methyl sulfone, 4, the base peak represented the loss of SO_2CH_3 from the molecular ion. (Scheme 1)

SCHEME 1

Mass spectral fragmentation of phenyl methyl sulfone and isomeric sulfinates



Since we had available a number of γ and δ sultines as a result of our new synthesis of these compounds and the fact that only a limited amount of mass spectral data on sulfinates of any type was available we decided to carry out a systematic study of the mass spectra of the cyclic esters.

The mass spectrum of 1,2-oxathiolane-2-oxide, 5, is recorded in figure 1. The spectrum was quite simple showing only five peaks (including a prominent molecular ion) above $m/e = 41$ having an intensity greater than 5% of the base peak; the genesis of each peak is easily understood. The molecular ion ($m/e = 106$) appeared to decompose by two or possibly three pathways. a) Loss of SO_2 gives rise to the base peak at $m/e = 42$ (C_3H_6^+) from which H^+ can be expelled to yield C_3H_5^+ at $m/e = 41$. b) Elimination of the elements of ethylene to form CH_2SO_2^+ ($m/e = 78$) which can further decompose by the loss of CH_2O to SO^+ at $m/e = 48$. Alternatively the SO^+ fragment can be formed directly from the parent ion by a formal cleavage of both the C-S and S-O bonds ($M - \text{C}_3\text{H}_6\text{O}$). It is also possible to arrive at $m/e = 41$ by the loss of SO_2H from the molecular ion. Unfortunately no metastable ions were apparent in the mass spectrum which might have allowed us to corroborate some of the above alternatives. The possible pathways of fragmentation are summarized in Scheme 2.

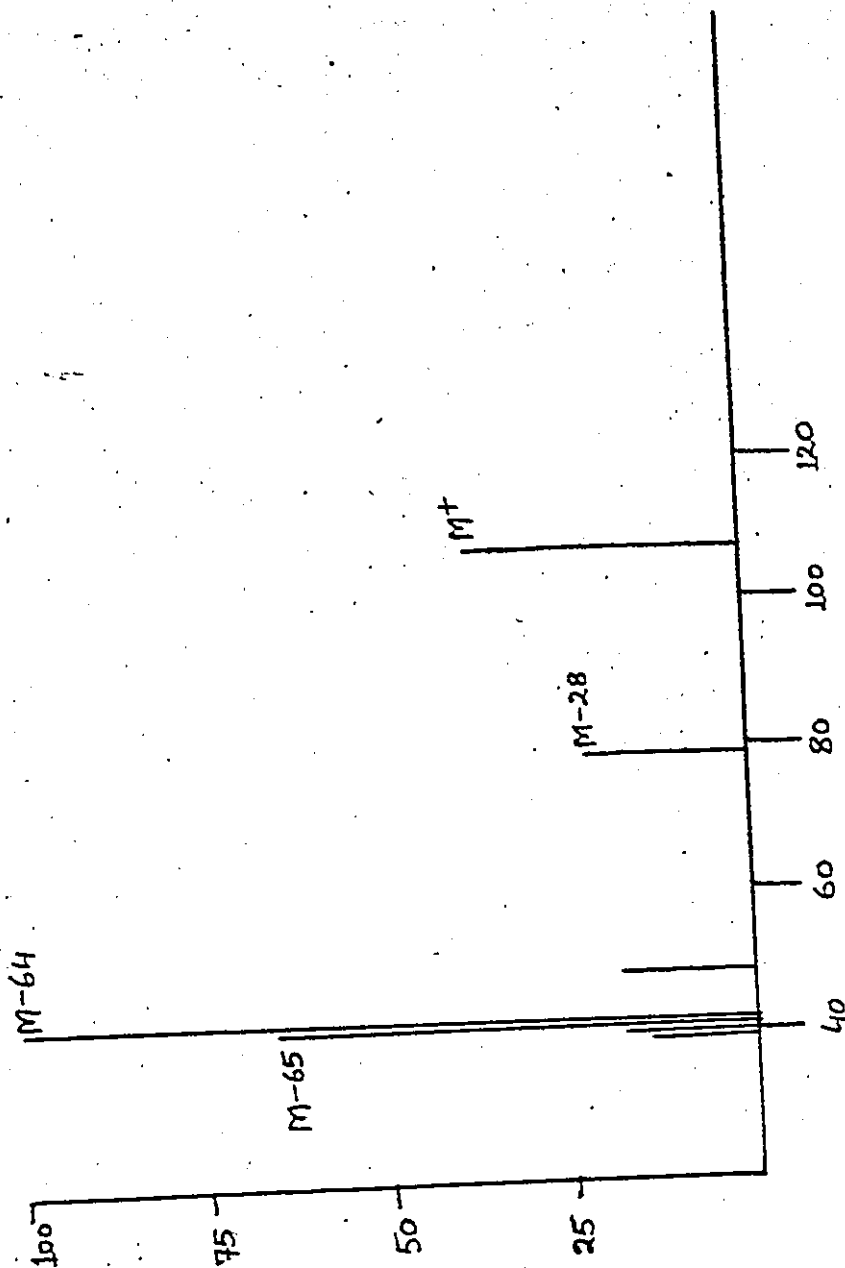
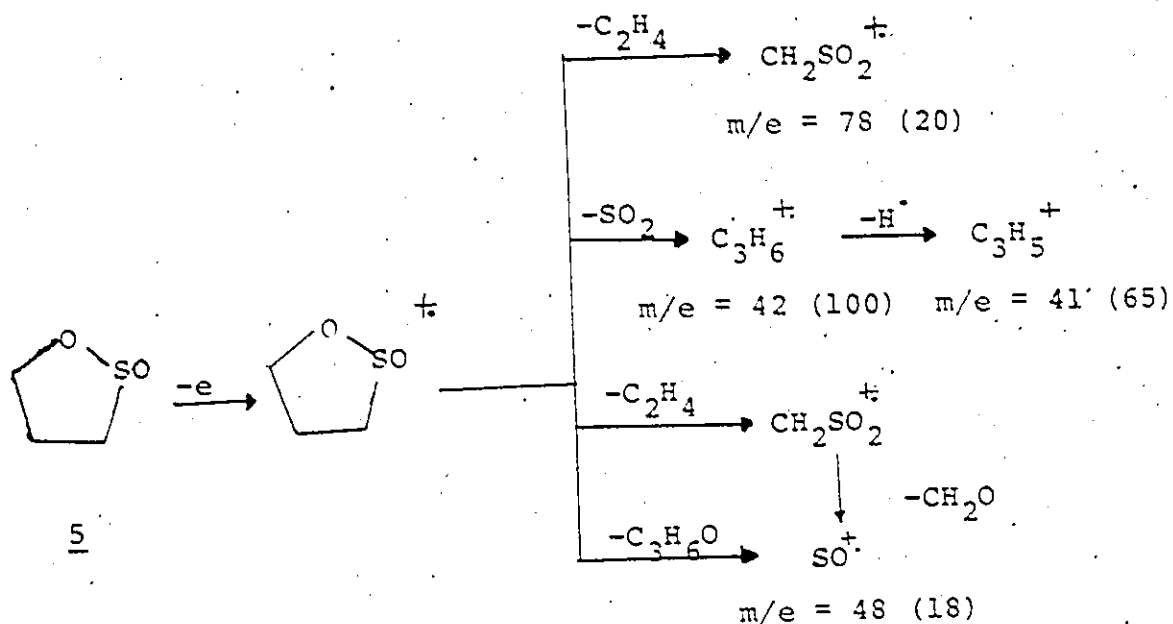


Figure 1: Mass spectrum of 1,2-oxathiolane-2-oxide

SCHEME 2

Fragmentation of 1,2-oxathiolane-2-oxide, 5.

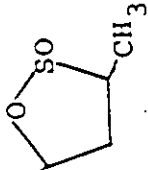
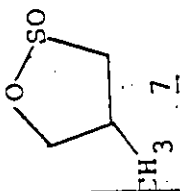
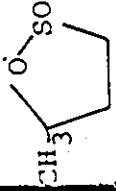


The important fragments observed in the mass spectra of the isomeric monomethyl γ -sultines (6 - 8) are recorded in Table I. The mass spectrum of 3-methyl-1,2-oxathiolane-2-oxide, 6, is recorded in figure 2.

The fragmentations of these sultines can be explained using the same general pathways discussed for the unsubstituted sultine 5 discussed above. All three sultines displayed prominent molecular ions at $m/e = 120$. Loss of ethylene from the molecular ion was again observed in each case to give $m/e = 92$. The $m/e = 91$ peak, probably due to the loss of $\text{H}^{\cdot}$ from 92, was also a significant peak. This fragmentation is easy to rationalize for both the 3- and 5-methyl isomers (6 and 8) but must

TABLE I

Mass Spectra of Monomethyl γ -sultines.

M^+	M-28	M-29	M-42	M-64	M-65	M-79
m/e (rel.ab.)	m/e (rel.ab.)	m/e (rel.ab.)	m/e (rel.ab.)	m/e (rel.ab.)	m/e (rel.ab.)	m/e (rel.ab.)
6	92 (16)	91 (34)	78 (29)	56 (12)	55 (100)	41 (61)
	120 (11)					
7	92 (10)	91 (15)	78 (12)	56 (37)	55 (33)	41 (100)
	120 (22)					
8	92 (20)	91 (34)	78 (22)	56 (15)	55 (100)	41 (64)
	120 (13)					

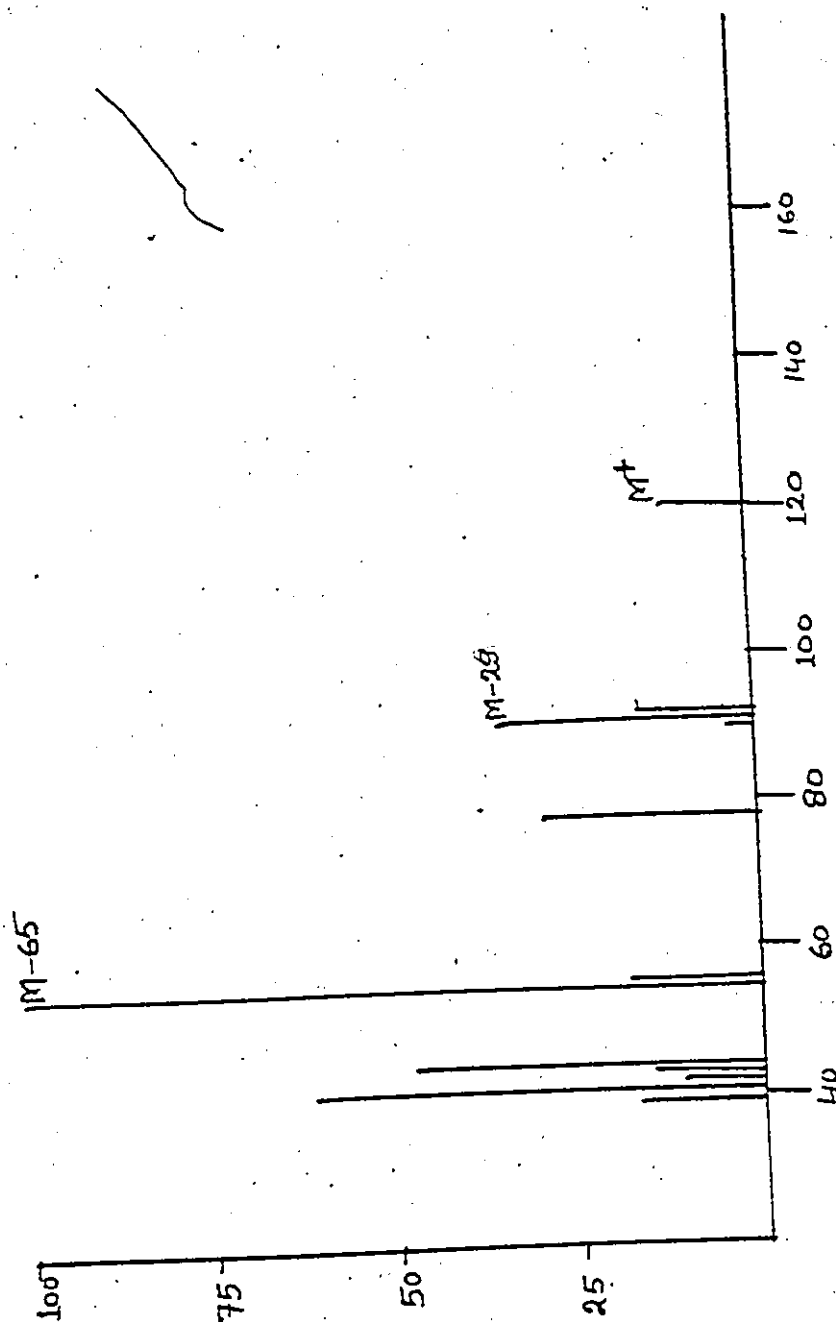
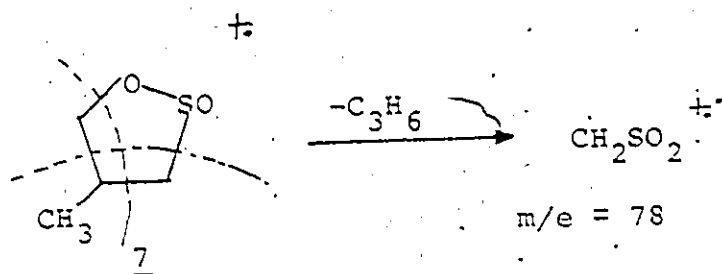


Figure 2: Mass spectrum of 5-methyl-1,2-oxathiolane-2-oxide.

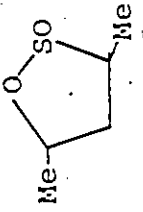
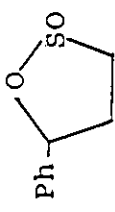
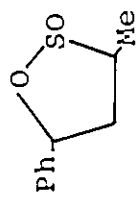
result from a prior reorganization of the carbon skeleton in 4-methyl-1,2-oxathiane-2-oxide, 7. The related loss of propylene resulting in a peak at $m/e = 78$ is surprisingly low in 7 compared to 6 and 8, considering that two possibilities exist in the former compound for the loss of this species and only one in the latter two.



In the parent compound 5, M-64 yielded the base peak, M-65 being approximately two thirds of that intensity. In contrast, in the isomers 6 and 8, M-65 (base peak) was found to be eight to ten times larger than M-64. The difference can be attributed to the greater inherent stability of C_3H_6^+ compared to C_4H_8^+ . For the 4-methyl isomer 7, the base peak was observed at $m/e = 41$ corresponding to the loss of $\text{CH}_3^\bullet$ from the C_4H_8^+ (M-64) fragment.

The mass spectrum of 3,5-dimethyl-1,2-oxathiolane-2-oxide, 9, (Table II) displayed a small peak at M-15 corresponding to the loss of $\text{CH}_3^\bullet$. Other prominent peaks were observed at M-42, M-64, M-65 and M-79. The genesis of these peaks can be explained using the same pathways suggested for the parent

TABLE 2
Mass spectra of substituted γ -sultines

Sultine	M^+ m/e (rel.ab.)	M-15 m/e (rel.ab.)	M-42 m/e (rel.ab.)	M-64 m/e (rel.ab.)	M-65 m/e (rel.ab.)	M-79 m/e (rel.ab.)
	134 (29)	119 (1.5)	92 (53)	70 (38)	69 (100)	55 (72)
	182 (2)	-	-	118 (84)	117 (100)	103 (-)
	196 (<1)	-	-	132 (60)	131 (10)	117 (100)

9

10

11

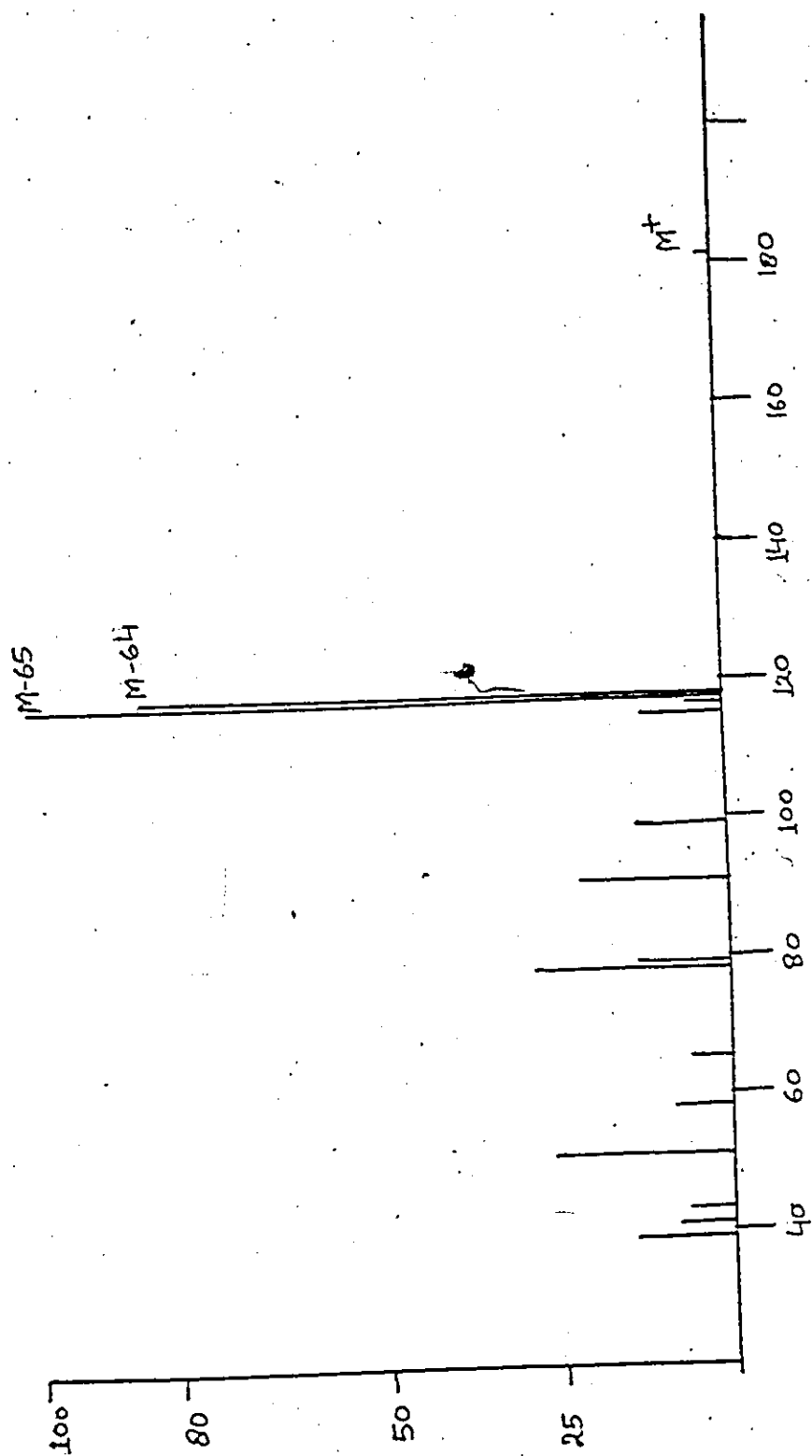


Figure 3: Mass spectrum of 5-phenyl-1,2-oxathiolane-2-oxide

and monomethyl derivatives.

Finally, for the 5-phenyl (10) and 5-phenyl-3-methyl (11) derivatives the initial extrusion of SO_2 followed by the loss of $\text{H}^\bullet$ for 10 and $\text{CH}_3^\bullet$ (mainly) or $\text{H}^\bullet$ for 11 constituted almost all of the ion current. The alternate routes e.g. loss of C_2H_4 or C_3H_6 are completely suppressed by this facile fragmentation ascribed to the weakening of the $\text{C}_5\text{-O}$ bond due to the presence of the phenyl group. There is a strong relationship between the mass spectral and photochemical behaviour of the 5-phenyl γ -sultines.

The mass spectrum of 1,2-oxathiane-2-oxide, 12 (figure 4) like its five membered ring analogue also showed a significant molecular ion. The spectra of these compounds show a strong similarity. As in 5, the loss of SO_2 (and $\text{SO}_2 + \text{H}^\bullet$) are very important though not the base peaks. Elimination of propylene, $\text{M}-42$, producing a peak at $m/e = 78$ (9% of the base peak) was somewhat less important than that of ethylene (20% of base peak) in 5. The peak at $m/e = 78$ was observed in a number of five and six membered ring sultines suggesting that this fragment can be considered as the molecular ion of sulfene (CH_2SO_2^+). The base peak in the mass spectrum of 12 occurred at $m/e = 41$; it is presumably formed from the molecular ion by the sequential loss of SO_2 and $\text{CH}_3^\bullet$ or, less likely, by the loss of CH_2SO_2 and $\text{H}^\bullet$. These fragmentation pathways are summarized in Scheme 3.

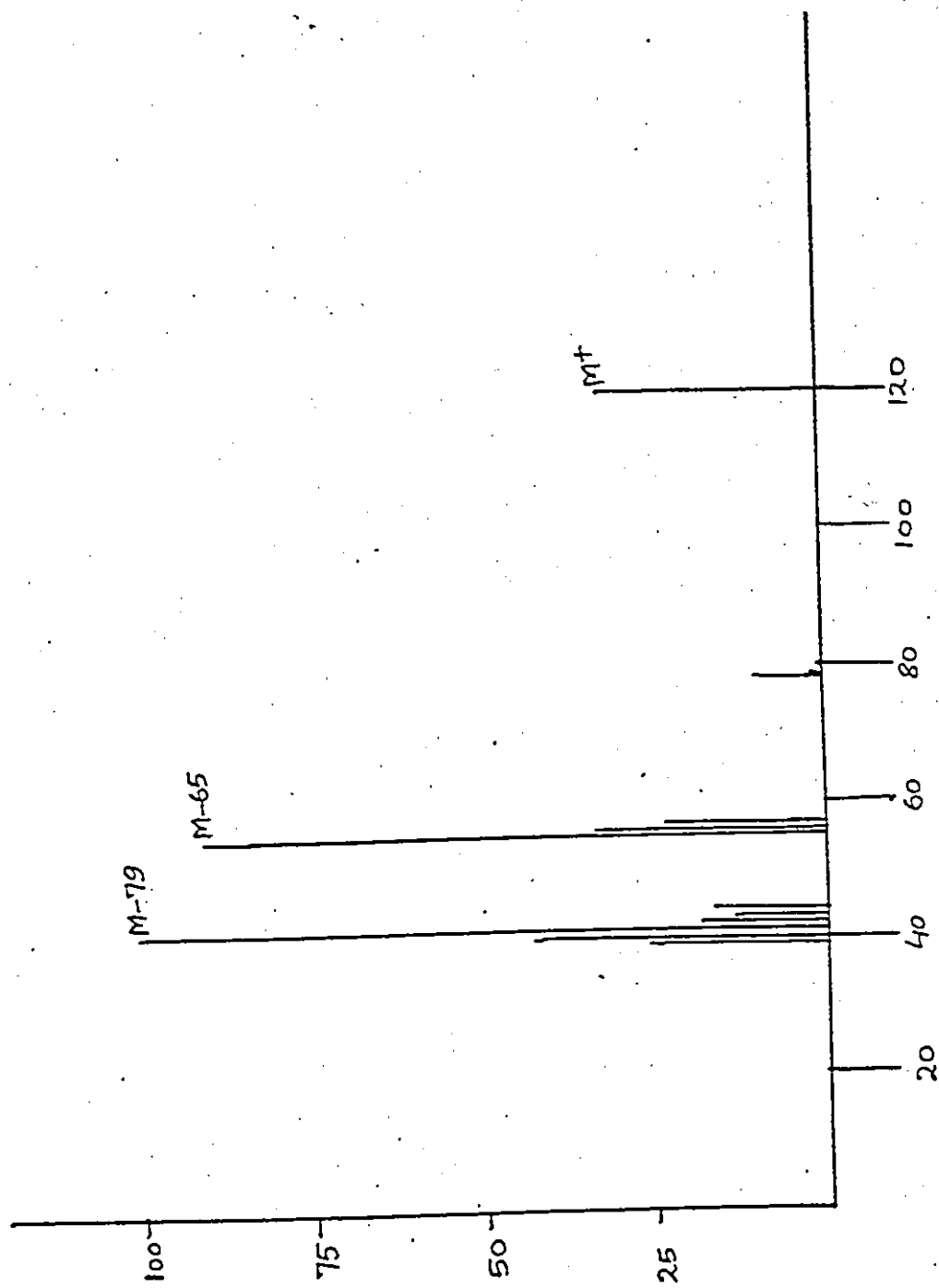
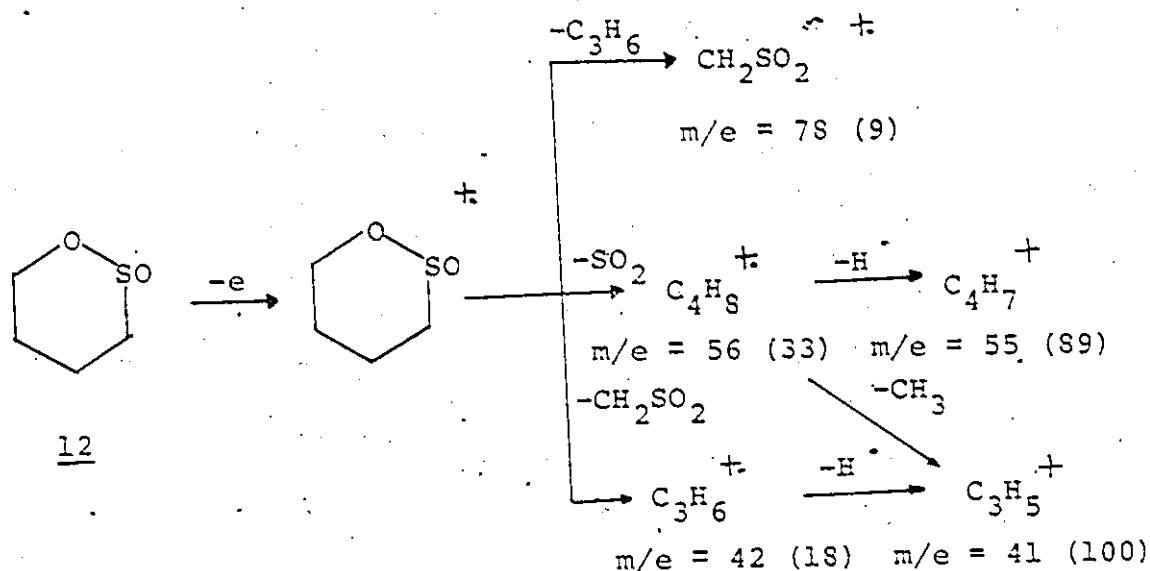


Figure 4: Mass spectrum of 1,2-oxathiane-2-oxide

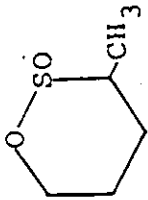
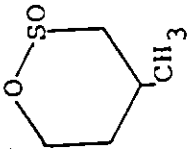
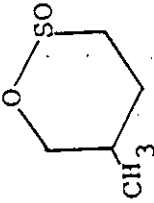
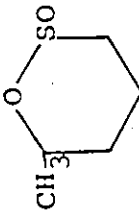
SCHEME 3

Fragmentation of 1,2-oxathiane-2-oxide, 12.

