ORGANIC SULFUR CHEMISTRY

I. CHLORINATION OF SULFOXIDES

II. α,β-EPOXY SULFOXIDES AND SULFONES

III. SULTONE SYNTHESIS

by

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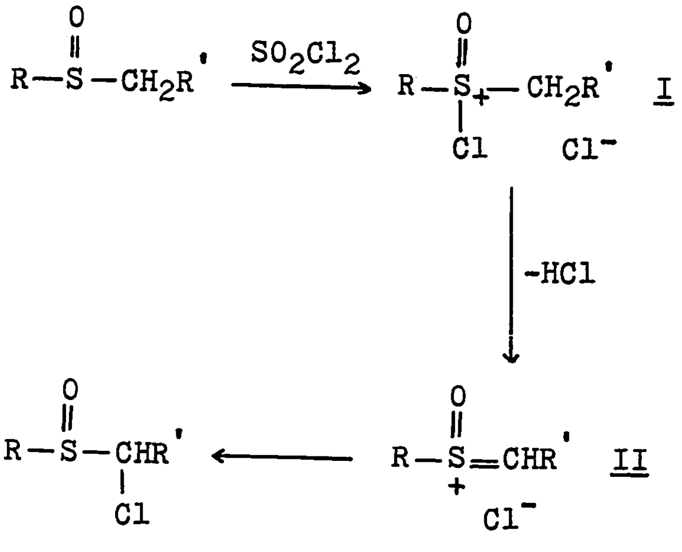
ABSTRACTS

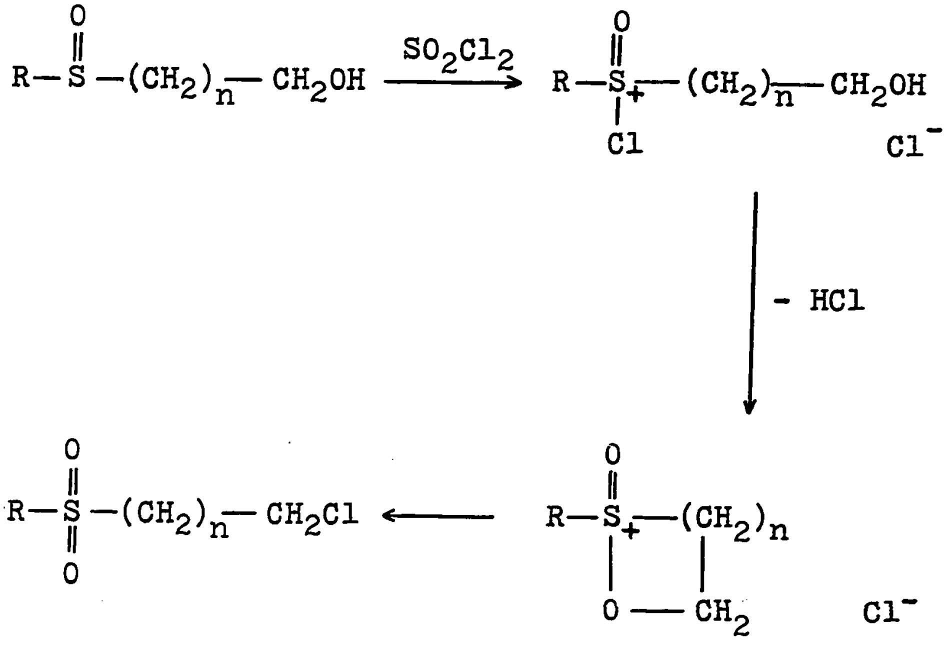
PART I

Chlorination of Sulfoxides with Sulfuryl Chloride

A number of α-chloro sulfoxides have been prepared by the reaction of sulfoxides with sulfuryl chloride *in the absence of base*. It is suggested that sulfuryl chloride reacts with the sulfoxide to form chloro-oxosulfonium ion I. α-Chloro sulfoxides can be obtained from I by a number of mechanisms. Elimination of HCl to the oxosulfenium ion II followed by addition of Cl^- is considered most likely.



Chlorination of $\beta, \gamma,$ and δ-hydroxy sulfoxides with sulfuryl chloride resulted in the formation of the corresponding $\beta, \gamma,$ and δ-chloro sulfones. Stereochemical evidence is presented that cyclic alkoxyoxosulfonium salts III (O-alkylated sulfones) are intermediates in these transformations. The chlorination of acid and amide sulfoxides was also investigated.

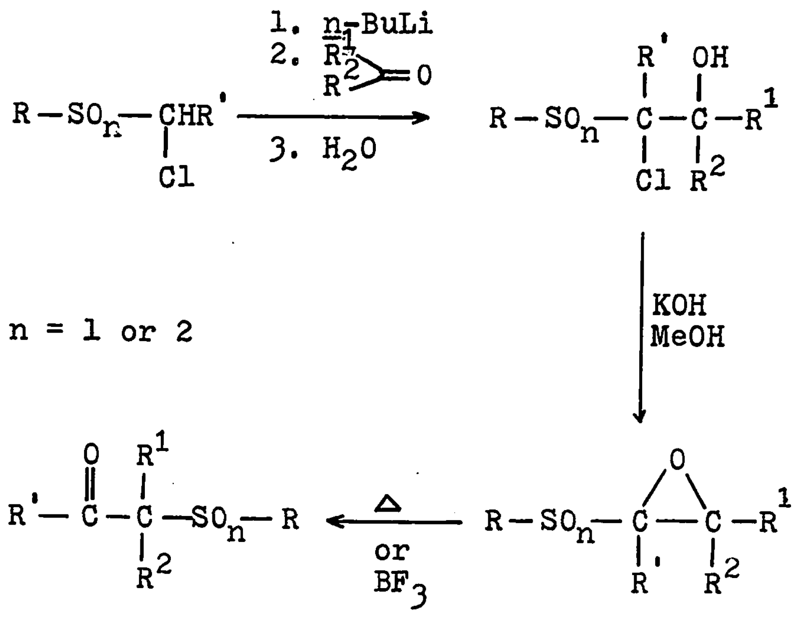


III

PART II

α,β-Epoxy Sulfoxides and Sulfones

The reaction of ketones with the α-lithio derivatives of a number of α-chloro sulfoxides and sulfones are reported. Treatment of the adducts with dilute methanolic KOH generally gave the corresponding α,β-epoxy sulfoxides and sulfones. The thermal and acid-catalyzed rearrangements of these epoxides have been investigated.

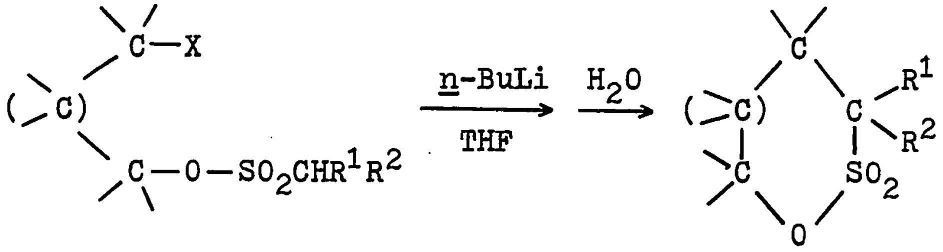


A study of the thermal decomposition of the lithio derivatives of chloromethyl phenyl sulfoxide and sulfone is also reported. These species do not yield carbene or carbenoid-type intermediates.

PART III

Sultone Synthesis

Treatment of 1,2- or 1,3-alkanedisulfonate esters with one equivalent of n-butyllithium in tetrahydrofuran affords 5- and 6-membered ring sultones. Similarly, alkane sulfonate esters of 1,2-halohydrins give 5-membered ring sultones. 1,2-Diols and 1,2-halohydrins of known stereochemistry were converted into 5-membered ring sultones in which the stereochemistry at 2 of the 3 ring carbon atoms is uniquely defined.



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Other members of the staff, especially Professor R.R. Fraser for help in interpretation of n.m.r. spectra and valuable advice;

My associates in 211 and the Chemistry Department, especially Messrs R. Viau, M. LeBelle, and C.W. Chiu in the course of these studies and in the writing of this thesis;

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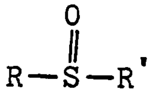
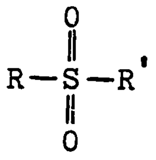
PART I

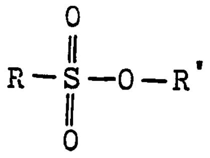
PART III

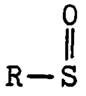
List of Sulfur Nomenclatures

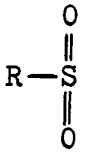
sulfide $R-S-R'$

sulfoxide 
$R-\overset{\overset{O}{\|}}{S}-R'$

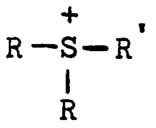
sulfone 
$R-\underset{\underset{O}{\|}}{\overset{\overset{O}{\|}}{S}}-R'$

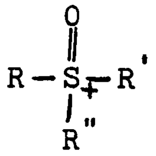
sulfonate ester 
$R-\underset{\underset{O}{\|}}{\overset{\overset{O}{\|}}{S}}-O-R'$

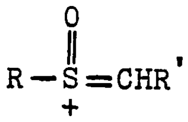
sulfinyl 
$R-\overset{\overset{O}{\|}}{S}$

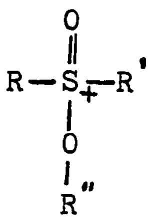
sulfonyl 
$R-\underset{\underset{O}{\|}}{\overset{\overset{O}{\|}}{S}}$

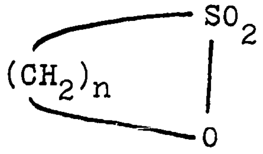
sulfenium $R-\overset{+}{S}=CHR'$

sulfonium 
$R-\underset{\underset{R}{|}}{\overset{+}{S}}-R'$

oxosulfonium 
$R-\underset{\underset{R''}{|}}{\overset{\overset{O}{\|}}{S}}\!{}^{+}-R'$

oxosulfenium 
$R-\underset{+}{\overset{\overset{O}{\|}}{S}}=CHR'$

alkoxyoxosulfonium 
$R-\underset{\underset{\underset{\underset{R''}{|}}{O}}{|}}{\overset{\overset{O}{\|}}{S}}\!{}^{+}-R'$

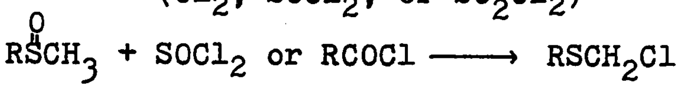
sultone 

PART 1

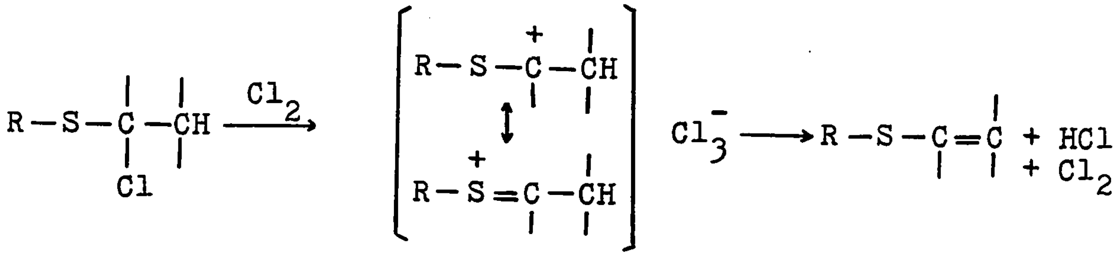
CHLORINATION OF SULFOXIDES

INTRODUCTION

In connection with a study of the metallation of α-chloro sulfoxides and sulfones (See Part II) we required a variety of these compounds. At the beginning of this study very few of these derivatives, especially in the sulfoxide series, had been reported. The most common route to these compounds was oxidation of the corresponding α-chloro sulfides. A number of methods for preparing α-chloro sulfides have been reported and are listed below.

1. $RSH + HCHO + HCl \longrightarrow RSCH_2Cl + H_2O$ (1)
2. $PhCH_2SCH_2OH + HCl \longrightarrow PhCH_2SCH_2Cl$ (2)
3. $H_2CN_2 + ArSCl \longrightarrow ArSCH_2Cl$ (3)
4. $RSCH_3$ + Chlorinating agents $\longrightarrow RSCH_2Cl$ (4)
   (Cl_2, $SOCl_2$, or SO_2Cl_2)
5.  $R\overset{O}{\overset{\|}{S}}CH_3 + SOCl_2$ or $RCOCl \longrightarrow RSCH_2Cl$ (4)

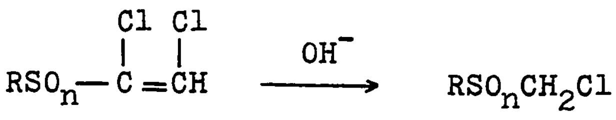
All of these methods are generally restricted to the preparation of aryl and alkyl chloromethyl sulfides. α-Chloro sulfides having a β-hydrogen are much difficult to obtain. Their preparation is generally accompanied by the formation of large amounts of vinyl sulfides. The formation of these materials has been explained as shown below. (4)



While our work was in progress a number of workers reported the direct chlorination of sulfoxides to α-chloro sulfoxides (See TABLE I). These methods especially the chlorination with NOCl/pyridine as reported by Loeppky and Chang (6) showed considerable synthetic scope.

In view of these results and in analogy with the α-chlorination of sulfides we decided to attempt the chlorination of sulfoxides with sulfuryl chloride or chlorine in the absence of added base. In dry methylene chloride such chlorinations work with surprising ease requiring but a few minutes even at -78° to give good yields of α-chloro sulfoxides.

Recently, Brown (11) has reported the preparation of chloromethyl sulfoxides and sulfones from the corresponding 1,2-dichlorovinyl sulfoxides and sulfones by treatment with dilute aqueous base.

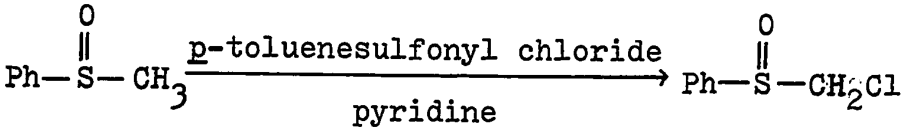


$$RSO_n-\overset{Cl}{C}=\overset{Cl}{CH} \xrightarrow{OH^-} RSO_nCH_2Cl$$

n = 1 and 2

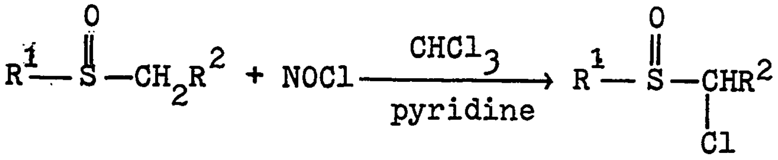
TABLE I

α-Chlorination of Sulfoxides in the Presence of Added Base

1. 

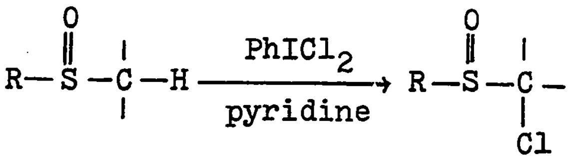
$$\mathrm{Ph{-}\overset{\underset{\|}{O}}{S}{-}CH_3} \xrightarrow[\text{pyridine}]{\underline{\text{p}}\text{-toluenesulfonyl chloride}} \mathrm{Ph{-}\overset{\underset{\|}{O}}{S}{-}CH_2Cl}$$

(5)

2. 

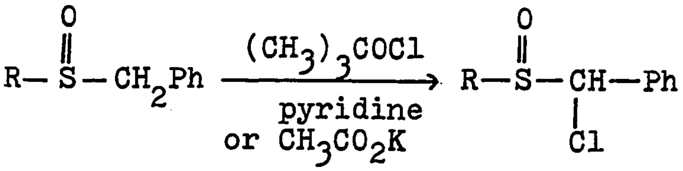
$$\mathrm{R^1{-}\overset{\underset{\|}{O}}{S}{-}CH_2R^2} + \mathrm{NOCl} \xrightarrow[\text{pyridine}]{\mathrm{CHCl_3}} \mathrm{R^1{-}\overset{\underset{\|}{O}}{S}{-}\underset{\underset{Cl}{|}}{C}HR^2}$$

(6)

3. 

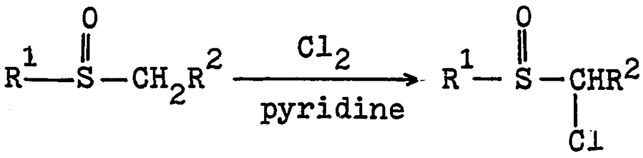
$$\mathrm{R{-}\overset{\underset{\|}{O}}{S}{-}\underset{|}{\overset{|}{C}}{-}H} \xrightarrow[\text{pyridine}]{\mathrm{PhICl_2}} \mathrm{R{-}\overset{\underset{\|}{O}}{S}{-}\underset{\underset{Cl}{|}}{\overset{|}{C}}{-}}$$

(7)

4. 

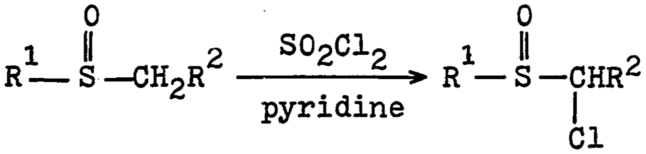
$$\mathrm{R{-}\overset{\underset{\|}{O}}{S}{-}CH_2Ph} \xrightarrow[\substack{\text{pyridine}\\ \text{or } \mathrm{CH_3CO_2K}}]{\mathrm{(CH_3)_3COCl}} \mathrm{R{-}\overset{\underset{\|}{O}}{S}{-}\underset{\underset{Cl}{|}}{C}H{-}Ph}$$

(8)

5. 

$$\mathrm{R^1{-}\overset{\underset{\|}{O}}{S}{-}CH_2R^2} \xrightarrow[\text{pyridine}]{\mathrm{Cl_2}} \mathrm{R^1{-}\overset{\underset{\|}{O}}{S}{-}\underset{\underset{Cl}{|}}{C}HR^2}$$

(9)

6. 

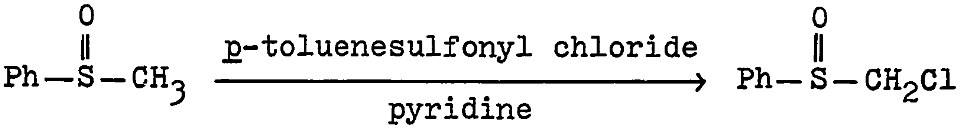
$$\mathrm{R^1{-}\overset{\underset{\|}{O}}{S}{-}CH_2R^2} \xrightarrow[\text{pyridine}]{\mathrm{SO_2Cl_2}} \mathrm{R^1{-}\overset{\underset{\|}{O}}{S}{-}\underset{\underset{Cl}{|}}{C}HR^2}$$

(10)

α-CHLORINATION OF SULFOXIDES

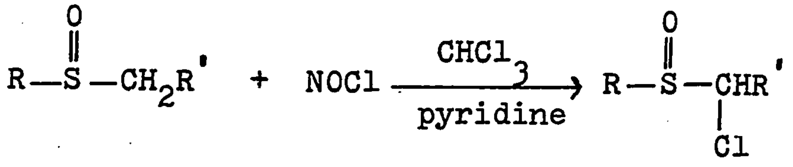
A. Synthetic Aspects:

Direct α-chlorination of sulfoxides was first reported by Hojo and Yoshida (5). In the presence of pyridine, p-toluenesulfonyl chloride reacted with methyl phenyl sulfoxide to give chloromethyl phenyl sulfoxide in 23% yield. In the absence of pyridine the reaction gave almost exclusively chloromethyl phenyl sulfide.



$$\mathrm{Ph{-}\overset{\overset{O}{\|}}{S}{-}CH_3} \xrightarrow[\text{pyridine}]{\text{p-toluenesulfonyl chloride}} \mathrm{Ph{-}\overset{\overset{O}{\|}}{S}{-}CH_2Cl}$$

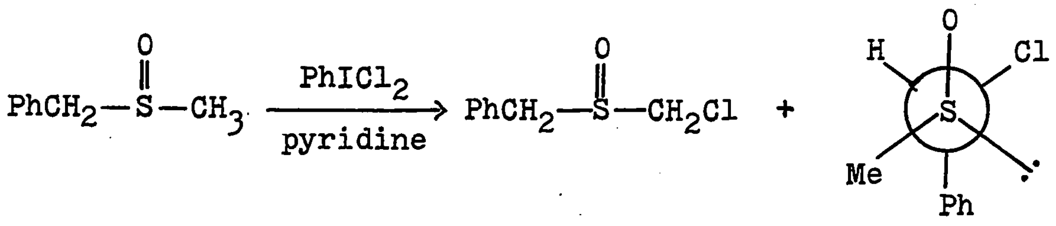
Loeppky and Chang (6) reported that a number of alkyl sulfoxides reacted smoothly with a nitrosyl chloride-pyridine mixture in chloroform to produce the corresponding α-chloro sulfoxides in high yields. The best yields of α-chloro sulfoxides were produced by using a sulfoxide : nitrosyl chloride : pyridine ratio of 1 : 3 : 3. The physical and spectroscopic properties of the products suggested that only one diastereomer was being produced in each case. This method appears to have general applicability. However the large amounts of pyridine and nitrosyl chloride required by the procedure make this method rather uneconomical and complicate the workup.



$$\mathrm{R}-\overset{\mathrm{O}}{\overset{\|}{\mathrm{S}}}-\mathrm{CH_2R'} + \mathrm{NOCl} \xrightarrow[\text{pyridine}]{\mathrm{CHCl_3}} \mathrm{R}-\overset{\mathrm{O}}{\overset{\|}{\mathrm{S}}}-\underset{\mathrm{Cl}}{\underset{|}{\mathrm{C}}}\mathrm{HR'}$$

R	R'	yield (%)
$PhCH_2$	Ph	89
$4\text{-}ClC_6H_4$	H	80
Ph	H	80
CH_3	H	61
Ph	Ph	83
$CH_3(CH_2)_3$	$CH_3(CH_2)_2$	81

Montanari and co-workers (7) have found that sulfoxides reacted with equimolar amounts of iodobenzene dichloride in pyridine at -40° to give α-chloro sulfoxides. Subsequently it was shown that iodobenzene dichloride acts as a controlled source of chlorine (7b). Benzyl methyl sulfoxide (1) was chlorinated to produce benzyl chloromethyl sulfoxide (2) and α-chlorobenzyl methyl sulfoxide (3) in 32 and 30% yields respectively. It was suggested that the latter consisted of only one of the two diastereomeric α-chlorobenzyl methyl sulfoxides. The configuration of this diastereomer was established as in 3 by showing that the proton diastereotopic to the one which was exchanged preferentially in $D_2O/NaOD$ (12, 13) was replaced by chlorine.*



1 2 (32%) 3 (30%)

The halogenation of optically active sulfoxides has also been reported by Montanari et al (7b). Under the conditions, $PhICl_2$/pyridine, the optically active α-chloro sulfoxides retained the original sulfur asymmetry. Chlorination in the presence of $AgNO_3$ or $Ni(NO_3)_2$ produced the enantiomer of the above derivative which must have involved inversion of the sulfur chirality. The latter result was claimed as "the first example of a reaction in which inversion of chirality occurs without any breaking of bonds at the chiral center or any diastereomeric interaction in the transition states."

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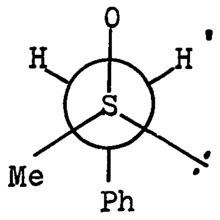
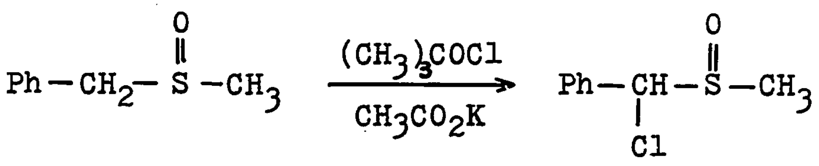
* The original assignment by Wolfe et al (12) that the proton (H') is preferentially exchanged for deuterium in $D_2O/NaOD$ has been shown to be in error by Baldwin et al (13). The proton (H) is in fact more rapidly exchanged.



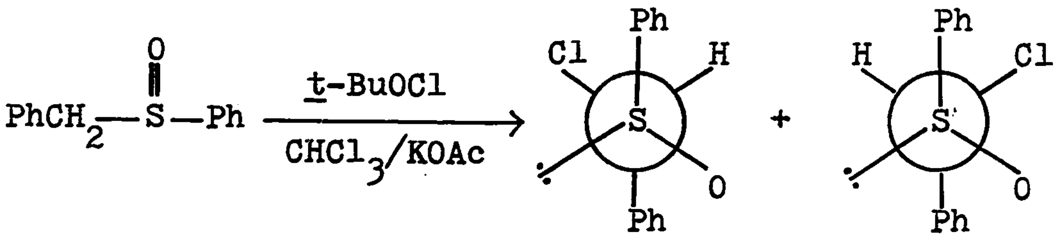
Iriuchijima and Tsuchihasi (8) have described the the chlorination of benzyl methyl sulfoxide and benzyl phenyl sulfoxide with t-butyl hypochlorite in the presence of anhydrous potassium acetate. Chlorination of the former gave α-chlorobenzyl methyl sulfoxide in 40% yield.



$$\mathrm{Ph-CH_2-\overset{O}{\overset{\|}{S}}-CH_3} \xrightarrow[\mathrm{CH_3CO_2K}]{\mathrm{(CH_3)_3COCl}} \mathrm{Ph-\underset{Cl}{\underset{|}{C}H}-\overset{O}{\overset{\|}{S}}-CH_3}$$

1 3

In the case of benzyl phenyl sulfoxide a 70 : 30 mixture of diastereomers was produced. The minor isomer obtained in this reaction was identical with the major isomer produced by chlorination with nitrosyl chloride, p-toluenesulfonyl chloride, iodobenzene dichloride or t-butyl hypochlorite in pyridine. Structure assignments to the diastereomeric α-chloro sulfoxides as 4 (major) and 5 (minor) were made on the basis of benzene and trifluoroacetic acid induced solvent shifts. The use of this method for assigning the configuration of conformationally mobile sulfoxides is suspect (14-16); in fact when applied to α-methyl benzyl sulfoxides the wrong configurations are predicted (17, 18).

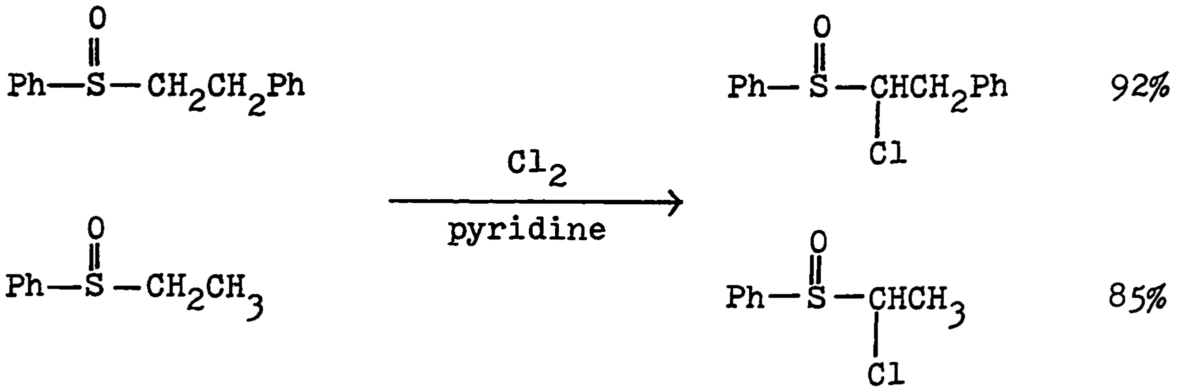


4 (major product)

5 (minor product)

The authors suggested that chlorination occurs by a free radical pathway. However ionic chlorinations using t-butyl hypochlorite have been reported by Johnson et al. (19) Mixtures of diastereomers are also obtained in the sulfuryl chloride chlorinations which do not occur via a free radical pathway.

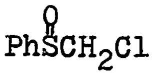
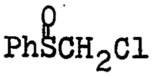
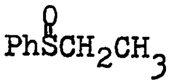
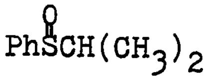
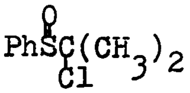
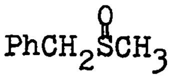
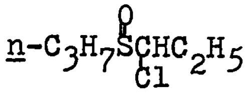
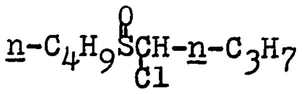
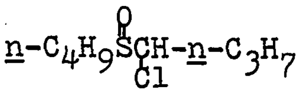
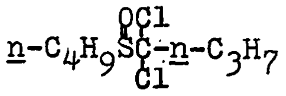
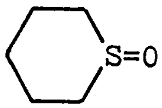
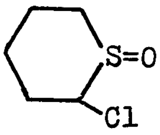
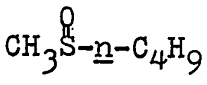
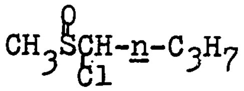
More recently the same authors described the chlorination of sulfoxides with chlorine (9) or sulfuryl chloride (10) in the presence of excess excess pyridine. These reactions, as all the other reactions which employed pyridine as base, gave mainly one diastereomer.



We have observed that α-chlorination of sulfoxides with sulfuryl chloride or chlorine occurs even in the absence of added base (20). Thus α-chlorination of sulfoxides with sulfuryl chloride in methylene chloride yielded α-chloro sulfoxides rapidly and generally in good yield. The reactions were carried out under anhydrous conditions at -78° for dialkyl sulfoxides and either at -78° or 0° for aralkyl sulfoxides. The reaction time was generally less than 15 minutes as indicated by thin layer chromatography. Standard workup and purification by basic alumina column chromatography gave pure α-chloro sulfoxides. (See TABLE II)

TABLE II

α-Chlorination of Sulfoxides with Sulfuryl Chloride

Sulfoxide	Temp(°C)	Time(hr)	Product	Yield(%)
 $\mathrm{Ph}\overset{O}{\mathrm{S}}\mathrm{CH_3}$	0	0.25	 $\mathrm{Ph}\overset{O}{\mathrm{S}}\mathrm{CH_2Cl}$	83
 $\mathrm{Ph}\overset{O}{\mathrm{S}}\mathrm{CH_2Cl}$	25	12	 $\mathrm{Ph}\overset{O}{\mathrm{S}}\mathrm{CHCl_2}$	72
 $\mathrm{Ph}\overset{O}{\mathrm{S}}\mathrm{CH_2CH_3}$	0	0.25	 $\mathrm{Ph}\overset{O}{\mathrm{S}}\underset{Cl}{\mathrm{C}}\mathrm{HCH_3}$	89
 $\mathrm{Ph}\overset{O}{\mathrm{S}}\mathrm{CH(CH_3)_2}$	-78	0.5	 $\mathrm{Ph}\overset{O}{\mathrm{S}}\underset{Cl}{\mathrm{C}}\mathrm{(CH_3)_2}$	71
 $\mathrm{PhCH_2}\overset{O}{\mathrm{S}}\mathrm{CH_3}$	-78	0.25	 $\mathrm{Ph}\underset{Cl}{\mathrm{C}}\mathrm{H}\overset{O}{\mathrm{S}}\mathrm{CH_3}$	25
$(\underline{n}\text{-}\mathrm{C_3H_7})_2\mathrm{S{=}O}$	-78	0.1	 $\underline{n}\text{-}\mathrm{C_3H_7}\overset{O}{\mathrm{S}}\underset{Cl}{\mathrm{C}}\mathrm{HC_2H_5}$	77
$(\underline{n}\text{-}\mathrm{C_4H_9})_2\mathrm{S{=}O}$	-78	0.1	 $\underline{n}\text{-}\mathrm{C_4H_9}\overset{O}{\mathrm{S}}\underset{Cl}{\mathrm{C}}\mathrm{H}\text{-}\underline{n}\text{-}\mathrm{C_3H_7}$	85
 $\underline{n}\text{-}\mathrm{C_4H_9}\overset{O}{\mathrm{S}}\underset{Cl}{\mathrm{C}}\mathrm{H}\text{-}\underline{n}\text{-}\mathrm{C_3H_7}$	-78	0.5	 $\underline{n}\text{-}\mathrm{C_4H_9}\overset{O}{\mathrm{S}}\overset{Cl}{\underset{Cl}{\mathrm{C}}}\text{-}\underline{n}\text{-}\mathrm{C_3H_7}$	70
	-78	0.1		76
 $\mathrm{CH_3}\overset{O}{\mathrm{S}}\text{-}\underline{n}\text{-}\mathrm{C_4H_9}$	-78	0.1	 $\mathrm{CH_3}\overset{O}{\mathrm{S}}\underset{Cl}{\mathrm{C}}\mathrm{H}\text{-}\underline{n}\text{-}\mathrm{C_3H_7}$	75

Since the α-chloro sulfoxides move much faster than their parent sulfoxides on either silica thin layer chromatography (t.l.c.) or basic alumina column, the combined technique provides a convenient way of following the reaction and purification of the product. For large scale preparation it was found advantageous to purify by vacuum distillation. Some care must be exercised to remove traces of acids from the crude product since these substances promote sulfoxide decomposition during distillation. We have found it advantageous in some cases to add dry CaO to the reaction mixture. This generally increases the yield and purity of the product since the HCl formed during the reaction is removed thereby preventing sulfoxide decomposition via Pummerer-type rearrangements (21). Calcium oxide also serves as a drying agent thus reducing by-product (sulfone) formation. (See page 25)

Sulfones do not react with sulfuryl chloride.* α-Chloro sulfones are generally obtained in excellent yields by m-chloroperbenzoic acid oxidation of the corresponding α-chloro sulfides and sulfoxides.

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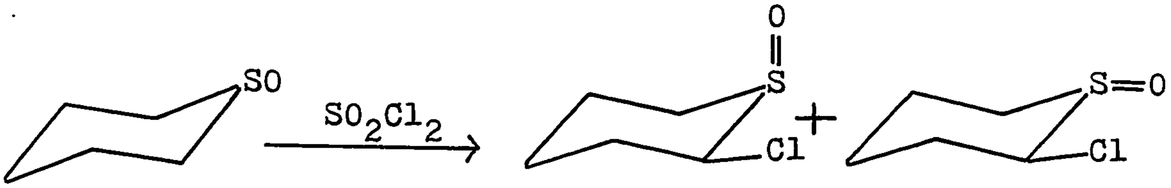
* Recently, I. Tabushi, Y. Tamaru and Y. Yoshida have reported that sulfones do react with SO_2Cl_2 at 60° to give mainly β-chloro sulfones. Tetrahedron Letters 3893 (1971).

Contrary to the chlorination carried out in the presence of pyridine (6-9), we found the present reaction to be generally non-stereospecific and, where possible, mixtures which contained considerable amounts of each diastereomer were obtained. The diastereomeric ratio could in most cases be determined by n.m.r. examination of the total crude reaction mixture. Thus the material obtained from chlorination of thiane-S-oxide showed a pair of equal intensity quartets at δ=4.90 (J=8.5 and 3.0Hz) and 4.92 (J=8.4 and 2.7Hz) assignable to hydrogen on carbon bearing chlorine and suggesting approximately equal amounts of the diastereomers 6 and 7. Oxidation of the mixture with excess m-chloroperbenzoic acid gave only α-chlorothiane-S, S-dioxide. (See page 115)



6 76% 7

The diastereomers of α-chloro-n-butyl methyl sulfoxide, also formed in nearly equal amounts, were separated by preparative t.l.c. and were shown to be configurationally stable under the reaction conditions. The spectroscopic data for the pure diastereomers are recorded in TABLE III.

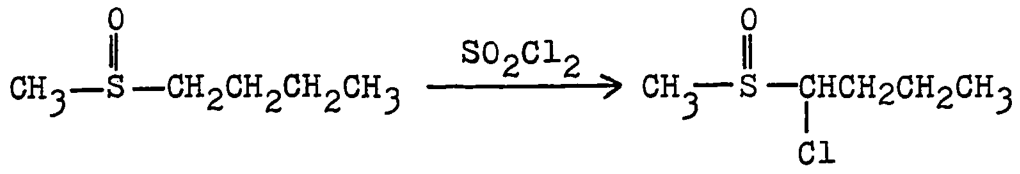
TABLE III

Spectroscopic Properties of the Diastereomers of α-Chloro-*n*-butyl Methyl Sulfoxide

	More Polar Isomer	Less Polar Isomer
N.m.r.	0.8 - 1.3 (m, 3H)	0.8 - 1.2 (m, 3H)
(CCl_4)	1.3 - 2.4 (m, 4H)	1.2 - 2.5 (m, 4H)
(δ)	2.50 (s, 3H)	2.46 (s, 3H)
	4.52 (q, J=9.0 and 4.0Hz, 1H)	4.46 (q, J=8.2 and 3.8Hz, 1H)
Infrared		
(CCl_4)	2850 (s)	2900 (s)
(cm^{-1})	1045 (s)	1040 (s)

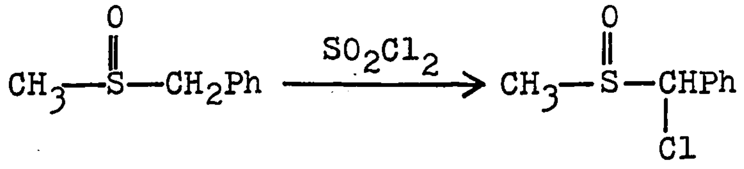
Mass Spect. Both of the diastereomers have parent molecular ions at m/e = 156 and 154 with the ratio of 1 to 3.

Sulfoxides which can be chlorinated at two possible positions show high regioselectivity and yield only the more highly substituted chlorides. For example n-butyl methyl sulfoxide gave a 75% yield of the α-chloro-n-butyl methyl sulfoxide (8). (See TABLE III) Similarly from benzyl methyl sulfoxide, we have been able to isolate only a diastereomeric mixture of 3, albeit in poor yield. The n.m.r. spectrum ($CDCl_3$) showed peaks at δ=2.20 and 2.58 (2 singlets, 3H), 5.40 and 5.58 (2 singlets, 1H) and 7.2 -7.5 (m, 5H). (8) These results again differ from those obtained with $PhICl_2$/pyridine and t-BuOCl/pyridine which gave on chlorination of benzyl methyl sulfoxide a mixture of chloromethyl benzyl sulfoxide and α-chlorobenzyl methyl sulfoxide in 1 : 1 and 1 : 3 ratio respectively.



$$CH_3-\overset{O}{\overset{\|}{S}}-CH_2CH_2CH_2CH_3 \xrightarrow{SO_2Cl_2} CH_3-\overset{O}{\overset{\|}{S}}-\underset{Cl}{CH}CH_2CH_2CH_3$$

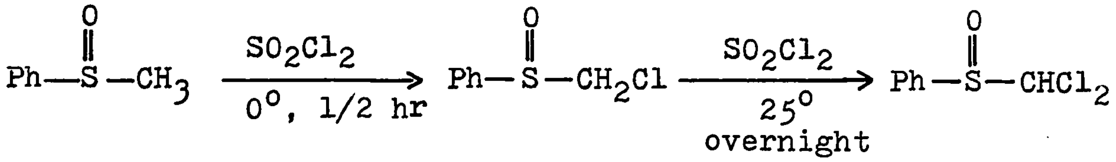
8



$$CH_3-\overset{O}{\overset{\|}{S}}-CH_2Ph \xrightarrow{SO_2Cl_2} CH_3-\overset{O}{\overset{\|}{S}}-\underset{Cl}{CH}Ph$$

3

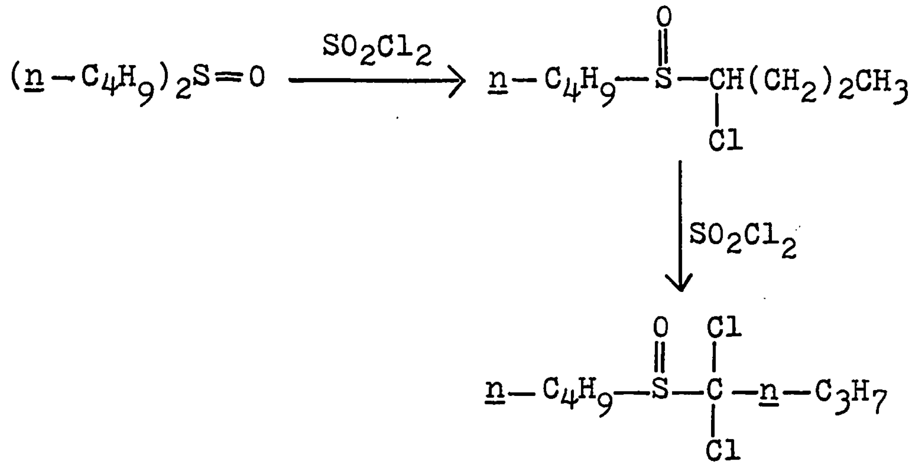
The monochlorinated sulfoxides are significantly less reactive toward sulfuryl chloride than their precursors thus allowing stepwise α-chlorinations and ready isolation of either the mono- or the dichlorinated sulfoxides. For example, the α-chlorination of methyl phenyl sulfoxide was complete within 1/2 hr at 0° whereas the second chlorination required more than 2 hr at 25°. The n.m.r. spectrum (CCl_4) of 9 was identical with that of an authentic sample (prepared from oxidation of chloromethyl phenyl sulfide). Spectroscopic properties of 10 were as follows : i.r. ($CHCl_3$), 1070 (s) and 1090 (s) cm^{-1}; n.m.r. peaks (CCl_4), δ=6.36 (s, 1H) and 7.30-7.90 (m, 5H). The structure of 10 was confirmed by oxidation to the corresponding sulfone m.p. 55-56° which was identical with that prepared from oxidation of the dichloromethyl phenyl sulfide (22).



$$Ph-\overset{O}{\overset{\|}{S}}-CH_3 \xrightarrow[0^\circ,\ 1/2\ hr]{SO_2Cl_2} Ph-\overset{O}{\overset{\|}{S}}-CH_2Cl \xrightarrow[25^\circ\ \text{overnight}]{SO_2Cl_2} Ph-\overset{O}{\overset{\|}{S}}-CHCl_2$$

9 10

Chlorination of n-butyl sulfoxide with sulfuryl chloride gave α-chloro-n-butyl n-butyl sulfoxide (11) in 85% yield. The subsequent chlorination of 11 with sulfuryl chloride afforded α,α-dichloro-n-butyl n-butyl sulfoxide(12) in preference to the α,α'isomer. The spectroscopic properties of these materials are in agreement with the assigned structures and are recorded in the Experimental Section.



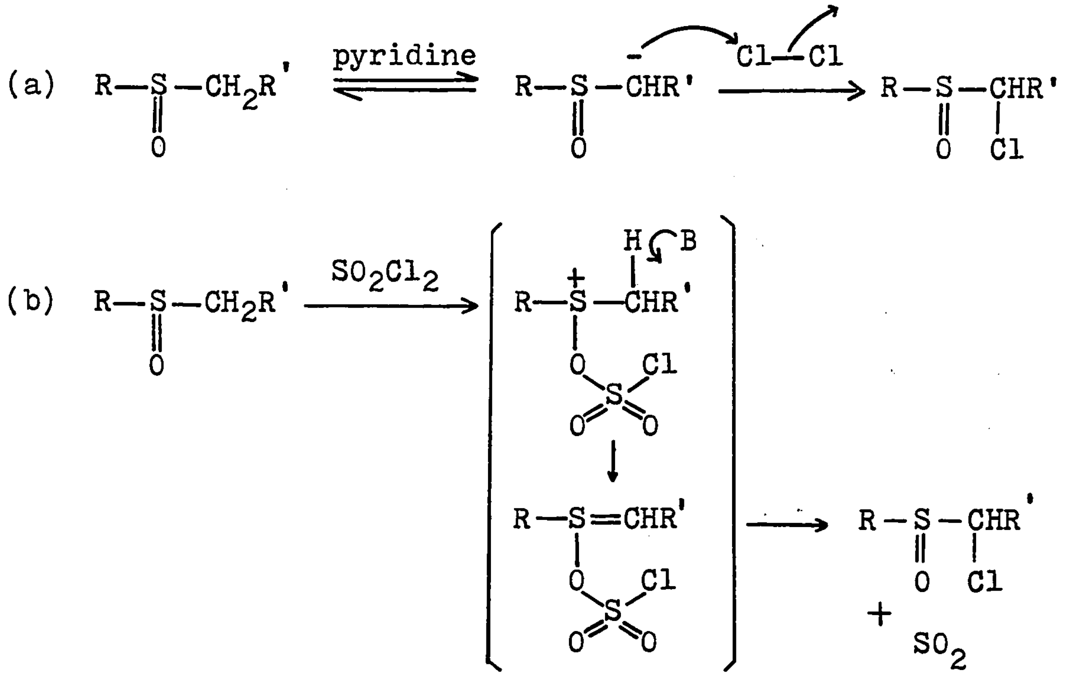
11 (85%)

12 (70%)

The chlorination of sulfoxides, as mentioned before, can also be carried out using chlorine in methylene chloride but the experimental difficulty of weighing relatively small amounts of chlorine make this route less desirable for laboratory use. Bromine does not react with sulfoxides under the conditions in which chlorination is rapid. For example, methyl phenyl sulfoxide was recovered after stirring for 24 hr at 25° with one equivalent of bromine in methylene chloride. α-Bromination of sulfoxides has however been reported using bromine in the presence of pyridine. (23)

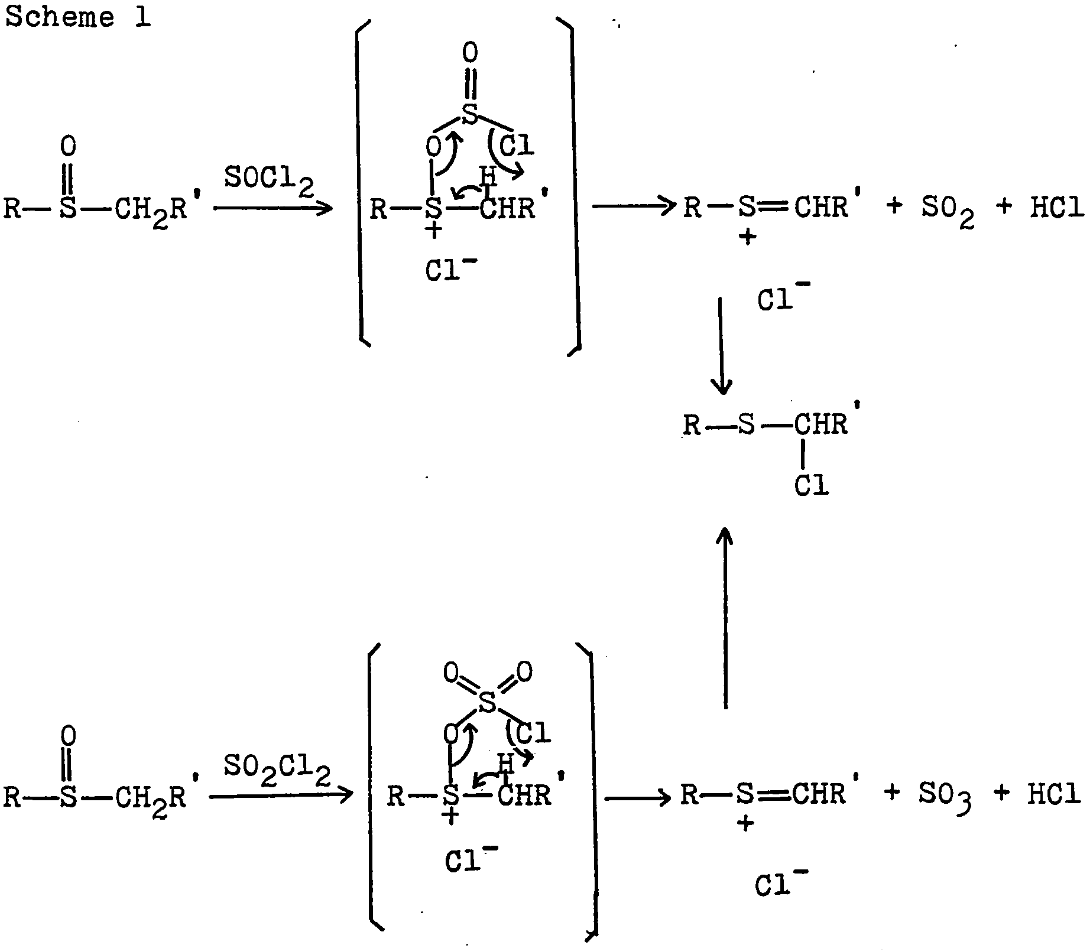
B. Mechanistic Aspect:

The Japanese group of Tsuchihashi have proposed the following mechanisms for the chlorination of sulfoxide in pyridine with chlorine (9) and sulfuryl chloride (10).