The data for monomethyl δ -sultines 13-16 are summarized in Table III. In each case there was a significant molecular ion and the spectra of the isomers were virtually identical. It is noteworthy that there was little loss of 28 or 42 mass units, an important pathway in the fragmentation of analogous γ -sultines. There was however observed a loss of 56 (C_4H_8) from the molecular ion giving rise to the ion fragment CH_2SO_2^+ ($m/e = 78$). The elimination of SO_2 (M-64) followed by either $\text{H}^\bullet$ (M-65) or $\text{CH}_3^\bullet$ (M-79) was again significant. The base peak in all four isomers was due to C_3H_5^+ representing loss of SO_2 , $\text{H}^\bullet$ and C_2H_4 or a combination thereof. Scheme 4 illustrates the various pathways encountered in the fragmentation of isomeric

TABLE 3

Mass spectra of monomethyl δ -sultines

Sultine	M^+ m/e (rel.ab.)	M-56 m/e (rel.ab.)	M-64 m/e (rel.ab.)	M-65 m/e (rel.ab.)	M-79 m/e (rel.ab.)	M-93 m/e (rel.ab.)
	134 (12)	78 (8)	70 (10)	69 (75)	55 (43)	41 (100)
	134 (15)	78 (9)	70 (10)	69 (75)	55 (57)	41 (100)
	134 (33)	78 (6)	70 (33)	69 (73)	55 (-)	41 (100)
	134 (14)	78 (12)	70 (10)	69 (82)	55 (20)	41 (100)

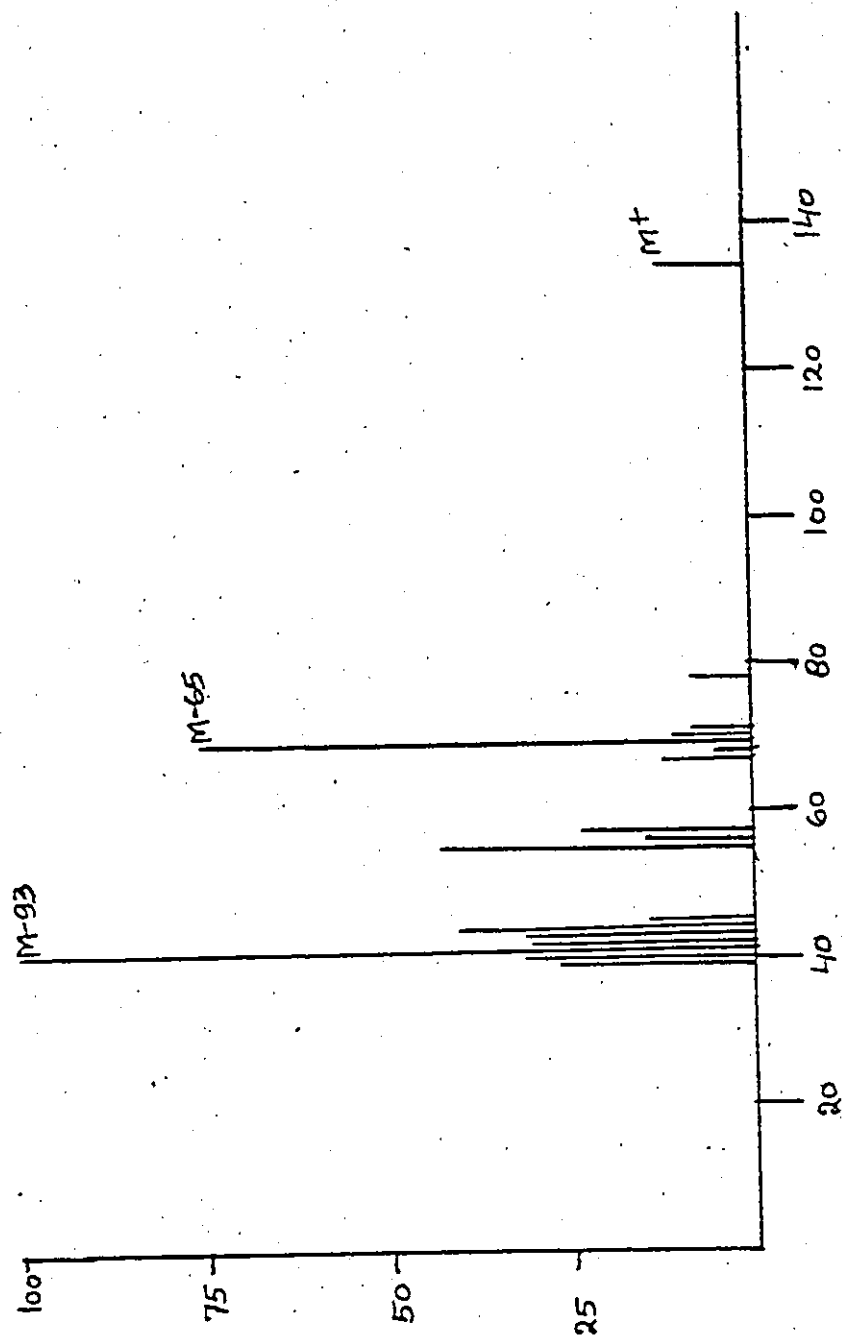
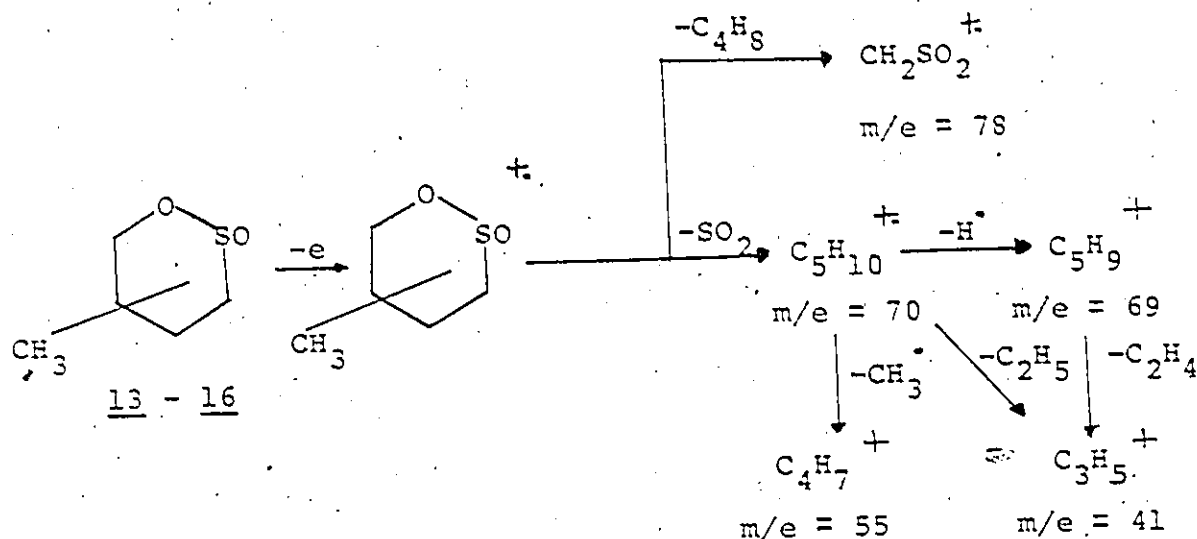


Figure 5: Mass spectrum of 4-methyl-1,2-oxathiane-2-oxide

monomethyl δ -sultines.

SCHEME 4

Fragmentation of monomethyl δ -sultines



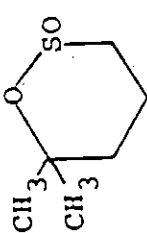
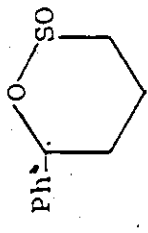
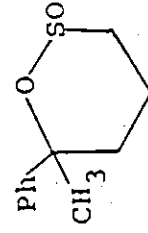
For the 6,6-dimethyl-1,2-oxathiane-2-oxide, 17, the peak resulting from the loss of SO_2 is relatively small.

Further decomposition of the M-64 fragment by the elimination of C_2H_5 or a combination thereof ($\text{H}^+ + \text{C}_2\text{H}_4$) yields the base peak at $m/e = 55$. The peak at $m/e = 42$ could have arisen via $\text{M} - \text{SO}_2 - \text{C}_3\text{H}_6$.

The 6-phenyl derivative 18 (figure 6) behaved quite similar to the 5,5-dimethyl sultine, 17 under electron impact. The initial ion formed by the loss of SO_2 appeared to fragment further via elimination of ethylene, thereby resulting in the base peak at $m/e = 104$. Compound 19 is the only sultine studied

TABLE 4

Mass spectra of substituted δ -sultines

<u>Sultine</u>	M^+ m/e (rel.ab.)	M-64		M-65		M-92		M-93		M-106	
		m/e	(rel.ab.)	m/e	(rel.ab.)	m/e	(rel.ab.)	m/e	(rel.ab.)	m/e	(rel.ab.)
	148 (11)	84 (5)		83 (10)		56 (-)		55 (100)		42 (44)	
<u>17</u>											
	196 (2)	132 (15)		131 (5)		104 (100)		103 (5)		90 (-)	
<u>18</u>											
	210 (-)	146 (-)		145 (6.0)		118 (16)		117 (11)		104 (100)	
<u>19</u>											

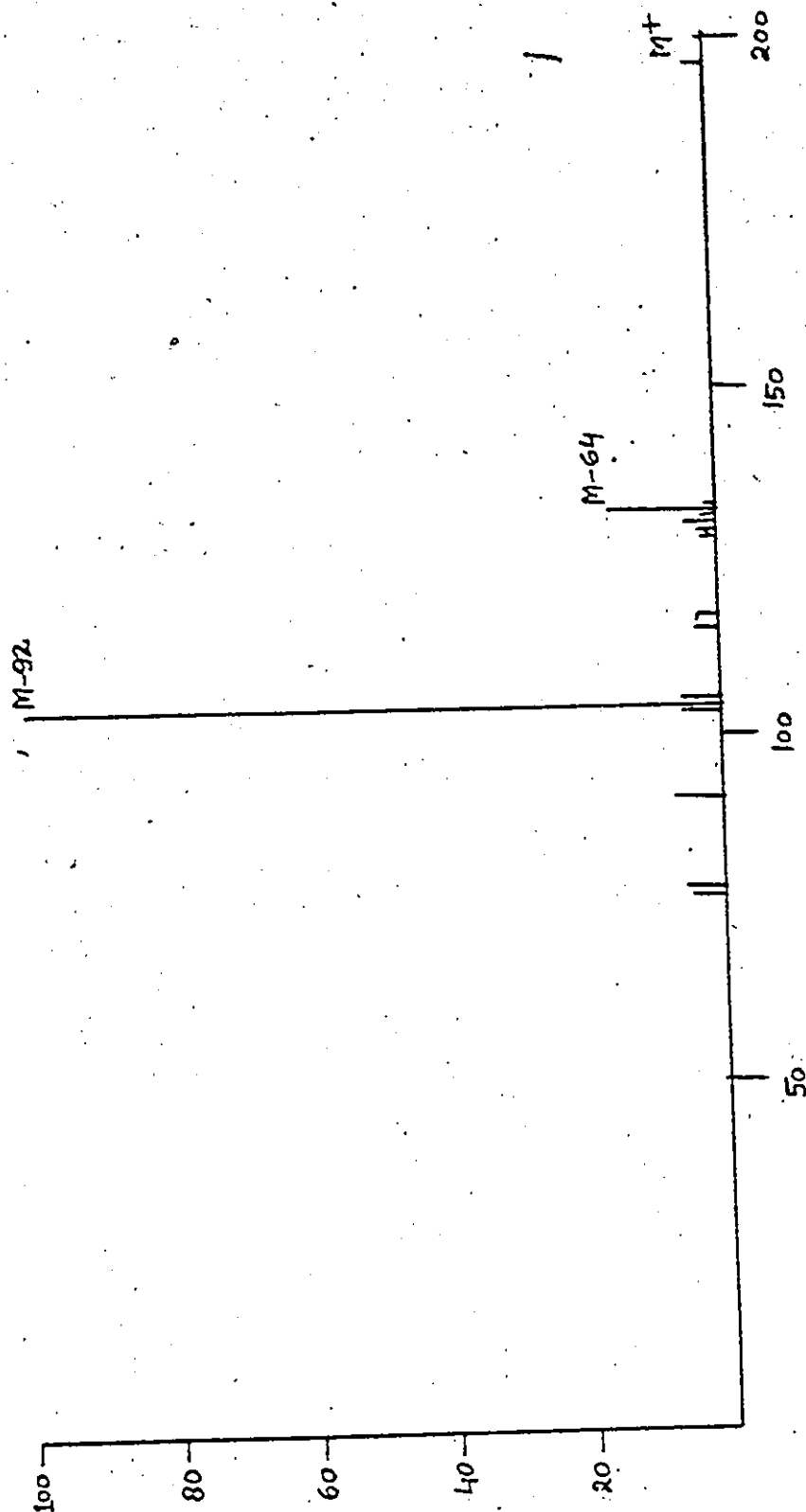


Figure 6: Mass spectrum of 6-phenyl-1-oxathiane-2-oxide, 18.

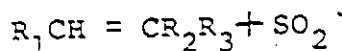
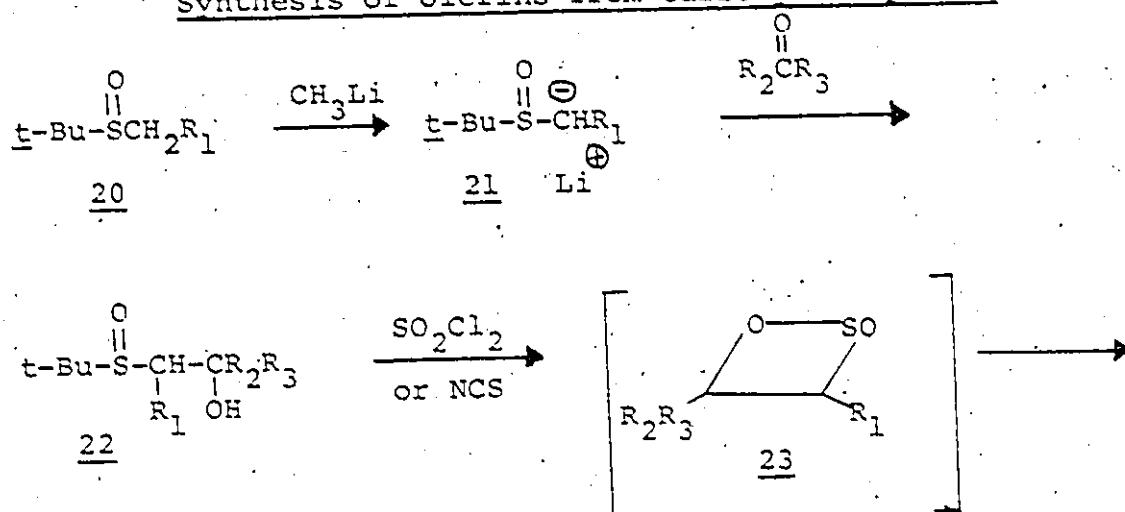
which did not give a molecular peak. The base peak at $m/e = 104$ can be arrived at most simply by sequential losses of SO_2 and C_3H_6 .

The mass spectra of the seven and eight membered ring sultines are relatively predictable; that of the seven membered ring species was remarkably similar to the monomethyl δ -sultines showing fragment ions at $m/e = 134$ (16), 78 (6), 70 (9), 69 (78), 55 (58), 42 (74) and 41 (100). For the eight membered ring compound the pattern was similar to the seven membered ring species, the peaks being displaced by required 14 mass units.

d) Thermal loss of SO_2 from 1,2-oxothietane-2-oxides (β -sultines)

Syntheses of five to eight membered ring sultines from the precursor t -butyl α -hydroxyalkyl sulfoxides have been described in detail in Chapter III. All initial attempts to synthesize β -sultines from β -hydroxysulfoxides by treatment with positive halogen species failed. It was found that β -sultines (1,2-oxathietane-2-oxides) have only limited thermal stability. They readily lose sulfur dioxide, in most cases within a few minutes at room temperature, to give olefins (Scheme 5).

SCHEME 5

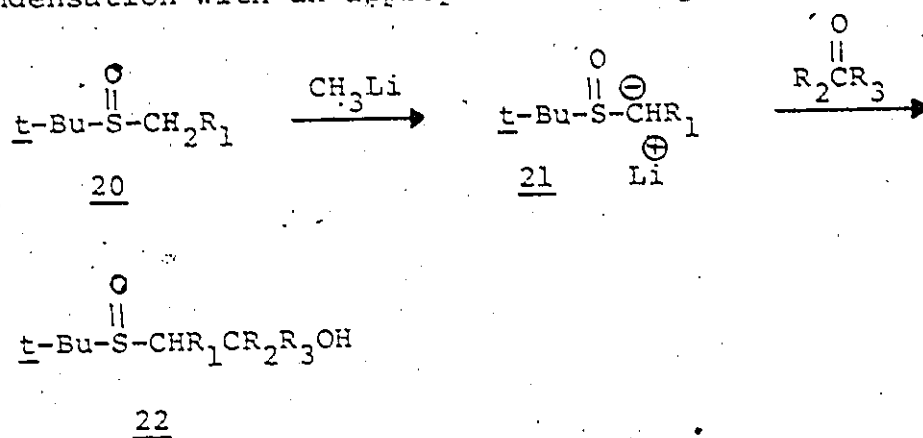
Synthesis of olefins from carbonyl compounds24

The work on the synthesis of olefins via β -sultines described in this section was carried out in collaboration with Dr. F. Jung who made the initial observations. The author's contributions were concentrated toward the isolation and/or characterization of a β -sultine, determination of the stereochemistry of the β -sultine decomposition and the synthesis of mono-substituted olefins utilizing the β -sultine route. For the sake of completeness some of the results obtained by Dr. Jung are included in the discussion.

The yields of olefins from β -hydroxysulfoxides were generally found to be good to excellent. The β -hydroxysulfoxides

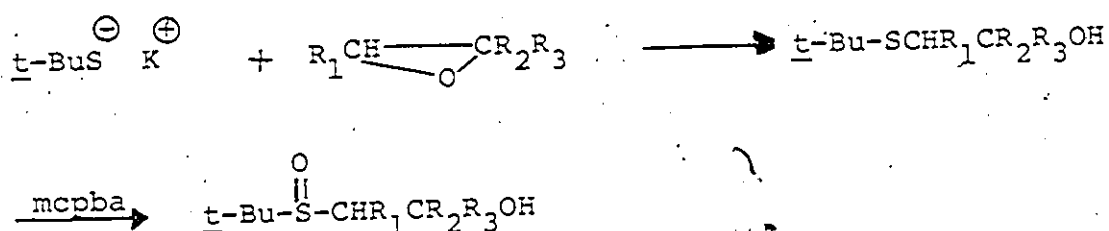
used in this study were prepared in one of the following two ways:

- i) Metallation of t-butyl alkyl sulfoxides followed by the condensation with an appropriate carbonyl compound.^{6,7}



As shown in Table V the yields for this route were good to excellent with a variety of both the sulfoxide and the carbonyl components.

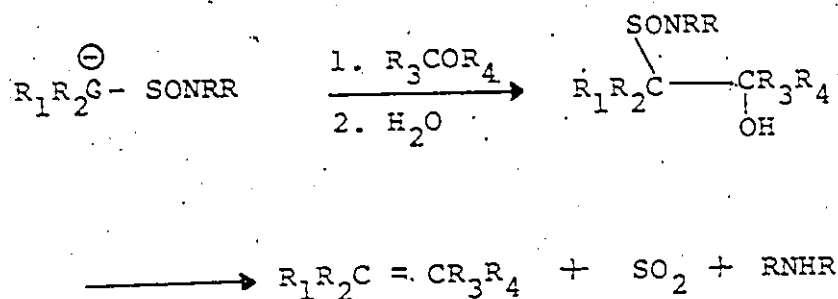
- ii) Reaction of t-butyl thiolate with an epoxide followed by m-chloroperbenzoic acid oxidation of thus formed hydroxysulfides.



Because of the stereospecific nature of the epoxide ring opening by the thiolate anion this was the method of choice for the preparation of β -hydroxysulfoxides (and thus the β -sulfine intermediates) of known stereochemistry.

The sequence comprising the condensation of the α -lithio-t-butyl sulfoxides with carbonyl compounds followed by the decomposition of the resultant β -hydroxysulfoxides (Scheme 5) has a close analogy to the Wittig olefin synthesis in which sulfur plays the role of heteroatom. Further consideration shows that the β -sultines, the α -lithio sulfoxides and t-butyl alkyl sulfoxides could be considered the equivalents of the oxaphosphetanes, phosphonium ylides and triphenyl alkyl phosphonium halides respectively.

An earlier rather limited Wittig like olefin synthesis based on sulfur as the heteroatom involved the thermal decomposition of β -hydroxy sulfinamides.⁸



A number of olefin syntheses have been reported in the last few years; several reviews on the subject are available.^{9,10,11,12}

Table V summarizes the yields of olefins together with those of the precursor hydroxysulfoxides.

TABLE V

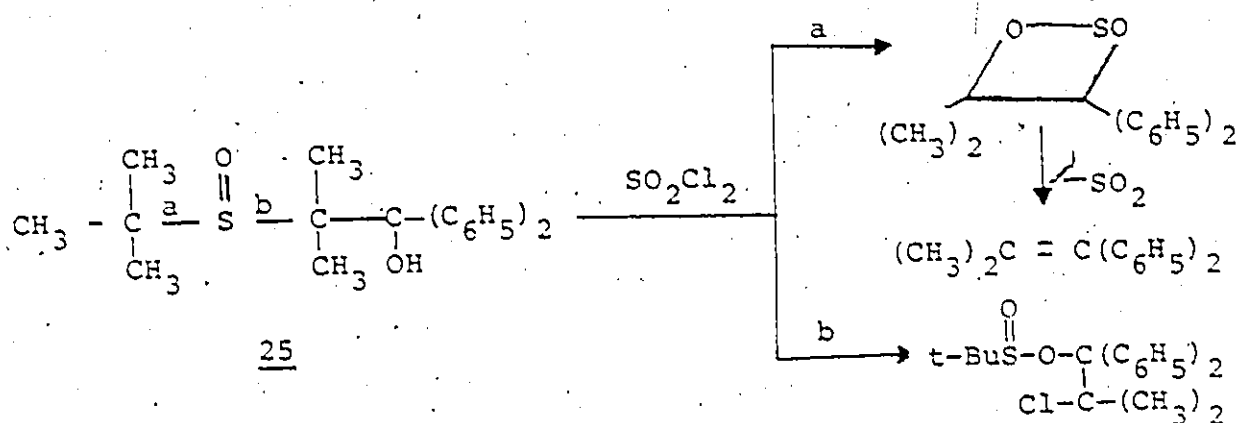
	t-Butyl alkyl sulfoxide alkyl	Carbonyl compound	Yield (%) ^a	
			Hydroxy Sulfoxide	Olefin ^b
I	Methyl	Benzaldehyde	95	82 ^a
II	Methyl	Cinnamaldehyde	95	75
III	Methyl	Δ^3 -Cyclohexene carboxaldehyde	75	62 ^a
IV	Methyl	Benzophenone	98	92
V	Methyl	Δ^5 -Cholesten-3-one	77	62
VI	Isopropyl	Benzophenone	97	53
VII	Ethyl	Benzophenone	97	92

a. All yields refer to the isolated yields except those noted by the superscript a; these are vpc yields.

b. Based on hydroxysulfoxide.

c. Entries IV, VI and VII taken from Dr. Jung's work.

As is evident from Table V, high yields (based on the precursor hydroxysulfoxides) were obtained when trisubstituted olefins were formed. The yields were more variable for the production of mono and disubstituted olefins. In the only example studied a tetrasubstituted olefin was obtained in 55% yield. This relatively poor yield is not surprising since the sulfoxide bond in the β -hydroxysulfoxide 25 is flanked by two tertiary carbon atoms and cleavage of either C-S bond can occur, one leading to the β -sulfones (olefins) and the other to sulfinate esters.



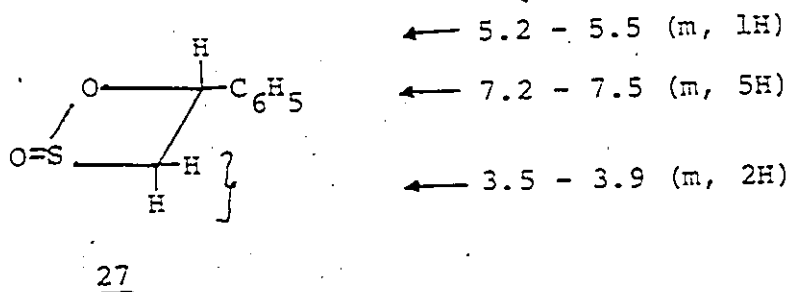
Although the overall yields of olefins via the β -sultine route is in many instances comparable to the Wittig synthesis a serious drawback of the sultine route is that it is necessarily a two step process requiring the isolation of the intermediate β -hydroxysulfoxides. This, however, in some instances may be advantageous. The diastereomeric β -hydroxy-sulfoxides formed by condensation of an aldehyde or a unsymmetrical ketone and 20 (R_1 = alkyl or aryl) can usually be separated by chromatography. Decomposition of the separated ¹³ isomers has been shown to lead to isomerically pure olefins.

Another advantage of the sultine route over the Wittig route is the ease of separation of the olefin from the byproducts, SO_2 and *t*-butyl chloride (or isobutylene) in the sultine synthesis vs triphenyl-phosphine oxide in the Wittig reaction.

One aspect which may dissuade others from utilizing the sultine route is rather unpleasant odours associated with sulfur chemistry. This aspect in reality is greatly reduced.

if one utilizes the t-butyl sulfides (many of which are available commercially); rather than t-butyl thiol as the starting material. The pure sulfoxides have no perceptible odour.

For quite some time the attempts to isolate β -sultines proved futile. However in several instances these species were found to have a sufficient life-time to allow the determination of some spectroscopic properties and interception by nucleophilic reagents. Thus the reaction of 26 (prepared by the condensation of t-butyl methyl sulfoxide with benzaldehyde) with sulfuryl chloride in methylene chloride at room temperature for fifteen minutes followed by the evaporation of the solvent in cold gave a crude product having n.m.r. spectral properties which could be ascribed to the β -sultine 27.