Mechanism (a) can be dismissed since chlorinations with either SO_2Cl_2 or Cl_2 occur in the absence of added base. In addition the rate of carbanion formation is much slower than the rate of chlorination (24). This also confirms the fact that an α-sulfinyl carbanion cannot be an intermediate in these reactions. The intermediate in mechanism (b) is very closely related to that proposed for the Pummerer rearrangement of sulfoxides with $SOCl_2$(21) and would be more likely to decompose to give a sulfenium ion and SO_3 rather than α-chloro sulfoxides and SO_2 as suggested by the authors. (See Scheme 1)

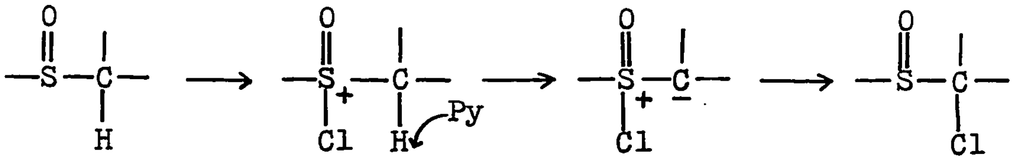
Scheme 1



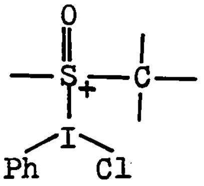
These authors have also suggested a free radical mechanism for the t-butyl hypochlorite chlorination. However, they have provided no evidence to show the intermediacy of free radicals. The use of t-butyl hypochlorite as an ionic reagent in the chlorination of sulfides (19) casts additional doubt on this mechanism.

Montanari and co-workers (7a) suggested that the formation of α-chloro sulfoxides is the result of initial

S-chlorination* 13 , followed by ylid formation and concerted intramolecular transfer of chlorine from sulfur to carbon.



13



14

The proposal was based on the following observations: (a) only one of the two diastereomeric α-chlorobenzyl methyl sulfoxides was formed and (b) a large primary isotope effect was observed. The selectivity for the formation of one diastereomer was attributed to the preferential removal of one of the diastereotopic hydrogens.

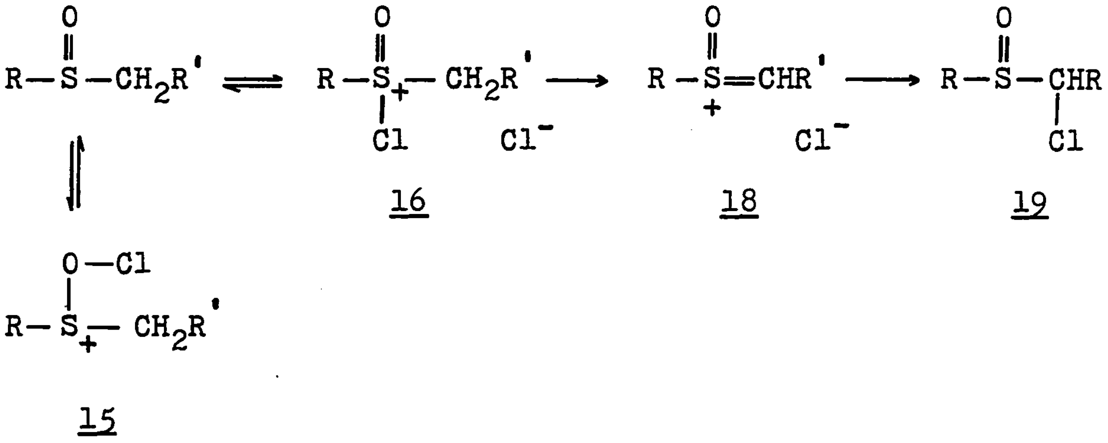
---

* Initially it was considered that $PhICl_2$ was the chlorinating agent and structure 14 was assigned to the first intermediate. However, later these authors reported that $PhICl_2$ acts only as controlled source of chlorine.(7b)

A more complete discussion of this mechanism is given on page 25-27.

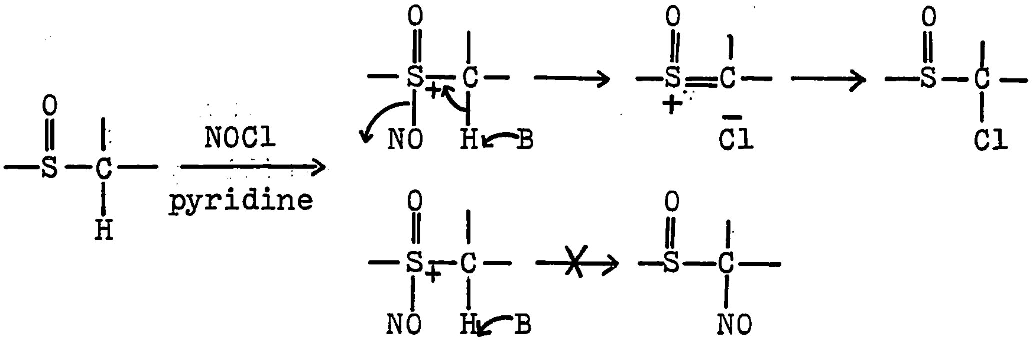
We would like to propose Scheme 2 to explain the results of the various chlorination reactions. Although some parts are rather tentative and not directly supported by experimental data we feel that it does allow us to offer a rationalization for the product differences observed in the presence and absence of pyridine.

Scheme 2

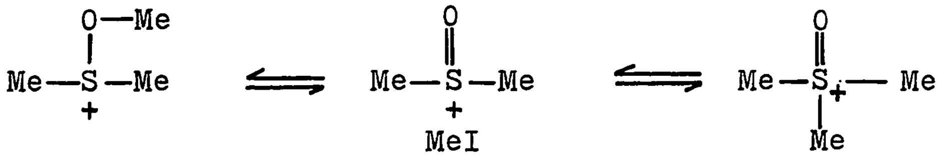


Scheme 2 also allows one to rationalize the NOCl chlorination. Nitrosyl chloride is polarized in the sense NO^+Cl^-(25). Addition of NO^+ to the sulfoxide should give rise to the nitroso-oxosulfonium ion 17. If ylid formation and intramolecular migration were to occur as proposed by Montanari et al (7), this reaction would give rise to α-nitroso sulfoxides rather than α-chloro sulfoxides. On the other hand, elimination of HNO to form an oxosulfenium ion followed by addition of Cl^- leads to α-chlorosulfoxides.

17



Smith and Winstein (26) have found that sulfoxides have two reactive centers for nucleophilic reactions. Thus dimethyl sulfoxide and methyl iodide can give rise to either the O-alkylated derivative 20 or the S-alkylated derivative 21. The kinetically preferred O-alkylated salt 20 isomerizes in solution to the thermodynamically more stable 21.



20

Kinetic Control

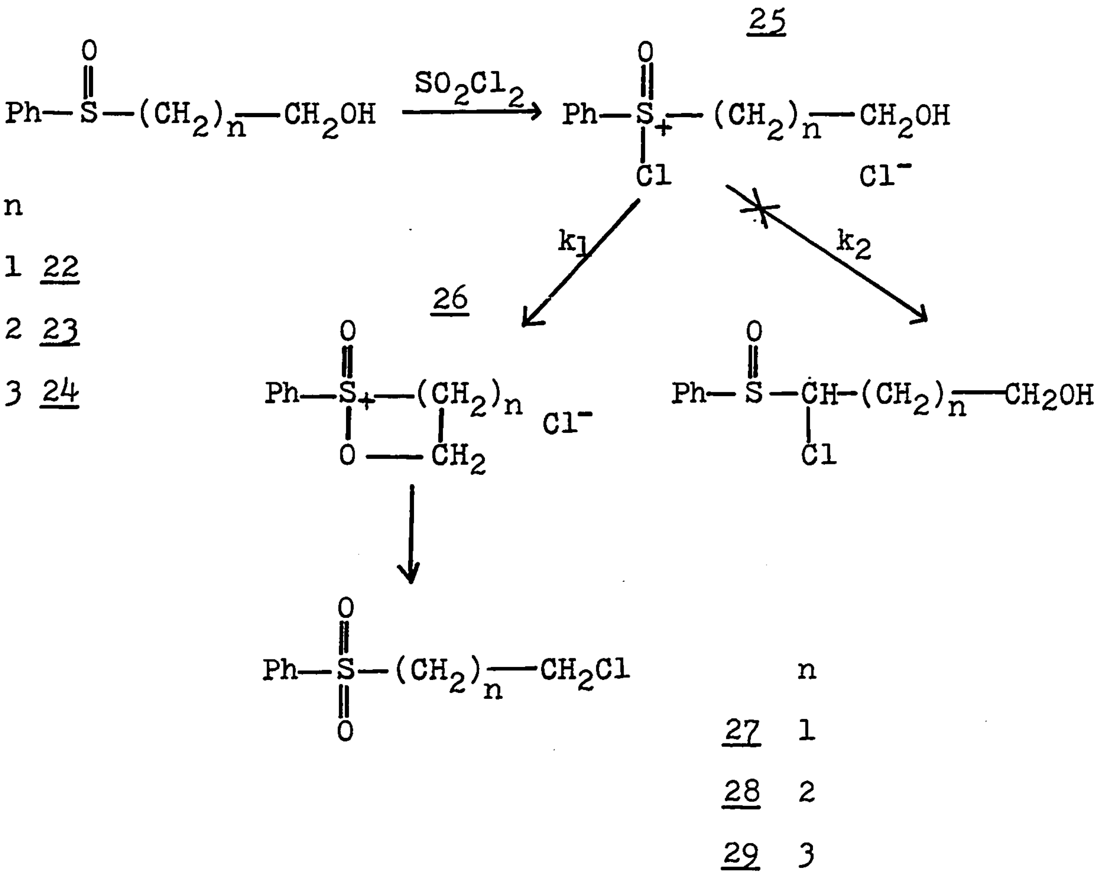
21

Thermodynamic Control

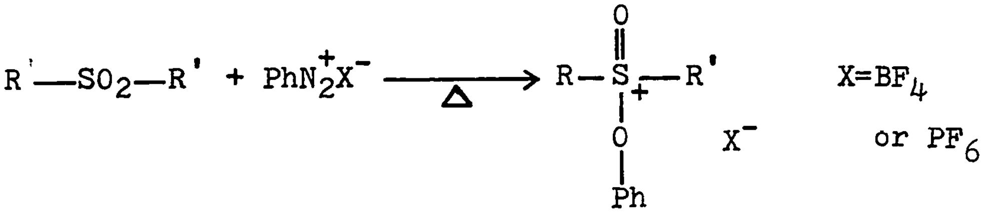
In analogy with the above results, reaction of the sulfoxide with the positive chlorine species can result in either O-chlorination or S-chlorination; S-chlorination resulting in the formation of the chloro-oxosulfonium ion 16. α-Chloro sulfoxides can be obtained from 16 via the elimination of HCl to give oxosulfenium ion 18 followed by the addition of chloride.

The overall mechanism has considerable similarity to that proposed for α-chlorination of sulfides (4) and to the Pummerer rearrangement of sulfoxides (21), the difference being the extra oxygen on sulfur. It was hoped that support for some of these intermediates especially the chloro-oxosulfonium ion could be obtained by trapping it with a suitably placed hydroxyl group. The chlorination of β-, γ-, and δ-hydroxy sulfoxides 22-24 at -78° gave the corresponding chloro sulfones 27-29 in high yields. (Structure determinations see page 123) These transformations can be rationalized as in Scheme 3. Displacement of chloride ion from chloro-oxosulfonium ion 25 by the remote hydroxyl group leads to the formation of a cyclic alkoxy-oxosulfonium chloride 26 which can be opened by S_N2 attack of chloride on carbon to give chloro sulfones.

Scheme 3



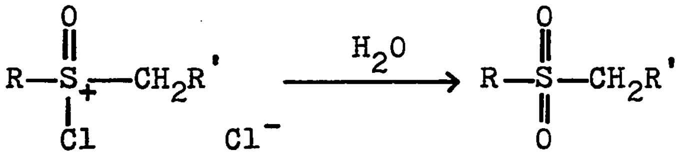
Aryloxysulfoxonium salts 30 which bear a close structure to postulated intermediate 26 have been isolated by Whiting et al last year from the thermal decomposition of phenyl diazonium salts in the presence of sulfones. (27)



$$R'-SO_2-R' + Ph\overset{+}{N_2}X^- \xrightarrow[\Delta]{} R-\overset{O}{\underset{O-Ph}{\overset{\|}{S^+}}}-R' \quad X^- \qquad X=BF_4 \text{ or } PF_6$$

30

Other data which supports the intermediacy of chloro-oxosulfonium ion is the formation of sulfones (corresponding to the starting sulfoxides). This by-product is generally obtained in less than 10% in the chlorination reaction. The formation of sulfone can be rationalized as due to displacement of chloride by water or OH^- followed by proton transfer. In agreement with this rationalization the addition of H_2O to the reaction mixture greatly increases the ratio of sulfone to α-chloro sulfoxide.

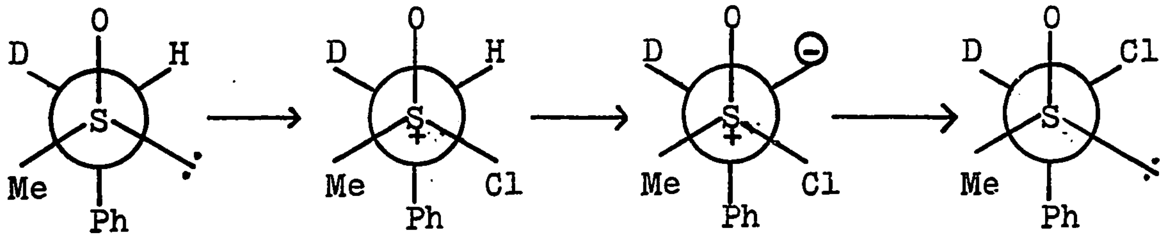


$$R-\overset{O}{\overset{\|}{\underset{\underset{Cl}{|}}{S^{+}}}}-CH_2R' \quad Cl^- \xrightarrow{H_2O} R-\overset{O}{\overset{\|}{\underset{\underset{O}{\|}}{S}}}-CH_2R'$$

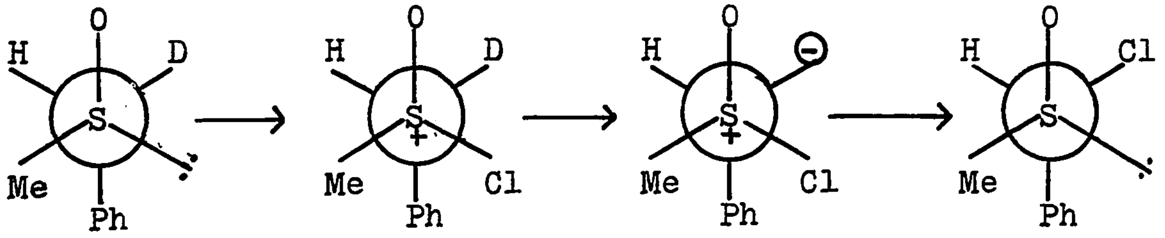
16 31

It is interesting to note the ease with which displacement of Cl^- from chloro-oxosulfonium ions can occur. In the case of an intramolecular displacement it completely dominates over the rapid α-chlorination. (Scheme 3, $k_1 \gg k_2$) Even the intermolecular displacement by water resulting in sulfone formation can effectively compete with the α-chlorination.

Two pathways have been considered for the conversion of chloro-oxosulfonium salts to α-chloro sulfoxides. The first proposed, by Montanari <u>et al</u> (7), involves formation of an ylid and intramolecular migration of chloride from sulfur to carbon. This proposal was based mainly on the observation that chlorination of the α-deuteriobenzyl methyl sulfoxide (32) led to specific replacement of hydrogen, whereas in the isomer (33), deuterium was replaced. The selective removal of one of the two benzylic hydrogens was considered evidence for the preferred formation of one of the two ylids. Stereospecific migration of chlorine would then result in the formation of mainly one α-chlorobenzyl methyl sulfoxide.



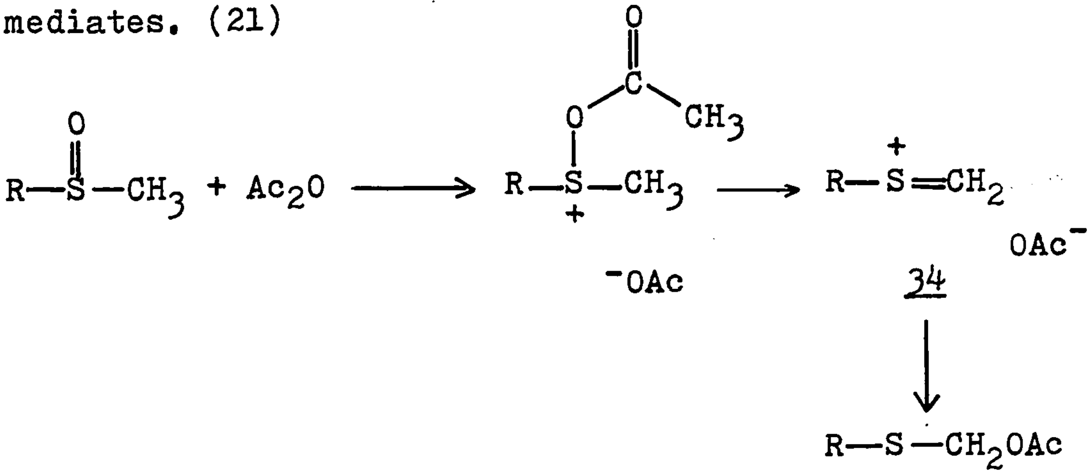
32



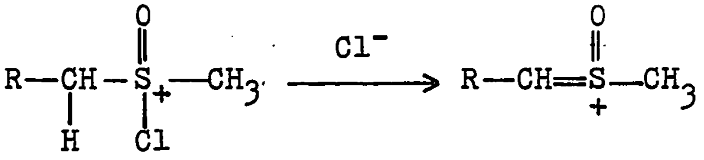
33

If one accepts this scheme it becomes difficult to understand why pyridine can differentiate so well between the diastereotopic benzylic protons and not between those of the benzyl and methyl groups, even though the latter should be much less acidic than either of the former. For example, in benzyl methyl sulfoxide the more slowly exchanging benzylic proton exchanges almost 500 times faster than the methyl protons (12 b). Furthermore, one would expect that the chlorinations with SO_2Cl_2 also be highly stereospecific since chloride ion is a smaller base than pyridine and ought to be at least as selective. These chlorinations, while highly regiospecific, generally give rise to mixtures of diastereomers.

A second pathway for the conversion of chloro-oxosulfonium ion 16 to α-chloro sulfoxide 19 (Scheme 2) is the elimination of HCl to form an oxosulfenium ion 18 followed by addition of Cl^-. In the related rearrangement of sulfoxides to α-acetoxysulfides on treatment with acetic anhydride, sulfenium ions e.g. 34 were suggested to be intermediates. (21)

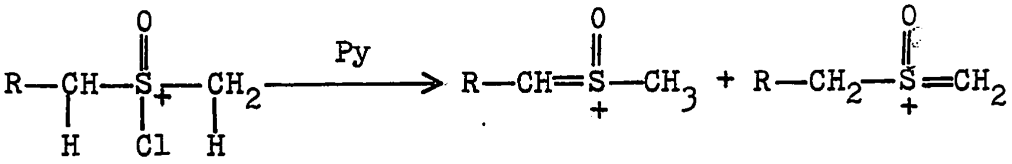


Such a pathway suggests a reason for the regioselectivity observed in the SO_2Cl_2 chlorinations and the lack in the pyridine-catalyzed process. In the elimination of HCl from 16 one might expect mainly internal elimination (Saytzeff) with Cl^-. The sterically larger base pyridine should be less selective and give rise to both of the oxosulfenium ions, 35 and 36. Such trends (i.e. mainly Saytzeff-type product with a small base and Hofmann-type product with a bulky base) are observed in the base-catalyzed elimination of HBr from alkyl halides. (28) The highly selective removal of one of the two benzylic protons might also be due more to a steric factor rather than differences in their acidity. The formation of mainly one diastereomeric α-chloro sulfoxide in the presence of pyridine and a mixture in its absence is difficult to explain and a convincing argument cannot be put forward at this time. That the diastereomeric mixtures observed in the sulfuryl chloride chlorinations represent the initial product mixture and are not due to a subsequent isomerization has been verified in the α-chloro-*n*-butyl methyl sulfoxide series. The possibility of isomerization in pyridine from a mixture to mainly one diastereomer, while admittedly a remote possibility, has not been ruled out.



$$R{-}\underset{\displaystyle H}{\underset{|}{C}}H{-}\overset{\displaystyle O}{\overset{\|}{\underset{\displaystyle Cl}{\underset{|}{S}}}}{}^{+}{-}CH_3 \xrightarrow{Cl^-} R{-}CH{=}\overset{\displaystyle O}{\overset{\|}{\underset{+}{S}}}{-}CH_3$$

35



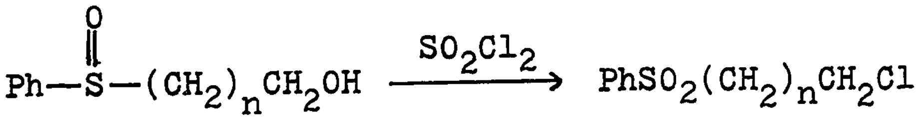
$$R{-}\underset{\displaystyle H}{\underset{|}{C}}H{-}\overset{\displaystyle O}{\overset{\|}{\underset{\displaystyle Cl}{\underset{|}{S}}}}{}^{+}{-}\underset{\displaystyle H}{\underset{|}{C}}H_2 \xrightarrow{Py} R{-}CH{=}\overset{\displaystyle O}{\overset{\|}{\underset{+}{S}}}{-}CH_3 + R{-}CH_2{-}\overset{\displaystyle O}{\overset{\|}{\underset{+}{S}}}{=}CH_2$$

35 36

One final possibility which must still be considered in view of the divergent results observed in the presence and absence of pyridine is that chlorination proceeds by different mechanisms under the different conditions. Rationalization of all the results by a single mechanism while intrinsically attractive may be doomed to failure.

CHLORINATION OF HYDROXY SULFOXIDES

In order to obtain further evidence supporting the intermediacy of chloro-oxosulfonium ions in the chlorination of sulfoxides and to examine some of their chemistry, we have carried out the chlorination of a number of sulfoxides bearing hydroxy groups at various position with the hope of trapping these intermediates. In all of the simple β-, γ- and δ-hydroxy sulfoxides such as <u>22</u>-<u>24</u>, we obtained in high yield, the products <u>27</u>-<u>29</u> in which the sulfur had been oxidized from sulfoxide to sulfone and the remote hydroxyl group replaced by chlorine. Spectroscopic and physical data supported the structure assignments (29). In particular the products showed the expected i.r. sulfone bands in the ranges 1300-1340 and 1145-1165 cm^{-1} and the absence of a hydroxyl group. The n.m.r. data are as expected and recorded in the Experimental Section.



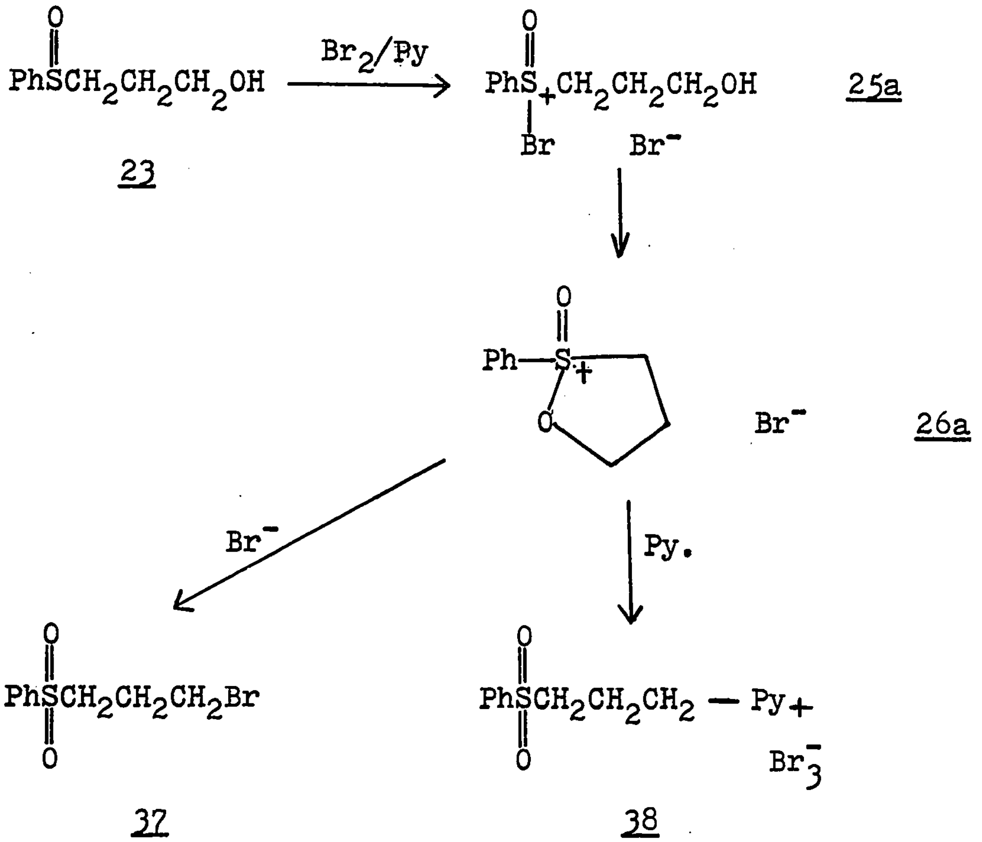
$$Ph-\overset{\overset{O}{\parallel}}{S}-(CH_2)_nCH_2OH \xrightarrow{SO_2Cl_2} PhSO_2(CH_2)_nCH_2Cl$$

n=1	<u>22</u>	<u>27</u>	95%
2	<u>23</u>	<u>28</u>	96%
3	<u>24</u>	<u>29</u>	88%

The formation of these chloro sulfones, presumably via chloro-oxosulfonium ion <u>25</u> and cyclic alkoxyoxosulfonium chloride 26 has been discussed in page 23. Other data supporting the intermediacies of the halo-oxosulfonium ions and the cyclic salts are shown in Scheme 4 and 5.

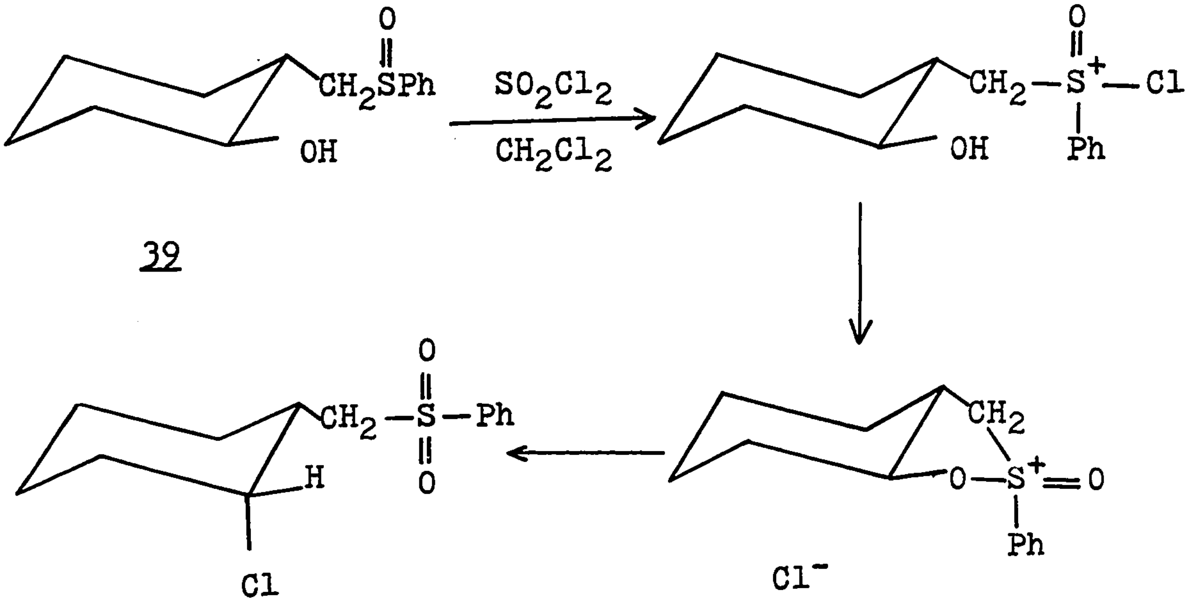
Bromination of the γ-hydroxy sulfoxide 23 in the presence of pyridine led to two products, the γ-bromo sulfone 37 and the γ-pyridinium sulfone perbromide 38. The n.m.r. spectrum of bromosulfone had peaks at δ=1.78-2.18 (m, 2H), 3.0-3.60 (m, 4H), and 7.35-7.95 (m, 5H); infrared bands at 1310 and 1150 cm^{-1}. The pyridinium salt was obtained as yellow flaky plates, m.p. 137° (dec.), from $MeOH-H_2O$. Analytical data was in agreement with the formula $C_{14}H_{16}Br_3NO_2S$. Its n.m.r. peaks ($DMSO-d_6$) occurred at δ=2.10-2.44 (m, 2H), 3.35-3.60 (m, 2H), 4.68 (t, J=7Hz, 2H) and 7.55-9.10 (m, 10H). The formation of the bromo and pyridinium sulfones is readily rationalized as the result of displacement of Br^- from bromo-oxosulfonium ion 25a by the hydroxyl group that leads to 26a and followed by ring opening of the alkoxyoxosulfonium ion 26a by bromide ion and pyridine respectively.

Scheme 4



Stereochemical studies also support the existence of the chloro-oxosulfonium and the cyclic alkoxyoxosulfonium intermediates. The trans-hydroxy sulfoxide 39, prepared by adding cyclohexene oxide to the lithio salt of methyl phenyl sulfoxide, was treated with sulfuryl chloride to give an 77% yield of cis-chloro sulfone 40. The cis assignment was based on n.m.r. spectroscopy. The low field proton on carbon bearing chlorine which occurred at δ=4.53 with a width at half-height of only 7Hz is consistent with its equatorial position. The formation of the cis-chloro sulfone from the trans-hydroxy sulfoxide is expected since nucleophilic opening of the cyclic intermediate results in inversion of configuration at the carbon initially bearing the hydroxyl group. This unusually hindered S_N2 displacement to form an axial chloride may be explained by the partial dissociation of the carbon-oxygen bond during the approach of Cl^-, i.e. the transition state has a considerable amount of S_N1 character. The structure of the chloro sulfone is further supported by infrared peaks at 1307 and 1150 cm^{-1} and by its mass spectrum $M^+ = 274$ and 272 (1 : 3 ratio).

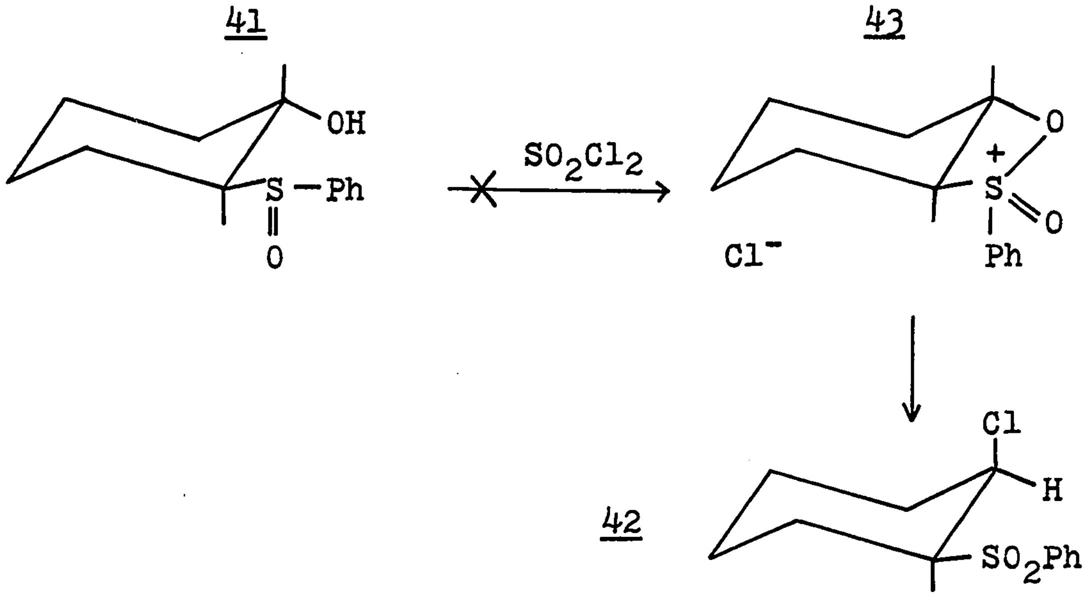
Scheme 5



39

40

In contrast to the above results, chlorination of the trans-hydroxy sulfoxide 41 gave a complex mixture of at least five components which have not been separated. N.m.r. inspection of the total mixture indicated the absence of significant amounts of the chloro sulfone 42. The failure to obtain 42 is not unexpected since its formation requires the intermediacy of 43 which contains the highly strained 6,4-trans fused ring system.

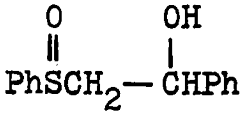
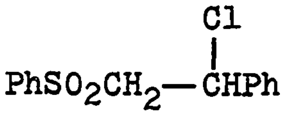
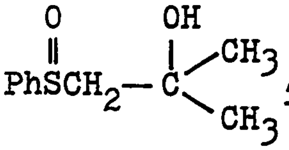
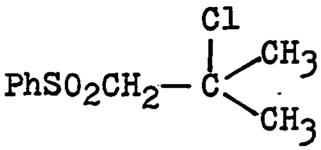
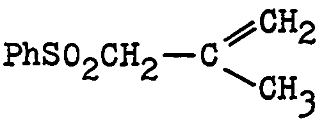
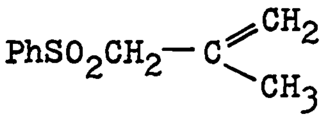
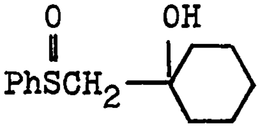
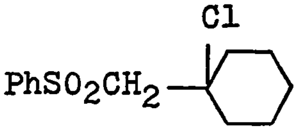
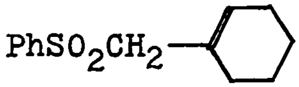
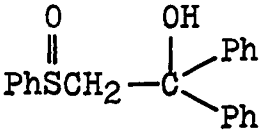
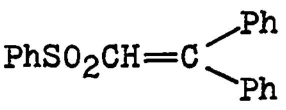


There were available from another study a number of highly substituted β-hydroxy sulfoxides 44-47. Each of these was found to react smoothly with sulfuryl chloride to give the corresponding β-chloro sulfones. Formally the formation of these compounds involves a very facile S_N2 at a tertiary carbon. Again as in the ring opening of the bicyclic alkoxyoxosulfonium ion the transition state probably has considerable S_N1 characteristics.

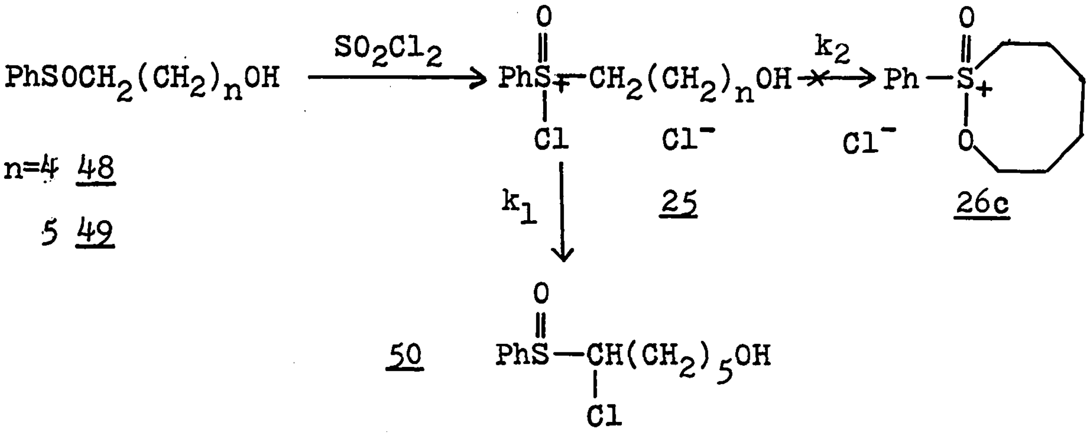
These β-chloro sulfones are extremely readily dehydrochlorinated. The product obtained from chlorination was found to depend on workup; β-chloro sulfones could be obtained by washing the reaction mixture with water followed by recrystallization (procedure 1), the corresponding unsaturated sulfones could be obtained by passing the crude product through a basic alumina column (procedure 2). These simple procedures provide an easy method of synthesizing base-sensitive β-chloro sulfones as well as unsaturated sulfones.

TABLE IV

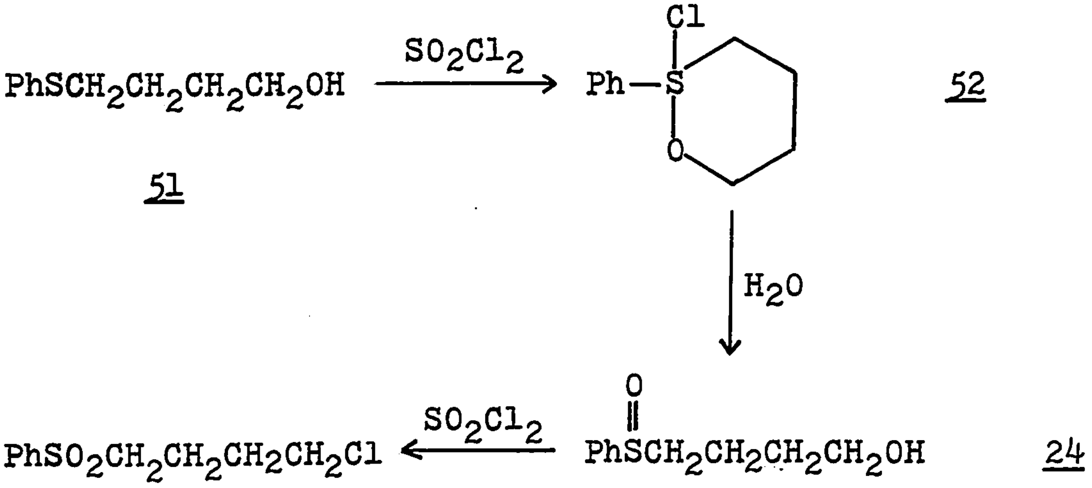
Chlorination of β-Hydroxy Sulfoxide with SO_2Cl_2

β-Hydroxy sulfoxide	Procedure 1 Yield(%)	Procedure 2 Yield(%)
 $PhS(O)CH_2-CH(OH)Ph$ 44	 $PhSO_2CH_2-CH(Cl)Ph$ 78%	$PhSO_2CH{=}CHPh$ 80%
 $PhS(O)CH_2-C(OH)(CH_3)_2$ 45	 $PhSO_2CH_2-C(Cl)(CH_3)_2$ 41% +  $PhSO_2CH_2-C(=CH_2)CH_3$ 34%	 $PhSO_2CH_2-C(=CH_2)CH_3$ 81%
 46	 73%	 92%
 $PhS(O)CH_2-C(OH)Ph_2$ 47	 $PhSO_2CH{=}CPh_2$ 89%	

In contrast to the β-, γ- and δ-hydroxy sulfoxides, chlorination of hydroxy sulfoxides having the hydroxyl group positions 5 and 6 do not give the corresponding chloro sulfones. The crude products from 48 and 49 were unstable colorless liquids which became brown on standing at room temperature. Purification of the crude product from 49 by chromatography gave a colorless oil. The n.m.r. spectrum ($CDCl_3$) had peaks at δ=0.8-2.4 (m, 8H), 3.15-3.60 (m, 2H), 4.38-4.62 (m, 1H) and 7.4-7.8 (m, 5H). The i.r. showed absorption at 1042 cm^{-1} (sulfoxide) and 3450 cm^{-1} (O-H). These spectroscopic properties are in agreement with the designation of the product as 6-chloro-6-phenylsulfinyl hexanol (50). Failure of 48 and 49 to yield chloro sulfones is reasonable because of the expected difficulty in forming 7- and 8-membered cyclic alkoxyoxosulfonium intermediates 26c from the chloro-oxosulfonium ions 25. (i.e. $k_2 \ll k_1$)

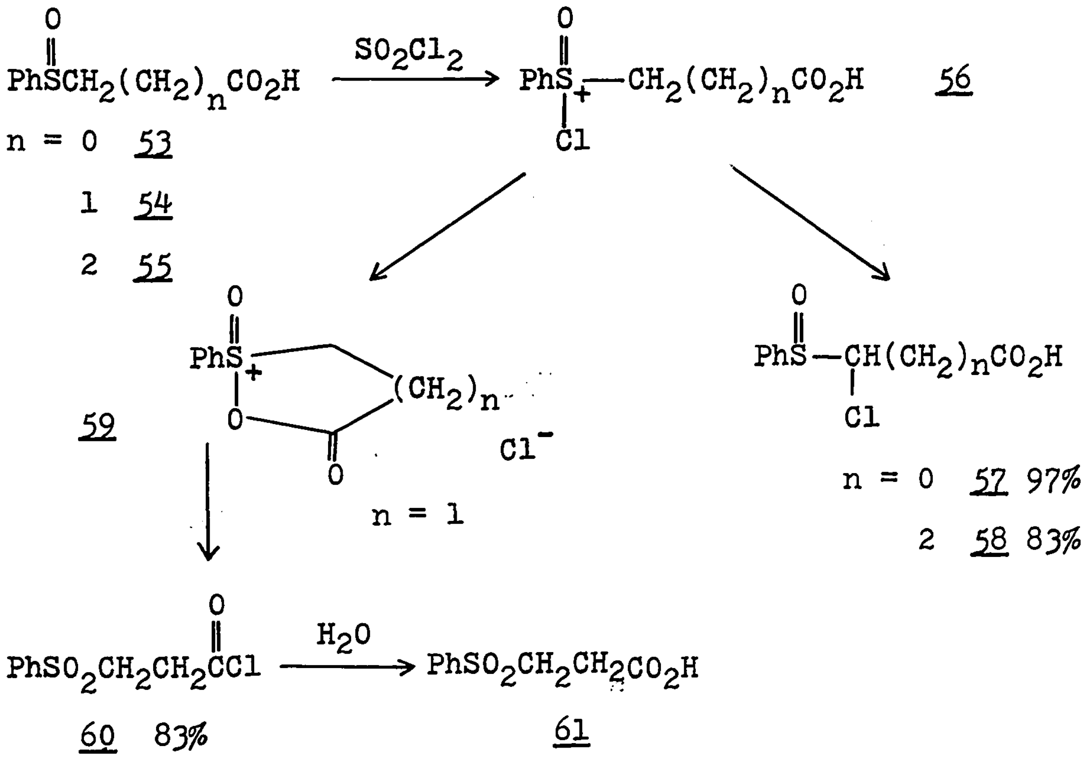


We have observed rather interesting results in the chlorination of 4-hydroxybutyl phenyl sulfide (51) with sulfuryl chloride. With one equivalent of sulfuryl chloride, 51 gave an intermediate formulated as 52 (19, 30) which was stable enough to be observed by n.m.r. absorption occurred at δ=1.6-2.6 (m, 4H), and 3.9-4.5 (m, 4H). Addition of water resulted in hydrolysis and formation of the corresponding hydroxy sulfoxide 24 (19). With two equivalents of sulfuryl chloride 51 is converted to the chloro sulfone presumably via 52 and 24.



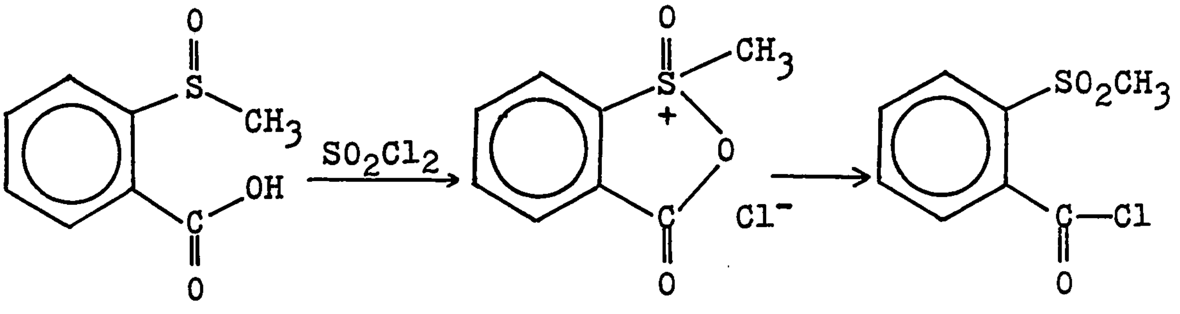
CHLORINATION OF ACID AND AMIDE SULFOXIDES

We have also investigated the interaction of other groups with chloro-oxosulfonium ions. Acids generally produce α-chlorosulfoxide acids via the chloro-oxosulfonium intermediate 56, except when a five membered ring intermediate 59 can be formed. In these cases, acid chloride sulfones were obtained. Their formation is explained by attack of Cl⁻ on the carbonyl carbon of 59 and expulsion of the sulfone.