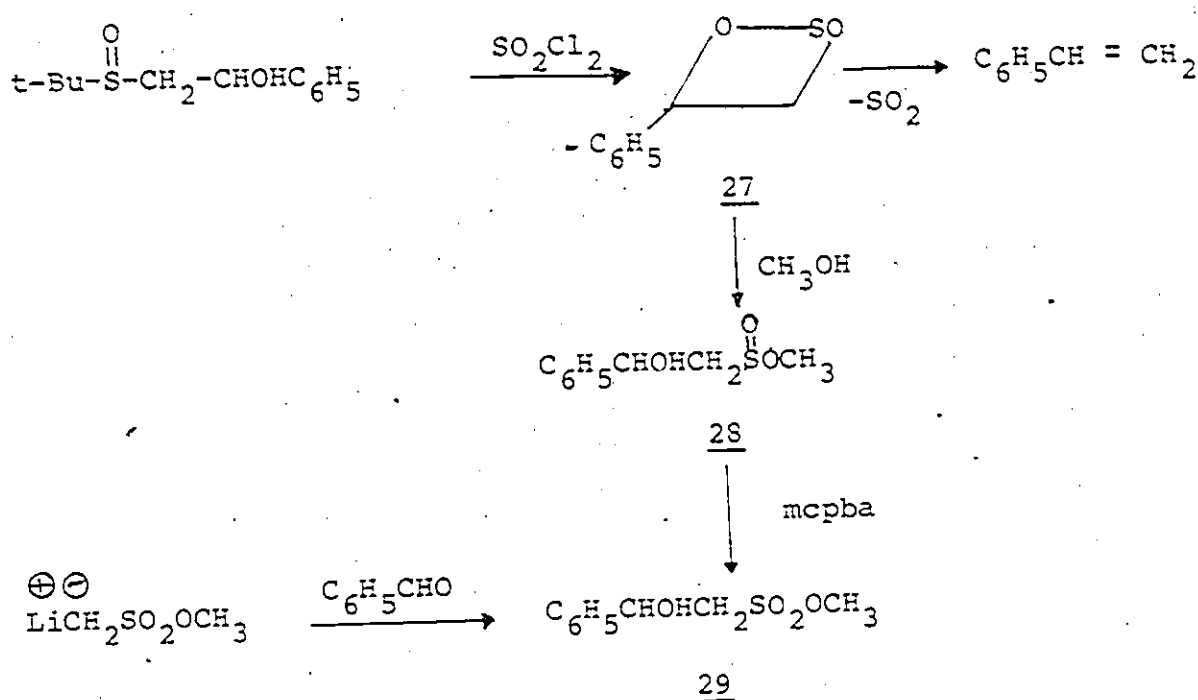


When the solution was allowed to stand at room temperature for several hours, the above peaks were replaced by those belonging to styrene. Addition of methanol to the reaction mixture prior to evaporation gave the β -hydroxysulfinate ester 28 formed by the attack of methanol on the sulfur in 27. The n.m.r. spectrum of ester 28 displayed the following features:

a multiplet at δ 1.9 - 2.6 (3H); a singlet at δ 3.83 (3H); a multiplet at δ 5.3 - 5.7 (1H) and a multiplet at δ 7.4 (5H). This ester was further characterized by its oxidation to the corresponding β -hydroxy sulfonate ester 29 which in turn was also synthesized from the α -lithio derivative of methyl methane sulfonate and benzaldehyde. (Scheme 6)

SCHEME 6

Interception of a β -sultine by nucleophilic reagent



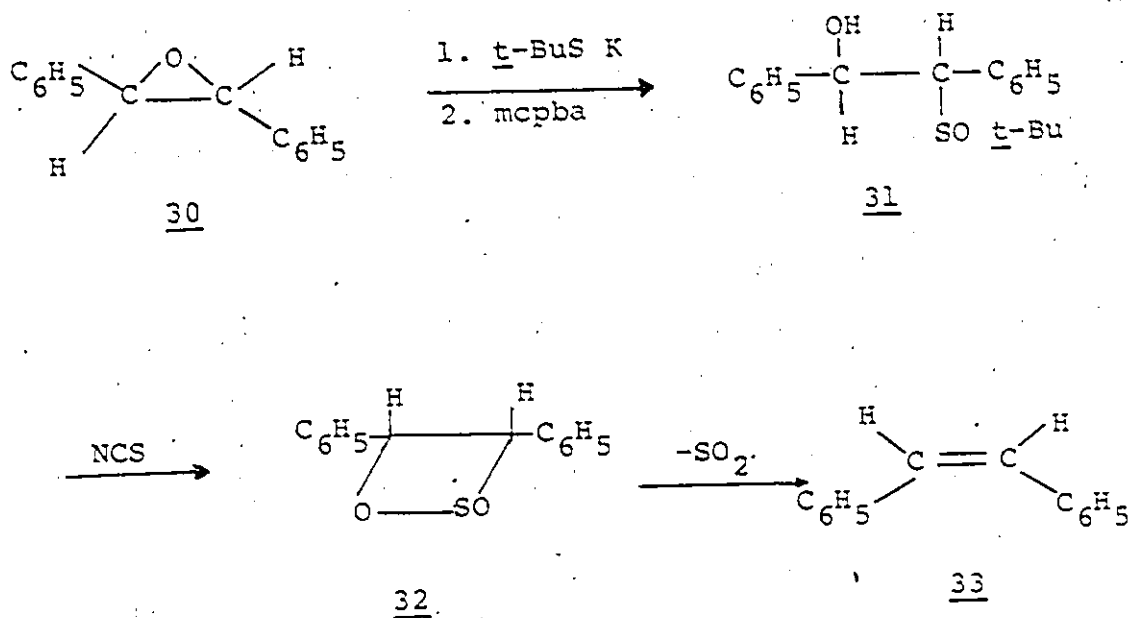
The loss of SO_2 from β -sultines was shown unambiguously to be ^astereospecific cis-elimination. Thus reaction of 31 with NCS in benzene at reflux temperature resulted in the formation of cis-stilbene, 33 in 50% isolated yield. No

trace of trans-stilbene could be detected either by T.L.C. analysis or n.m.r. spectroscopy of the total crude product.

(Scheme 7)

SCHEME 7

Stereochemistry of the decomposition of β -sultines.

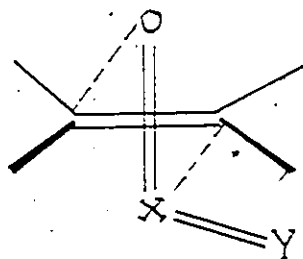


Since the stereochemistry at the two benzylic carbons of the β -sultine is known, being related by a stereospecific ring opening to trans-stilbene oxide, the β -sultine formed by the cyclization of 31 must necessarily have the two phenyl groups in a relationship as shown in 32.

The exclusive formation of cis-stilbene, 33, despite the fact that it is thermodynamically much less stable than the trans-isomer underscores the stereochemical integrity of

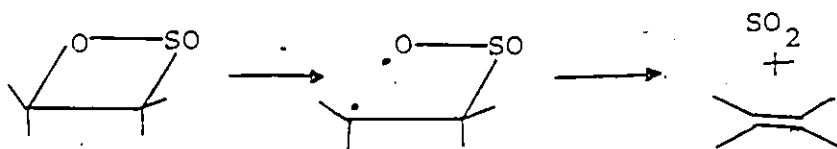
the SO_2 elimination process.

The decomposition of β -sultines is reminiscent of the stereospecific cis-elimination of CO_2 and isocyanates from β -lactones and β -lactams, respectively. These decompositions generally occur at a considerably higher temperature (about 150°C for the β -lactones and above 450°C for β -lactams) than the SO_2 loss from the β -sultines. The loss of CO_2 and $\text{R-N} = \text{C} = \text{O}$ have been designated by Paquette as examples of $\pi 2s + \pi 2a$ cycloreversion with the cumulative system being the $\pi 2a$ component. Similar designation could perhaps be made for the sultine decomposition although no orbital correlations have as yet been made.



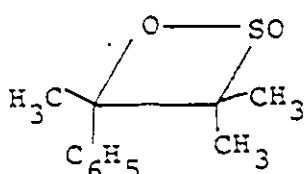
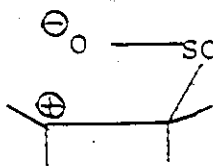
$x = \text{C or S}$
 $y = \text{O or NR}$

Several alternative mechanisms for the sultine decomposition can be considered. For example homolytic cleavage of the C-O bond could lead to a diradical intermediate from which the loss of SO_2 would furnish the olefin. In such a case the SO_2 loss would have to be considerably faster than the C-C bond rotation to account for the stereospecificity.

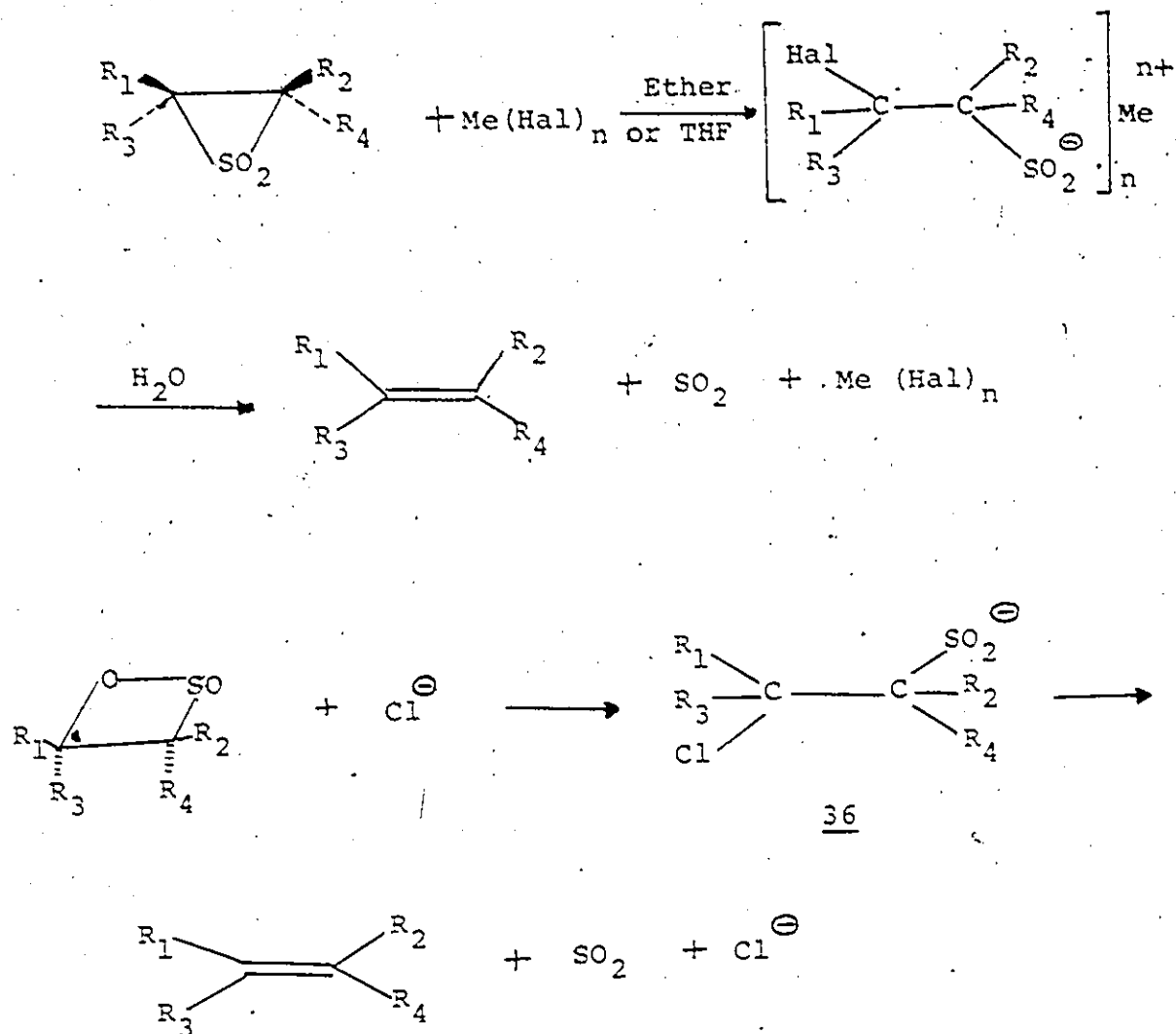


16

The fact that B.Gimbarzevsky has been able to isolate the sulfone 34 as a relatively stable material argues against this mechanism since cleavage of the C-O bond in 34 would lead to a relatively stable diradical. Similar considerations can also be used to discriminate against a dipolar intermediate such as 35.

3435

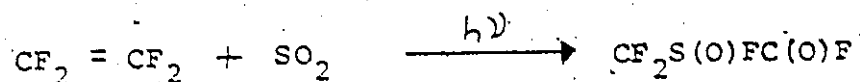
Another possible mode of decomposition under certain conditions was suggested by the work of Vilsmaier and coworkers who converted episulfones to olefins via the intermediacy of β -halo sulfinates, a reaction which represents an overall stereospecific cis elimination. Thus chloride ion which is present to a considerable extent under the usual decomposition conditions could conceivably attack at C₄ to yield the β -chloro-sulfinate 36 which would, based on the above result, form the olefin.



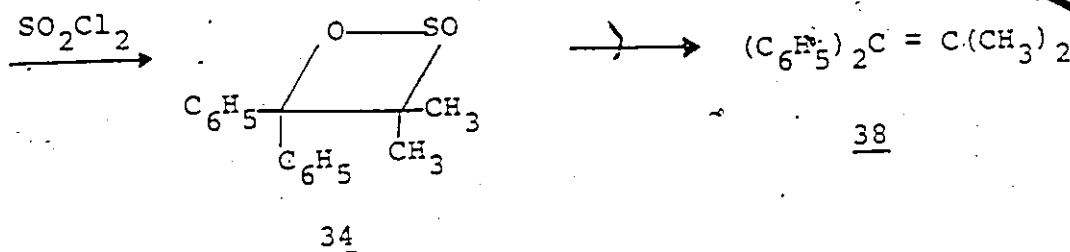
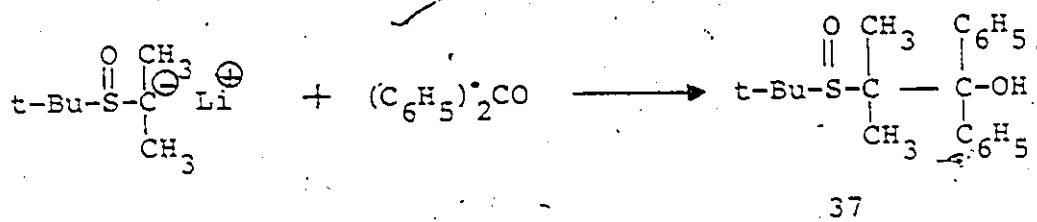
This possibility is however considered unlikely in view of the usual attack of nucleophiles on the sulfinyl sulfur^{18,19} in the sulfinate esters. In particular, as shown above, methanol opens the β -sultine by S-O rather than C-O bond cleavage.

β -Sultines, in contrast to β -sultones, especially polychlorinated and polyfluorinated β -sultones, have not been

previously isolated. A polyfluorinated β -sultine has been suggested as an intermediate in the following reaction:



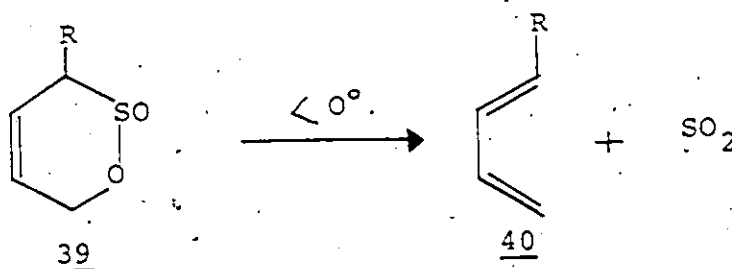
As referred to above, a stable β -sultine has been isolated in this laboratory during the past year. Thus reaction of the β -hydroxysulfoxide 37, prepared from α -lithio-*t*-butyl *iso*-propyl sulfoxide and benzophenone, gave the sultine 34 in 50% yield.



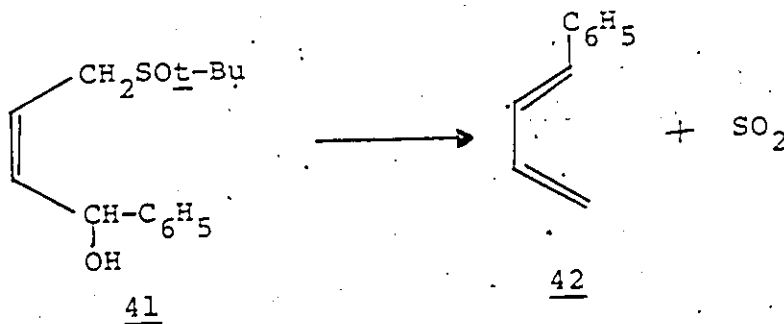
The crystalline sultine showed a strong S=O absorption in the infrared at 1150 cm^{-1} and n.m.r. singlets at $\delta 1.30$ and 1.43 due to the two nonequivalent methyl groups. At its melting point, $92-94^\circ$, the sultine decomposed to the expected olefin 38 (100%) and SO_2 .

The sultine 34 is in all likelihood nonplanar allowing for optimum distance between the bulky substituents on C-3 and C-4. In the transition state due to the shortening of the C-C bond and the necessity for bringing all the carbon substituents into the same plane, there is expected to be a significant increase in steric hinderance. This in effect raises the transition state energy relative to the ground state thus increasing the thermal stability of the sultine.

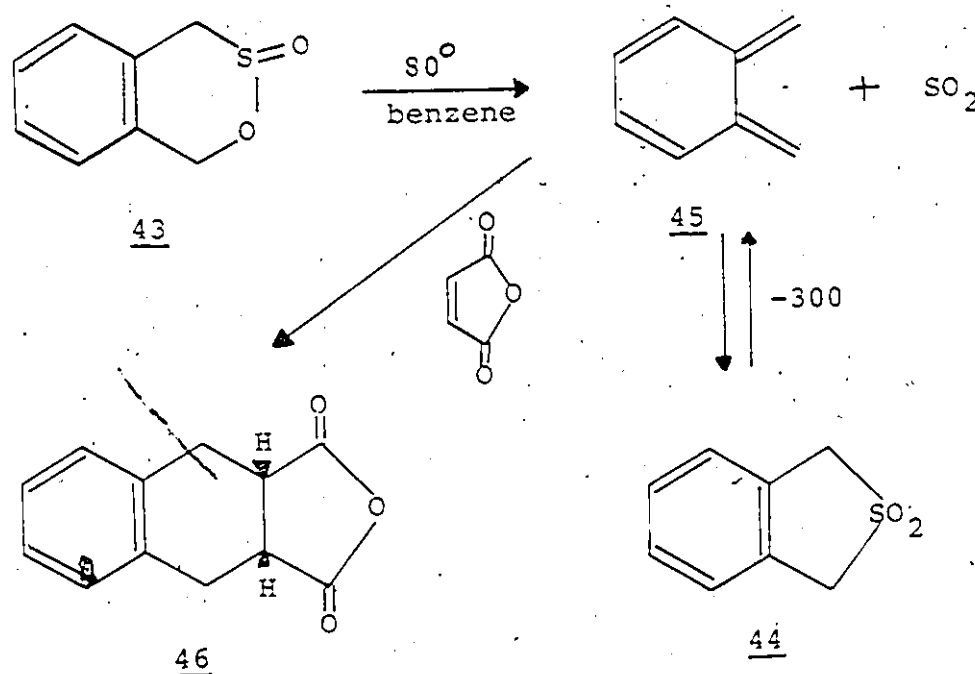
While the thermal elimination of sulfur dioxide from β -sultines was being studied, it was also found that 3,6-dihydro-1,2-oxathian-2-oxides 39 fragment into SO_2 and 1,3-dienes 40 below 0°C .²¹ This stereospecific transformation appears to be the first example of the formation of SO_2 and 1,3-dienes via a $\pi 4_s + \pi 2_s$ cycloreversion.



The stereospecific nature of this decomposition was shown by the conversion of the *cis*-hydroxysulfoxide 41 to isomerically pure *trans*-1-phenyl-1,3-butadiene, 42.



The benz-fused sultine 43 has presented some novel and synthetically interesting results. When heated in refluxing benzene it cleanly isomerized to 1,3-dihydro benzo (c)-thiophene-2,2-dioxide, 44 ($t_1 = 6$ hrs). That this isomerization represented a cycloreversion to o-quinodimethane 45 and SO_2 followed by a typical $\text{SO}_2 + 1,3$ -diene cycloaddition was shown by carrying out the thermolysis in presence of a very reactive dienophile such as maleic anhydride. Under these conditions tetrahydronaphthalene derivative 46 was obtained in over 95% yield.



This route represents a very mild and effective approach to these reactive dienes and has been used to prepare several derivatives bearing substituents in the exocyclic methylene group.²¹

- e) Synthesis and characterization of 3,4,6,7-tetraphenyl-1,5-dioxa-2-thiepane-2-oxide. (Attempted isolation of 3,4-diphenyl-1,2-oxathietane-2-oxide)

Encouraged by the isolation and characterization of the β -sultine 34, the sulfonyl chloride reaction with the hydroxysulfoxide 31 was repeated at low temperature with the hope of isolating the β -sultine 32. Based on the rationalization given for the stability of 34, the β -sultine 32 having two phenyl groups cis to each other was expected to have reasonable thermal stability.

Treatment of 31 with 1.1 equivalents of sulfonyl chloride in dichloromethane at -70° resulted in the complete disappearance of the starting material within fifteen minutes (as evidenced by TLC). The solvent was carefully removed in cold under vacuum and the crude residue subjected to column chromatography on silica gel. Elution with methylene chloride furnished initially diphenyl-acetaldehyde, 47, and subsequently a colorless solid to which the structure 48 was assigned based on the evidence outlined below. The yields of 47 and 48 were 30% and 60% respectively.

Similar results were obtained when the above reaction was carried out with NCS at room temperature. These results are completely different than those described in the previous section regarding the stereochemistry of the sultine decomposition in which it was claimed that 31 and NCS in refluxing benzene gave pure cis-stilbene in 50% yield.

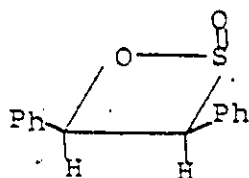
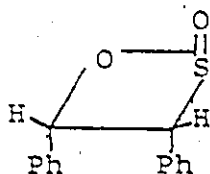
Both sets of reaction conditions were repeated several times to ensure their validity. Examination of the crude reaction products obtained under both conditions showed that there was no cross-over i.e. no cis-stilbene was obtained at -70° nor was any of 48 observed when the reaction was carried out in refluxing benzene. Furthermore 48 was eliminated as a possible intermediate in the cis-stilbene formation by the observation that no cis-stilbene was obtained when the NCS reaction was first carried out at room-temperature and then, after the disappearance of the starting sulfoxide, the reaction mixture was refluxed for a considerably longer period of time than was required to produce cis-stilbene under the initial reflux conditions.

Compound 48 was crystallized from methylene chloride/pentane to furnish a colorless powder (m.p. $160-162^{\circ}$), homogeneous on T.L.C. The infrared spectrum showed absorption at 1125 cm^{-1} , characteristic of the O-S=O grouping. The proton n.m.r. spectrum showed the following features:

δ 3.49 (d, 3.0Hz, 1H); 4.53 (d, 3.0Hz, 1H); 6.17 (d, 3.0Hz, 1H); 6.67 (d, 3.0Hz, 1H) and 6.7-7.4 (m, 20H).

Decoupling experiments established that the protons at δ 3.49 and 4.53 were coupled with those resonating at 6.17 and 6.67 respectively. The carbon-13 n.m.r. spectrum showed four aliphatic carbons at 55.3, 66.3, 73.9 and 94.3 ppm in addition to the aromatic absorption at 132-136 ppm.

At first sight these spectra could be interpreted in terms of a 1:1 mixture of the diastereomeric β -sultines 49 and 50.

4950

However the unusual thermal stability of the compound (no change was observed when the compound 48 was refluxed in benzene for 48 hours) cast doubt upon this explanation. Furthermore repeated recrystallizations failed to give any change in the relative size of the integrals for the various protons. Thus the unknown compound 48 cannot be accommodated by the β -sultine structures.

Elemental analysis bore out the above fact. The found analytical values for 48 are shown in Table VI. They are in good agreement with the molecular formula $C_{28}H_{24}O_3S$ but rather far from the values calculated for the β -sultine formula ($C_{14}H_{12}O_2S$). A molecular weight determination by osmometry, 416 ± 13 , was not far from the value 440 required for $C_{28}H_{24}O_3S$.

Based on the above results, and on some of the chemistry described on the following pages, the 7-membered sultine structure, 3,4,6,7-tetraphenyl-1,5-dioxo-2-thiepane-2-oxide,

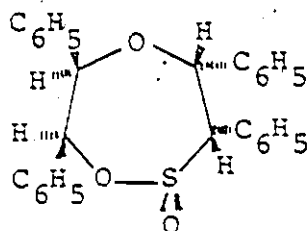
was assigned to the unknown 48.

For example the structure 48 requires four aliphatic protons each coupled to one other proton as is observed. The required four different aliphatic carbon atoms were present in the carbon-13 spectrum. Selective proton decoupling of the carbon-13 spectrum showed that the hydrogens resonating at $\delta = 3.49, 4.53, 6.17$ and 6.67 were attached to the carbons appearing at $66.3, 55.3, 73.9$ and 94.3 ppm respectively assuming that the highest field hydrogen ($\delta = 3.49$) is attached to the carbon α to the sulfinyl group and the lowest field hydrogen ($\delta = 6.72$) to the carbon bearing the ester oxygen.

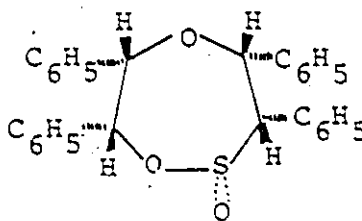
Although there are a number of unusual features, for example, an 18 ppm difference in the chemical shifts of rather similar C_4 and C_6 and a 1.64 ppm difference between the hydrogens attached to these carbons, the above assignments are much more reasonable than any of the alternatives. The chemical shift difference referred to above appears to be at least qualitatively in the right direction. If the C_4 hydrogen is in a syn 1,3-"diaxial" relationship with the sulfinic oxygen a large deshielding, similar to that observed for the 6-axial hydrogen in the δ -sultines (0.8 ppm), is possible. Under these conditions the C_4 resonance would be expected to be shifted upfield due to the γ -steric effect (See Chapter IV).