The acid chloride sulfone 60 obtained from chlorination of 54 is colorless powder, m.p. 68-70°. The n.m.r. spectrum ($CDCl_3$) had peaks at $\delta=3.45$ (t, J=4.5Hz, 4H) and 7.5-8.0 (m, 5H) and the i.r. had strong bands at 1782, 1312 and 1146 cm^{-1}. The structure of 60 was confirmed by hydrolysis to the corresponding acid sulfone 61 m.p. 124-126°. (reported m.p. 125.5-127°). (31)

Chlorination of *o*-methylsulfinyl benzoic acid (62) which can also form a five membered ring intermediate 63, gave the acid chloride sulfone 64. The n.m.r. had peaks at $\delta=3.28$ (s, 3H) and 7.6-8.3 (m, 4H); infrared bands occurred at 1785, 1320 and 1150 cm^{-1}.

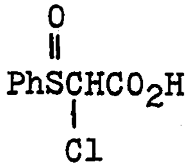


62 63 64

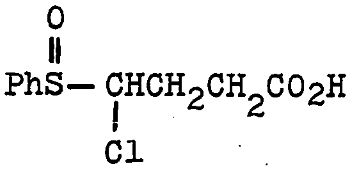
Chlorination of 53 and 55 in methylene chloride at -78° gave mixtures of diastereomers of α-chlorosulfoxide acids 57 and 58; each mixture showed 2 signals for the methine hydrogen. The spectroscopic properties (TABLE V) are in agreement with their structures which are also confirmed by elementary analysis.

TABLE V

Spectroscopic Properties of 2-Chloro-2-phenylsulfinylacetic Acid (57) and 4-Chloro-4-phenylsulfinylbutyric Acid (58)



$\mathrm{Ph\overset{\overset{O}{\|}}{S}\underset{\underset{Cl}{|}}{C}HCO_2H}$ 57

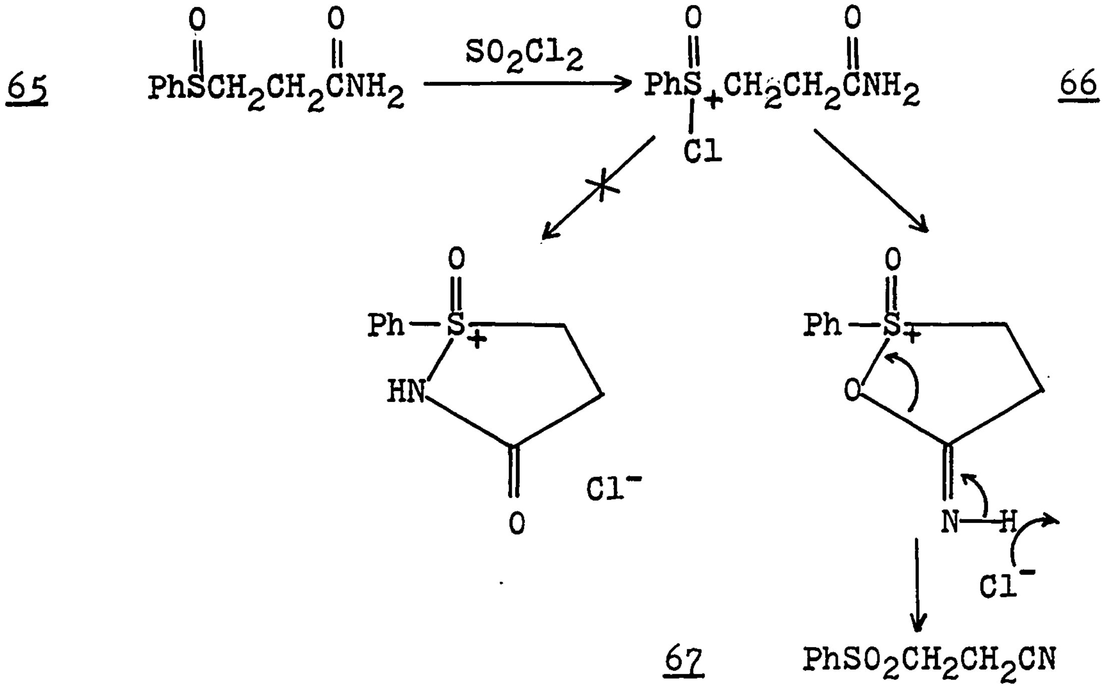


$\mathrm{Ph\overset{\overset{O}{\|}}{S}-\underset{\underset{Cl}{|}}{C}HCH_2CH_2CO_2H}$ 58

	57	58
n.m.r. (δ)	Two singlets at 5.20	1.72-2.94 (m, 4H)
($CDCl_3$)	and 5.34 with a ratio	4.65-5.00 (m, 1H)
	of 2 to 1. (1H)	7.38-7.84 (m, 5H)
	7.45-7.95 (m, 5H)	10.34 (s, 1H)
	9.20 (s, 1H)	
i.r. (cm^{-1})	3500-2300 (broad peak)	3400-2500 (broad peak)
($CHCl_3$)	1735	1720
	1200	1200
	1080	1090
	1032	1042

The fact that 4-membered ring intermediate 56 (n=0) is not formed can be easily explained by the extra ring strain due to the carbonyl group. However, the complete failure to obtain products via a 6-membered ring intermediate 56 (n=2) is rather surprising. A more gradual transition from sulfone formation to α-chlorination on the basis of an entropy effect would have been expected.

Reaction of the primary sulfinyl amide 65 with sulfuryl chloride afforded the sulfonyl nitrile 67 in 95% yield. Thus attack by oxygen on the chloro-oxosulfonium ion 66 is preferred over attack by nitrogen. The structure of 67 was confirmed by spectroscopic data and satisfactory elementary analysis. The i.r. ($CHCl_3$) showed sulfone absorption at 1145 and 1325 cm^{-1}, and a nitrile band at 2230 cm^{-1}. The n.m.r. spectrum ($CDCl_3$) had peaks at δ=2.62-3.0 (m, 2H), 3.30-3.62 (m, 2H) and 7.52-8.10 (m, 5H). The mass spectrum showed the parent molecular ion at m/e = 195 and other strong peaks at m/e = 141, ($PhSO_2^+$) and 77 (Ph^+). The metastable ion at m/e = 101.8 confirmed the loss of 54 (CH_2CH_2CN) from the parent ion.

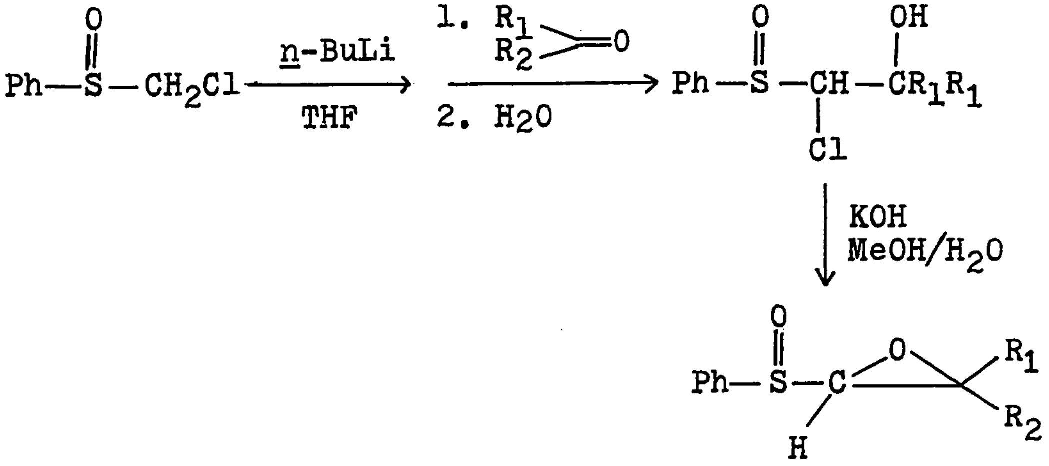


PART II

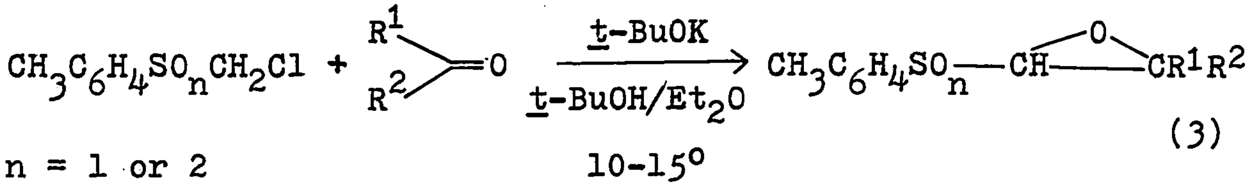
α,β-EPOXY SULFOXIDES AND SULFONES

INTRODUCTION

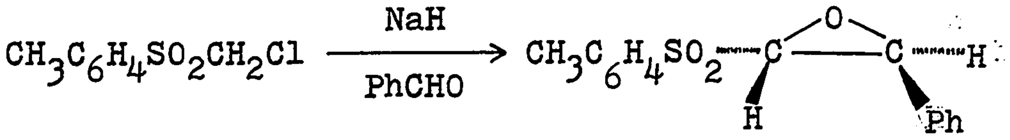
A recent report from this laboratory (1) described the metallation and subsequent hydroxyalkylation of chloromethyl phenyl sulfoxide. The α-chloro-β-hydroxy sulfoxides thus obtained were readily converted by base into α,β-epoxy sulfoxides which could be oxidized to the α,β-epoxy sulfones. Since this constituted a ready route to the epoxy sulfoxides (a new functional group) and to epoxy sulfones (substances not readily available by previously published procedures (2), it was decided to investigate the generality of this synthesis and to study some of the chemistry of these compounds.



Since the initial report (1), a number of preparations of α,β-epoxy sulfoxides and sulfones have appeared. Tavares and co-workers have shown that the reaction of chloromethyl aryl sulfones and sulfoxides with ketones and aldehydes in the presence of potassium t-butoxide leads directly to α,β-epoxy sulfones (3) and sulfoxides (4) respectively. (The Darzens Condensation) The extension of the Tavares procedure may be limited to sulfones and sulfoxides which cannot undergo a Ramberg-Baecklund type rearrangement. (3,5) The Darzens condensation with α-chloro sulfones (NaH as base) has also been reported by Bohlmann and Haffer (6).

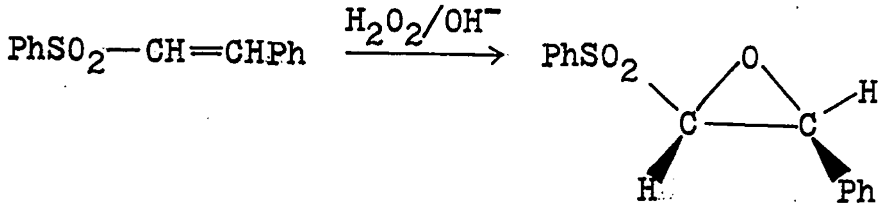


(3)



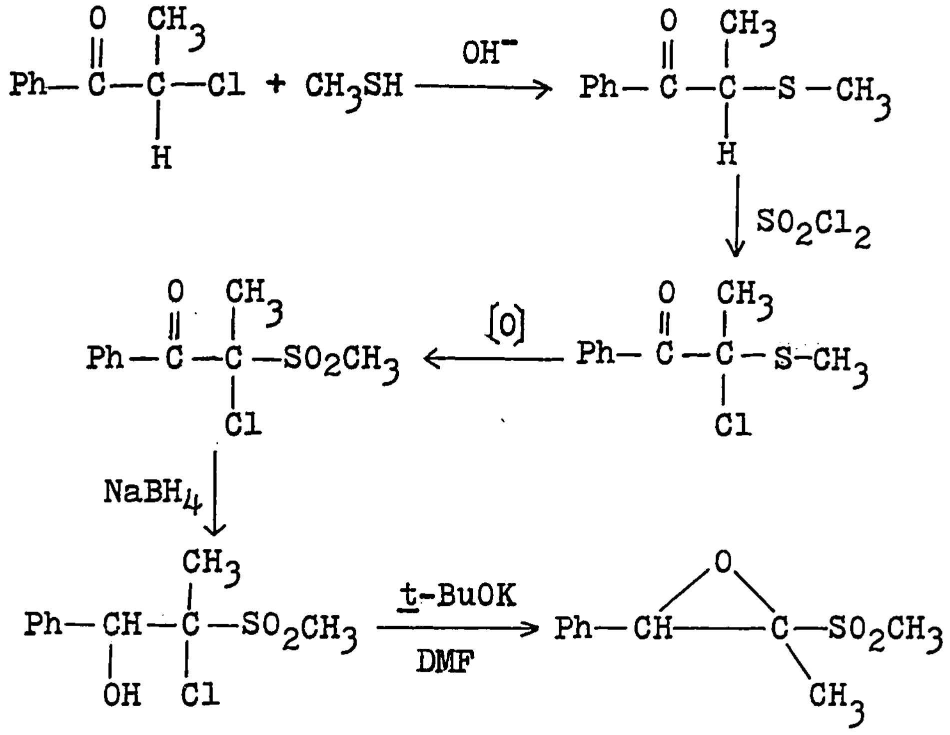
(6)

Zwanenburg and Wiel (7) have described the synthesis of α,β-epoxy sulfones by alkaline H_2O_2 epoxidation of α,β-unsaturated sulfones. This reaction appears to be highly stereoselective. Irrespective of the configuration of the starting material a single stereoisomer (trans-epoxide) is obtained. The general application of this method is probably restricted by the availability of α,β-unsaturated sulfones. α,β-Unsaturated sulfones are known to isomerize to the β,γisomer under basic conditions (8) and may do so prior to epoxidation.

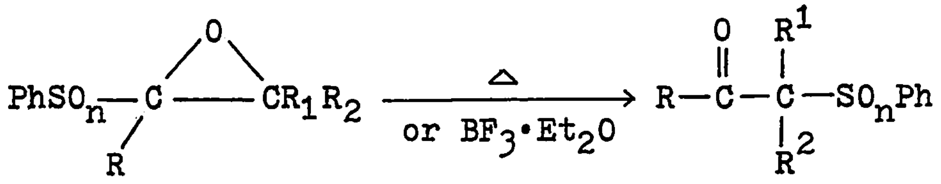


cis (or trans) trans.

Bohlmann and Haffer(6)have reported the synthesis of α,β-epoxy sulfones via chlorohydrin sulfones. However their synthesis starting from a β-keto sulfide, involves a chlorination, oxidation, reduction and cyclization and is much less attractive than the syntheses utilizing the α-halo sulfones. Furthermore, no β,β-disubstituted α,β-epoxy sulfones could be obtained by this method.



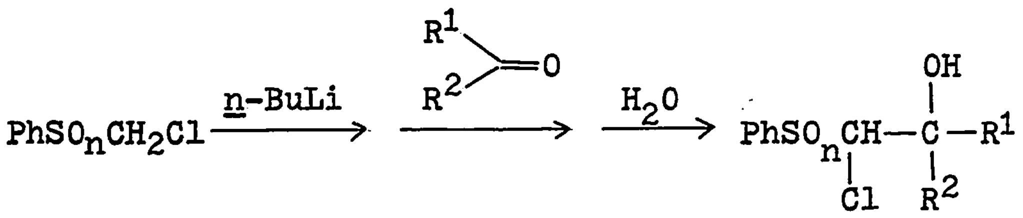
In the course of investigating the epoxide formation from the adducts of chloromethyl phenyl sulfoxide and sulfone, a thermal and acid catalyzed rearrangement was discovered which parallels those reported for a number of other negatively substituted epoxides, for example, α-halo (9) α-keto (10), α-carbomethoxy (11) and α-phosphonate ester epoxides (12). We have observed generally the fission of the oxirane ring, followed by intramolecular migration of the sulfinyl or sulfonyl group. Very similar observations have been made by Professor Tavares and his group; their results will also be discussed in this thesis.



n = 1 or 2

METALLATION AND HYDROXYALKYLATION OF α-CHLORO SULFOXIDES AND SULFONES

Chloromethyl phenyl sulfoxide (1) and sulfone (2) have been successfully hydroxyalkylated with ketones and aldehydes via their lithio derivatives in this laboratory (1). The unusually high stereoselectivity in the formation of the ketone adducts from 1 and the generally high yields in these reactions, were of sufficient interest and novelty to warrant an investigation of the application of these reactions to other α-chloro sulfoxides and sulfones.

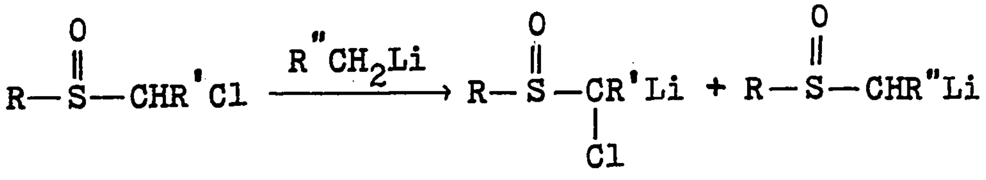


n = 1	1	$R^1R^2 = (CH_2)_5$	79%
		$R^1 = R^2 = CH_3$	75%
		$R^1 = R^2 = Ph$	68%
n = 2	2	$R^1R^2 = (CH_2)_5$	94%
		$R^1 = R^2 = CH_3$	71%
		$R^1 = H$, $R^2 = Ph$	94%

The generation of α-chloro sulfinyl and sulfonyl carbanions was carried out at -78° under nitrogen atmosphere.

Addition of 1.2 equivalents of methyllithium* or n-butyllithium to the α-chloro sulfoxide or sulfone in tetrahydrofuran usually caused formation of a bright yellow or greenish-yellow color. Addition of one equivalent of aldehyde or ketone at -78° discharged the color immediately and yielded after hydrolysis the corresponding α-chloro-β-hydroxy sulfoxides or sulfones. (In some cases these adducts could not be isolated, however epoxides resulting from cyclization of the intermediate chloroalkoxides were obtained. The products were purified by recrystalization or column chromatography (basic alumina); yields refer to purified products.

In the reaction of α-chloro sulfoxides with alkyllithium, two types of processes were generally observed. In addition to the expected metallation we have also observed significant amounts of products derived from a displacement of the chloroalkyl group of the sulfoxide by the alkyllithium.

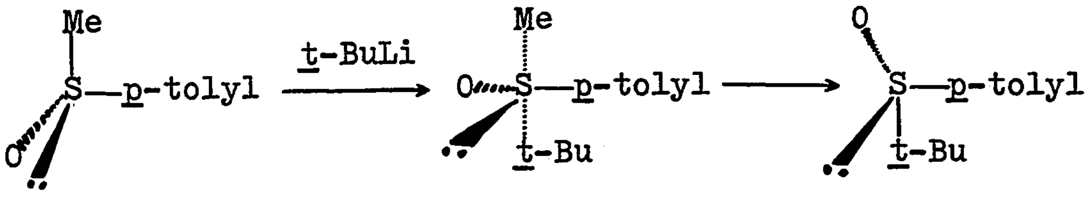


$$R-\overset{\overset{O}{\|}}{S}-CHR'Cl \xrightarrow{R''CH_2Li} R-\overset{\overset{O}{\|}}{S}-\underset{\underset{Cl}{|}}{C}R'Li + R-\overset{\overset{O}{\|}}{S}-CHR''Li$$

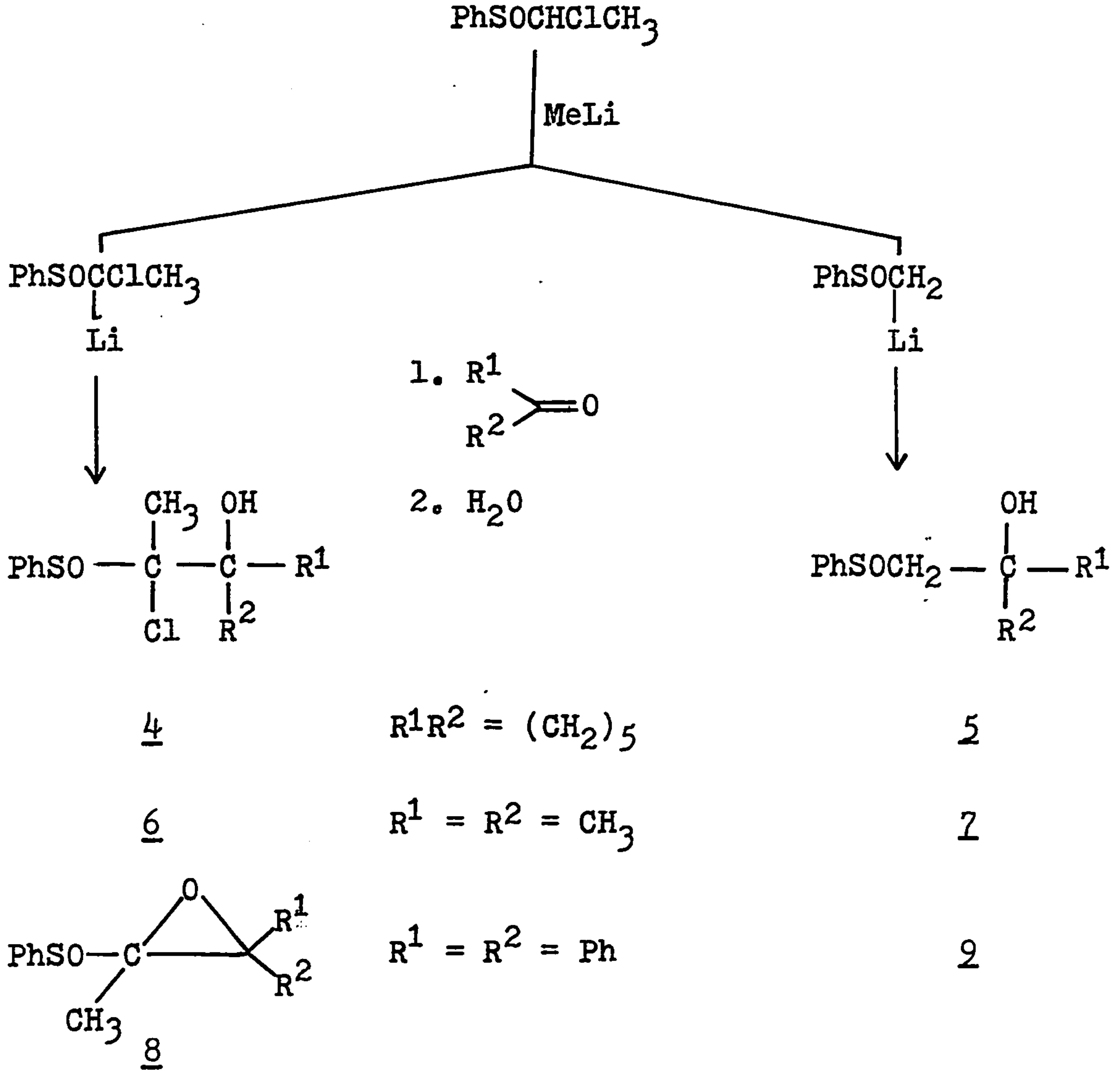
---

* Generally 10 to 20% excess of alkyllithium was added to take care of small amount of water which might be present in the reaction mixture.

Franzen has reported the exchange of the methyl groups of DMSO with the alkyl group of various alkyllithiums (13). Whether this exchange is a direct displacement or involves a bipyramidal intermediate as suggested by Mislow (15) for the racemization of PhS(O)CH_3 with MeLi is not known. A more recent study of the reaction has been carried out by LeBelle (14) who found that the reaction of optically active methyl p-tolyl sulfoxide with t-butyllithium gave t-butyl p-tolyl sulfoxide with inversion of configuration. Such a result points to either a simple S_N2-type displacement or the formation of a bipyramidal intermediate which ejects an alkyl group (alkyl lithium) prior to pseudorotation.