Based on the relative stereochemistry of the phenyl groups in the starting material the most likely structure for 48 is one with the geometry of the two bibenzylic units

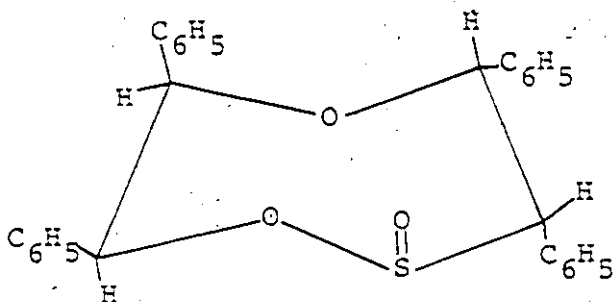
retained i.e. either 48a or 48b.



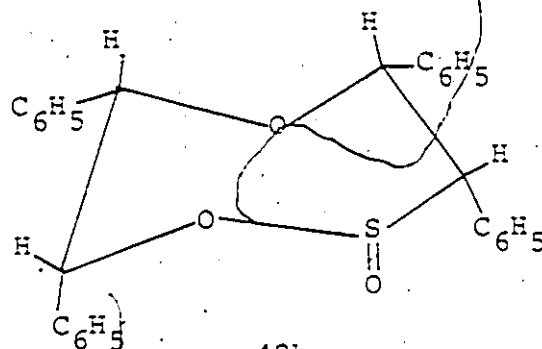
48a



48b



48a



48b

Inspection of molecular models indicated that 48a could more readily take up a conformation which would allow the rationalization of the large shifts observed in the proton and carbon-13 n.m.r. spectra. These conclusions are obviously extremely tentative. An X-ray structure determination would seem to be the best way to resolve the problem.

Since the structure of 48 had a phenyl group α to the sulfinate oxygen and experience had indicated that such

esters are photochemically labile (see next section) it was decided to carry out a photolysis of 48. In the event, irradiation of 48 in benzene-acetone solution with a medium pressure mercury lamp, using corex filter, for thirty minutes resulted in the formation of an isomer of 48, compound 51 (m.p. 162-164°) in quantitative yield. The analytical and spectroscopic data of 51 are listed in Table VI.

The n.m.r. spectrum of 51 like that of 48 showed four sets of doublets at δ 4.02, 4.43, 5.86 and 6.67. The 4.02 and 5.86 peaks were related by an 11.0Hz coupling constant; that between the other two protons was 4.0Hz. Thus the protons were assigned to positions 3,6,4 and 7 in order of increasing δ -values.

Since the photolysis of the other sultines bearing a phenyl group α to oxygen proceeds via the cleavage of C-O bond it seems reasonable to believe that in this case the isomerization occurred in a similar manner. Thus the sultine 51 may be assigned the structure (using 48a as precursor) shown below.

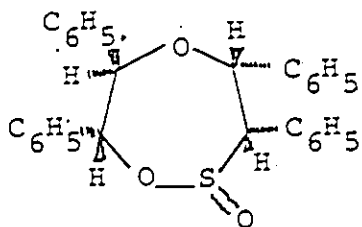
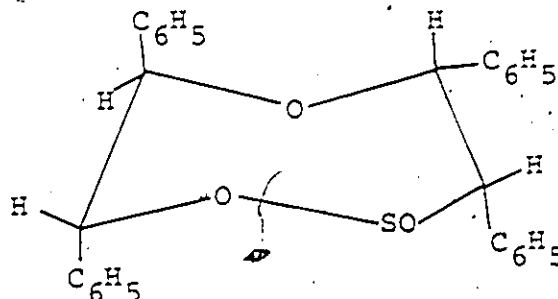
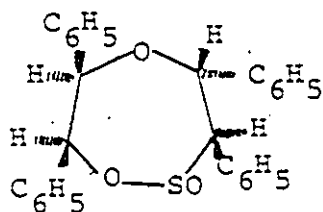
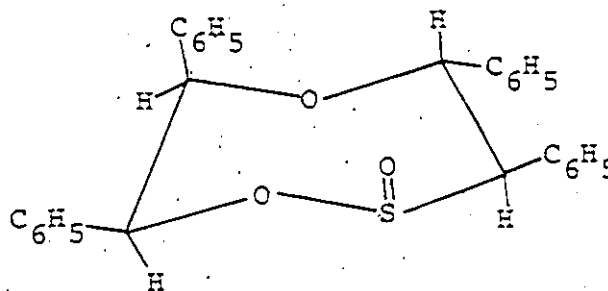
51a51a

TABLE VI

Properties of sultines 48 and 51

	<u>48</u>	<u>51</u>
<u>m.p.</u>	160 - 162°	162 - 164°
<u>ir.</u>	1125 cm ⁻¹	1128 cm ⁻¹
<u>n.m.r.</u>	3.49 (d, J = 3.0Hz, 1H); 4.53 (d, J = 3.0Hz, 1H); 6.17 (d, J = 3.0Hz, 1H); 6.67 (d, J = 3.0Hz, 1H); 6.7 - 7.4 (m, 2OH)	4.02 (d, J = 11.0Hz, 1H); 4.43 (d, J = 4.0Hz, 1H); 5.86 (d, J = 11.0Hz, 1H); 6.67 (d, J = 4.0Hz, 1H); 6.7 - 7.4 (m, 2OH).
<u>Analysis</u>	C, 76.72; H, 5.66; S, 7.15	C, 76.57; H, 5.45; S, 7.15
<u>C₂₈H₂₄O₃S</u> <u>requires:</u>		C, 76.35; H, 5.45; S, 7.2
<u>C₁₄H₁₂O₂S</u> (or C ₂₈ H ₂₄ O ₄ S ₂) <u>requires:</u>		C, 68.84; H, 4.95; S, 13.10
<u>Molecular weight</u> (<u>Osmometry</u>)	416 ± 13	418 ± 13
<u>C₂₈H₂₄O₃S</u> <u>requires:</u>		440

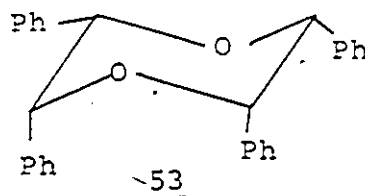
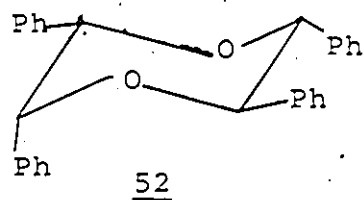
In order to explain the chemical shift differences between the hydrogens on C_4 and C_6 , a syn 1,3-"diaxial" arrangement would still be needed thus leading to 51a. It must be admitted that it is difficult to envisage a conformation of 51a which could explain the 11.0Hz coupling constant between the protons at C_3 and C_4 . A structure which would be in "agreement" with both the observed chemical shift differences and the coupling constants is 51b. The formation of this structure from 48a is however difficult to rationalize chemically. Again X-ray structure determination might resolve the problem.

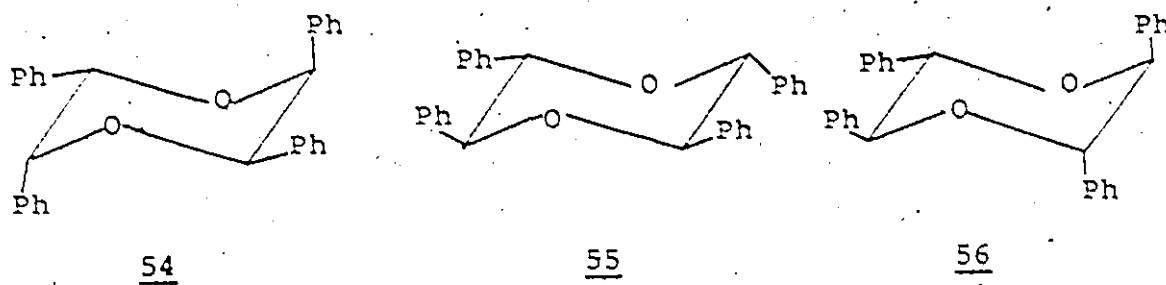
51b51b

The gross ring structure of 48 and 51 was supported by the reduction of both substances with lithium aluminium-hydride. Reduction of either 48 or 51 gave rise to a mixture of two products whose spectroscopic data were consistent with their designation as 2,3,5,6-tetraphenyl dioxanes. The two compounds were separated by preparative thin layer chromatography using methylene chloride as the developing solvent.

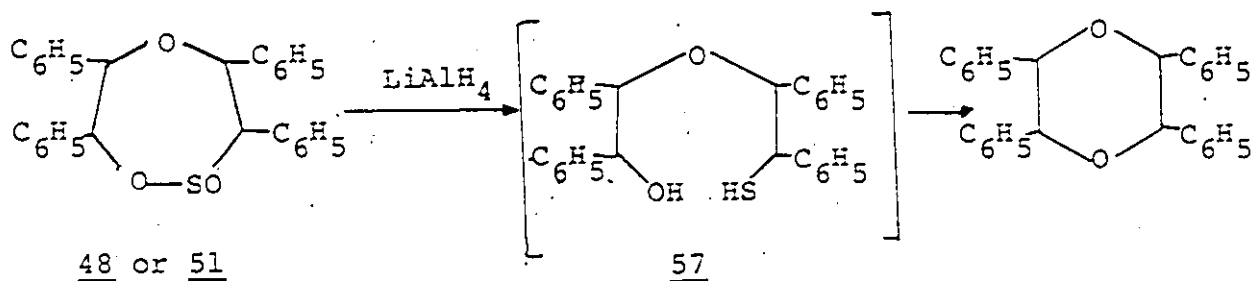
They were obtained as waxy oils which could not be crystallized. Because of the relatively small amounts of pure materials available no analyses have as yet been obtained.

The infrared spectrum of each isomer showed a strong band at 1095 attributable to the ether function of the dioxane ring. 1,4-Dioxane itself has its ether band at 1100 cm^{-1} .⁴ The n.m.r. spectrum of the major isomer (more polar) showed two singlets at $\delta = 4.20$ and 7.30 in a 1:5 ratio. These were attributed to the hydrogens on carbon bearing phenyl and oxygen and the aromatic hydrogens respectively. The spectrum of the minor isomer had absorption at $\delta = 4.70$ (s) and a multiplet centred at $\delta = 7.3$ in the integral ratio 1:5. The mass spectra of both isomers were identical. Unfortunately the molecular ion, expected at $m/e = 392$ was not visible. The only intense peaks at $m/e > 100$ in the spectra occurred at $m/e = 167$ due to the $(\text{C}_6\text{H}_5)_2\text{CH}^+$, a reasonable fragment based on the tetraphenyl-1,4-dioxane structure. Of the five possible isomeric 2,3,5,6-tetraphenyl-1,4-dioxanes only one (52) is not symmetrical and thus could not be accommodated by the n.m.r. A distinction between the other structures 53 - 56, based on the data available is not possible.





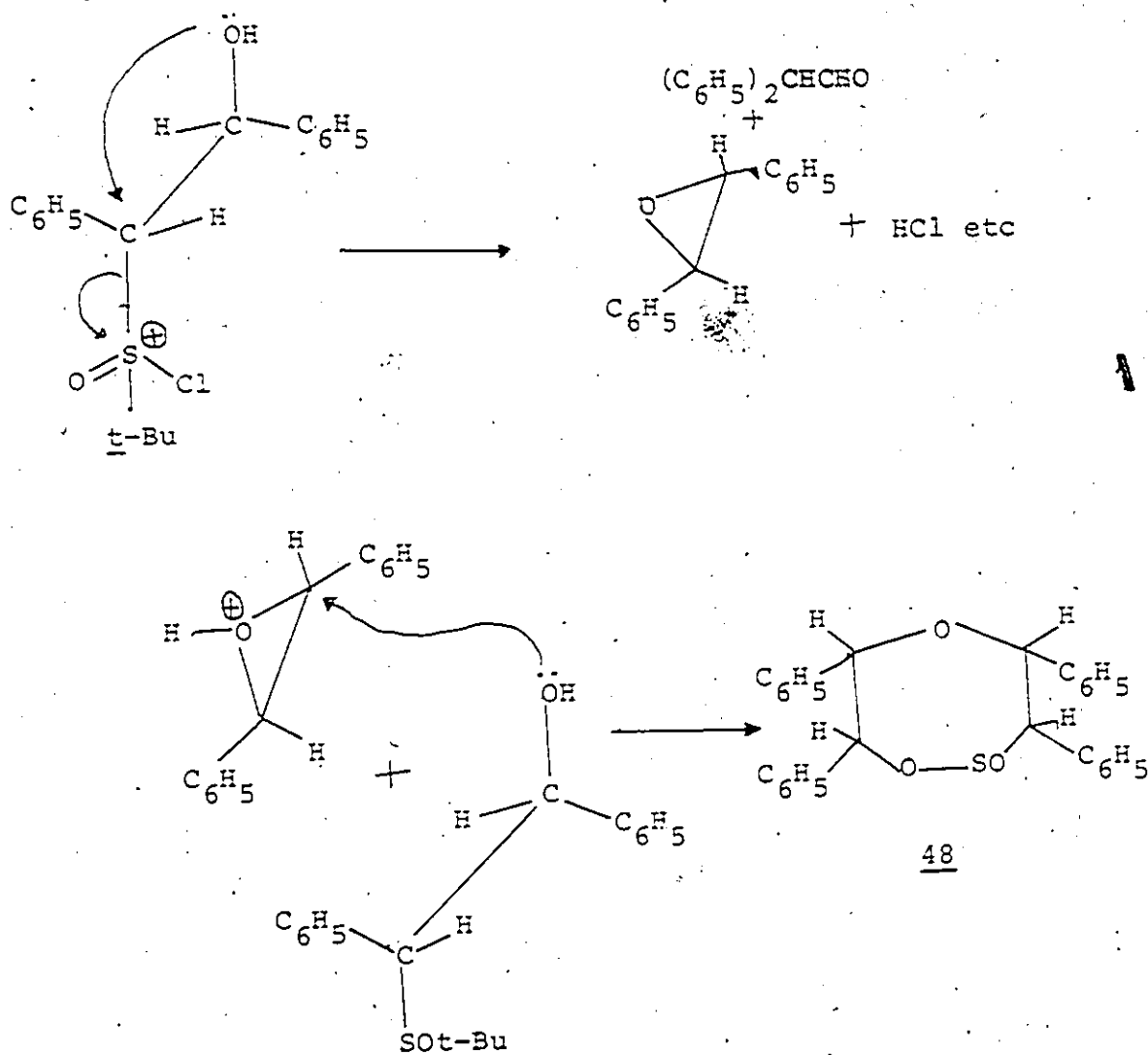
The lithium aluminium hydride reductions were done with the expectation of obtaining the hydroxy mercaptan 57 so as to confirm the order in which the ring atoms are joined to each other. The formation of the dioxanes is surprising but may be rationalized in the following manner. Complexation of the thiol with an aluminium species may sufficiently weaken the benzylic carbon-sulfur bond to allow formation of the cyclic ether structure.



The formation of trans-stilbene in approximately 85% yield upon refluxing either 48 or 51 in benzene containing a trace of p-toluene sulfonic acid for twenty four hours is again rather surprising.

The mechanism of this transformation is by no means obvious. The formation of stilbene in 50% or less yield, together with an equimolecular amount of stilbene oxide or diphenyl acetaldehyde could have been easily explained. The mass spectra of 48 and 51 obtained under low voltage (15 ev) conditions showed prominent peaks at $m/e = 244$ ($C_{14}H_{12}O_2S$) and 180 ($C_{14}H_{12}$).

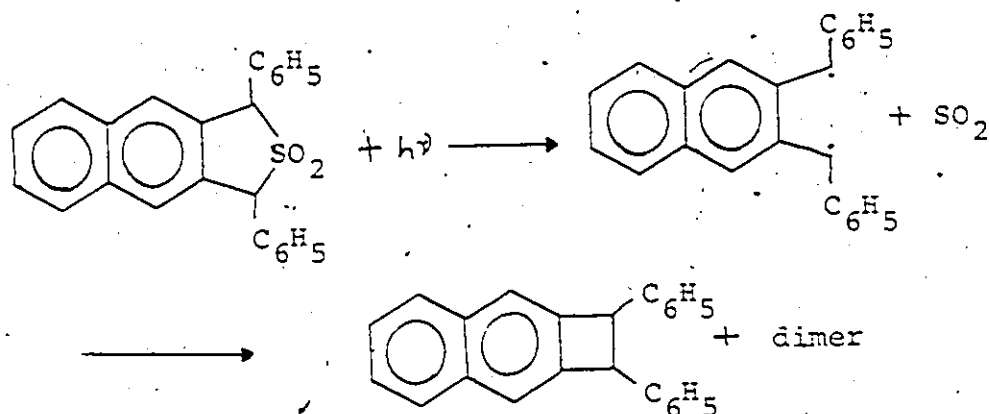
A tentative, as yet unproven, route to 48 from 31 is shown in the scheme below:



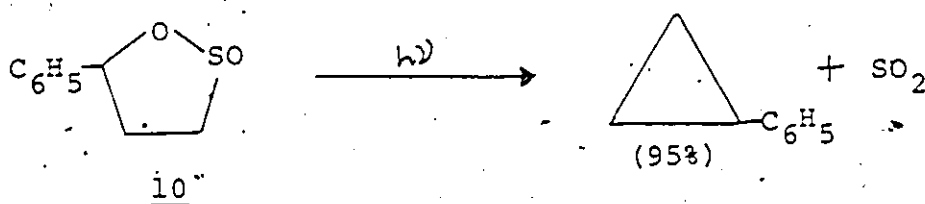
f) Photochemical extrusion of SO₂ (cyclopropane synthesis):

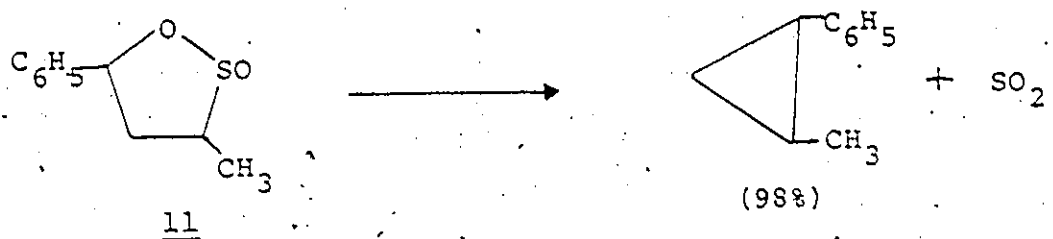
In contrast to the β -sultines, γ -sultines were found to be thermally stable. Photolytic extrusion of sulfur dioxide was therefore examined with the hope of obtaining cyclopropanes.

It has been shown by Cava and coworkers²⁴ that ultraviolet irradiation of benzene solutions of benzylic sulfones (under nitrogen at 15°) causes loss of sulfur dioxide, presumably via a diradical intermediate.



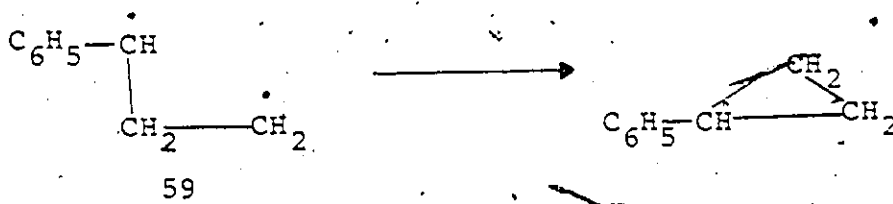
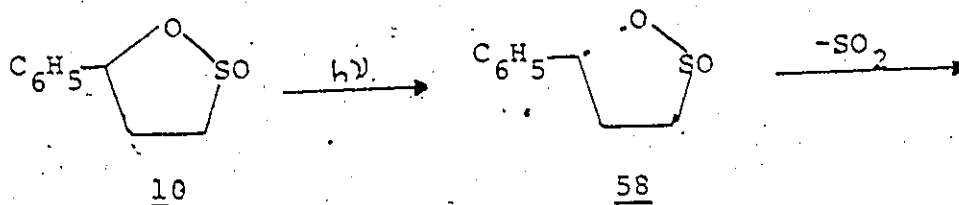
Our hopes of obtaining cyclopropanes were rewarded in the case of the 5-phenyl-1,2-oxathiolane-2-oxide, 10, which produced phenyl cyclopropane in 95% yield. Similarly 1-phenyl-2-methyl cyclopropane was obtained in 98% yield from 5-phenyl-3-methyl-1,2-oxathiolane-2-oxide, 11.



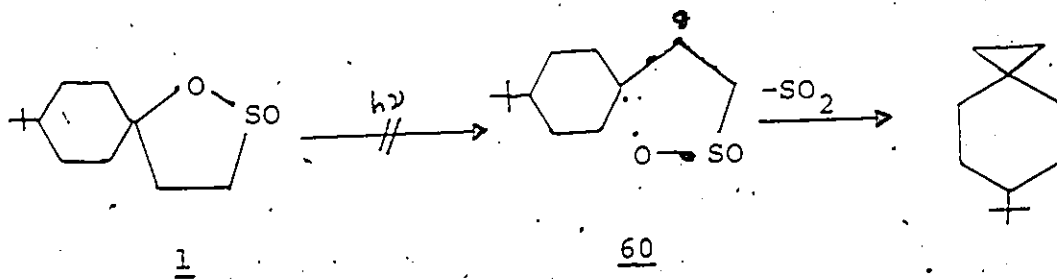


Unfortunately the photolysis of sultines which did not have a phenyl group α to oxygen yielded no cyclopropanes. This was very discouraging since we had hoped that the γ -sultines might be generally useful for the preparation of cyclopropanes. Prof. D.J.H. Smith of the University of Leicester, England, has thermolyzed at 600° using flash vacuum pyrolysis technique, a sample of 5-phenyl-1,2-oxathiolane-2-oxide, supplied by us, and obtained phenyl cyclopropane in high yield. Thus a fairly general synthesis of cyclopropanes is still possible.

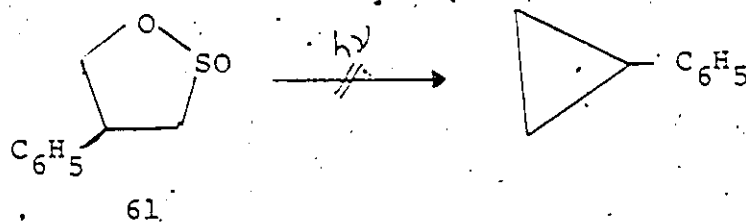
It appears, therefore, that the phenyl group plays a special role in the photolytic cleavage. In all likelihood it facilitates the cleavage of the C-O bond by stabilizing the intermediate diradical 58, from which loss of SO₂ leads to a second diradical 59. Cyclopropanes would form as a result of intramolecular ring closure of this diradical.



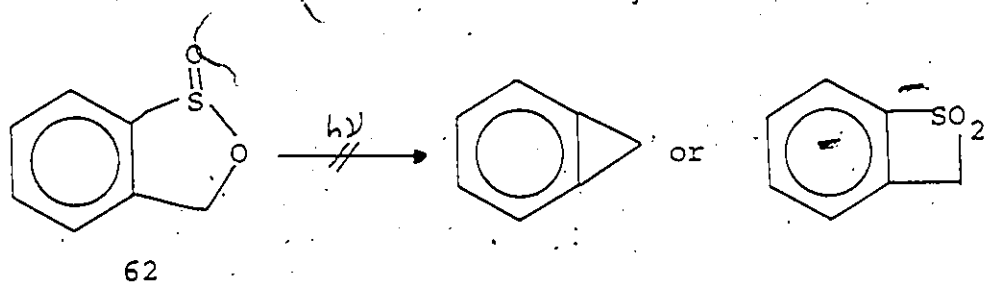
The low wavelength ($\lambda_{\text{max}} 230$) coupled with a low extinction coefficient ($\epsilon = 300$) observed for the parent γ -sultine suggests the possibility that the light may be absorbed by the phenyl group and not by the sultine function. The cleavage of the α C-O bond may be similar to that observed ²⁵ for aryl substituted epoxides. Such an explanation would be in agreement with the observation that the 5,5-dialkyl substituted sultine 1 did not undergo ready photolysis despite the fact that the intermediate diradical 60 would be expected to have comparable stability with the initial diradical 59 formed in the photolysis of 10.



A phenyl group at position 4 does not promote the cyclopropane formation. Thus 4-phenyl-1,2-oxathiolane-2-oxide, 61, under photolytic conditions (which suffice for the formation of phenyl cyclopropane from 10) was recovered unchanged. As usual, prolonged photolysis led to intractable materials.



Somewhat surprisingly the benzofused sultine 62, having the necessary aryl function α to oxygen, did not undergo any reaction under the standard photolytic conditions.

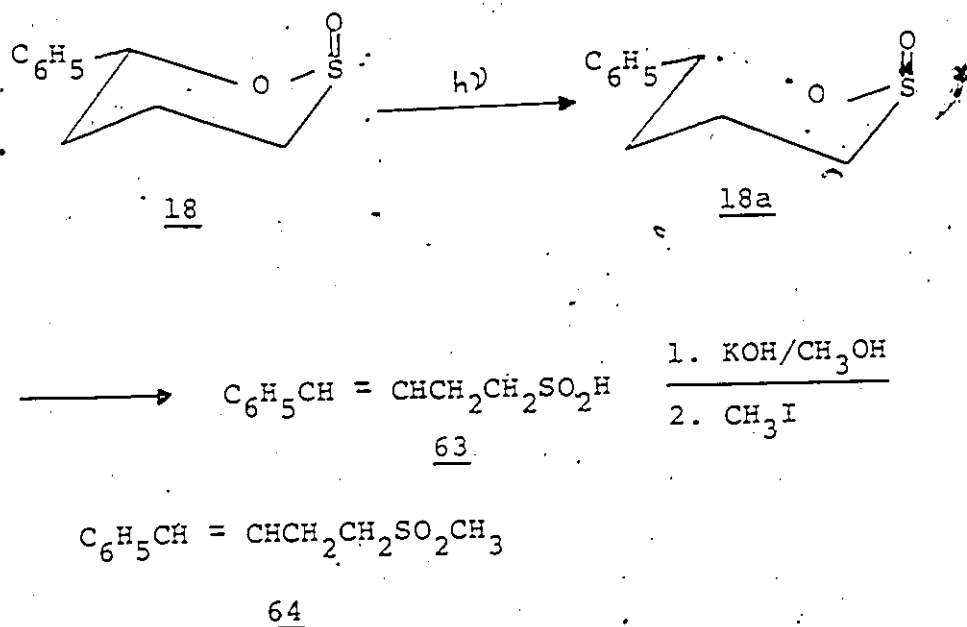


Presumably the diradical formed in this case prefers to recyclize to the 5-membered ring rather than isomerize to a 4-membered ring sulfone or lose SO_2 .