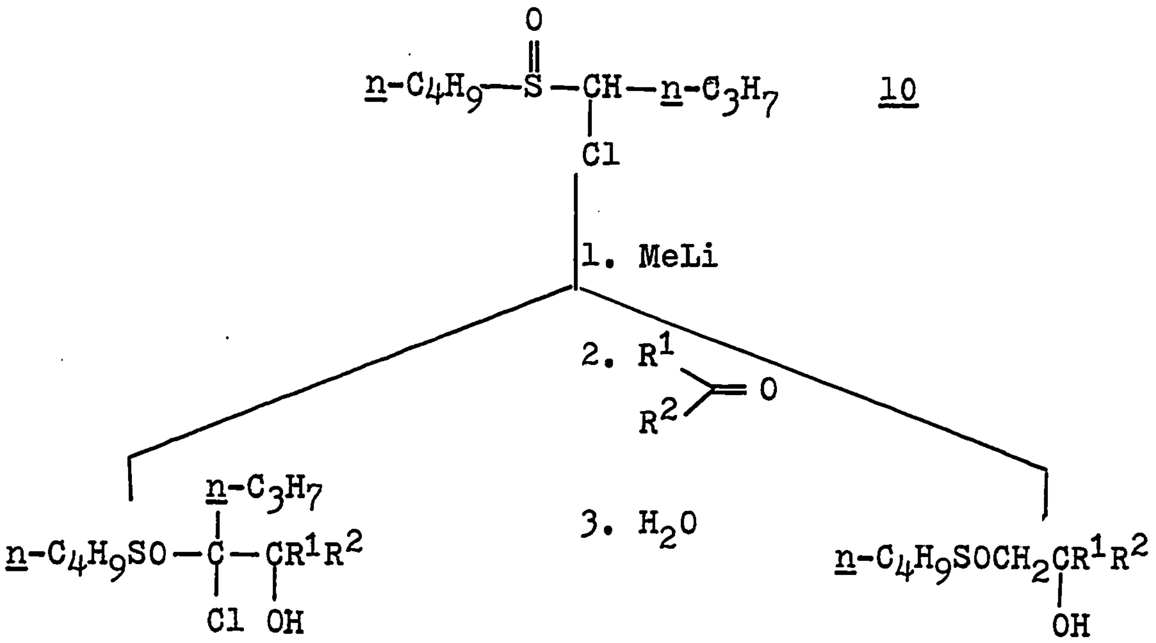
Thus for example, reaction of α-chloroethyl phenyl sulfoxide (3) with methyllithium at -78° followed by addition of cyclohexanone gave the chlorohydrin sulfoxide 4 and the hydroxy sulfoxide 5 in 45 and 55% yield respectively. When acetone was added to the metallation mixture the corresponding sulfoxides 6 and 7 were obtained in 34 and 18% yield; with benzophenone the results were epoxide 8 (69%) and hydroxy sulfoxide 9 (31%). There is considerable variation in the ratio of metallation to substitution. LeBelle (14) has found that such variations can be due to a number of factors including rate of addition and the amount of excess alkyllithium employed.



The structure of the hydroxy sulfoxides 5, 7 and 9 were proved by independent synthesis involving MeLi metallation of methyl phenyl sulfoxide followed by addition of the appropriate ketone.

As in the case of chloromethyl phenyl sulfoxide metallation and hydroxyalkylation appears to give only one diastereomer. Thus in the n.m.r. spectrum of 4 only one signal for the methyl group (δ=1.46, 3H) was observed. Similarly the n.m.r. spectrum of the chlorohydrin sulfoxide 6 indicated the presence of only one diastereomer. The spectroscopic properties of all of the chlorohydrin sulfoxides discussed in this section are in agreement with the structure assignments and are recorded in TABLE I.

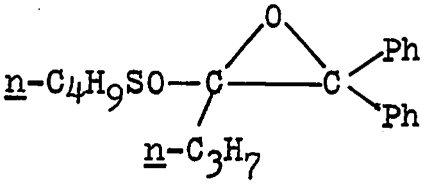
Results similar to those obtained above were observed in the reaction of α-chloro-*n*-butyl *n*-butyl sulfoxide (10) with MeLi. When the reaction mixture was quenched with cyclohexanone a 71% yield of the chlorohydrin sulfoxide 11 and a 14% yield of the hydroxy sulfoxide 12 was obtained. Acetone afforded the product 13 from direct metallation (66%); no hydroxy sulfoxide could be isolated in this instance. Benzophenone gave products from metallation 14 and displacement 15 in 34 and 11% yield respectively.



10

11 $R^1R^2 = (CH_2)_5$ 12

13 $R^1 = R^2 = CH_3$

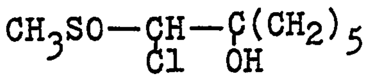
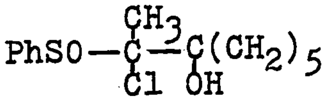
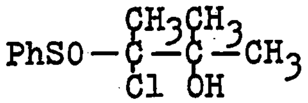
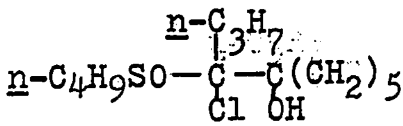
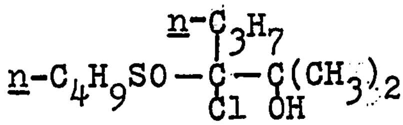
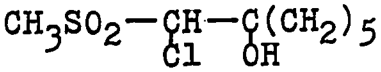
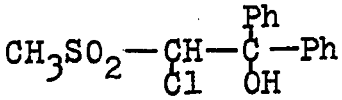


$R^1 = R^2 = Ph$ 15

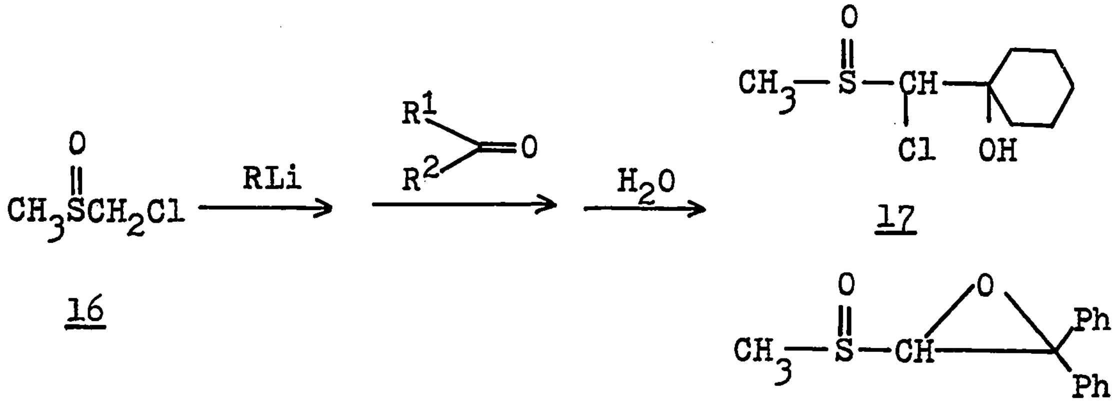
14

TABLE I

Spectroscopic Properties of Ketone Adducts of α-Chloro Sulfoxides and Sulfone

	N.m.r. $(CDCl_3)$ (δ)	Infrared $(CHCl_3)(cm^{-1})$
 $CH_3SO-\underset{Cl}{CH}-\underset{OH}{C}(CH_2)_5$ 17	1.4-2.1(m, 10H); 2.65(s, 3H) 2.94(OH); 4.36(s, 1H)	3450, 2978, 1065
 $PhSO-\overset{CH_3}{\underset{Cl}{C}}-\underset{OH}{C}(CH_2)_5$ 4	0.8-2.4(m, 10H); 1.46(s, 3H) 3.4(OH); 7.4-7.9(m, 5H)	3400, 2980, 1082, 1038
 $PhSO-\overset{CH_3}{\underset{Cl}{C}}-\overset{CH_3}{\underset{OH}{C}}-CH_3$ 6	1.48(s, 6H); 1.72(s, 3H) 4.18(OH); 7.4-7.85(m, 5H)	3440, 3005, 1088, 1025
 $n\text{-}C_4H_9SO-\overset{n\text{-}C_3H_7}{\underset{Cl}{C}}-\underset{OH}{C}(CH_2)_5$ 11	0.8-1.2(m,6H); 1.2-2.4(m,18H) 2.6-3.3(m,2H); 3.8(OH)	3400, 2978, 1450, 1010
 $n\text{-}C_4H_9SO-\overset{n\text{-}C_3H_7}{\underset{Cl}{C}}-\underset{OH}{C}(CH_3)_2$ 13	0.8-1.2(m, 6H); 1.47(s, 3H) 2.01(s, 3H); 1.2-2.2(m, 8H) 2.4-3.2(m, 2H); 4.4(OH)	3400, 2900, 1018
 $CH_3SO_2-\underset{Cl}{CH}-\underset{OH}{C}(CH_2)_5$ 21	1.3-2.1(m, 10H); 3.08(s, 3H) 3.20(OH); 4.67(s, 1H)	3520, 2965, 1315, 1126
 $CH_3SO_2-\underset{Cl}{CH}-\overset{Ph}{\underset{OH}{C}}-Ph$ 20	2.67(s, 3H); 4.18(OH) 5.75(s, 1H); 7.2-7.8(m, 10H)	3460, 3030, 1310, 1125

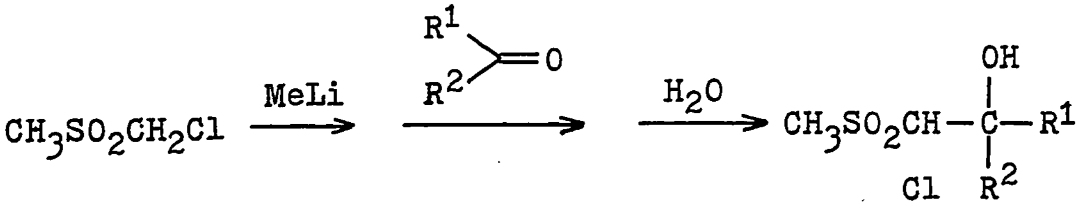
Methyllithium or n-butyllithium metallation of chloromethyl methyl sulfoxide (16) was not very satisfactory. The metallated sulfoxide was trapped with benzophenone and cyclohexenone to give the products 17 and 18 in 15 and 17% yield respectively. No adducts of the DMSO carbanion (the displacement product) were isolated.



16 17 18

No evidence of a stable lithio salt of the α-chlorothiane-S-oxide was obtained. Attempted trapping of this intermediate with the usual ketone gave no hydroxy sulfoxide. Most of the starting sulfoxide disappeared presumably due to decomposition of the lithio derivative.

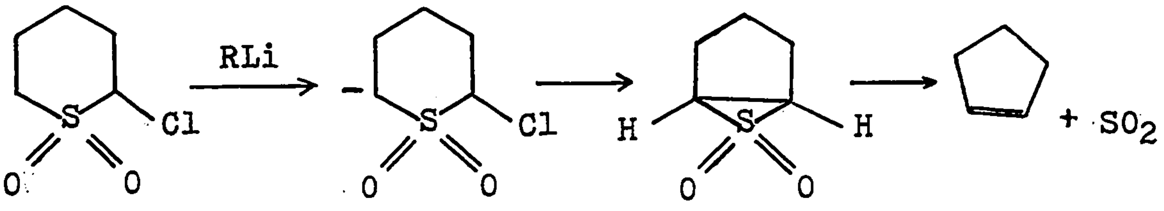
Reaction of chloromethyl methyl sulfone (19) and α-chlorothiane-S,S-dioxide (22) with MeLi also gave contrasting results. Whereas the former yielded a stable α-lithio derivative in reasonable yield as shown by the usual trapping reactions (benzophenone adduct 20 52%, cyclohexanone adduct 21 78%), the latter gave no chlorohydrin sulfones under similar conditions. Attempt trapping of the lithio salt with D_2O gave no deuterium incorporation. Careful workup of such a reaction and examination of the crude product by n.m.r. showed in addition to some nondeuterated starting material, a broad peak at δ=3.6-3.9. In addition, methylene peaks not belonging to the starting material were present. When the crude product was heated the material giving the δ=3.6-3.9 peak disappeared, the remaining material was shown to be essentially pure 22. These changes are interpretable in terms of a Ramberg-Baecklund reaction (5) the transient product being the episulfone 23, which forms cyclopentene on heating. The absorption at δ=3.6-3.9 is attributed to the hydrogens on the 3-membered ring. The reasons for the different behaviour of the chloro sulfones 19 and 22 toward alkyllithiums are not understood.



19

R^1=R^2=Ph 20 52%

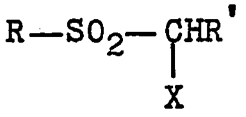
R^1R^2=$(CH_2)_5$ 21 78%



22

23

The Ramberg-Baecklund rearrangement of α-halo sulfones (5) limits the generality of Darzens condensation (3,6) as a route to epoxy sulfones. Vogt and Tavares have reported that their procedure can be applied only to α-halo sulfones of the general formula 24 which do not bear any α' hydrogen (3). The fact that some of the α-chloro sulfoxides and sulfones which have α' hydrogens gave ketone adducts after metallation in reasonably good yields has shown that the low temperature metallation is not as restricted as the Darzens route.



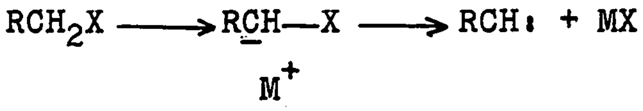
$R{-}SO_2{-}\underset{\displaystyle X}{\underset{|}{C}}HR'$

24

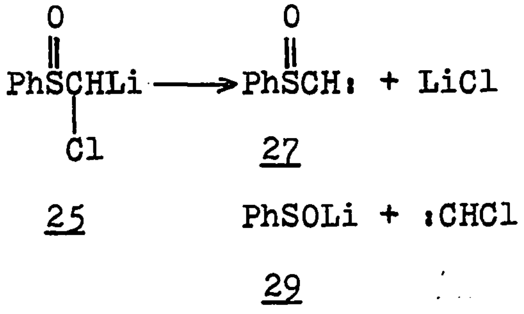
R = aryl or *t*-butyl
R' = H, alkyl or aryl
X = Cl, Br

THERMAL DECOMPOSITION OF THE LITHIO CHLOROMETHYL PHENYL SULFOXIDE AND SULFONE

A general route to carbenoid species is the base-catalyzed α-elimination of hydrogen halides from alkyl halides (16). The availability of the lithio chloromethyl phenyl sulfoxide (25) and sulfone (26) via low temperature metallation with alkyllithiums suggested these materials as potential sources of α-sulfinyl and α-sulfonyl carbenes. The lithio salts 25 and 26 can decompose in two possible ways (a) loss of LiCl to give phenyl sulfinyl carbene 27 and phenyl sulfonyl carbene 28, or (b) elimination of lithium sulfenate 29 and lithium sulfinate 30 to give chlorocarbene.



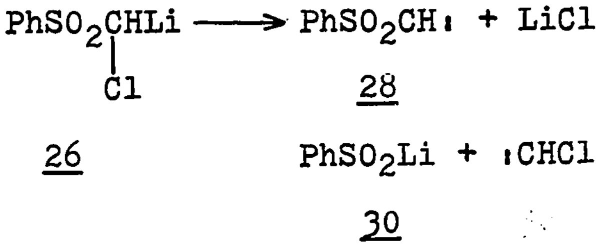
$$\mathrm{RCH_2X} \longrightarrow \mathrm{R\underset{M^{+}}{\underline{C}}H{-}X} \longrightarrow \mathrm{RCH\!:} + \mathrm{MX}$$



$$\mathrm{Ph\overset{O}{\overset{\|}{S}}\underset{Cl}{C}HLi} \longrightarrow \mathrm{Ph\overset{O}{\overset{\|}{S}}CH\!:} + \mathrm{LiCl}$$

$$\mathrm{PhSOLi} + \mathrm{:CHCl}$$

25 27 29



$$\mathrm{PhSO_2\underset{Cl}{C}HLi} \longrightarrow \mathrm{PhSO_2CH\!:} + \mathrm{LiCl}$$

$$\mathrm{PhSO_2Li} + \mathrm{:CHCl}$$

26 28 30

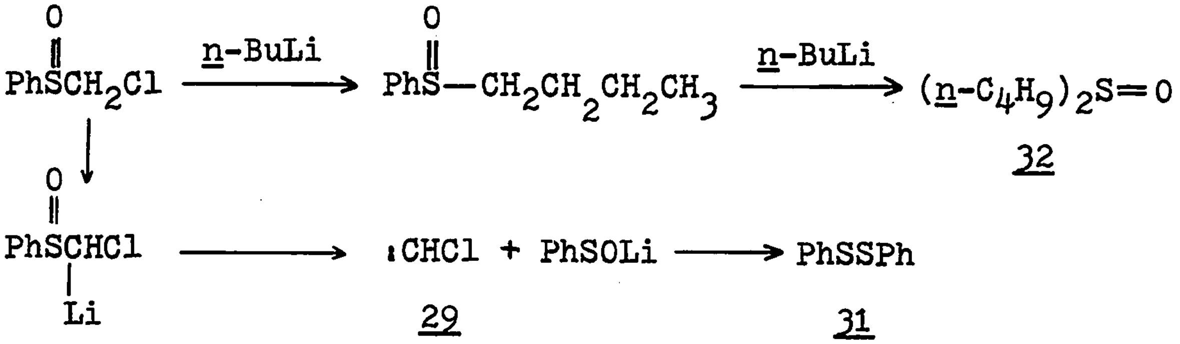
α-Sulfonyl carbenes have been prepared by Strating et al (17a) via photolytic decomposition of the corresponding diazo compounds. Their chemistry has been investigated by these authors (17b). α-Sulfinyl carbenes have not been studied.

$$\mathrm{ArSO_2\overset{-}{C}H\overset{+}{N}_2 \xrightarrow{h\nu} ArSO_2CH\!:}$$

As mentioned on page 48, the lithio salts 25 and 26 are stable for extended periods at -78° as judged by trapping experiments and the retention of the clear yellow color of the solution. When warmed to above -40° the reaction mixtures became brown; at 0° they became black. Decomposition occurred at slightly higher temperatures for the sulfone 26 than for the sulfoxide 25.

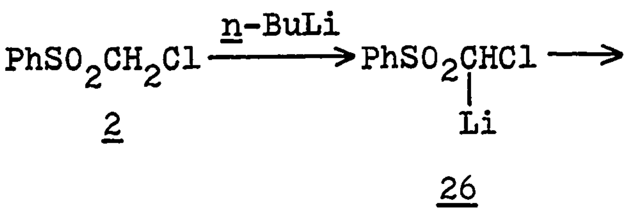
A complex mixture was obtained from the decomposition of the lithio sulfoxide 25 from which only diphenyl disulfide 31 (22%) and n-butyl sulfoxide 32 (3%) could be isolated. The structure of these materials were confirmed by comparison of their spectroscopic properties with those of the authentic materials.

The formation of 31 is rationalizable in terms of decomposition of 25 to chlorocarbene 29 and lithium phenyl sulfenate. Sulfenic acids are known to be sources of disulfides (18). Trapping of the chlorocarbene with cyclohexene or tetramethylethylene was not successful. The formation of n-butyl sulfoxide was unexpected but could be due to a double displacement at the sulfoxide by n-butyllithium. (See also page 49-51)



$$\begin{tikzcd} \mathrm{Ph}\overset{O}{\overset{\|}{S}}CH_2Cl \arrow[r, "n\text{-BuLi}"] \arrow[d] & \mathrm{Ph}\overset{O}{\overset{\|}{S}}{-}CH_2CH_2CH_2CH_3 \arrow[r, "n\text{-BuLi}"] & (n\text{-}C_4H_9)_2S{=}O \ \underline{32} \\ \mathrm{Ph}\overset{O}{\overset{\|}{S}}\underset{Li}{\underset{|}{C}}HCl \arrow[r] & :CHCl\ \underline{29} + PhSOLi \arrow[r] & PhSSPh\ \underline{31} \end{tikzcd}$$

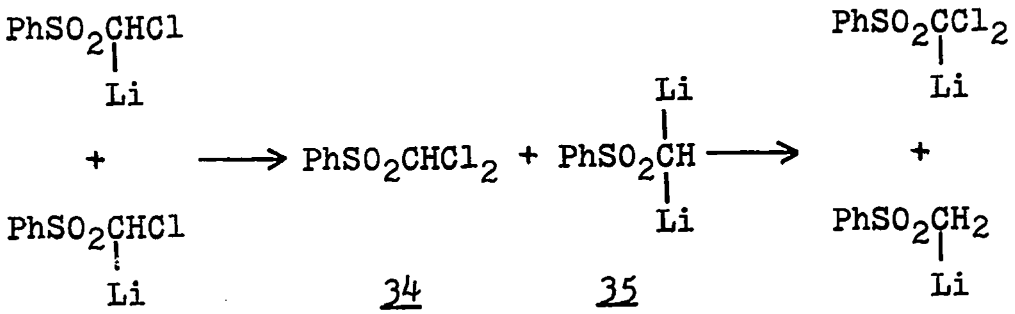
From the decomposition of the lithio sulfone three compounds were isolated: methyl phenyl sulfone 33, chloromethyl phenyl sulfone 2 and dichloromethyl phenyl sulfone 34. In a typical experiment the yields of these were 10, 19 and 9% respectively. The n.m.r. spectra of these products were identical with those of the authentic sulfones prepared by oxidation of the corresponding sulfides.



$$PhSO_2CH_2Cl\ \underline{2} \xrightarrow{n\text{-BuLi}} PhSO_2\underset{Li}{\underset{|}{C}}HCl\ \underline{26} \longrightarrow$$

		Yield(%)	Ratio
$PhSO_2CH_3$	33	9	1
$PhSO_2CH_2Cl$	2	19	2
$PhSO_2CHCl_2$	34	10	1

The constant ratio of 33 to 34 (1:1) obtained in several experiments suggested one possible pathway may be nucleophilic attack of one anion on the chloride of another would give the dichloride 34 and the dianion 35. These would react with each other in an acid-base reaction giving the lithio salts of 34 and 33 respectively.

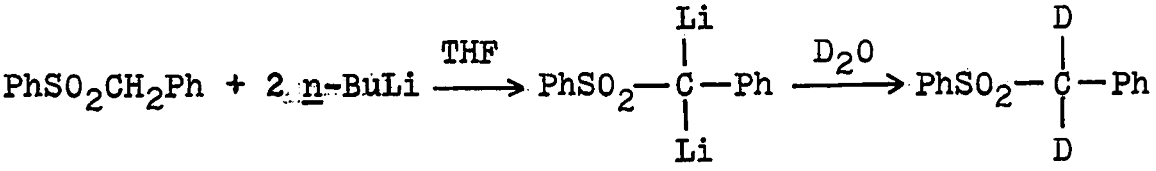


$$\mathrm{PhSO_2\underset{Li}{C}HCl + PhSO_2\underset{Li}{C}HCl \longrightarrow PhSO_2CHCl_2 + PhSO_2\overset{Li}{\underset{Li}{C}}H \longrightarrow PhSO_2\underset{Li}{C}Cl_2 + PhSO_2\underset{Li}{C}H_2}$$

34 35

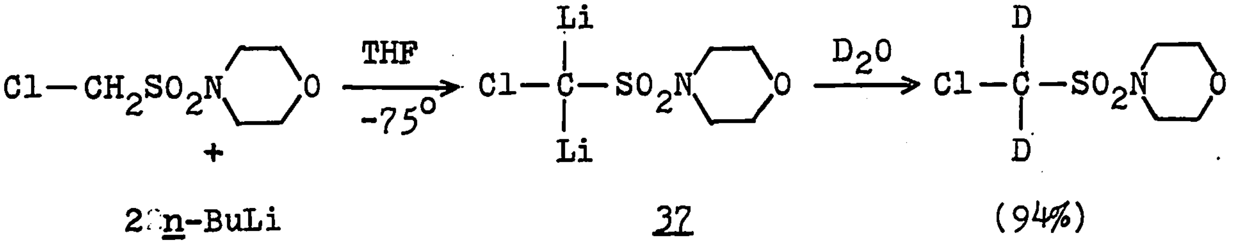
Such explanation would require that long reaction periods would lead to complete consumption of the monochlorolithium salt 26. However, reaction time varying from 5 to 24 hr still gave essentially the same proportions of the sulfones 33, 2 and 34.