Photolysis of 6-phenyl-1,2-oxathiane-2-oxide, 18, in benzene-acetone, for sixty minutes, resulted into the formation of a very polar compound 63 in 88% yield. It was assigned the unsaturated sulfinic acid structure on the basis of its n.m.r. spectrum which showed the following features.

δ 2.5 - 3.0 (m, 4H); 5.3 - 5.6 (m, 2H); 7.2 (m, 5H); 9.8 (bs, exchangeable with D_2O , 1H).

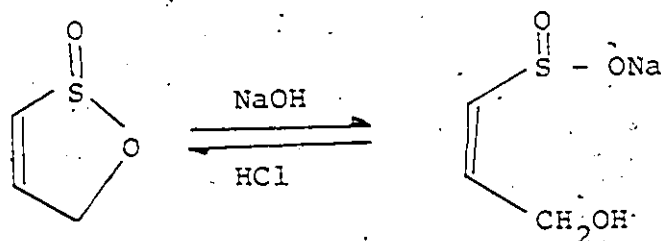
The sulfinic acid structure for 63 was supported by the conversion of its potassium salt to the sulfone 64 (82%) on treatment with methyl iodide. The sulfone 64 (m.p. 112°) showed characteristic sulfone absorption at 1120 and 1300 cm^{-1} . The n.m.r. spectrum had singlets at δ 2.9 and 3.0 (total area 3H); multiplets at 3.0 - 3.4 (4H); 5.3 - 6.6 (2H) and 7.2 (5H).



It appears that the diradical 18a produced from 18 undergoes intramolecular hydrogen transfer (rather than the loss of SO_2) resulting into the formation of the observed unsaturated sulfinic acid 63.

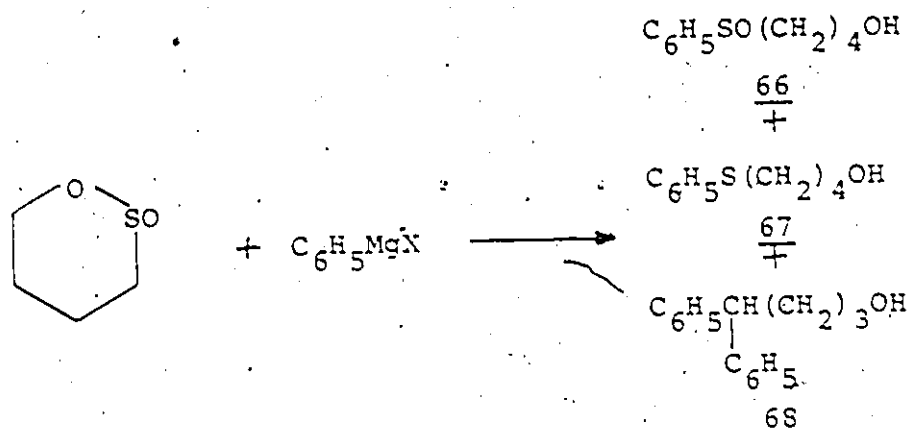
g) Nucleophilic Displacement on sulfur:

King et al¹⁸ have shown that in dilute sodium hydroxide soln, sultines can be cleaved to the corresponding hydroxy-sulfinates which when acidified with HCl recyclize to the starting sultine.

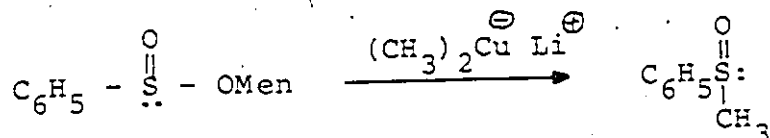


Somewhat similar behaviour was observed with 5-phenyl-1,2-oxathiolane-2-oxide, 10. When the sultine was treated with 0.1 equivalent of dil. sodium hydroxide the starting material almost completely disappeared. The product appeared to be the hydroxy sulfinic acid 65 as indicated by n.m.r. [δ 2.1 - 2.5 (m, 2H); 3.3 - 3.6 (m, 2H); 4.8 (t, $J = 6\text{Hz}$, 1H); 6.5 (bs, 2H); 7.3 (s, 5H)]. However, the material did not recyclize to the sultine in good yield. Most of the hydroxy sulfinic acid remained in the aqueous solution.

such as 67 and 68.

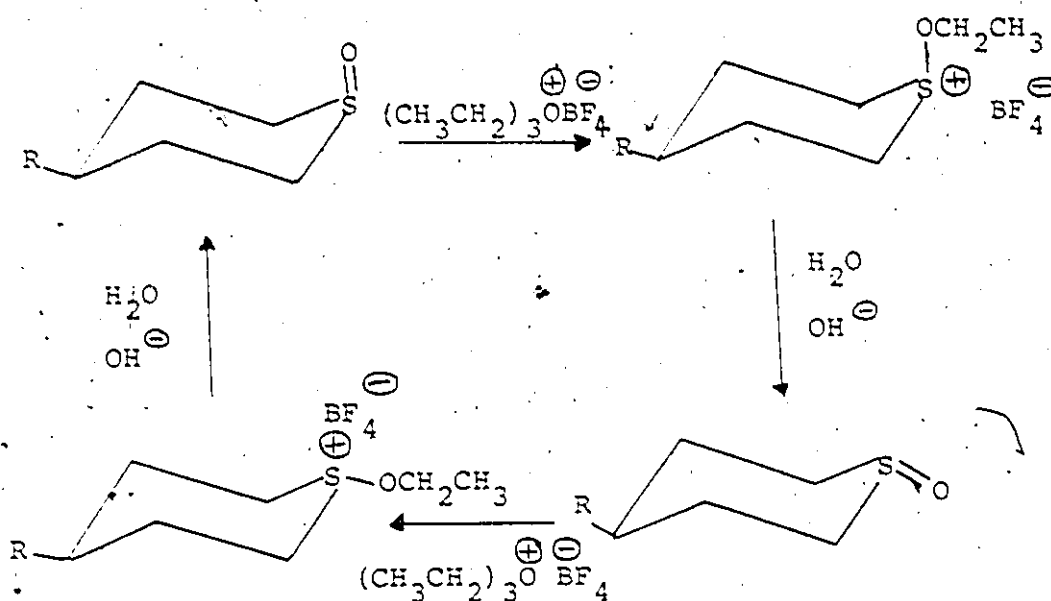


In an effort to improve the scope of this reaction, the use of organocopper reagents was explored. It was found that these reagents act as an effective replacement for the Grignard in the nucleophilic displacement reaction in that the number and amount of by-products is greatly reduced.



The copper reagents appeared to react with inversion of configuration at sulfinyl sulfur.

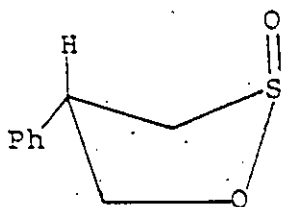
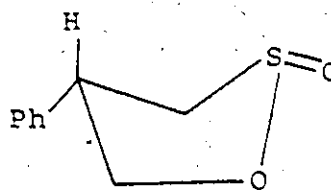
Johnson et al⁴⁴ showed that the hydrolysis of alkoxy sulfonium salts, obtained by the O-alkylation of sulfoxides, proceeds with inversion of configuration of the sulfur atom. The method was successfully employed to interconvert the cis and trans sulfoxides derived from a series of 4-substituted thianes.



45

Recently Fraser and Schuber have employed this method for the inversion of the sulfoxide in 1,11-dimethyl-5,7-dihydrodibenz-(c,e)-thiepin S-oxide.

Preliminary results suggest that this method can be extended to sultines as well. Dr. F. de Reinach has recently been able to separate the two isomers of the sultine 69 by column chromatography over silica. On the basis of n.m.r., more polar isomer was tentatively assigned the structure a in which the phenyl group and sulfinyl oxygen are trans to each other. Thus the less polar isomer b should have these two groups cis.

69a69b

n.m.r. 3.0 - 3.5 (m, 2H),
 4.0 - 4.5 (m, 2H); 5.0 - 5.2 (m, 1H)
 7.2 - 7.4 (m, 5H)

n.m.r. 3.0 - 4.0 (m, 4H);
 4.6 - 4.9 (m, 1H);
 7.3 - 7.4 (m, 5H)

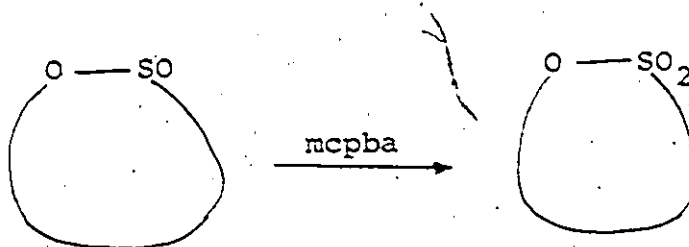
Sultine 69a was used as the starting material for studying the epimerization. Triethyloxonium fluoroborate (0.190 g, 1 mmole) was added to a solution of 69a (1mmole) in 5 ml of methylene chloride and stirred for twenty four hours at room temperature. TLC of the reaction mixture indicated disappearance of the starting material. Addition of anhydrous ethyl ether at 0° did not result into the precipitation of a white solid but produced a gummy mass instead. Hence 0.1N aqueous sodium hydroxide (10 ml) was added to it and the reaction mixture was stirred for another two hours. After workup the reaction product appeared to be a 50:50 mixture of the isomers 69a and 69b as judged by n.m.r.

At this point it is very difficult to say anything about the mechanism of the reaction. It does seem appropriate

to point out that epimerization, if successful in general, should help in understanding the stereochemical aspects of γ and δ sultines.

h) Oxidation of Sultines:

The sultines were readily oxidized to the corresponding sultones (cyclic sulfonate esters). In fact many of the sultines were characterized by the comparison of the oxidized materials with the known sultones.



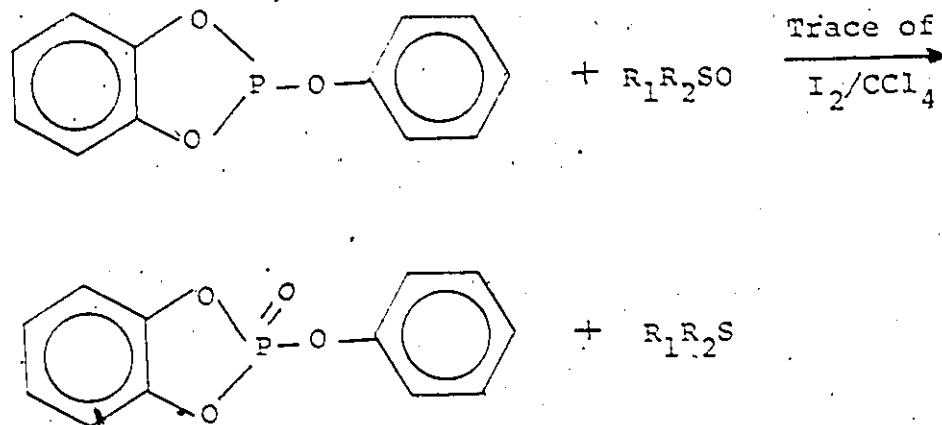
i) Attempted Deoxygenation of Sultines:

Sulfoxides can be reduced to sulfides by lithium²⁹ aluminium hydride³⁰ and a variety of other reagents (e.g. sulfur,³¹ sodium borohydride, cobalt chloride, saturated aqueous sodium hydrogen sulfite,³² bromine-hydrobromic acid³³ iron pentacarbonyl³⁴ etc.).

The very method of choice, however, seems to be³⁵ the one reported by Kaiser and coworkers employing stannous chloride - acetyl chloride in acetonitrile: dimethyl formamide at 0°.

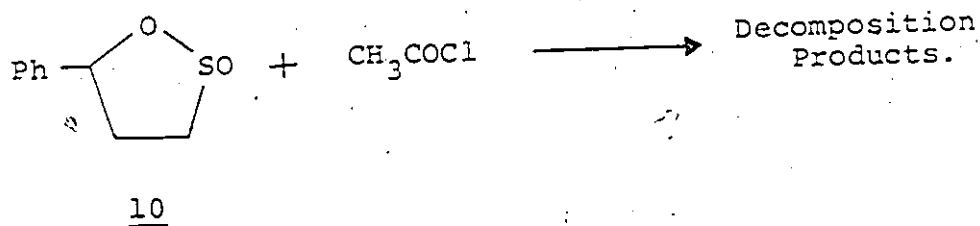
In addition trivalent phosphorus compounds have been³⁶⁻³⁸ extensively employed for the reduction of sulfoxides to sulfides.

Very recently deoxygenation of sulfoxides using 2-phenoxy-1,3,³⁹
2-benzodioxaphosphole has been reported. The reaction was
found to be catalysed by a trace of iodine and generally com-
plete within three hours in refluxing benzene.



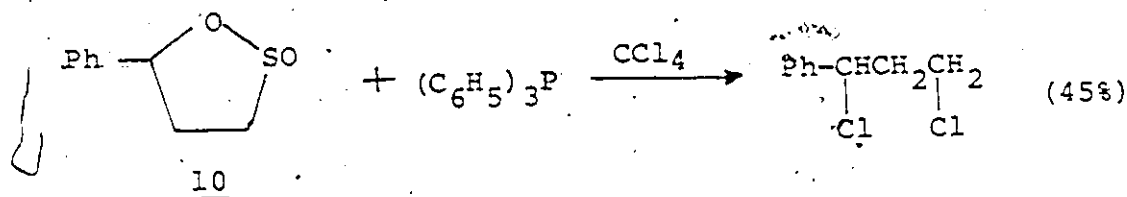
It was of interest to examine the behaviour of
sultines towards the mild deoxygenating reducing agents. The
expected products, cyclic sulfenate esters, have not been
reported in literature thus far.

When the sultine 10 was treated with acetyl chloride
in methylene chloride no apparent reaction was observed for
several hours. When left overnight the material decomposed
presumably via Pummerer type rearrangement.



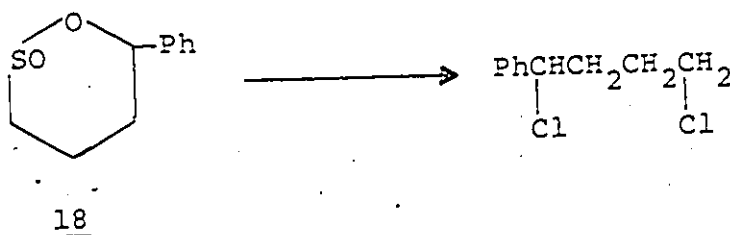
When the reduction was attempted with stannous chloride-acetyl chloride in CH_3CN — DMF no transformation appeared to take place at least for twenty four hours. Starting material was recovered.

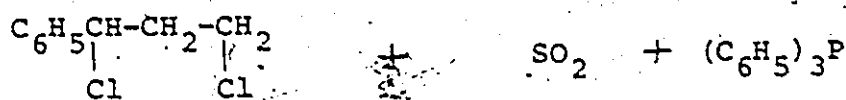
Finally using triphenyl-phosphine in refluxing carbon tetrachloride the starting material did disappear after 48 hours. The product was identified as 1-phenyl-1,3-dichloropropane from its n.m.r. and mass spectral data. [n.m.r. 2.3 - 2.6 (m, 2H), 3.3 - 3.8 (m, 2H), 5.0 - 5.2 (m, 1H), 7.3 - 7.5 (m, 5H); m.s. M^+ 188, other peaks at m/e 153, 125, 117, 115 and 91]. The yield of the dichloride was 45%.



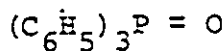
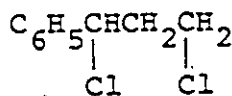
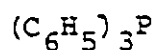
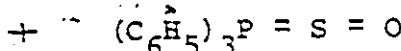
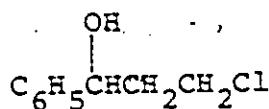
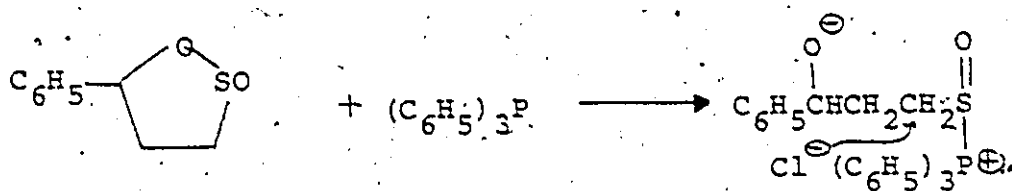
Similarly n.m.r. of the crude material obtained from 18 was in agreement with the structure $\text{C}_6\text{H}_5\text{CH}(\text{Cl})\text{CH}_2\text{CH}_2\text{CH}_2(\text{Cl})$ (25%).

The acyclic sulfinic acid $\text{C}_9\text{H}_{19}\text{SO}_2\text{OCH}_3$ led to the formation of $\text{C}_9\text{H}_{19}\text{Cl}$ (30%).

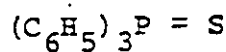




b) Nucleophilic attack of phosphorus on sulfinyl sulfur.

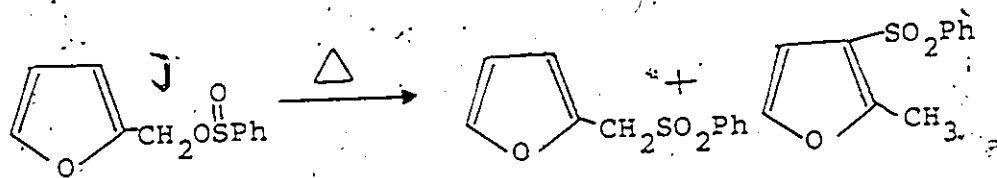


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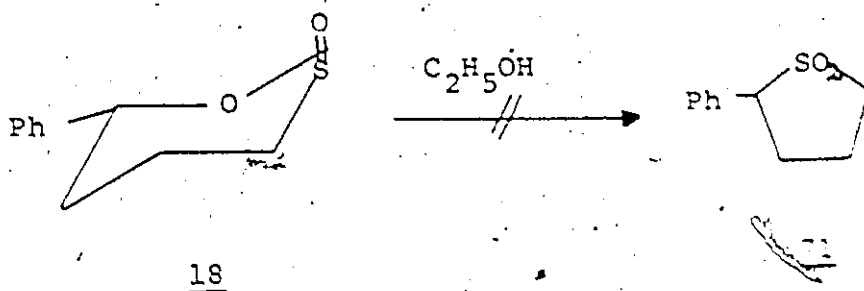


j) Solvolysis reactions: (Isomerisations)

Cope and coworkers⁴⁰ examined the thermal stability of allylic arene sulfinates and observed that allyl benzene sulfinate and some of its derivatives on heating underwent rearrangement to sulfones in low yields. Sulfinates in general undergo solvolysis with relatively little sulfone formation.⁴¹ The solvolysis of arene sulfinates may proceed either by sulfur-oxygen or by carbon-oxygen bond fission. It has been observed that the sulfur-oxygen bond fission mechanism prevails for benzyl arene sulfinates whereas a carbon-oxygen bond fission by an ionization mechanism proceeds in the case of the corresponding *p*-methoxybenzyl ester.⁴² Very recently Braverman and Globberman⁴³ observed that under buffered non-solvolytic conditions, furfuryl benzene sulfinate undergoes thermal rearrangement to a mixture of furfuryl phenyl sulfone and 2-methyl-3-furyl phenyl sulfone.



It was therefore hoped that δ -sultines with a phenyl group on C₆ (carbon α -to oxygen) might rearrange to the isomeric sulfones. However no such isomerisation was observed in the case of 6-phenyl-1,2-oxathiane-2-oxide and only the starting sultine could be recovered.



When the S-sultine 18 was heated strongly (distilled under vacuum with a small flame) most of the compound decomposed and the residue appeared to be mainly the sulfone 71, as examined by n.m.r.

Experimental

Melting points were determined with a Thomas Hoover apparatus and are uncorrected. Similarly all boiling points reported are uncorrected. All n.m.r. spectra were recorded on a Varian HA-100 or T-60 spectrometers using CDCl_3 as solvent (unless otherwise specified). The peak positions are given in ppm downfield from T.M.S. Infrared spectra were obtained using a Beckman IR-20 or IR 20-A spectrophotometer. The spectra of solid compounds were obtained using CHCl_3 as solvent; liquids or oils were generally used neat. Mass spectra were obtained using either a Hitachi RMU-6 spectrometer or an AEI MS-9 spectrometer. Ultraviolet spectra were recorded on a Perkin Elmer 202 ultraviolet visible spectrophotometer. Carbon-13 n.m.r. spectra were obtained at 25.2 MHz, most commonly under conditions of complete proton noise decoupling, using a varian XL-100 spectrometer operating in the Fourier Transform mode. Carbon-13 chemical shifts are given in ppm downfield from TMS.

Elemental analyses were carried out by National Research Council of Canada, Ottawa, Chemalytics, Inc. Tempe, Arizona or Hoffman La Roche Inc. Nutley, New Jersey.

The chemicals used during the course of this work were supplied by Aldrich chemical Co., Fisher Scientific, Chemical samples Co. and Canlab Ltd. The solvents used meet A.C.S. specifications. Alkylolithiums were supplied by the

Foot Mineral Co., or Ventron Corp., Alfa Products. The silica gel used for T.L.C. was supplied by Macherey-Nagel and Co., Düren (Germany). Silica gel 60., supplied by Brinkmann Instruments (Canada) Ltd. was used for column chromatography.

Usual workup refers to partitioning the reaction mixture between water and an organic solvent, generally methylene chloride, drying the organic extract with anhydrous magnesium sulfate and evaporating the solvent using a rotary evaporator.

CHAPTER II (Experimental)

Preparation of benzyl methyl sulfoxide, 25

From 13.7 g of benzyl methyl sulfide (0.1 mole) and 20.0 g (0.1 mole) of *m*-chloroperbenzoic acid, 12.5 g (82%) of sulfoxide, m.p. 52-53° (lit. m.p. 53-54°¹⁶), were obtained. The sulfoxide sublimed rapidly at 50°/5 μ .

IR. 1030 (S=O) cm^{-1} .

N.M.R. 2.44 (s, 3H); 3.98 (ABq; $\delta_A = 4.05$, $\delta_B = 3.91$, $J = 13$ Hz, 2H); 7.43 (s, 5H)

Reaction of 25 with NCS in methylene chloride

NCS (670mg, 5 mmole) was added to a solution containing 770mg (5 mmole) of 25 in 10 ml of methylene chloride. The reaction mixture was stirred at room temperature for thirty minutes. After removing the solvent, the residue was chromatographed on silica using ethyl acetate as the eluent. The yield of α -chlorobenzyl methyl sulfoxide, 26, was 990mg (91%).

N.M.R. 2.20 and 2.58 (2 singlets in the ratio 4:1, 3H); 5.6 (s, 1H); 7.3 (m, 5H).

Reaction of 25 with NBS in methylene chloride

NBS (890mg, 5 mmole) was added to a solution containing 770mg (5 mmole) of 25 in 10 ml of methylene chloride.

The reaction mixture was stirred at room temperature for thirty

minutes. After removing the solvent, the residue was chromatographed on silica using ethylacetate as the eluent. The yield of α -bromobenzyl methyl sulfoxide, 27, was 870 mg (75%).

IR. 1005 (S=O) cm^{-1} .

N.M.R. 2.42 (s, 3H); 4.89 (s, 1H); 7.2 - 7.5 (m, 5H).

Reaction of 25 with SO_2Cl_2 in methylene chloride

Sulfuryl chloride (280 mg) was added to a solution of 25 (300 mg) in methylene chloride (10 ml). The reaction product was a complex mixture from which α -chlorobenzyl methyl sulfoxide, 26, (95 mg, 25%) was isolated by column chromatography over silica using ethyl acetate as the eluent.

Reaction of 25 with NCS in methylene chloride: methanol (95:5)

The reaction was carried out as above using 462 mg (3.0 mmole) of benzyl methyl sulfoxide and 400 mg (3.0 mmole) of NCS in 10 ml of 5% $\text{CH}_3\text{OH}/\text{CH}_2\text{Cl}_2$. The total product was chromatographed on 25 g. of silica gel using CH_2Cl_2 as eluent and collecting 25 ml fractions. The first two fractions were found to contain 32 mg (9%) of PhCH_2Cl and 22 mg (5%) of benzyl methyl sulfide. From later fractions there was isolated 36 mg (12%) of benzaldehyde and 340 mg (60%) of α -chlorobenzyl methyl sulfoxide, 26.

Reaction of 25 with NCS in 1:1 methylene chloride: methanol

The reaction and product analysis were carried out as above. The relative yields of products were: benzyl methyl ether (12%), benzyl methyl sulfide (8%), benzaldehyde (10%), benzyl chloride (5%) and α -chloro sulfoxide (50%).

Reaction of 25 with NCS in methanol

This reaction was carried out on 912 mg (6.0 mmole) of the sulfoxide. The relative yields of the various products as estimated by n.m.r. were: benzyl methyl ether (33%), benzyl methyl sulfide (18%), benzaldehyde (12%), benzyl chloride (6%) and α -chlorobenzyl methyl sulfoxide, 26, (9%). The ratio of the first four products were also verified by VPC (6 ft, 10% Carbowax, 180). The retention times of the components matched those of authentic samples.

In a second experiment (products analyzed by column chromatography) the yields of products were within 15% of the values quoted above.

Reaction of benzyl phenyl sulfoxide, 36, with NCS in CH_2Cl_2

NCS (334 mg, 2.5 mmole) was added to a solution of benzyl phenyl sulfoxide (500 mg, 2.3 mmole) in methylene chloride (25 ml). The reaction mixture was refluxed for 48 hours. Crude reaction product showed the presence of unreacted starting material and the desired α -chloro sulfoxide (ca. 50:50).

Reaction of benzyl phenyl sulfoxide with NCS in benzene

NCS (334 mg, 2.5 mmole) was added to a solution of benzyl phenyl sulfoxide (498 mg, 2.3 mmole) in benzene (20 ml). The reaction mixture was refluxed for one hour. Usual workup afforded α -chlorobenzyl phenyl sulfoxide, (545 mg) in 94% yield m.p. 38-39° (lit. m.p. 38.5 - 39.5°)

IR. 1015 (S=O) cm^{-1} .

N.M.R. 5.52 (s, 1H); 7.0 - 7.5 (m, 10H).

Reaction of 36 with NCS in benzene: methanol (95:5)

NCS (334 mg, 2.5 mmole) was added to a solution of benzyl phenyl sulfoxide (500 mg, 2.3 mmole) in benzene: methanol (20 ml, 95:5). The reaction mixture was refluxed for 24 hours. Crude reaction product showed the presence of unreacted starting material ($\approx 50\%$) in addition to the desired α -chloro-sulfoxide and several other products.