Initially it might be considered that dilithio salts such as 35 would be difficult to form. Treatment of methyl phenyl sulfone with 2.4 equivalents of n-butyllithium at -78°, and then warming to room temperature followed by DCl addition gave a mixture of deuterated sulfones in which the dideuterated sulfone $PhSO_2CHD_2$ was formed to the extent of 18 %. Jacobus and Mislow (15) have carried the metalation of methyl phenyl sulfoxide with 2 equivalents of MeLi in ether at room temperature for 2 minutes, quenched with excess D_2O and also observed essentially the same deuterium distribution. Dilithio salts of benzyl phenyl sulfone (36) (19) and the chlorosulfonamide (37) (20) have been reported. These dimetallated species are readily formed in excellent yields.



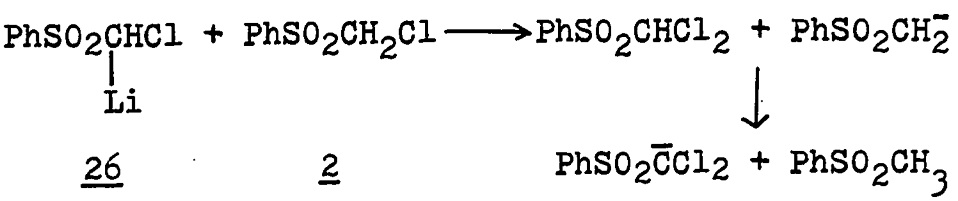
$$PhSO_2CH_2Ph + 2\ n\text{-}BuLi \xrightarrow{THF} PhSO_2-\underset{Li}{\overset{Li}{C}}-Ph \xrightarrow{D_2O} PhSO_2-\underset{D}{\overset{D}{C}}-Ph$$

36 (95%)



37 (94%)

An alternative source of positive chlorine should be the monochlorosulfone 2 (starting material). Some of this might be formed during partial decomposition.



$$PhSO_2\underset{Li}{C}HCl + PhSO_2CH_2Cl \longrightarrow PhSO_2CHCl_2 + PhSO_2CH_2^-$$

$$\downarrow$$

$$PhSO_2\bar{C}Cl_2 + PhSO_2CH_3$$

This scheme would not require the formation of dilithio sulfone. Such a scheme should be facilitated by an increased concentration of the chloride source. However when the decomposition of $PhSO_2CH_2Cl$ was carried out under the same conditions using only one half equivalent of n-BuLi (i.e. ensuring the presence of considerable $PhSO_2CH_2Cl$) the ratio of the sulfones $PhSO_2CH_3$, $PhSO_2CH_2Cl$ and $PhSO_2CHCl_2$ formed was 1 : 4.5 : 1. Thus $PhSO_2CH_2Cl$ does not appear to be involved in the formation of methyl phenyl and dichloromethyl phenyl sulfone.

α-Chloro-α-lithio sulfoxides and sulfones do not appear to be sources of α-sulfinyl and α-sulfonyl carbenes.

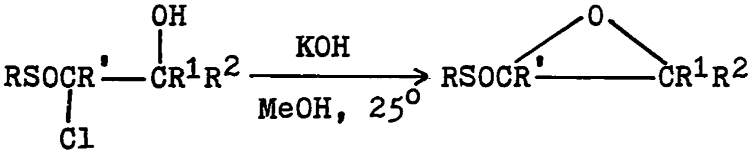
FORMATION OF α,β-EPOXY SULFOXIDES AND SULFONES

A. α,β-Epoxy Sulfoxides

Treatment of the α-chloro-β-hydroxy sulfoxides obtained from chloromethyl phenyl sulfoxide with dilute methanolic KOH was reported to give the corresponding epoxides in high yield.(1) The α-chloro-β-hydroxy sulfoxides described in this thesis were similarly converted into epoxides;yields being greater than 90%. (TABLE II) The ease of intramolecular displacement of chloride ion from these chlorohydrin sulfoxides contrasts with the great difficulty which is generally encountered in displacing chloride ion from α-chloro sulfoxides by external nucleophiles (21-23).

TABLE II

Formation of α,β-Epoxy Sulfoxides from α-Chloro-β-hydroxy Sulfoxides



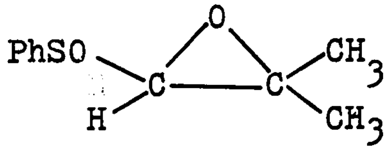
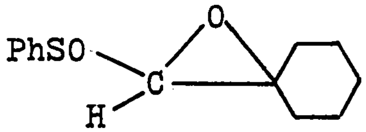
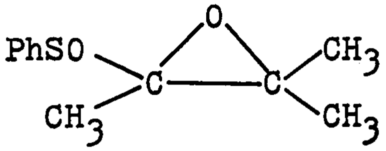
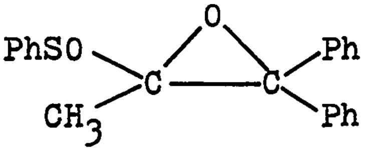
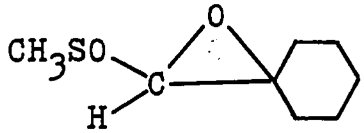
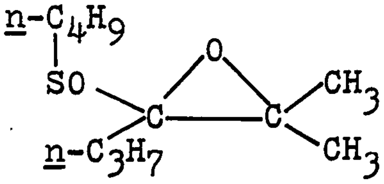
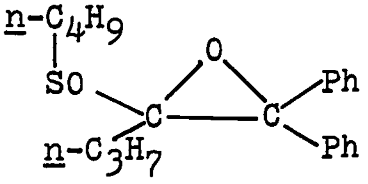
α,β-Epoxy Sulfoxides	R	R'	R¹	R²	Yield(%)	Ref.
37	Ph	H	CH_3	CH_3	91	(1)
39	Ph	H	$-(CH_2)_5-$		91	(1)
40	Ph	H	Ph	Ph	(100)	(1)
41	Ph	CH_3	CH_3	CH_3	96	
42	Ph	CH_3	$-(CH_2)_5-$		99	
43	n-C_4H_9	n-C_3H_7	CH_3	CH_3	92	
44	CH_3	H	$-(CH_2)_5-$		96	

The structures of the α,β-epoxy sulfoxides were generally confirmed by n.m.r., i.r., mass spectrometry and elementary analysis. For example, epoxide <u>42</u>, colorless granules of m.p. 60-62° (methylene chloride-pentane) had n.m.r. peaks ($CDCl_3$) at δ=1.31 (s, 3H), 1.4-2.5 (m, 10H), and 7.4-7.8 (m, 5H); i.r. peaks ($CHCl_3$) at 3080, 2970,1090 and 1045 cm^{-1}. The n.m.r. data of α,β-epoxy sulfoxides are given in TABLE III; other data supporting their structures are recorded in the Experimental Section.

We have found that most of these epoxy sulfoxides decompose slowly at room temperature. Tavares and co-workers have made similar observations with both their α,β-epoxy sulfoxides (24) and sulfones (25). The room temperature decomposition was not investigated. However we have briefly studied the more rapid thermal decomposition of α,β-epoxy sulfoxides at temperatures above 100°. (See page 72-78)

TABLE III

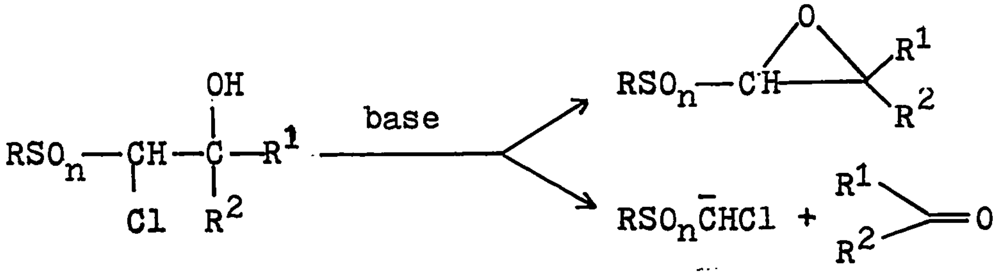
N.m.r. Data of α,β-Epoxy Sulfoxides in $CDCl_3$ (δ)

	38	1.41 (s, 3H); 1.74 (s, 3H); 3.66 (s, 1H) and 7.4-7.8 (m, 5H).
	39	1.4-2.3 (m, 10H); 3.66 (s, 1H) and 7.4-7.8 (m, 5H).
	41	1.52 (s, 3H); 1.63 (s, 3H); 1.81 (s, 3H) and 7.4-7.9 (m, 5H).
	8	1.2 (s, 3H) and 7.2-7.8 (m, 15H).
	44	1.4-2.1 (m, 10H); 2.68 (s, 3H) and 3.65 (s, 1H).
	43	0.8-1.2 (m, 6H); 1.2-2.2 (m, 8H); 1.50 (s, 3H); 1.62 (s, 3H) and 2.5-2.8 (m, 2H).
	14	0.6-1.0 (m, 6H); 1.0-2.4 (m, 8H); 2.6-2.9 (m, 2H) and 7.18-7.66 (m, 10H).

B. α,β-Epoxy Sulfones

Contrary to the quantitative epoxidation of halohydrin sulfoxides, the corresponding halohydrin sulfones formed epoxides in generally much poorer yields. Thus treatment of the acetone adduct 45 and the cyclohexanone adduct 46 of chloromethyl phenyl sulfone, with methanolic KOH for 10 min at room temperature gave in addition to the epoxides 47 and 48 considerable amounts of chloromethyl phenyl sulfone and the corresponding ketone. (Reverse of the condensation reaction) The crude n.m.r. spectra showed that the epoxides 47 and 48 were formed in 10 and 40% yield respectively. Bohlmann and Haffer (6) have also observed the same fragmentation of halohydrin sulfones with KOH to chloro sulfones and ketones. In contrast, 21, the cyclohexanone adduct of chloromethyl methyl sulfone, gave a 94% yield of the α,β-epoxy sulfone 49. (See TABLE III)

Thus, two competing processes are observed in the reaction of halohydrin sulfoxides and sulfones with base. The difference in the ratio of epoxidation vs fragmentation in the two series could be explained by (a) the ease of displacement of chlorine and (b) the stability of the fragmentation products (i.e. the sulfonyl and sulfinyl carbanions and the ketones).



45 R=Ph, $R^1=R^2=CH_3$

46 R=Ph, $R^1R^2=(CH_2)_5$

21 R=CH_3, $R^1R^2=(CH_2)_5$

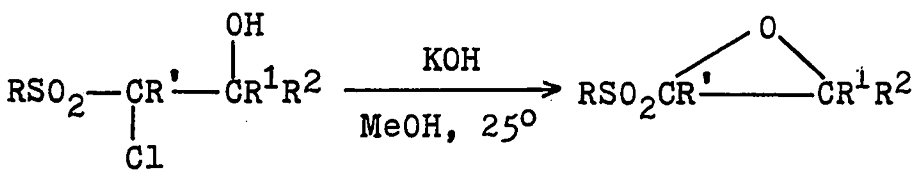
Results of the thermal decomposition experiments indicated that $\mathrm{PhSO_2CH(Li)Cl}$ is more stable than PhSOCH(Li)Cl. Furthermore, Bordwell et al (21) have shown that chlorine α to a phenyl sulfonyl group is at least 12 times less reactive toward S_N2 displacement than chlorine α to the phenyl sulfinyl group. Both of these factors favor the fragmentation process in the phenyl sulfone series and indeed this is the major pathway. In the adduct 21, where fragmentation is less favorable than above, because the $\mathrm{CH_3SO_2\bar{C}HCl}$ anion is less stable than $\mathrm{PhSO_2\bar{C}HCl}$, epoxide formation dominates again.

Because of the variable yields of α,β-epoxy sulfones obtained it was decided to prepare these compounds via m-chloroperbenzoic acid oxidation of the more readily available α,β-epoxy sulfoxides.

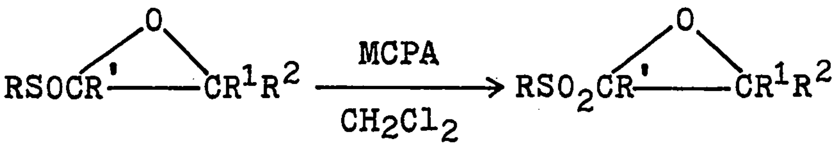
TABLE IV

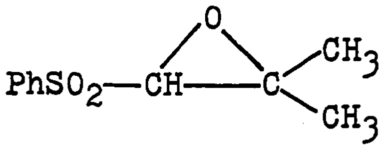
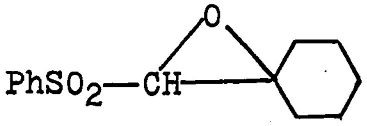
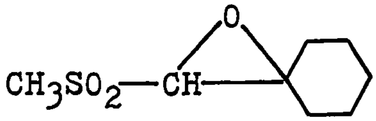
Synthesis of α,β-Epoxy Sulfones

Method A:



Method B:

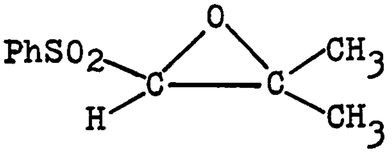
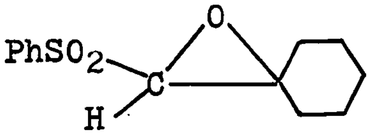
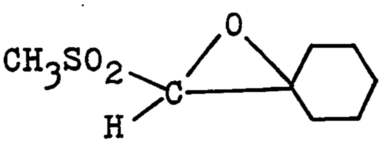


		Method A	Method B
	47	10%	95%
	48	40%	93%
	49	94%	72%

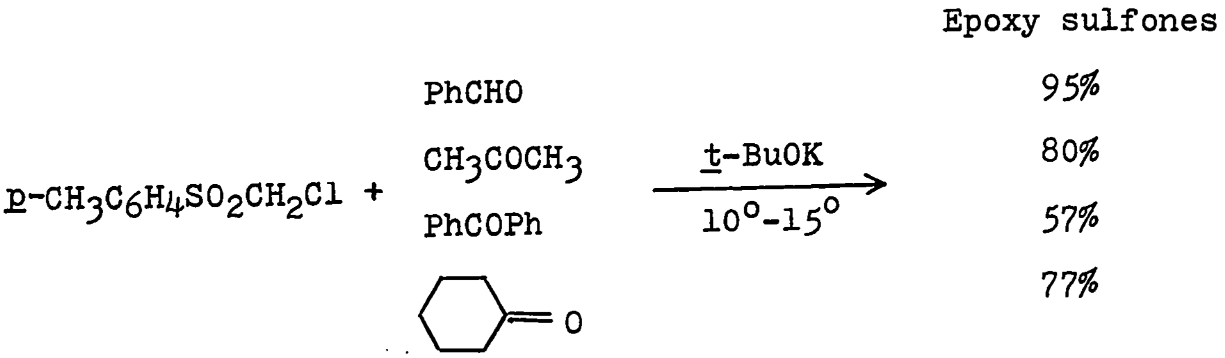
The spectroscopic properties of these epoxides clearly supported the structure assignments. In particular they showed sulfone bands at about 1310 and 1150 cm^{-1} in the i.r.. The n.m.r. data are shown below in TABLE V..

TABLE V

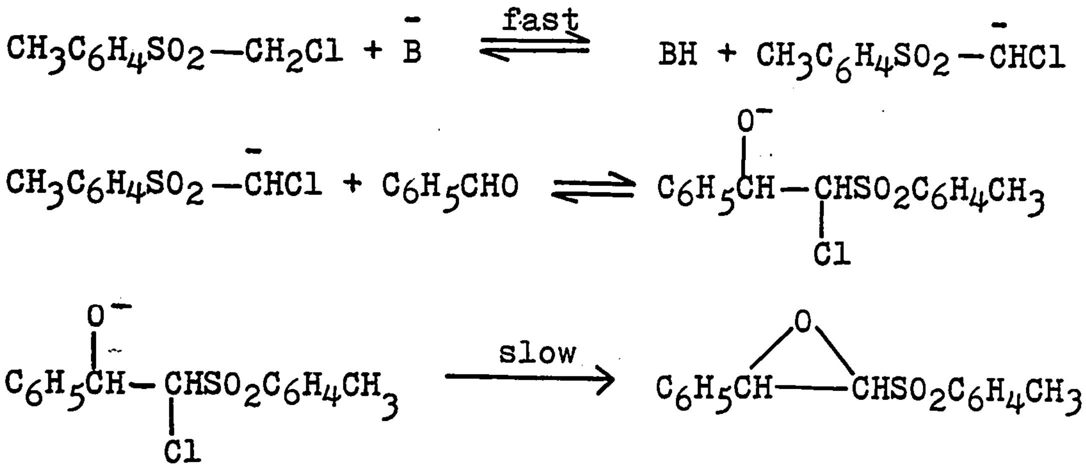
N.m.r. Data of α,β-Epoxy Sulfones

	47	1.42 (s,3H); 1.84 (s, 3H); 3.82 (s,1H) and 7.4-8.15(m, 5H).
	48	1.4-2.4 (m, 10H); 3.8 (s, 1H); and 7.4-8.2 (m, 5H).
	49	1.38-2.32 (m, 10H); 3.02 (s, 3H) and 3.86 (s, 1H).

Finally, we would like to mention the direct synthesis of α,β-epoxy sulfones from α-halosulfones and carbonyl compounds by Darzens condensation. This method is useful for preparation of aryl sulfonyl epoxides as reported Tavares et al (3) and Bohlmann and Haffer (6).

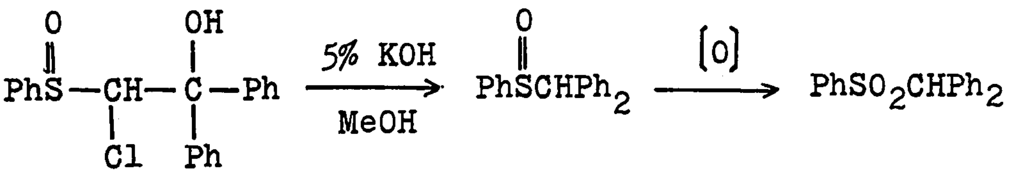


Both groups have established that the epoxides obtained by condensation with aldehyde had exclusively the trans configuration. The following detailed mechanism for the epoxidation was proposed by Vogt and Tavares. (3)



THERMAL AND ACID-CATALYZED REARRANGEMENTS OF α,β-EPOXY SULFOXIDES AND SULFONES

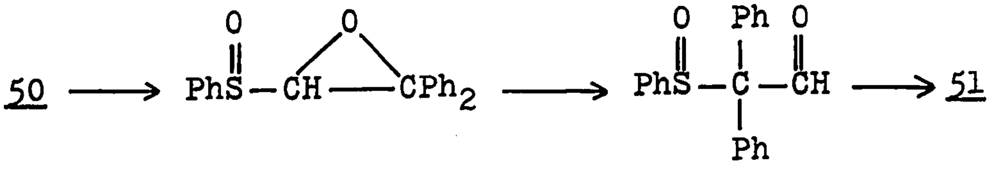
In the course of investigating the epoxide formation from the benzophenone adduct of chloromethyl phenyl sulfoxide 50, a quantitative yield of benzhydryl phenyl sulfoxide (51) instead of the expected epoxide 52 was obtained. The product was identified by oxidation to benzhydryl sulfone (53).



$$\mathrm{Ph}\overset{\overset{\textstyle O}{\|}}{\mathrm{S}}-\underset{\underset{\textstyle Cl}{|}}{\mathrm{CH}}-\overset{\overset{\textstyle OH}{|}}{\underset{\underset{\textstyle Ph}{|}}{\mathrm{C}}}-\mathrm{Ph} \xrightarrow[\text{MeOH}]{5\%\ \text{KOH}} \mathrm{Ph}\overset{\overset{\textstyle O}{\|}}{\mathrm{S}}\mathrm{CHPh_2} \xrightarrow{[O]} \mathrm{PhSO_2CHPh_2}$$

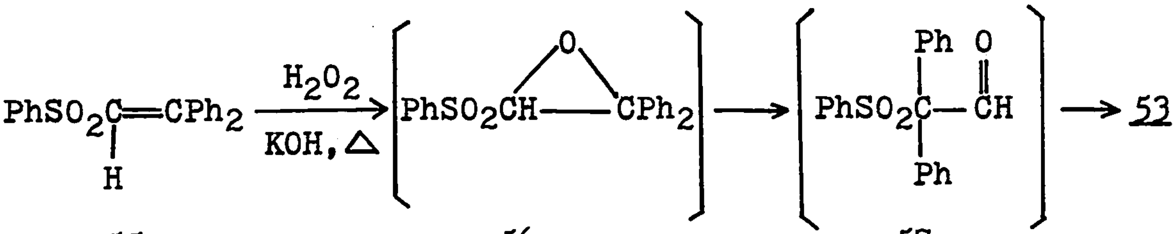
50 51 53

The formation of 51 can be rationalized as involving initial formation of epoxide 52, followed by rearrangement to the aldehyde sulfoxide 54 and finally deformylation.



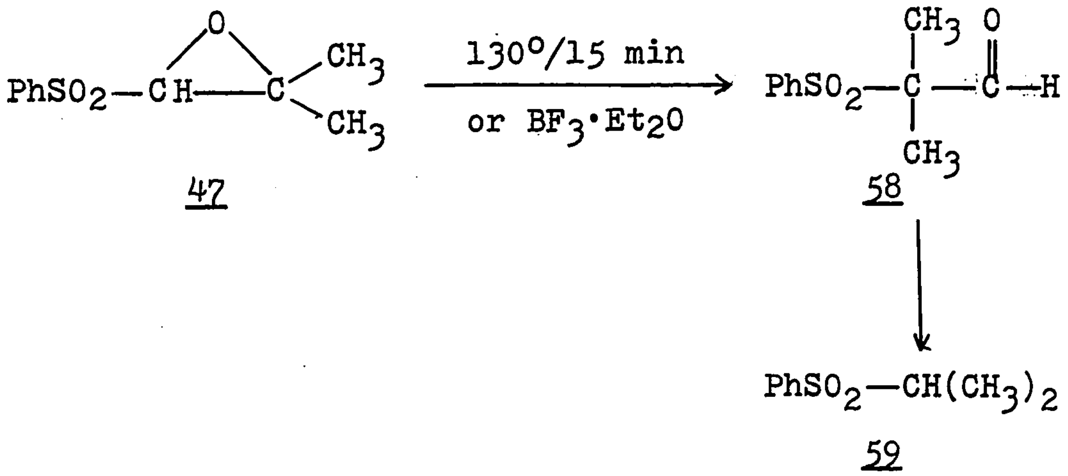
52 54

Support for this mechanism was obtained by showing that the unsaturated sulfone 55 reacted with hot basic hydrogen peroxide to give 53. (26) The only reasonable initial products in this and the above reaction are the epoxides 56 and 52 respectively. The isolation of the other postulated intermediate i.e. the aldehyde sulfoxide was successful in the rearrangement of other α,β-epoxy sulfoxides and sulfones. This epoxide rearrangement which involves the migration of phenyl sulfinyl (or sulfonyl) group is similar to a number of other reported negatively substituted epoxides (9-12). The nearly quantitative transformation of 50 to 51 and the availability of epoxy sulfoxides and sulfones has allowed us to study the mechanism of this rearrangement and its generality. The results of this study are shown in TABLE VI.