Reaction of t-butyl methyl sulfoxide with NCS in CH_2Cl_2

Reaction of t-butyl methyl sulfoxide (360 mg, 3.0 mmole) with NCS (400 mg, 3.0 mmole) in CH_2Cl_2 , after usual workup, gave 40 mg of a bad smelling liquid which could not be characterized properly.

Reaction of *t*-butyl methyl sulfoxide with SO_2Cl_2 in CH_2Cl_2

Reaction of *t*-butyl methyl sulfoxide (360 mg, 3.0 mmole) with SO_2Cl_2 (410 mg, 3.0 mmole) in CH_2Cl_2 , after usual workup, gave 60 mg of a yellow liquid which could not be characterized.

CHAPTER III (Experimental)

Synthesis of Sulfides:

General procedure:

To a solution of the appropriate thiol (1.0 equivalent) in methanol (25 ml) containing KOH (1.2 equivalents) was added in a dropwise fashion a solution of alkyl halide (1.1 equivalents) in methanol (15 ml). The reaction mixture was stirred overnight and the precipitate formed was filtered. The filtrate was diluted with H_2O (50 ml) and extracted with CH_2Cl_2 (4 x 50 ml). The combined organic extract was washed with 10% aqueous KOH (2 x 25 ml), dried, and the solvent removed. The crude products were generally purified by distillation under reduced pressure.

Synthesis of Sulfoxides:

General procedure:

Oxidation of sulfides was carried out with one of the following reagents:

- a) m-chloroperbenzoic acid.
- b) t-butyl hypochlorite.
- c) H_2O_2 - acetic anhydride.

a) Oxidation with m-chloroperbenzoic acid:³ The appropriate sulfide (1.0 eq) was dissolved in methylene chloride and the solution cooled in ice. To this was added slowly (over two to four hours depending on the scale) with stirring a 10% solution of m-chloroperbenzoic acid (1.1 eq, Aldrich chemical, 85% purity) in methylene chloride. A colorless precipitate appeared after addition was complete. The mixture was stirred for one hour at room temperature, washed with dilute sodium sulfite solution and then with dilute KOH solution. The organic layer was dried and the solvent evaporated to give the crude sulfoxide. Purification was achieved by distillation, recrystallization or column chromatography.

b) Oxidation with t-butyl hypochlorite:³ To the sulfide (1 eq.) dissolved in methanol at -70° was added dropwise t-butyl hypochlorite (1.2 eq.) (freshly prepared from t-butanol, commercial bleach and acetic acid). When the temperature of the bath reached -40° anhyd. sodium carbonate (0.5 g) was added. After stirring at room temperature for one hour the reaction mixture was stripped of methanol by evaporation on a rotary evaporator. The residue was dissolved in water and extracted several times with CH_2Cl_2 . The organic extracts were dried over MgSO_4 and the solvent evaporated on a rotary evaporator. The crude sulfoxides were purified as in (a).

c) Oxidation with H_2O_2 - acetic anhydride:¹⁸ At room temperature, with stirring, 30% H_2O_2 (1.1 eq) was added dropwise to sulfide

(1.0 eq) in acetic anhydride (30-100 ml depending on the scale). Stirring was continued for 5-8 hours or until the test for peroxide was negative. The reaction mixture was diluted with methylene chloride and the acetic anhydride was removed with a saturated aqueous solution of potassium carbonate. The CH_2Cl_2 solution was dried and the solvent evaporated. The crude sulfoxides were purified as in (a).

Cyclization of Hydroxy Sulfoxides to Sultines:

General Procedure:

Sulfuryl chloride (1.1 eq) was added to a solution of hydroxy sulfoxide (1.0 eq) in methylene chloride at room temperature (some of the later syntheses were carried out at -70°). The progress of the reaction was followed by thin layer chromatography. After the disappearance of starting material (fifteen minutes to one hour), the volatile matter was removed on a rotary evaporator. The crude product was examined by n.m.r. and purified by column chromatography over silica gel. Further purification was done by distillation under reduced pressure or by crystallization. Because of the instability of some of the new sultines, a number of them could not be analyzed. Their structures were assigned on the basis of their mode of preparation, their n.m.r., ir and mass spectra, and by oxidation to the corresponding sultones.

Oxidation of Sultines to Sultones: Excess of m-chloroperbenzoic acid (ca. 2 equivalents) was added to the solution of the pertinent sultine in methylene chloride. The reaction mixture was stirred at room temperature until disappearance of the sultine (TLC). After stripping the mixture of the solvent the residue was subjected to column chromatography over silica. The sultones were generally known compounds and characterized by comparison of their IR. and/or N.M.R. spectra with those reported in the literature.

Parent Sultines

1) Synthesis of 1,2-oxathiolane-2-oxide, 5.

i) 3-t-Butylthio-1-propanol.

This compound was prepared in 90% yield from t-butyl thiol and 3-bromo-1-propanol. The hydroxy-sulfide boiled at 53-55°/5 μ .

IR. 3325 (OH) cm^{-1} .

N.M.R. 1.33 (s, 9H); 1.87 (m, 2H); 2.70 (t, J= 6Hz, 2H); 3.8 (t, J= 6Hz, 2H); 1.93 (bs, exchangeable with D₂O, 1H).

ii) 3-t-Butylsulfinyl-1-propanol, 1.

From 14.8 g of above hydroxy-sulfide (0.1 moles) and 13.0 g. of t-butyl hypochlorite (0.12 moles) were obtained 12.4 g. (75%) of the hydroxy sulfoxide 1.

IR. 3325 (OH) and 1000 (S=O) cm^{-1} .

N.M.R. 1.30 (s, 9H); 1.83 - 2.4 (m, 2H); 2.53 - 2.86 (m, 2H); 3.75 (t, J= 6Hz, 2H); 4.5 (bs, exchangeable with D₂O, 1H).

iii) 1,2-Oxathiolane-2-Oxide, 5.

Hydroxy-sulfoxide 1 (1.48 g.) was dissolved in methylene chloride (25 ml) at room temperature and a solution of sulfuryl chloride (1.4 g., 1.15 equivalents) in methylene chloride (5.0 ml) was added to it. The crude product was purified by column chromatography over silica (ethyl acetate:

hexanes 2:1) to give 730 mg. (83%) of the sultine 5.

U.V. $\lambda_{\max}$ 225 (360).

IR. 1110 (S=O) cm^{-1} .

N.M.R. 1.66 - 3.15 (m, 4H); 4.0 - 4.7 (m, 2H).

M.S. Calculated for $\text{C}_3\text{H}_6\text{O}_2\text{S}$: 106
Found: 106

iv) 1,2-Oxathiolane-2,2-dioxide, 9

Sultine 5 (220 mg) was oxidized with 400 mg. of m-chloroperbenzoic acid in methylene chloride to give 192 mg. (94%) of the sultone 9.

IR. 1320, 1130 and 890 (SO_2) cm^{-1} .

N.M.R. 2.3 - 2.9 (m, 2H); 3.07 - 3.46 (m, 2H);
4.43 (t, $J = 7\text{Hz}$, 2H).

2) Synthesis of 1,2-oxathiane-2-oxide, 6.

i) 4-t-Butylthio-1-butanol: This hydroxy sulfide was obtained in 70% yield from t-butyl thiol and 4-chloro-1-butanol. The liquid boiled at $70^\circ / .01 \text{ mm}$.

IR. 3290 (OH) cm^{-1} .

N.M.R. 1.26 (s, 9H); 1.3 - 2.0 (m, 4H); 2.0 - 2.6 (m, 2H); 3.2 - 3.7 (m, 3H).

ii) 4-t-Butylsulfinyl-1-butanol, 2. Oxidation of 4-t-butylthio-1-butanol with t-bu. hypochlorite in methanol at -70° afforded

the desired hydroxy sulfoxide in 75% yield.

IR. 3300 cm^{-1} (OH) and 1000 cm^{-1} (S=O).

N.M.R. 1.23 (s, 9H); 1.6 - 2.3 (m, 4H); 2.3 - 2.8 (m, 2H); 3.3 - 4.0 (m, 3H).

iii) 1,2-Oxathiane-2-Oxide, 6. When 1.35 g. of hydroxy-sulfoxide 2 were reacted with 1.28 g. of sulfuryl chloride in methylene chloride, the reaction mixture afforded 670 mg. (75%) of 1,2-oxathiane-2-oxide. (b.p. 59-60° / 0.5 mm, Lit: 60-61° / 0.5 mm)

IR. 1120 (S=O) cm^{-1} .

N.M.R. 1.5 - 2.2 (m, 3H); 2.2 - 3.0 (m, 3H); 3.6 - 3.8 (m, 1H); 4.28 - 4.66 (m, 1H).

M.S. Calculated for $\text{C}_4\text{H}_8\text{O}_2\text{S}$: 120.0247

Found: 120.0245

Analysis Calculated for $\text{C}_4\text{H}_8\text{O}_2\text{S}$: C, 39.98; H, 6.71; S, 26.68

Found: C, 39.86; H, 6.75; S, 26.42.

iv) 1,2-Oxathiane-2,2-dioxide, 10. Sultine 6 (120 mg.) on oxidation with 200 mg. of m-chloroperbenzoic acid in methylene chloride gave 126 mg. (90%) of butane sultone.

IR. 1335, 1150 and 920 (SO_2) cm^{-1} .

N.M.R. 1.5 - 2.4 (m, 4H); 3.1 (t, 6Hz, 2H); 4.33 (t, 5.5Hz, 2H).

3) Synthesis of 1,2-oxathiepane-2-oxide, 7.

i) 5-t-Butylthio-1-pentanol: This hydroxy-sulfide was obtained

in 85% yield from t-butyl thiol and 5-chloro-1-pentanol. The hydroxy-sulfide boiled at $68-70^{\circ}/5\mu$.

IR. 3340 (OH) cm^{-1} .

N.M.R. 1.33 (s, 9H); 1.5 - 2.0 (m, 7H); 2.3 - 2.6 (m, 2H); 3.5 - 3.7 (m, 2H).

ii) 5-t-Butylsulfinyl-1-pentanol, 3. The above hydroxy-sulfide (17.6 g., 0.1 moles) on oxidation with t-butyl hypochlorite (13.0 g., 0.12 moles) afforded 13.6 g. (72%) of the hydroxy-sulfoxide 3.

IR. 3330 (OH) and 1005 (S=O) cm^{-1} .

N.M.R. 1.30 (s, 9H); 1.4 - 2.0 (m, 7H); 2.3 - 2.6 (m, 2H); 3.5 - 3.7 (m, 2H).

iii) 1,2-Oxathiepane-2-oxide, 7. Reaction of 3 (1.9 g., 0.01 moles) with sulfuryl chloride (1.4 g., 0.01 moles) in CH_2Cl_2 (25 ml) afforded 796 mg. (58%) of the sulfone 7.

IR. 1100 (S=O) cm^{-1} .

N.M.R. 1.2-2.2 (m, 6H); 2.6 - 2.8 (m, 2H); 3.8 - 4.2 (m, 2H).

M.S. Calculated for $\text{C}_5\text{H}_{10}\text{O}_2\text{S}$: 134

Found : 134

Analysis Calculated for $\text{C}_5\text{H}_{10}\text{O}_2\text{S}$: C, 44.75; H, 7.51; S, 23.89.

Found : C, 44.84; H, 7.41; S, 23.04.

iv) 1,2-Oxathiepane-2,2-dioxide, 11. ^{7a}

Sultine 7 (134 mg.) was oxidized with 200 mg. of m-chloroperbenzoic acid in methylene chloride to give 130 mg. (90%) of the sultone 11.

IR. 1338, 1150 and 895 ($\text{O}-\text{SO}_2$) cm^{-1} .

N.M.R. 1.6 - 2.2 (m, 6H); 3.2 - 3.6 (m, 2H);

4.2 - 4.5 (m, 2H).

4) Synthesis of 1,2-oxathiocane-2-oxide, 8.

i) 6-t-Butylthio-1-hexanol. This hydroxy-sulfide was obtained in 80% yield from t-butyl thiol and 6-chloro-1-hexanol. The hydroxy sulfide boiled at $74 - 76^\circ/5\mu$.

IR. 3325 (OH) cm^{-1} .

N.M.R. 1.33 (s, 9H); 1.5 - 2.0 (m, 9H); 2.4 - 2.7

(m, 2H); 3.5 - 3.7 (m, 2H).

ii) 6-t-Butylsulfinyl-1-hexanol, 4. The above hydroxy-sulfide (19.0 g., 0.1 mole) on oxidation with t-butyl hypochlorite (13.0 g., 0.12 moles) yielded 14.0 g. (70%) of the hydroxy sulfoxide 4.

IR. 3340 (OH) and 1005 ($\text{S}=\text{O}$) cm^{-1} .

N.M.R. 1.32 (s, 9H); 1.4 - 2.0 (m, 9H); 2.3 - 2.7

(m, 2H); 3.5 - 3.7 (m, 2H).

iii) 1,2-Oxathiocane-2-oxide, 8. Reaction of 4 (2.0 g., 0.01 moles) with sulfuryl chloride (1.4 g., 0.01 moles) in CH_2Cl_2 (25 ml) yielded 670 mg (45%) of the sultine 8.

IR. 1110 (S=O) cm^{-1} .

N.M.R. 1.2 - 2.2 (m, 8H); 2.5 - 3.0 (m, 2H);

3.8 - 4.2 (m, 2H).

M.S. Calculated for $\text{C}_6\text{H}_{12}\text{O}_2\text{S}$: 148

Found: 148

Analysis Calculated for $\text{C}_6\text{H}_{12}\text{O}_2\text{S}$: C, 48.64; H, 81.6;

S, 21.60.

Found : C, 48.21; H, 8.04;

S, 22.12.

Sultines bearing substituents α to sulfur

- 1) Synthesis of 3-Methyl-1,2-oxathiolane-2-oxide, (15).
- i) 3-t-Butylsulfinyl -1-butanol, (13). Methyl-lithium (18.3 ml, 2.2 equivalents) was introduced via syringe into a solution of the hydroxy-sulfoxide 1 (2.46 g., 1 equivalent) in 25 ml of dry THF (under nitrogen) at 0°. After stirring for five minutes 2.5 g. of methyl iodide was added. Stirring was continued for an additional hour after which the contents were poured into water and extracted with 3 x 50 ml of methylene chloride; workup gave 2.13 g., (82%) of the desired hydroxy-sulfoxide as a slightly yellowish oil which was purified by column chromatography (silica, ethyl acetate).
- IR. 3330 (OH) and 1000 (S=O) cm^{-1} .
- N.M.R. 1.3 (s, 9H); 1.3 - 1.34 (2d, 3H); 1.6 - 2.3 (m, 2H); 2.7 - 3.35 (m, 1H); 3.4 - 4.0 (m, 2H).
- ii) 3-Methyl-1,2-oxathiolane-2-Oxide, (15). From 1.55 g. of hydroxy-sulfoxide 13 and 1.35 g. of sulfoxyl chloride were obtained, after purification via silica gel chromatography, 720 mg (72%) of sultine 15.
- IR. 1100 (S=O) cm^{-1}
- N.M.R. 1.22 and 1.38 (d, J= 7Hz, 3H); 1.75 - 3.5 (m, 3H); 4.2 - 4.9 (m, 2H).
- M.S. Calculated for $\text{C}_4\text{H}_8\text{O}_2\text{S}$: 120 .
Found : 120 .

Calculated for $C_4H_8O_2S$: C, 39.98; H, 6.71.

Found : C, 39.67; H, 6.37.

iii) 3-methyl-1,2-oxathiolane-2,2-dioxide, (17).¹⁰

Sultine 15 (120 mg) was oxidized with 240 mg of m-chloroperbenzoic acid in methylene chloride to give 110 mg (80%) of the sultone 17.

IR. 1325, 1130 and 880 (SO_2) cm^{-1} .

N.M.R. 1.46 (d, J = 7Hz, 3H); 2.08 - 2.9 (m, 2H);
3.2 - 3.6 (m, 1H); 4.24 - 4.6 (m, 2H).

2) Synthesis of 3-methyl-1,2-oxathiane-2-oxide, 16.

i) 4-t-Butylsulfinyl-1-pentanol, 14.

Methyl lithium (14.1 ml, 0.02 moles) was introduced into a solution of 4-t-butylsulfinyl-1-butanol, 2, (1.78 g, 0.01 moles), in anhydrous THF (30 ml) at 0° under nitrogen. After stirring for five minutes iodomethane (1.56 g., 1.1 eq.) was added. On usual workup the reaction mixture afforded the desired hydroxy-sulfoxide 14 (1.5 g., 80%) as a viscous oil.

IR. 3300 (OH) and 1005 ($S=O$) cm^{-1} .

N.M.R. 1.1 - 1.3 (m, 12H); 1.3 - 2.0 (m, 4H);
2.2 - 2.9 (m, 1H); 3.4 - 3.6 (m, 2H); 4.0
(bs, exchangeable with D_2O , 1H).

ii) 3-Methyl-1,2-oxathiane-2-oxide, 16.

Sulfuryl chloride (950 mg, 1.1 eq.) was added to a solution of the hydroxy-sulfoxide 14 (1.21 g., 0.006 moles)

in methylene chloride (30 ml) at room temperature. The reaction mixture after usual workup and purification afforded the desired sultine 16 (640 mg., 78%).

3) Attempted Synthesis of 3-Phenyl-1,2-Oxathiolane-2-Oxide, 21.

i) Methyl 3-Phenyl 3-t-butylthio propanoate, 18.

Methyl cinnamate (14.8 g., 0.1 moles) was added to a solution of 9.0 g. (0.1 moles) of t-butyl thiol and 6.0 g. of KOH in 25 ml of methanol. The reaction mixture was stirred overnight, stripped of methanol, poured into water and extracted several times with 50 ml of methylene chloride. The combined organic extracts were dried and evaporated to give 12.0 g.

(50%) of crude methyl 3-phenyl-2-t-butylthio propanoate, 18.

N.M.R. 1.22 (s, 9H); 2.8 (d, J = 7.5 Hz, 2H);
3.6 (s, 3H); 3.75 (t, J = 7.5 Hz, 1H);
7.1 - 7.6 (m, 5H).

ii) 3-Phenyl-3-t-butylthio-1-propanol, (19).

The crude ester 18 (6.0 g.) was reduced with 0.9 g. of lithium aluminium hydride in 30 ml of anhydrous ether to give 5.2 g. (quantitative) of the required hydroxy-sulfide.

IR. 3400 (OH) cm^{-1} .

N.M.R. 1.2 (s, 9H); 1.7 - 2.35 (m, 2H); 2.5 (bs, exchangeable with D_2O , 1H); 3.3 - 4.5 (m, 3H);
7.0 - 7.3 (m, 5H).

iii) 3-Phenyl-3-t-butylsulfinyl-1-propanol, (20).

From 5.3 g. of hydroxy-sulfide 19 (0.25 moles) and 2.9 g. of t-butyl hypochlorite (0.27 moles) were obtained 2.7 g. (50%) of the hydroxy-sulfoxide 20 as a white solid, which was recrystallized from ethyl acetate: hexane (m.p. 94-96°).

IR. 3360 (OH) and 1005 (S=O) cm^{-1} .

N.M.R. 1.03 (s, 9H); 1.9 - 2.6 (m, 3H); 3.3 - 4.2 (m, 3H); 7.2 - 7.5 (m, 5H).

Analysis Calculated for $\text{C}_{13}\text{H}_{20}\text{O}_2\text{S}$: C, 64.98; H, 8.39; S, 13.32.

Found : C, 64.95; H, 8.42; S, 13.65.

iv) Reaction of 20 with N-chlorosuccinimide:

A solution, containing 2.4 g. of hydroxy-sulfoxide 20 and 1.4 g. of NCS in 50 ml of CCl_4 , was refluxed for thirty minutes. After cooling, the insoluble material was removed by filtration and the solution stripped of solvent, to give 2.0 g. of a crude, light yellow oil.

N.M.R. 1.33 (s, 9H); 2.0 - 2.3 (m, 2H); 3.7 - 4.0 (m, 2H); 7.2 (s, 5H).

Attempted purification of this residue via column chromatography led only to further decomposition of the material.

v) Reaction of 20 with sulfuryl chloride.

Sulfuryl chloride (2.7 g.) was added to a solution of 4.8 g. of 20 in 100 ml of methylene chloride. The resultant

solution was stirred at room temperature for 30 minutes and then stripped of volatile material by evaporating on a rotary evaporator to give 4.0 g. of crude material.

N.M.R. 1.33 (s, 9H); 2.0 - 2.3 (m, 2H); 3.7 - 4.0 (m, 2H); 7.2 (s, 5H).

Attempted purification of this residue via column chromatography did not give any pure substance.

Sultines bearing substitution α to oxygen

1) Synthesis of 5-methyl-1,2-oxathiolane-2-oxide, 23.

i) 4-t-Butylsulfinyl-2-butanol, 22.

Methyl lithium (18.4 ml, 1.1 equivalents) was introduced into a solution of 3.6 g. of t-butyl methyl sulfoxide (1 equivalent) in anhydrous THF under nitrogen at 0°, followed after 5 minutes by 1.8 g. (1 equivalent) of propylene oxide. The reaction mixture was stirred for another three hours, poured into water and extracted with 4 x 50 ml of methylene chloride. The combined organic extract after drying and evaporation followed by chromatography of the crude residue afforded 4.7 g. (88%) of the required hydroxy-sulfoxide.

IR. 3320 (OH) and 1000 (S=O) cm^{-1} .

N.M.R. 1.3 - 1.4 (m, 12H); 1.6 - 2.9 (m, 4H); 3.4 (bs, exchangeable with D_2O , 1H); 3.7 - 4.25 (m, 1H).

ii) 5-Methyl-1,2-oxathiolane-2-oxide, 23.

Sulfuryl chloride (1.8 g.) was added to a solution of 2.24 g. of the hydroxy-sulfoxide 22 in 100 ml of methylene chloride. Workup followed by chromatography afforded 1.05 g. (70%) of the sultine 23.

IR. 1120 (S=O) cm^{-1} .

N.M.R. 1.39 and 1.59 (d, $J = 6\text{Hz}$, 3H); 2.2 - 3.42 (m, 3H); 4.7 - 5.2 (m, 1H).

M.S. Calculated for $C_4H_8O_2S$: 120

Found : 120

Analysis: Calculated for $C_4H_8O_2S$: C, 39.98; H, 6.71;
S, 26.68.

Found : C, 40.00; H, 6.47;
S, 26.01.

iii) 5-Methyl-1,2-oxathiolane-2,2-dioxide.⁵

Oxidation of 500 mg. of the above sultine with 900 mg. of m-chloroperbenzoic acid in methylene chloride afforded 442 mg. (80%) of the sultone.

IR. 1160 and 1350 (SO_2) cm^{-1} .

N.M.R. 1.5 (d, $J = 6Hz$, 3H); 2.0 - 3.35 (m, 4H);
4.5 - 4.9 (m, 1H).

2) Synthesis of 5-phenyl-1,2-oxathiolane 2-oxide, (25).i) 1-Phenyl 3-*t*-butylsulfinyl-1-propanol, (24).

Methyl lithium (18.4 ml, 1.1 equivalents) was introduced into a solution of 3.6 g. of *t*-butyl methyl sulfoxide (1 equivalent) in anhydrous THF under nitrogen at 0°, followed after 5 minutes by 3.6 g. (1 equivalent) of styrene oxide. The reaction mixture was stirred for another three hours, poured into water and extracted with 4 x 50 ml of methylene chloride. The combined organic extract after drying and evaporation followed by chromatography of the crude residue afforded 6.15 g. (85%) of the required hydroxy-sulfoxide.

IR. 3325 (OH) and 1000 (S=O) cm^{-1} .

N.M.R. 1.25 (s, 9H); 2.02 - 2.7 (m, 4H); 4.3 - 5.0 (m, 2H); 7.0 - 7.35 (m, 5H).

ii) 5-Phenyl-1,2-oxathiolane-2-oxide, 25.

Sulfuryl chloride (3.78 g.) was reacted with 6.2 g. of the above hydroxy-sulfoxide in 500 ml of methylene chloride for fifteen minutes. The reaction mixture after usual workup followed by purification via chromatography on silica afforded 4.5 g. (96%) of the substance 25.

IR. 1110 (S=O) cm^{-1} .

N.M.R. 2.5 - 3.5 (m, 4H); 5.45 and 6.0 (m, 1H);
7.2 - 7.5 (m, 5H).

M.S. Calculated for $\text{C}_9\text{H}_{10}\text{O}_2\text{S}$: 182.

Found : 182.

Analysis: Calculated for $C_9H_{10}O_2S$: C, 59.31; H, 5.53; S, 17.59.

Found : C, 59.60; H, 5.75; S, 17.40.

iii) 5-Phenyl-1,2-oxathiolane-2,2-dioxide.

The above sultine (300 mg) was oxidized with 650 mg of m-chloroperbenzoic acid in methylene chloride to yield 300 mg (94%) of the desired sultone.

IR. 1350, 1160 and 900 (SO_2) cm^{-1} .

N.M.R. 2.5 - 3.0 (m, 2H); 3.3 - 3.7 (m, 2H);

5.56 (d of d; $J = 6Hz$ and $9Hz$; 1H); 7.2 - 7.5 (m, 5H).

3) Synthesis of 3-Methyl-5-phenyl-1,2-oxathiolane-2-oxide, 27.

i) 1-Phenyl-3-*t*-butylsulfinyl-1-butanol, (26).

This hydroxy-sulfoxide was prepared in 88% yield from 3.6 g. styrene oxide and 4.0 g. of t-butyl ethyl sulfoxide (cf syntheses of 22 and 24). The crude product was recrystallized from ether: pentane to a white crystalline solid (m.p. 67 - 69° C)

IR. 3330 (OH) and 1000 ($S=O$) cm^{-1} .

N.M.R. 1.23 (s, 9H); 1.3 (d, $J = 4Hz$, 3H); 1.6 - 3.3 (m, 3H); 3.8 (bs, exchangeable with D_2O , 1H); 4.9 - 5.0 (m, 1H); 7.1 - 7.4 (m, 5H).

Analysis: Calculated for $C_{14}H_{22}SO_2$: C, 65.87;

H, 8.62.

Found: C, 65.66; H,

8.49.

ii) 3-Methyl-5-phenyl-1,2-oxathiolane-2-oxide, 27.

The reaction of 2.3 g. of sulfuryl chloride and 4.0 g. of the hydroxy-sulfoxide 26 afforded after chromatography (elution with ethyl acetate) 3.1 g. (96%) of the sultone 27.

IR. 1105 (S=O) cm^{-1} .

N.M.R. 1.25 and 1.31 (d, $J = 6Hz$, 3H); 2.0 - 3.0 (m, 2H); 3.3 - 3.6 (m, 1H); 5.36 - 6.04 (m, 1H); 7.1 - 7.4 (m, 5H).

M.S. Calculated for $C_{10}H_{12}O_2S$: 196

Found : 196

Analysis: Calculated for $C_{10}H_{12}O_2S$: C, 61.79; H,

6.16; S, 16.03.

Found : C, 61.95; H, 6.44;

15.41.

iii) Oxidation of 27.

Attempted oxidation of 27 with m-chloroperbenzoic acid led to the complete decomposition of the material. None of the desired sultone could be isolated.

4) Synthesis of 3,5-dimethyl-1,2-oxathiolane-2-oxide, 29.i) 4-t-Butylsulfinyl-2-pentanol, 28.

t-Butyl ethyl sulfoxide (3.45 g.) was dissolved in THF and treated with 15.7 ml of methyl lithium (1.1 equivalents). Propylene oxide (1.64 g, 1 equivalent) was added and the reaction mixture was stirred overnight. Workup followed by purification via column chromatography over silica (eluted with ethyl acetate) afforded 4.45 g. (90%) of the required hydroxy-sulfoxide as a viscous oil.

IR. 3340 (OH) and 1010 (S=O) cm^{-1} .

N.M.R. 1.0 - 1.4 (m, 15H); 1.5 - 2.4 (m, 3H);
2.9 - 3.4 (m, 1H); 3.2 - 4.1 (m, 1H).

ii) 3,5-Dimethyl-1,2-oxathiolane-2-oxide, 29.

From 2.0 g. of the above hydroxy-sulfoxide and 1.55 g. of sulfuryl chloride, were obtained, after chromatography on silica gel (eluted by ethyl acetate), 1.34 g. (90%) of the desired sultine.

IR. 1105 (S=O) cm^{-1} .

N.M.R. 1.1 - 1.6 (4 d'S, 6H); 1.7 - 2.7 (m, 2H);
2.8 - 3.5 (m, 1H); 4.5 - 5.3 (m, 1H).

M.S. Calculated for $\text{C}_5\text{H}_{10}\text{SO}_2$: 134; Found: 134.

Analysis. Calculated for $\text{C}_5\text{H}_{10}\text{SO}_2$: C, 44.75; H, 7.51;
S, 23.98.

Found : C, 44.71; H, 7.56;
S, 23.37.

iii) 3,5-Dimethyl-1,2-oxathiolane-2,2-dioxide.

Oxidation of 400 mg. of the sultine 29 with 1.2 g. of m-chloroperbenzoic acid in methylene chloride afforded 360 mg. (80%) of the desired sultone.

IR. 1325, 1140 and 900 (SO_2) cm^{-1} .

N.M.R. 1.43 and 1.45 (d'S, $J = 6\text{Hz}$, 6H); 1.7 - 2.85 (m, 2H); 3.3 - 3.7 (m, 1H); 4.5 - 5.0 (m, 1H).

5) Synthesis of sultine 31.

i) Epoxidation of 4-t-butyl cyclohexanone.

Sodium hydride (0.54 g.) was washed with 4 x 10 ml of anhydrous ether. It was placed in a 100 ml two-necked flask and 4.4 g. of trimethyl oxosulfonium iodide (0.02 moles) was added to it. The suspension was stirred under nitrogen at 0° for fifteen minutes. Dry DMSO (20 ml) was carefully added via a hypodermic syringe and the stirring continued for an additional ten minutes. The ice bath was then removed and the ylide solution stirred for further thirty minutes at room temperature.

A solution of 3.1 g. of 4-t-butyl cyclohexanone (0.02 moles) in 15 ml of anhydrous THF was added to the ylide solution and the contents allowed to stir overnight. The reaction mixture was poured into 100 ml of water and extracted with 4 x 100 ml of methylene chloride. This organic extract,

when dried and stripped of the solvent, afforded 3.0 g. of the crude epoxide which was further purified by chromatograph on silica (eluted with ethyl acetate: hexanes 1:2). The yield of purified epoxide was 2.42 g. (75%).

N.M.R. 0.9 (s, 9H); 0.92 - 2.0 (m, 9H); 2.43 (s, 2H).

ii) Synthesis of 30.

Methyl-lithium (9.5 ml, .017 moles) was added to a solution of 1.8 g. of t-butyl methyl sulfoxide (.015 moles) in anhydrous THF under nitrogen at 0°C, followed after five minutes by 2.4 g. of the above epoxide (.015 moles). The reaction mixture was stirred for another two hours, poured into water and extracted with 4 x 50 ml of methylene chloride. The combined organic extract, after drying and evaporation, furnished a brown solid which was recrystallized from ethyl-acetate: hexanes. The yield of recrystallized material was 2.6 g. (60%, m.p. 140° d)

IR. 3370 (OH) and 1010 (S=O) cm^{-1} .

N.M.R. 0.9 (s, 9H); 1.28 (s, 9H); 1.0 - 2.9 (m, 13H); 3.1 (bs, exchangeable with D_2O , 1H).

iii) Synthesis of 31.

Hydroxy-sulfoxide 30 (1.4 g.) was dissolved in 25 ml of methylene chloride at room temperature and a solution of 800 mg of sulfuryl chloride (1.1 equivalents) in 5 ml of methylene chloride was added to it. The crude product was purified

by column chromatography over silica (eluted with ethyl acetate) to give 1.0 g. (88%) of the sultine 31 as a white solid (m.p. 114-116°)

IR. 1110 (S=O) cm^{-1} .

N.M.R. 0.86 (s, 9H); 1.3 - 2.5 (m, 11H); 2.95 - 3.15 (m, 2H).

M.S. Calculated for $\text{C}_{12}\text{H}_{22}\text{SO}_2$: 230.

Found : 230.

Analysis. Calculated for $\text{C}_{12}\text{H}_{22}\text{SO}_2$: C, 62.58; H, 9.63; S, 11.40.

Found : C, 62.46; H, 9.54;

S, 11.82.

iv) Oxidation of Sultine 31.

Sultine 31 (100 mg) was oxidized with 200 mg. of m-chloroperbenzoic acid in 20 ml of methylene chloride to give 92 mg. (88%) of the corresponding sultone (m.p. 104-108°, d)

IR. 1140 and 1330 (SO_2) cm^{-1} .

N.M.R. 0.88 (s, 9H); 1.3 - 2.5 (m, 11H); 3.3 (t, J = 8Hz, 2H).

6) Synthesis of 6,6-dimethyl-1,2-oxathiane-2-oxide, 38.

i) 2-Methyl-4-pentene-2-ol:

Allyl bromide (24.2 g, 0.2 moles) was added dropwise to 9.6 g. of magnesium (0.4 moles) in ether. After

refluxing for one hour the reaction mixture was cooled and 11.6 g. (0.2 moles) of acetone was added. Usual workup afforded 12.0 g. of 2-methyl-4-pentene-2-ol (60%). The product boiled at 115-116°.

N.M.R. 1.13 (s, 6H); 1.2 (bs, 1H); 2.2 (d, 6Hz, 2H);
4.6 - 6.0 (m, 3H).

ii) 2-Methyl 5-t-butylthio 2-pentanol, 32.

A mixture of 4.5 g. of t-butyl mercaptan (0.05 moles) and 5.0 g. of 2-methyl-4-pentene-2-ol (0.05 mole) with trace of AIBN was refluxed for four hours. The reaction mixture was distilled to obtain 7.5 g. (80%) of the hydroxy-sulfide 32 (b.p. 85-90 /2mm).

N.M.R. 1.13 (s, 6H); 1.3 (s, 9H); 1.4 - 1.68
(m, 5H); 1.9 - 2.4 (m, 2H).

iii) 2-Methyl 5-t-butylsulfinyl 2-pentanol, 35.

Hydroxy-sulfide 32 (5.0 g., 0.025 moles) on oxidation with 5.5 g. of m-chloroperbenzoic acid (0.027 moles) in methylene chloride (60 ml) afforded 3.6 g. (70%) of the required hydroxy-sulfoxide 35 (m.p. 47-49°) and 0.65 g. (10%) of the corresponding sulfone (m.p. 66-67°).

Hydroxy-sulfoxide:

IR. 3340 (OH) and 1010 (S=O) cm^{-1} .

N.M.R. 1.14 (s, 6H); 1.18 (s, 9H); 1.4 - 2.2
(m, 4H); 2.3 - 2.6 (m, 2H); 3.76 (bs, ex-
changeable with D_2O , 1H).

Hydroxy-sulfone:

IR. 3325 (OH); 1300 and 1160 (SO₂) cm⁻¹.

N.M.R. 1.2 (s, 6H); 1.38 (s, 9H); 1.4 - 2.3 (m, 4H);
2.6 - 3.1 (m, 3H).

Analysis. Calculated for C₁₀H₂₂O₃S: C, 54.02;
H, 9.97.

Found : C, 54.38;
H, 10.37

iv) 6,6-Dimethyl-1,2-oxathiane-2-oxide, 38.

When 2.06 g. of hydroxy-sulfoxide 35 (0.01 moles) were treated with 1.4 g. of sulfuryl chloride (1.1 equivalents), the reaction mixture afforded 920 mg. (70%) of the expected sultine.

IR. 1135 (S=O) cm⁻¹.

N.M.R. 1.25 (s, 3H); 1.57 (s, 3H); 1.6 - 1.9 (m, 3H);
2.35 - 2.75 (m, 3H).

M.S. Calculated for C₆H₁₂O₂S: 148.056

Found : 148.056

Analysis. Calculated for C₆H₁₂O₂S: C, 48.64; H, 8.16.

Found : C, 48.14; H, 8.31.

v) 6,6-Dimethyl-1,2-oxathiane-2,2-dioxide

Sultine 38 (100 mg) on oxidation with 200 mg. of m-chloroperbenzoic acid in methylene chloride produced 95 mg. (90%) of the desired sultone.

IR. 1380 and 1165 (O-SO_2) cm^{-1} .

N.M.R. 1.58 (s, 6H); 1.8 - 2.9 (m, 4H); 3.2 - 3.5 (m, 2H).

7) Synthesis of 6-phenyl-1,2-oxathiane-2-oxide, 39.

i) 1-Phenyl-3-buten-1-ol.

Allyl bromide (12.2 g., 0.1 moles) was added dropwise to a suspension of 4.8 g. (0.2 moles) of magnesium in 100 ml of anhydrous ether. After refluxing for one hour, the reaction mixture was cooled and 10.6 g. (0.1 moles) of benzaldehyde was added dropwise. Usual workup afforded 11.8 g. (80%) of 1-phenyl-3-buten-2-ol. The product boiled at $60-62^\circ / 10\mu$.

N.M.R. 2.3 (bs, exchangeable with D_2O , 1H); 2.4 - 2.8 (m, 2H); 4.6 - 4.9 (m, 1H); 5.0 - 6.0 (m, 3H); 7.3 (m, 5H).

ii) 4-t-Butylthio -1-phenyl-1-butanol, 33.

A mixture of 4.5 g. of t-butyl mercaptan (0.05 moles) and 7.4 g. (0.05 moles) of 1-phenyl-3-buten-1-ol with a trace of AIBN was refluxed for six hours. The reaction mixture was distilled to remove the unreacted starting material (3.0 g. of homo allylic alcohol). The residue (7.0 g., 95% based on the used alcohol) was characterized as the required 4-t-butylthio-1-phenyl-1-butanol, 33, from its spectral properties.

IR. 3300 (OH) cm^{-1} .

N.M.R. 1.25 (s, 9H); 1.5 - 2.2 (m, 4H) 2.3 - 2.6
(m, 3H); 4.5 - 4.6 (m, 1H); 7.3 (s, 5H).

iii) 4-t-Butylsulfinyl-1-phenyl-1-butanol, 36.

Oxidation of 9.2 g. of the hydroxy-sulfide 33 with m-chloroperbenzoic acid (8.0 g.) in methylene chloride (200 ml) yielded the hydroxy-sulfoxide 36 (7.0 g., 70%, m.p. 56-59°) together with the corresponding hydroxy-sulfone (1.5 g., 15% m.p. 94-95°).

Hydroxy-sulfoxide:

IR. 3320 (OH) and 1010 (S=O) cm^{-1} .

N.M.R. 1.20 (s, 9H); 1.6 - 2.0 (m, 4H); 2.1 - 2.7
(m, 3H); 4.5 - 4.7 (m, 1H); 7.15 (s, 5H).

Hydroxy-sulfone:

IR. 3350 (OH); 1300 and 1155 (SO₂) cm^{-1} .

N.M.R. 1.36 (s, 9H); 1.6 - 2.0 (m, 5H); 2.6 - 3.0
(m, 2H); 4.5 - 4.7 (m, 1H); 7.2 (s, 5H).

Analysis. Calculated for C₁₄H₂₂O₃S: C, 62.19;
H, 8.20.

Found : C, 62.63; H, 8.46.

iv) 6-Phenyl-1,2-oxathiane-2-oxide, 39.

Reaction of sulfonyl chloride (270 mg.) with the hydroxy-sulfoxide 36 (510 mg.) in methylene chloride (20 ml) yielded the sultine 39 (288 mg., 72%) as a colorless liquid.

IR. 1125 (S=O) cm^{-1} .

N.M.R. 1.2 - 2.2 (m, 3H); 2.5 - 2.9 (m, 3H);
5.37 (d of d, $J = 9\text{Hz}$ and 6Hz , 1H); 7.3
(m, 5H).

M.S. Calculated for $\text{C}_{10}\text{H}_{12}\text{O}_2\text{S}$: 196.056.
Found : 196.056.

Analysis: Calculated for $\text{C}_{10}\text{H}_{12}\text{O}_2\text{S}$: C, 61.19; H, 6.16
Found : C, 61.07; H, 6.26.

8) Synthesis of 6-methyl-6-phenyl-1,2-oxathiane-2-oxide, 40.

i) 2-Phenyl-4-penten-2-ol.

This alcohol was obtained in 92% yield by the reaction of allyl magnesium bromide with acetophenone in ether. The product boiled at $52-55^\circ/10\mu$.

N.M.R. 1.53 (s, 3H); 2.3 (bs exchangeable with D_2O , 1H); 2.4 - 2.9 (m, 2H); 4.9 - 6.2 (m, 3H);
7.1 - 7.6 (m, 5H).

ii) 5-*t*-Butylthio-2-phenyl-2-pentanol, 34.

A mixture of 4.5 g. of *t*-butyl mercaptan (0.05 moles) and 8.1 g. (0.05 moles) of the above unsaturated alcohol with a trace of AIBN was refluxed for one hour. The reaction mixture was distilled to give 10.5 g. (83%) of 34 boiling at $120-125^\circ/15\mu$.

IR. 3300 (OH) cm^{-1} .

N.M.R. 1.25 (s, 9H); 1.53 (s, 3H); 1.6 - 2.3 (m, 5H);
2.4 - 2.7 (m, 2H); 7.2 - 7.5 (m, 5H).

iii) 5-t-Butylsulfinyl-2-phenyl-2-pentanol, 37.

Oxidation of 13.0 g. of 34 with m-chloroperbenzoic acid (11.0 g.) in methylene chloride (200 ml) yielded the hydroxy-sulfoxide 37 (7.9 g., 60%, m.p. 80-81°) together with the corresponding sulfone (2.5 g., 20%, m.p. 104-105°).

Hydroxy-sulfoxide:

IR. 3320 (OH) and 1005 (S=O) cm^{-1} .

N.M.R. 1.13 (s, 9H); 1.53 (s, 9H); 1.6 - 2.1 (m, 2H);
2.2 - 2.7 (m, 2H); 3.3 (bs, 1H); 7.1 - 7.5
(m, 5H).

Analysis. Calculated for $\text{C}_{15}\text{H}_{24}\text{O}_2\text{S}$: C, 67.12; H, 9.01;
S, 11.95.

Found : C, 66.73; H, 8.59;
S, 11.82.

Hydroxy-sulfone:

IR. 3340 (OH); 1300 and 1160 (SO_2) cm^{-1} .

N.M.R. 1.33 (s, 9H); 1.53 (s, 3H); 1.6 - 2.1 (m, 4H);
2.3 (bs, exchangeable with D_2O , 1H); 2.6 - 3.0
(m, 2H); 7.1 - 7.5 (m, 5H).

Analysis. Calculated for $\text{C}_{15}\text{H}_{24}\text{O}_3\text{S}$: C, 63.34; H, 8.51;
S, 11.27.

Found : C, 63.47; H, 8.74;
S, 11.11.

iv) 6-Methyl-6-phenyl-1,2-oxathiane, 2-oxide, 40.

Reaction of sulfuryl chloride (270 mg.) with the

hydroxy-sulfoxide 37 (536 mg.) in methylene chloride (25 ml) yielded the sultine 40 (380 mg.) in 90% yield.

IR. 1125 (S=O) cm^{-1} .

N.M.R. 1.89 (s, 3H); 2.0 - 3.2 (m, 6H); 7.0 - 7.7 (m, 5H).

Analysis: Calculated for $\text{C}_{11}\text{H}_{14}\text{O}_2\text{S}$: C, 62.82; H, 6.71.

Found: C, 62.96; H, 6.87.

9) Synthesis of 4,6-dimethyl-1,2-oxathiane-2-oxide, 47.

i) 5-t-Butylthio-4-methyl-2-pentanol, 43.

This hydroxy-sulfide was obtained in 90% yield (b.p. 101-104°/4 mm) by the radical addition of t-butyl thiol to 4-methyl-4-pentene-2-ol.

N.M.R. 0.98 (d, J = 6Hz, 3H); 1.03 (d, J = 6Hz, 3H);

1.26 (s, 9H); 1.3 - 2.0 (m, 4H); 2.2 - 2.5

(m, 2H); 3.6 - 4.0 (m, 1H).

ii) 5-t-Butylsulfinyl-4-methyl-2-pentanol, 45.

Hydroxy-sulfide 43 (7.6 g., 0.04 moles) on oxidation with 8.0 g. of m-chloroperbenzoic acid yielded 5.2 g. (65%) of the hydroxy-sulfoxide 45.

IR. 3380 (OH) and 1010 (S=O) cm^{-1} .

N.M.R. 0.9 - 1.2 (15H); 1.3 - 2.0 (m, 4H); 2.2 - 2.5 (m, 2H); 3.6 - 4.0 (m, 1H).

iii) 4,6-Dimethyl-1,2-oxathiane-2-oxide, 47.

Hydroxy-sulfoxide 45 (2.0 g.) on treatment with sulfuryl chloride (1.5 g.) in methylene chloride (40 ml) yielded 1.04 g. (70%) of the sulfone 47.

IR. 1120 (S=O) cm^{-1}

N.M.R. 0.94 (d, J = 6Hz, 3H); 1.28 (d, J = 6Hz, 3H);
1.4 - 2.4 (m, 5H); 3.8 - 4.2 (m, 1H).

10) Synthesis of 5,6-dimethyl-1,2-oxathiane-2-oxide, 48.

i) 5-t-Butylthio-3-methyl-2-pentanol, 44.

This hydroxy-sulfide was obtained in 82% yield (b.p. 85-89°/4 mm) by the radical addition of t-butyl thiol to 3-methyl-4-pentene-2-ol.

N.M.R. 0.86 (d, J = 6Hz, 3H); 1.08 (d, J = 6Hz, 3H);
1.26 (s, 9H); 1.3 - 2.0 (m, 4H); 2.2 - 2.5 (m, 2H); 3.4 - 3.7 (m, 1H).

ii) 5-t-Butylsulfinyl-3-methyl-2-pentanol, 46.

Hydroxy-sulfide 44 (7.6 g., 0.04 moles) was oxidized with 8.0 g. of m-chloroperbenzoic acid to obtain 5.0 g. (65%) of the hydroxy-sulfoxide 46.

IR. 3360 (OH) and 1000 (S=O) cm^{-1} .

N.M.R. 0.9 - 1.2 (15H); 1.3 - 2.0 (m, 4H); 2.2 - 2.5 (m, 2H); 3.5 - 3.8 (m, 4H).

iii) 5,6-Dimethyl-1,2-oxathiane-2-oxide, 48.

Hydroxy-sulfoxide 46 (2.0 g.) on treatment with sulfuryl chloride (1.5 g.) in methylene chloride (25 ml) yielded 1.02 g. (69%) of the sulfine 48.

IR. 1125 (S=O) cm^{-1} .

N.M.R. 0.93 (d, J = 6Hz, 3H); 1.28 (d, J = 6Hz, 3H);
1.5 - 2.9 (m, 5H); 4.2 - 5.0 (m, 1H).

11) Synthesis of 6-methyl-1,2-oxathiane-2-oxide, 52.

i) 5-t-Butylthio-2-pentanone, 49.

5-Chloro-2-pentanone (6.0 g., 0.05 moles) was added to solution containing 4.5 g. of t-butyl thiol (.05 moles) and 2.8 g. of KOH in 25 ml of methanol. After stirring overnight the reaction mixture was poured into water and extracted with 4 x 50 ml of methylene chloride. Methylene chloride extract was dried and stripped of the solvent. Crude ketone was purified by distillation (b.p. $110^{\circ}/4$ mm) to obtain 4.0 g. (45%) of the product.

N.M.R. 1.3 (s, 9H); 1.6 - 2.1 (m, 2H); 2.13 (s, 3H);
2.33 - 2.7 (m, 4H).

ii) 5-t-Butylthio-2-pentanol, 50.

When 3.2 g. of above keto-sulfide was reduced with excess of sodium borohydride in methanol, 3.0 g. of hydroxy-sulfide 50 (95%) was obtained.

N.M.R. 1.21 (d, 6Hz, 3H); 1.3 (s, 9H); 1.4 - 2.2 (m, 5H); 2.3 - 2.7 (m, 2H); 3.6 - 3.8 (m, 2H).

iii) 5-t-Butylsulfinyl-2-pentanol, 51.

Oxidation of 50 with m-chloroperbenzoic acid in CH_2Cl_2 yielded 51 in 80% yield.

IR. 3360 (OH) and 1005 (S=O) cm^{-1} .

N.M.R. 1.2 and 1.26 (d, J = 3Hz 3H); 1.25 (s, 9H); 1.4 - 2.2 (m, 4H); 2.3 - 2.9 (m, 2H); 3.2 - 4.0 (m, 2H).

iv) 6-Methyl-1,2-oxathiane-2-oxide, 52.

Hydroxy-sulfoxide 50 (200 mg.) and N-chlorosuccinimide (140 mg.) in 30 ml. of carbontetrachloride were refluxed for fifteen minutes. The reaction mixture was filtered and the filtrate evaporated to give 120 mg. of the desired sultine which was purified by chromatography to obtain 115 mg. (85%) of the pure material.

IR. 1110 cm^{-1} (O-SO)

N.M.R. 1.22 (d, 6Hz, 3H); 1.45 - 2.0 (m, 3H); 2.3 - 2.8 (m, 3H); 4.5 - 4.9 (m, 1H).

M.S. Calculated for $\text{C}_5\text{H}_{10}\text{O}_2\text{S}$: 134.035.

Found : 134.040 $\pm$.003.

v) 6-Methyl-1,2-oxathiane-2,2-dioxide, 53.

50 mg. of the sultine on oxidation with 100 mg. of m-chloroperbenzoic acid furnished 48 mg. (95%) of the sultone.

IR. 1350, 1150 and 920 (SO_2) cm^{-1} .

N.M.R. 1.45 (d, 6Hz, 3H); 1.5 - 2.2 (m, 4H);
2.8 - 3.3 (m, 2H); 4.4 - 5.0 (m, 1H).

Sultines bearing substituents β to
oxygen or sulfur

1) Synthesis of 4-methyl-1,2-oxathiolane 2-oxide, 57.

i) Methyl 2-methyl-3-t-butylthio propanoate, 54.

Methyl methacrylate (10.0 g., 0.1 moles) was added to a solution containing 9.0 g. (0.1 moles) of t-butyl thiol and 6.0 g. of KOH in 25 ml of methanol. The reaction mixture was stirred overnight, stripped of methanol, poured into water and extracted several times with 50 ml of methylene chloride. The combined organic extracts were dried and evaporated to give 2.2 g. of methyl 2-methyl-3-t-butylthio propanoate, 54. The aqueous layer was acidified with HCl and again extracted with methylene chloride. Further workup gave 14.4 g. of 2-methyl-3-t-butylthiopropionic acid (combined yield 90%).

ii) 2-Methyl-3-t-butylthio-1-propanol, 55.

The acid and the ester obtained above were combined and reduced with lithium aluminium hydride in ether. The yield of 2-methyl-3-t-butylthio-1-propanol was 75%.

IR. 3325 (OH) cm^{-1} .

N.M.R. 0.98 (d, $J = 7\text{Hz}$; 3H); 1.3 (s, 9H);

1.5 - 2.3 (m, 2H); 2.3 - 2.8 (m, 2H); 3.5
(d, $J = 6\text{Hz}$, 2H).

iii) 2-Methyl-3-*t*-butylsulfinyl 1-propanol, (56).

8.5 g. of the sulfide alcohol 55 was oxidized with 5.8 g. of *t*-butyl hypochlorite in methanol to yield 6.6 g. (70%) of hydroxy-sulfoxide 56.

IR. 3325 (OH) and 1005 (S=O) cm^{-1} .

N.M.R. 1.0 - 1.35 (m, 12H); 1.9 - 3.0 (m, 3H);
3.1 - 3.9 (m, 2H); 4.5 (bs, exchangeable
with D_2O , 1H).

iv) 4-Methyl-1,2-oxathiolane-2-oxide, 57.

From 2.5 g. of the hydroxy-sulfoxide 56 and 2.1 g. of sulfuryl chloride, 1.3 g. (70%) of sultine 57 was obtained.

IR. 1110 cm^{-1} (S=O).

N.M.R. 1.07 and 1.18 (d, $J = 7\text{Hz}$, 3H); 2.24 - 4.9
(m, 5H).

M.S. Calculated for $\text{C}_4\text{H}_8\text{O}_2\text{S}$: 120.

Found : 120.

Analysis: Calculated for $\text{C}_4\text{H}_8\text{O}_2\text{S}$: C, 39.98; H, 6.71.

Found : C, 39.76; H, 6.75.

v) 4-Methyl-1,2-oxathiolane-2,2-dioxide, (58).

Sultine 57 (100 mg.) was oxidized with 220 mg. of *m*-chloroperbenzoic acid in methylene chloride to give 96 mg. (89%) of the sultone 58.

IR. 1340, 1160 and 950 (SO_2) cm^{-1} .

N.M.R. 1.3 (d, $J = 6\text{Hz}$, 3H); 2.5 - 4.5 (m, 5H).

2) Synthesis of 4-methyl-1,2-oxathiane-2-oxide, 61.i) 3-Methyl-4-t-butylthio-1-butanol, 59.

A mixture of 9.0 g. (0.1 moles) of t-butyl thiol and 8.6 g. (0.1 moles) of 3-methyl-3-butene-1-ol was refluxed with trace of AIBN for twenty four hours. Volatile matter was removed in vacuo and the residue was distilled to furnish 15.0 g. (85%) of the hydroxy-sulfide 59 (b.p. 95-98°/0.4 mm).

IR. 3330 (OH) cm^{-1} .

N.M.R. 1.0 (d, $J = 6\text{Hz}$, 3H); 1.3 (s, 9H); 1.35 - 2.2 (m, 3H); 2.2 - 2.7 (m, 2H); 2.8 (bs, 1H); 3.56 (t, 6Hz , 2H).

ii) 3-Methyl-4-t-butylsulfinyl-1-butanol, 60.

When 7.0 g. of the hydroxy-sulfide 59 (0.04 moles) were oxidized with 8.0 g. of mcpba (1.0 equivalent) in methylene chloride, the crude reaction product after chromatography afforded 4.0 g. (60%) of the hydroxy-sulfoxide 60 and 1.0 g. (15%) of sulfone.

Sulfoxide:

IR. 3340 (OH) and 1010 (S=O) cm^{-1}

N.M.R. 1.0 - 1.3 (m, 12H); 1.3 - 2.7 (m, 5H); 3.3 - 4.0 (m, 3H)

Sulfone:

IR. 3420 (OH); 1260 and 1090 (SO_2) cm^{-1} .

N.M.R. 1.20 (d, $J = 6\text{Hz}$, 3H); 1.38 (s, 9H); 1.4 - 1.85 (m, 2H); 2.15 - 3.3 (m, 4H), 3.6 (t, 6Hz).

iii) 4-Methyl-1,2-oxathiane-2-oxide, 61.

When 3.8 g. of hydroxy-sulfoxide 60 was allowed to react with 2.7 g. of sulfuryl chloride in methylene chloride the reaction mixture afforded 2.0 g. (80%) of the sultine.

IR. 1105 (S=O) cm^{-1} .

N.M.R. 1.0 (d, $J = 6\text{Hz}$, 3H); 1.2 - 1.9 (m, 2H); 2.3 - 2.8 (m, 3H); 3.75 - 4.0 (m, 1H); 4.4 - 4.7 (m, 1H).

M.S. Calculated for $\text{C}_5\text{H}_{10}\text{O}_2\text{S}$: 134.040

Found : 134.039

Analysis:

Calculated: C, 44.75; H, 7.51.

Found : C, 44.89; H, 7.72.

3) Synthesis of 5-methyl-1,2-oxathiane-2-oxide, 67.

i) 4-*t*-Butylthio butanoic acid, 63.

Methyl 4-chlorobutanoate, 62, (13.6 g.) was added to a solution containing 9.0 g. of *t*-butyl thiol and 6 g. of potassium hydroxide in 30 ml of methanol. The reaction mixture was stirred overnight after which another equivalent of potassium hydroxide was added. The reaction mixture was washed with ether and the aqueous layer after acidification with HCl was extracted with methylene chloride. Methylene

chloride extract was dried (anhydrous MgSO_4) and evaporated. Crude product was distilled to obtain 6.0 g. (40%) of acid sulfide (b.p. 110-115°, 2 mm).

N.M.R. 1.35 (s, 9H); 1.6 - 2.2 (m, 2H); 2.4 - 2.7 (m, 4H); 11.2 (bs, 1H).

ii) 2-Methyl-4-t-butylthio butanoic acid, 64.

A solution of lithium di-isopropyl amide in THF was prepared by introducing 20 ml of methyl lithium (.04 moles) into a solution of 4.04 g. of di-isopropyl amine (.04 moles) in 40 ml of THF under nitrogen at -20°C. To the well stirred solution was added 3.52 g. of 4-t-butylthio butanoic acid, 63, (.02 moles). After stirring for five minutes, 3.0 g. of methyl iodide ($\gg$.04 moles) were introduced. The reaction mixture was allowed to stir for thirty minutes. Workup afforded 3.45 g. (90%) of the crude alkylated acid which was used without further purification for the subsequent reaction.

N.M.R. 1.2 (d, $J = 7.0\text{Hz}$, 3H); 1.3 (s, 9H); 1.4 - 2.8 (m, 4H); 3.3 - 3.6 (m, 1H); 11.3 (bs, 1H)

iii) 2-Methyl-4-t-butylthio -1-butanol; 65.

Crude acid 64 (3.45 g.) on reduction with lithium aluminium hydride in ether afforded 2.8 g. of required alcohol 65 (yield 85%).

IR. 3364 (OH) cm^{-1} .

N.M.R. 0.95 (d, $J = 6\text{Hz}$, 3H); 1.33 (s, 9H); 1.46 - 2.1 (m, 4H); 2.76 (t, $J = 7.0\text{ Hz}$, 2H); 3.5 (d, $J = 5\text{H}_3$, 2H).

iv) 2-Methyl-4-t-butylsulfinyl-1-butanol, 66.

Hydroxy-sulfide 65 (1.6 g.) was oxidized with 1.9 g. of m-chloroperbenzoic acid in methylene chloride to obtain 0.92 g. (60%) of 2-methyl-4-t-butylsulfinyl-1-butanol.

IR. 3340 (OH) and 1000 (S=O) cm^{-1} .

N.M.R. 0.94 and 0.95 (2d each with $J = 6\text{Hz}$, 3H);
1.25 (s, 9H); 1.56 - 1.88 (m, 3H); 1.9 -
2.4 (m, 3H); 3.2 (d, 5Hz, 2H).

v) 5-Methyl-1,2-oxathiane-2-oxide, 67.

When 770 mg. of hydroxy-sulfoxide 66 were allowed to react with 550 mg. of sulfuryl chloride in methylene chloride the reaction mixture gave 320 mg. (65%) of the required sulfine.

IR. 1105 (S=O) cm^{-1} .

N.M.R. 0.87 (d, $J = 6\text{Hz}$, 3H); 1.3 - 3.0 (m, 5H);
3.6 - 3.8 (m, 1H); 4.0 - 4.5 (m, 1H).

M.S. Calculated for $\text{C}_5\text{H}_{10}\text{O}_2\text{S}$: 134.040
Found : 134.040

Analysis: Calculated for $\text{C}_5\text{H}_{10}\text{O}_2\text{S}$: C, 44.75; H, 7.51
Found : C, 44.64; H, 7.42.

Synthesis of benzfused sultines

1) Synthesis of 3H-2,1-benzoxathiole-1-oxide, 69.

i) 2-(α -Phenyl-ethyl-thio)-benzoic acid, 70.

The sulfide acid was prepared in 85% yield from o-mercaptobenzoic acid and α -phenyl ethyl bromide. Crude acid was used as such for the next step.

N.M.R. (crude) 1.7 (d, J = 8Hz, 3H); 4.5 (q, J = 8Hz, 1H); 7.1 - 7.7 (m, 8H); 7.8 - 8.0 (m, 1H); 11.5 (bs, 1H).

ii) 2-(α -Phenyl-ethyl-thio)-benzyl alcohol, 71.

Reduction of the sulfide acid 70 with lithium aluminium hydride in ether afforded the desired sulfide alcohol in 92% yield.

IR. 3360 (OH) cm^{-1} .

N.M.R. 1.6 (d, J = 7Hz, 3H, 1H exchangeable with D_2O)
4.25 (q, 7Hz, 1H); 4.9 (s, 2H); 7.0 - 7.4 (m, 9H).

iii) 2-(α -Phenyl-ethyl-sulfinyl)-benzyl alcohol, 72.

Oxidation of 4.9 g. of the hydroxy-sulfide 71 (0.02 moles) with 4.5 g. of m-chloroperbenzoic acid (0.0225 moles) in 100 ml of methylene chloride afforded 4.4 g. (85%) of the required hydroxy-sulfoxide.

IR. 3360 (OH) and 1005 (S=O) cm^{-1} .

N.M.R. 1.55 (d, $J = 7.0\text{Hz}$, 2H); 3.5 (bs, exchangeable with D_2O , 1H); 3.9 - 4.7 (m, 3H); 6.9 - 7.5 (m, 5H).

iv) 3H-2,1-benzoxathiole-1-oxide, 69.

Sultine 69 was prepared in 60% yield by the reaction of sulfuryl chloride with the hydroxy-sulfoxide 72 in the usual manner (m.p. $39-40^\circ$, literature ¹³ m.p. $39-40^\circ$).

IR. 1120 (S=O) cm^{-1} .

N.M.R. 5.60 (AB quartet, $\delta_A = 5.42$, $\delta_B = 5.78$, $J_{AB} = 13.5\text{Hz}$, 2H); 7.2 (m, 4H).

2) Attempted synthesis of 3H-1,2-benzoxathiole-2-oxide, 68.

i) 2-t-Butylthiomethyl phenol, 73.

α -Bromo o-cresyl acetate (6.9 g., 0.03 moles) was added to a solution containing 2.7 g. of t-butyl thiol (0.03 moles) and 1.7 g. of KOH in 25 ml. of methanol. After thirty minutes another equivalent of KOH was introduced and the reaction mixture stirred for an additional thirty minutes. After acidification with HCl the organic matter was extracted with ether. The ether extract was dried and evaporated to furnish 5.4 g. (92%) of the phenol sulfide 73.

N.M.R. 1.33 (s, 9H); 3.76 (s, 2H); 5.5 (bs, 1H); 6.5 - 7.3 (m, 4H).

ii) 2-t-Butylsulfinylmethyl phenol, 74.

Phenolic sulfide 73 was oxidized with m-chloroperbenzoic acid in methylene chloride to obtain the phenolic sulfoxide 74 in 80% yield (m. 154-156°).

N.M.R. 1.4 (s, 9H); 4.16 (AB quartet, $\delta_{H_A} = 3.86$,

$\delta_{H_B} = 4.46$, $J_{AB} = 12\text{Hz}$, 2H); 6.7 - 7.4 (m, 5H).

Analysis:

Calculated for $C_{11}H_{16}O_2S$: C, 62.25; H, 7.60;
S, 15.08

Found : C, 62.14; H, 7.62;
S, 15.84

iii) Reaction of 74 with sulfuryl chloride:

Reaction of 74 with sulfuryl chloride in CH_2Cl_2 gave a crude material which appeared to be a mixture of 3H-1,2-benzoxathiol-2-oxide, 68, and o-chloro methyl phenyl ester of t-butyl sulfinic acid. However the product deteriorated rapidly and could not be separated into its constituents.

iv) Reaction of 74 with N-chlorosuccinimide:

Reaction of 74 with N-chlorosuccinimide in CCl_4 was carried out until the starting material had disappeared. The products however deteriorated too rapidly and could not be identified.

v) 2-(p-Methoxybenzylthiomethyl) Phenol:

This phenol was prepared in 92% yield from p-methoxy

benzyl thiol and α -bromo *o*-cresyl acetate in the same manner as 73.

N.M.R. 3.6 (s, 2H); 3.7 (s, 2H); 3.8 (s, 3H);
6.7 - 7.5 (m, 9H).

vi) 2-(p-Methoxybenzylsulfinylmethyl) Phenol, 76.

Phenolic sulfide obtained above was oxidized with *m*-chloroperbenzoic acid in methylene chloride to obtain a 60% yield of the required phenolic sulfoxide (m. 105-107°).

N.M.R. 3.8 (s, 3H); 3.6 - 4.2 (m, 4H); 6.7 - 7.5 (m, 9H).

Analysis: Calculated for $C_{15}H_{16}O_3S$: C, 65.21;
H, 5.84; S = 11.59.
Found : C, 65.36; H, 5.74;
S = 11.82.

vii) Reaction of 76 with sulfuryl chloride:

When 310 mg. of sulfuryl chloride was added to a solution of 600 mg. of 76 in methylene chloride the reaction product appeared to be a mixture of the expected sulfone (AB quartet, $\delta_{H_A} = 4.16$, $\delta_{H_B} = 4.56$, $J_{AB} = 16\text{Hz}$, 2H) and *p*-methoxy benzyl chloride [3.90, s (3H); 4.66, s, (2H)]. However on column chromatography only *p*-methoxy benzyl chloride and *p*-methoxy benzyl alcohol were isolated.

viii) Reaction of 76 with N-chlorosuccinimide:

Treatment of hydroxy-sulfoxide 76 with N-chlorosuccinimide in carbon tetrachloride gave the same mixture as obtained

with sulfonyl chloride. However in this case also the required sultine decomposed prior to isolation.

In a second attempt, the reaction mixture was oxidized with *m*-chloroperbenzoic acid. The crude reaction product showed a singlet at 4.63 δ suggesting the presence of 3H-1,2-benzoxathiole-2,2-dioxide. Unfortunately it could not be isolated in its pure state.

II) Synthesis of 3,4-dihydro-1,2-benzoxathiin-2-oxide, 78.

i) 2-(2-*t*-Butylsulfinyl ethyl) phenol, 81.

Phenol 81 was obtained in 70% yield by the reaction of α -lithiomethyl *t*-butyl sulfoxide with α -bromo *o*-cresyl acetate in THF.

IR. 3360 (OH) and 1010 (S=O) cm^{-1} .

N.M.R. 1.25 (s, 9H); 1.6 - 2.2 (m, 4H); 6.9 - 7.3 (m, 5H).

ii) Reaction of 81 with sulfonyl chloride.

Reaction of 81 with 1.1 equivalents of sulfonyl chloride in methylene chloride gave the sultine 78 in a crude yield of 95%.

N.M.R. 2.3 - 3.5 (m, 4H); 6.8 - 7.4 (m, 4H).

iii) Oxidation of 78.

Without isolation 78 was oxidized with *m*-chloroperbenzoic

acid in methylene chloride to the sultone 82 (75%) (m.p. 108-110^o, lit. m.p. 108-109^o).

IR. 1360, 1140 and 900 (O-SO₂) cm⁻¹.

N.M.R. 3.3 - 3.6 (m, 4H); 6.8 - 7.5 (m, 4H).

CHAPTER V (Experimental)

Olefin synthesis: (Thermal Extrusion of SO_2 from sultines)

1) cis-Stilbene:

a) Epoxy trans-stilbene 30.

trans-Stilbene (1.8 g.) and m-chloroperbenzoic acid (2.25 g., 1.1 equivalents) were allowed to react in 25 ml of methylene chloride at room temperature for four hours. The usual work up yielded 1.9 g. (Quantitative yield) of the epoxide, m.p. $69-70^\circ$.

N.M.R. 4.35 (s, 2H); 7.2 (s, 10H)

b) erythro-1,2-Diphenyl-2-t-butylthio ethanol:

trans-Stilbene epoxide (1.96 g.), t-butyl mercaptan (0.99 g., 1.1 eq.) and KOH (0.6 g. 1.1 eq.) were allowed to reflux in 20 ml. of n-propanol for eight hours. The reaction mixture was cooled, poured into water and extracted with 50 x 3 ml. of methylene chloride. Organic extract was dried and evaporated. The crude product was distilled at $150-160^\circ$ (0.05 mm) to give 2.2 g. (75%) of a pale yellow oil which solidified to a pale yellow solid (m.p. $59-61^\circ$).

IR. 3350 (OH) cm^{-1} .

N.M.R. 1.2 (s, 9H); 2.5 (bs, 1H); 4.2 (d, 6Hz, 1H):

5.0 (d, 6Hz, 1H); 7.2 (m, 10H)

c) erythro-1,2-Diphenyl-2-t-butylethanol, 31.

erythro 1,2-Diphenyl-2-t-butylthio ethanol (5.6 g., 0.02 moles) was oxidized with 4.4 g. of m-chloroperbenzoic acid in 200 ml. of methylene chloride to obtain 4.5 g. (75% yield) of the hydroxy-sulfoxide 31.

IR. 3340 (OH) and 1010 (S=O) cm^{-1} .

N.M.R. 1.12 (s, 9H); 3.95 (d, 3Hz, 1H); 5.5 (d, 3Hz, 1H); 7.0 (m, 11H)

Analysis: Calculated for $\text{C}_{18}\text{H}_{22}\text{O}_2\text{S}$: C = 71.50,

H = 7.33, S = 10.68

Found : C = 71.27,

H = 7.03, S = 10.24

d) cis-Stilbene, 33.

Hydroxy-sulfoxide 31 (604 mg.) and N-Chlorosuccinimide (280 mg.) were refluxed in 100 ml. of benzene for sixty minutes. The reaction mixture was cooled and stripped of the solvent on a rotary evaporator. The crude residue was subjected to column chromatography on silica gel using methylene chloride: hexanes(1:1). First fraction afforded 185 mg. (51%) of cis-stilbene (99% pure from n.m.r.)

N.M.R. 6.55 (s, 2H); 7.2 (s, 10H).

2) Styrene:a) 1-Phenyl-2-t-butylsulfinyl ethanol, 26.

t-butyl methyl sulfoxide (6 g., 0.05 mole) was diluted

in 100 ml of THF and cooled at -78° . Methyl lithium (30.5 ml, 0.05 mole) was added, followed five minutes later by the addition of 5.3 g. (0.05 mole) of benzaldehyde. After thirty minutes, the reaction mixture was hydrolysed and the product extracted with methylene chloride. A white crystalline solid (9.8 g., 87%) was obtained and recrystallized from methylene chloride hexane (m.p. $94-6^{\circ}$).

IR. 3320 (OH) and 1005 (S=O) cm^{-1} .

N.M.R. 1.3 (s, 9H); 2.3 (m, 2H); 4.2 (m, 1H);
5.5 (bs, 1H); 7.5 (s, 5H).

Analysis: Calculated for $\text{C}_{12}\text{H}_{18}\text{O}_2\text{S}$: C, 63.70; H, 8.02.

Found : C, 63.64; H, 8.21.

b) Styrene

A mixture of above hydroxy-sulfoxide (452 mg.) and N-chlorosuccinimide (280 mg.) in 50 ml of benzene was refluxed for fifteen minutes. Usual workup afforded 145 mg. (70%) of styrene (vpc yield 82%).

N.M.R. 5.0 - 5.8 (2H); 6.4 - 6.9 (1H); 7.2 (5H).

3) 3-Vinyl-1-cyclohexene.

a) 2-t-Butylsulfinyl-1-(2-cyclohexenyl) ethanol:

This hydroxy sulfoxide was prepared in 75% yield from t-butyl methyl sulfoxide and Δ^3 -cyclohexene carboxaldehyde in the usual manner (m.p. $72-75^{\circ}$).

IR. 3280 (OH) and 1015 (S=O) cm^{-1} .

N.M.R. 1.26 (s, 9H); 1.3 - 2.6 (m, 9H); 3.8 - 4.2 (m, 1H); 4.3 (bs, exchangeable with D_2O , 1H); 5.6 - 5.7 (bs, 2H).

Analysis: Calculated for $\text{C}_{12}\text{H}_{22}\text{O}_2\text{S}$: C, 62.58; H, 9.63
Found : C, 62.36; H, 9.59

b) 3-Vinyl-1-cyclohexene.

When the above hydroxy-sulfoxide (460 mg.) was refluxed with 280 mg. of NCS in carbontetrachloride, 3-vinyl-1-cyclohexene was obtained (vpc yield 62%).

IR. 890 ($\text{C} = \text{CH}_2$) and 705 $\left(\begin{array}{c} \text{---C} = \text{C---} \\ | \quad | \\ \text{H} \quad \text{H} \end{array} \right) \text{cm}^{-1}$.

N.M.R. 1.5 to 2.0 (m, 6H); 2.75 (broad signal, 1H); 4.2 to 6.1 (olefinic protons, 5H).

4) 1-Phenyl-1,3-butadiene:

a) 1-t-Butylsulfinyl-4-phenyl but-3-en 2-ol.

This hydroxy-sulfoxide was prepared in 95% yield from t-butyl methyl sulfoxide and cinnamaldehyde in the usual manner. (m.p. $125-127^\circ$).

IR. 3280 (OH) and 1010 (S=O) cm^{-1} .

N.M.R. 1.23 (s, 9H); 2.6 - 2.8 (m, 2H); 4.7 - 5.0 (m, 1H); 5.7 - 7.0 (m, 3H); 7.2 (m, 5H).

Analysis: Calculated for $\text{C}_{14}\text{H}_{20}\text{O}_2\text{S}$: C, 66.64; H, 7.99.
Found : C, 66.48; H, 7.89.

B) 1-Phenyl-1,3-butadiene:

Reaction of the above hydroxy-sulfoxide with NCS in refluxing CCl_4 afforded 1-phenyl 1,3-butadiene in 75% isolated yield.

N.M.R. 6.4 - 6.8 (2H); 7.2 - 7.6 (7H); 9.66 (d, J = 8Hz, 1H).

5) 3-Methylene- Δ^5 -Cholestene.

a) 3-t-Butylsulfinylmethyl- Δ^5 -cholesten-3-ol:

This hydroxy-sulfoxide was prepared in 77% yield from t-butyl methyl sulfoxide and Δ^5 -cholesten-3-one. (m.p. 163-166°).

IR. 3320 (OH) and 1015 (S=O) cm^{-1} .

N.M.R. 1.23 (t-butyl singlet); 5.1 - 5.3 (olefinic proton at C_5).

b) 3-methylene- Δ^5 -cholestene:

Reaction of the above hydroxy-sulfoxide with NCS in refluxing carbon tetrachloride gave 3-methylene- Δ^5 -cholestene in 62% isolated yield.

N.M.R. 5.1 - 5.3 (olefinic proton at C_5); 5.3 - 5.6 (= CH_2 protons).

Characterization of β -sultine 27.

i) 2-Hydroxy-2-phenyl ethane sulfinic acid methyl ester, 28.

Hydroxy-sulfoxide 26 (130 mg.) was dissolved in methylene chloride (10 ml) and sulfonyl chloride (90 mg.) was added to it. After stirring at room temperature for fifteen minutes, methanol (5 ml) was added and the reaction mixture stirred for another sixty minutes. The solvent was removed in vacuo and the residue was examined by n.m.r.

N.M.R. 2.9 - 3.6 (m, 3H); 3.83 (s, 3H);

5.3 - 5.7 (m, 1H); 7.4 (m, 5H).

ii) Oxidation of 28.

Oxidation of 28 with m-chloroperbenzoic acid afforded 29 which was examined by n.m.r.

N.M.R. 3.2 - 3.4 (m, 3H); 3.90 (s, 3H);

5.3 - 5.7 (m, 1H); 7.4 (m, 5H).

iii) Synthesis of 29 from methyl methane sulfonate:

β -hydroxy-sulfonate ester 29 was prepared in 60%
7a
yield from methyl methane sulfonate and benzaldehyde. Its spectral properties were identical to those of 29 obtained by the oxidation of 28.

Synthesis of 3,4,6,7-tetraphenyl-1,5-dioxo-2-thiepane-2-oxide, 48.

Sulfuryl chloride (1.35 g., 0.01 mole) was added to a solution of 31 (2.7 g., 0.009 mole) in methylene chloride (100 ml) at -70° . After ten minutes the volatile material was removed in vacuo and the crude residue was subjected to column chromatography over silica using methylene chloride as eluent. Diphenyl acetaldehyde (580 mg. 30%) and 48 (1.25 g., 60%) were obtained as the major products. 48 had m.p. 160 - 162 $^{\circ}$.

IR. 1125 (S=O) cm^{-1} .

N.M.R. 3.49 (d, J = 3.0Hz, 1H); 4.53 (d, J = 3.0Hz, 1H); 6.17 (d, J = 3.0Hz, 1H); 6.67 (d, J = 3Hz, 1H); 6.7 - 7.4 (m, 20H).

Analysis:

Calculated for $\text{C}_{28}\text{H}_{24}\text{O}_3\text{S}$: C, 76.35; H, 5.45; S, 7.2.

Found : C, 76.72; H, 5.66; S, 7.15

Photolysis of 48.

A solution containing sultine 48 (300 mg.) in benzene: acetone (40 ml + 10 ml) was irradiated for thirty minutes using a 500 watt Hanovia lamp and a corex filter. The solvent was removed in vacuo and the residual sultine 51 was crystallized from methylene chloride-pentane to yield 295 mg. of a fluffy white material (m.p. 162-164 $^{\circ}$).

IR. 1120 (S=O) cm^{-1} .

N.M.R. 4.02 (d, J = 11.0Hz, 1H);
 4.43 (d, J = 4.0Hz, 1H);
 5.86 (d, J = 11.0Hz, 1H);
 6.67 (d, J = 4.0Hz, 1H);
 6.7 - 7.4 (m, 20H).

Analysis:

Calculated for $\text{C}_{28}\text{H}_{24}\text{O}_3\text{S}$: C, 76.35; H, 5.45; S, 7.2.

Found : C, 76.57; H, 5.45, S, 7.15.

Reduction of 48 with lithium aluminium hydride.

Sultine 48 (60 mg.) in ether (5 ml) was added to a suspension of lithium aluminium hydride (10 mg.) in ether (20 ml). Usual workup afforded the dioxane mixture (42 mg. 75%). Spectral properties have already been described in the text.

Reduction of 51 with lithium aluminium hydride.

A similar reduction of 51 with lithium aluminium hydride yielded the same dioxane mixture in 80% yield.

Photolysis of 5-phenyl-1,2-oxathiolane-2-oxide, 10.

A solution containing sultine 10 (300 mg.) in benzene : acetone (40 ml + 10 ml) was irradiated for three hours using a 500 watt Hanovia lamp and a corex filter. The solvent was removed in vacuo and the residual phenyl cyclopropane (185 mg., 95%) was characterized spectroscopically.

N.M.R. 0.5 - 1.0 (m, 4H); 1.6 - 2.2 (m, 1H);
6.9 - 7.2 (m, 5H).

Photolysis of 3-methyl-5-phenyl-1,2-oxathiolane-2-oxide, 11.

Similar photolysis of 11 yielded 1-methyl-2-phenyl cyclopropane in 98% yield.

N.M.R. 0.5 - 1.6 (m, 6H); 1.6 - 2.2 (m, 1H);
7.0 - 7.2 (m, 5H).

Photolysis of 1.

When 1 (300 mg.) was photolyzed for three hours and the reaction mixture worked up, only the unreacted sultine was recovered. Prolonged irradiation resulted into the formation of brown decomposition material.

Photolysis of 62.

When 62 was photolyzed for periods up to 24 hours, no change in the spectrum of recovered material was noted.

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Claims to original research.

- 1) Halogenation of benzyl methyl sulfoxide was studied in several systems. The effect of various nucleophiles on the course of this reaction was discussed.
- 2) The generality of the sultine synthesis based upon C-S bond cleavage of t-butyl alkyl sulfoxides was established. The reaction was used to synthesize a variety of sultines differing in ring size and substitution pattern.
- 3) Thermal decomposition of β -sultines leading to olefins was explored. Several monosubstituted olefins were synthesized. The stereochemistry of the reaction was investigated.
- 4) Conformational aspects of δ -sultines were studied.
- 5) Mass spectra of various sultines were studied in detail. Important fragmentation pathways were suggested.
- 6) Isolation and characterization of a seven membered sultine, 3,4,6,7-tetraphenyl-1,5-dioxo-2-thiepane-2-oxide was described.



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