55 56 57

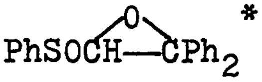
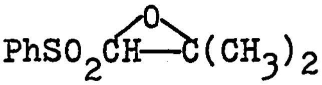
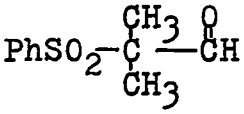
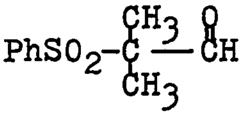
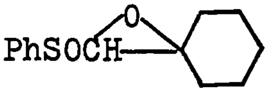
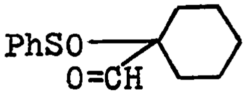
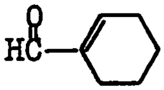
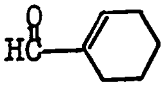
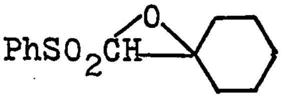
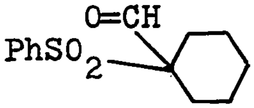
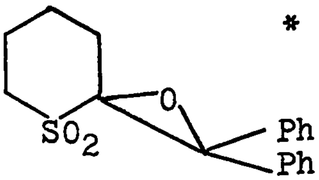
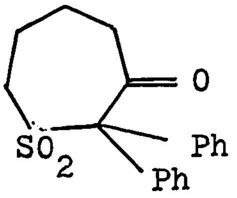
Thermal rearrangement of epoxide 47 was carried out by heating at 130° for 15 minutes. The resultant dark brown oil was separated by preparative t.l.c. (ether-pentane) to give the aldehyde sulfone 58, as colorless needles m.p. 100.5-101.5° (ether-pentane). The spectroscopic properties were in agreement with its designated structure. N.m.r. ($CDCl_3$) peaks occurred at δ=1.46 (s, 6H), 7.6-8.1 (m, 5H), and 9.80 (s, 1H); infrared ($CHCl_3$) had strong bands at 1735, 1310 and 1140 cm^{-1}. Treatment of 58 with dilute KOH in methanol afforded the deformylated sulfone 59 in 93% yield thereby further confirming the feasibility of the proposed transformation 50 to 51. The structure of 59 was proved by unambiguous synthesis (oxidation of isopropyl phenyl sulfide).



The above epoxide rearrangement could be done better in benzene or ether solution in the presence of $BF_3 \cdot Et_2O$. The reaction was complete in 15 minutes at room temperature, workup gave 72% yield of 58. Both the acid and thermal rearrangements have also been reported by Tavares et al (4).

TABLE VI

Thermal and Acid-Catalyzed Rearrangements of α,β-Epoxy Sulfoxides and Sulfones

Epoxide	Rearr. Method	Product	Yield(%)
 $\mathrm{PhSO\overbrace{CH-C}^{O}Ph_2}$ *	thermal	$\mathrm{PhSOCHPh_2}$ #	95
 $\mathrm{PhSO_2\overbrace{CH-C}^{O}(CH_3)_2}$	$\mathrm{BF_3 \cdot Et_2O}$	 $\mathrm{PhSO_2-\underset{CH_3}{\overset{CH_3}{C}}-\overset{O}{\overset{\|}{C}}H}$	72
	thermal	 $\mathrm{PhSO_2-\underset{CH_3}{\overset{CH_3}{C}}-\overset{O}{\overset{\|}{C}}H}$	38
	$\mathrm{BF_3 \cdot Et_2O}$	 +	36
			60
	thermal		66
	$\mathrm{BF_3 \cdot Et_2O}$		34
 *	thermal/ acid		91

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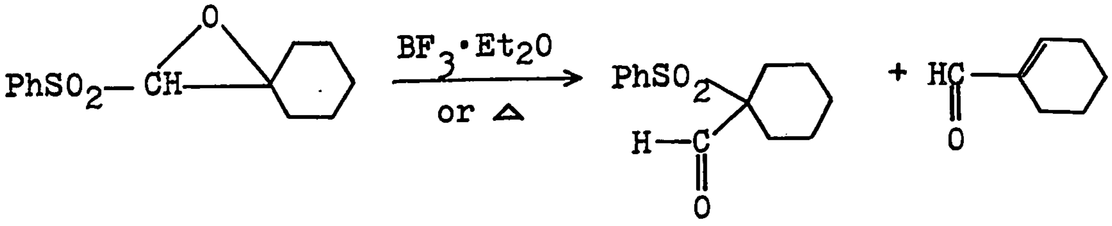
* Epoxide not isolated.

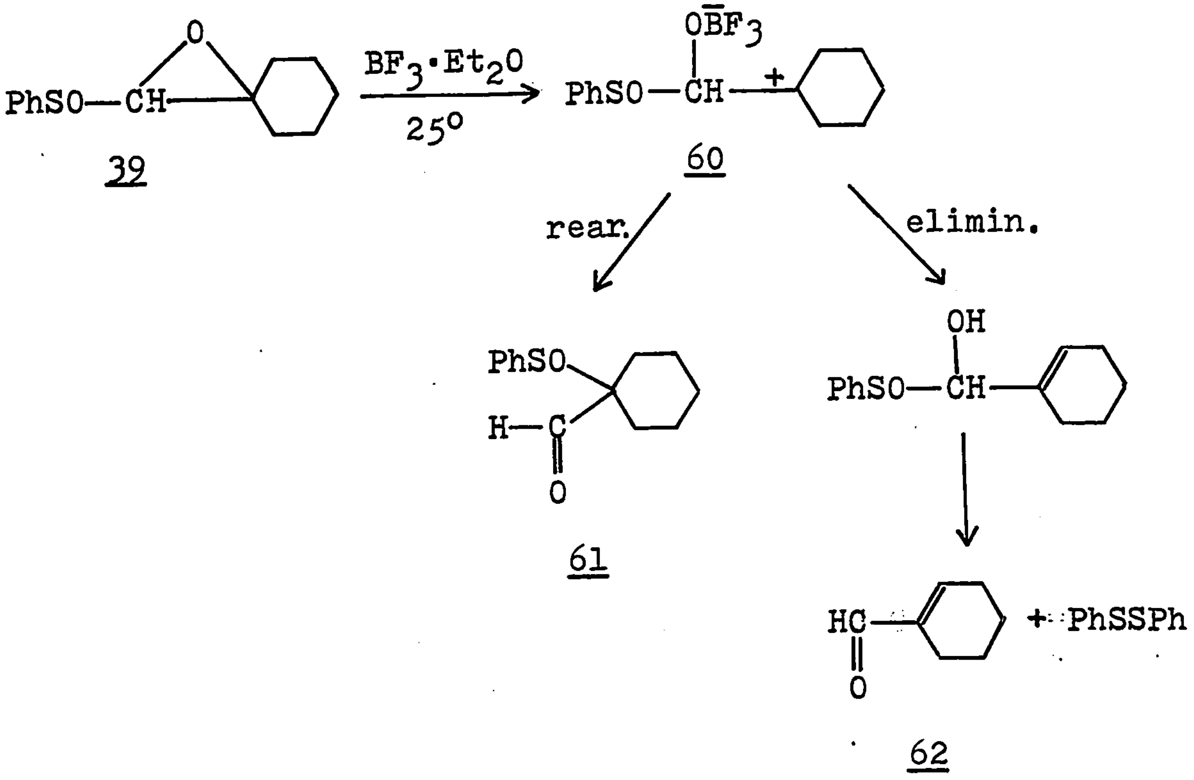
\# Product derived from subsequent deformylation of initial rearrangement product.

In the acid-catalyzed rearrangement of 39 it was possible to isolate in addition to the aldehyde sulfoxide 61 (36%) a 60% yield of Δ-1-cyclohexene carboxaldehyde 62 (as DNP derivative). When 39 was heated to 190° the unsaturated aldehyde 62 distilled from the reaction mixture and was obtained in 68% yield. From the black residue of sulfur moiety was isolated in the form of diphenyl disulfide (91%). The i.r. spectrum of 62 showed the absorption of the conjugated aldehyde at 1685 cm^{-1}, and C=C stretch at 1645 cm^{-1}. The n.m.r. spectrum ($CDCl_3$) showed four methylene protons from δ=1.40 to 2.00 (multiplet), four protons from 2.00 to 2.58 (multiplet), one olefinic proton from 6.70 to 6.95 (multiplet) and one aldehyde proton at 9.48 (singlet). The epoxy sulfone 48 corresponding to the epoxy sulfoxide 39 gave qualitatively the same results, *i.e.* both aldehyde sulfone and unsaturated aldehyde were obtained in the thermal and acid-catalyzed rearrangement. The aldehyde sulfoxide 61 and sulfone 63 were related by oxidation.



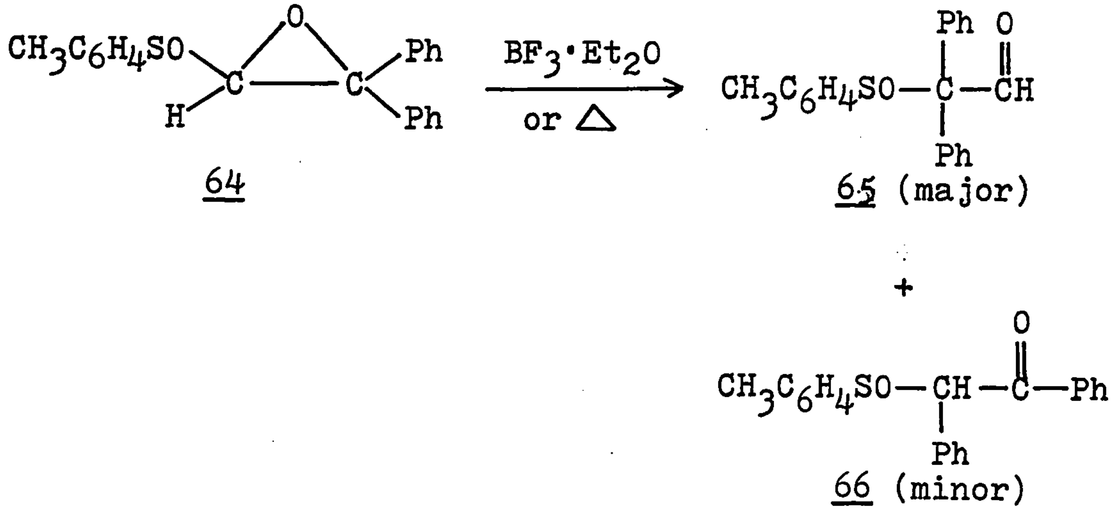
48 63 62

A detailed mechanism for the BF_3 catalyzed process is given in the scheme below.



Complexation of BF_3 to the epoxide followed by ring cleavage would be expected to give the dipolar species 60. Such a species could undergo either rearrangement to 61 or proton elimination to 62.

Generally we have observed migration of the sulfur moiety. Tavares and co-workers have found one example where phenyl migration 66 also was observed (4). Apparently the migratory aptitude is $PhSO_2$ or $PhSO > Ph > CH_3$ or H. This differs from the relative aptitudes of other electronegatively substituted epoxides where Ph migrates generally in preference over the electronegative substituent.



64

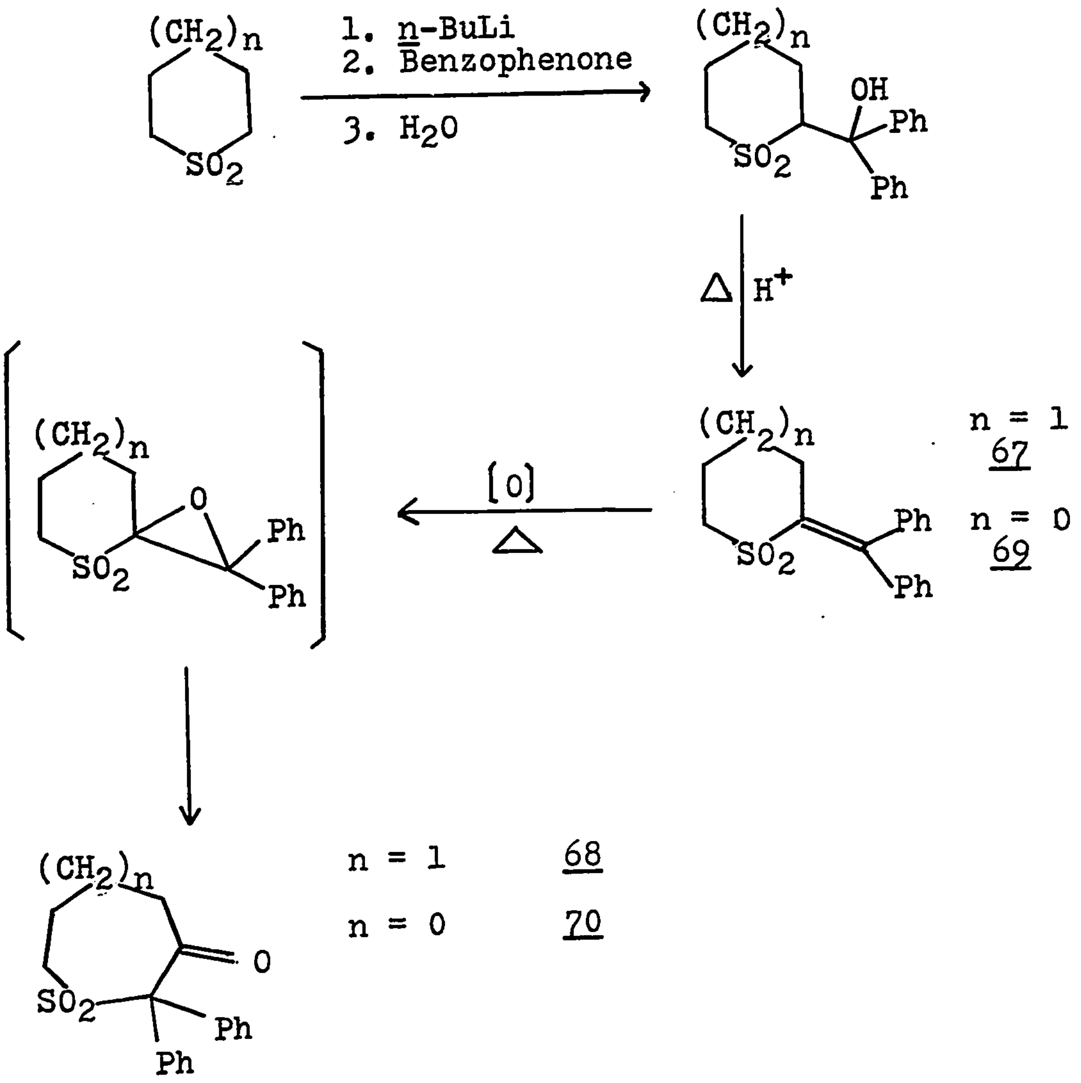
65 (major)

66 (minor)

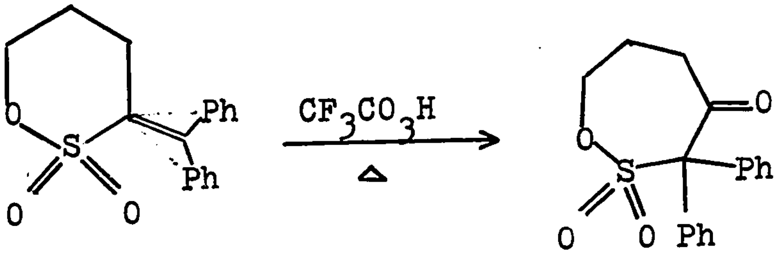
The rearrangement of epoxy sulfoxides and sulfones represented an interesting possibility for ring enlargement and thus a potential route to medium size sulfur containing rings which are often difficult to prepare from acyclic precursors.

Several successful examples have been carried out. For example, epoxidation of 67 (prepared from hydroxyalkylation of thiane-S,S-dioxide and followed by dehydration) with m-chloroperbenzoic acid in refluxing benzene gave directly the 7-membered ring product 68 in 91% yield. The structure of 68, colorless crystals, m.p. 198° (CH_2Cl_2-pentane) was determined by spectroscopic and analytical methods. The n.m.r. spectrum ($CDCl_3$) had peaks at δ= 1.08-3.20 (m, 8H), and 7.04-7.66 (m, 10H). The i.r. spectrum

($CHCl_3$) showed strong bands at 1725 cm^{-1} (carbonyl), 1315 and 1123 cm^{-1} (sulfone). The mass spectrum gave the parent molecular ion at m/e = 314. Epoxidation of 5-membered ring sulfone 69 and rearrangement to the 6-membered ring β-keto sulfone 70 had also been done in this laboratory (27).



Attempts to epoxidize the sultone 71 with m-chloroperbenzoic acid were not successful. However we have been able to isolate some of 7-membered ring sultone 72 in the trifluoroperacetic acid oxidation. The β-keto sultone 72, colorless granules, m.p. 151°, had i.r. ($CHCl_3$) absorption at 1725, 1373, 1185 and 995 cm^{-1}. The n.m.r. spectrum ($CDCl_3$) had peaks at δ=1.80-2.26 (m, 2H), 3.02-3.35 (m, 2H), 4.62 (t, J=5Hz, 2H) and 7.2-7.6 (m, 10H).



71

72

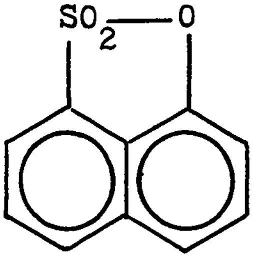
From the work described above and that of Tavares et al (4) it is apparent that the ease of rearrangement is dependent on the ability of the substituents to stabilize a positive charge. Two phenyl substituents allow the rearrangement to occur at room temperature, two α-methyl substituents require 130°. It is doubtful that rearrangement of an α,β-epoxy sulfoxide or sulfone bearing one or no alkyl group would occur at temperatures below 200-250°. At these temperatures side reactions probably would also occur, thus limiting the generality of the rearrangement.

PART III

SULTONE SYNTHESIS

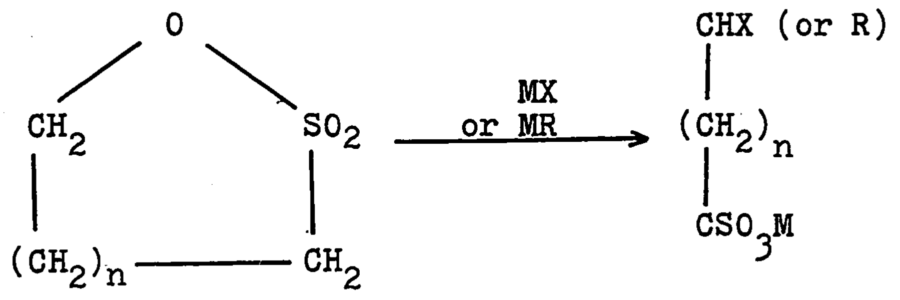
INTRODUCTION

Sultones are internal esters of hydroxy sulfonic acids. The name "Sultone", corresponding to lactone, was first used by Erdman (1) who confirmed the structure of the first member of the series 1,8-naphthosultone (1).



1

Sultones especially 1,3-propane sultones are of considerable industrial importance. They react readily with a variety of nucleophilic reagents according to the following equation to give derivatives of sulfonic acids. The result of this is the introduction of a water-solubilizing group into a variety of organic molecules. The products of these reactions have been found useful as detergents, photographic chemicals, plasticizers, pharmaceuticals, insecticides and intermediates for the manufacture of dyes (2).



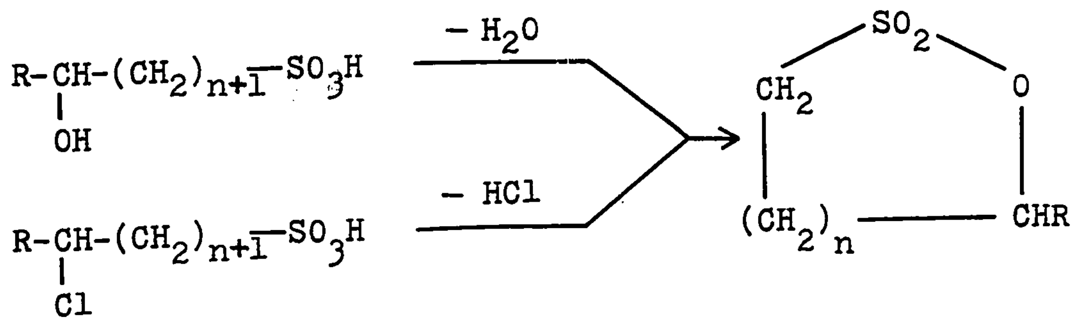
n = 1 or 2

R : H, alkyl, aryl etc.

M : K, Na, H etc.

X : NH_3, CN, SCN, halogen, alkoxy, carboxylate etc.

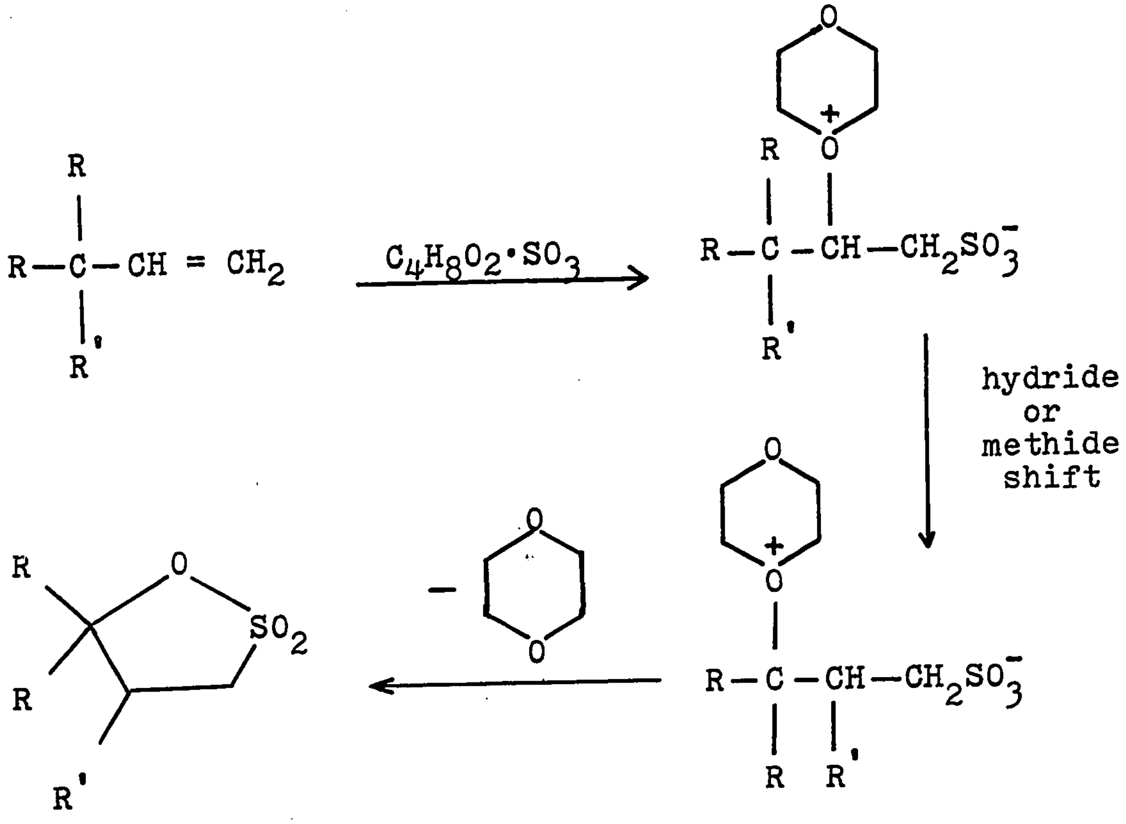
The synthesis of sultones is generally carried out either by cyclization of the appropriate halo- or hydroxyalkanesulfonic acid (2) or by sulfonation of olefins with dioxane and sulfur trioxide (2,3). Relatively few substituted sultones have been reported (3) probably because the above methods are limited in scope. The cyclization of the halo- or hydroxy sulfonic acids suffers from a lack of ready preparation of all but the most simple of the starting materials.



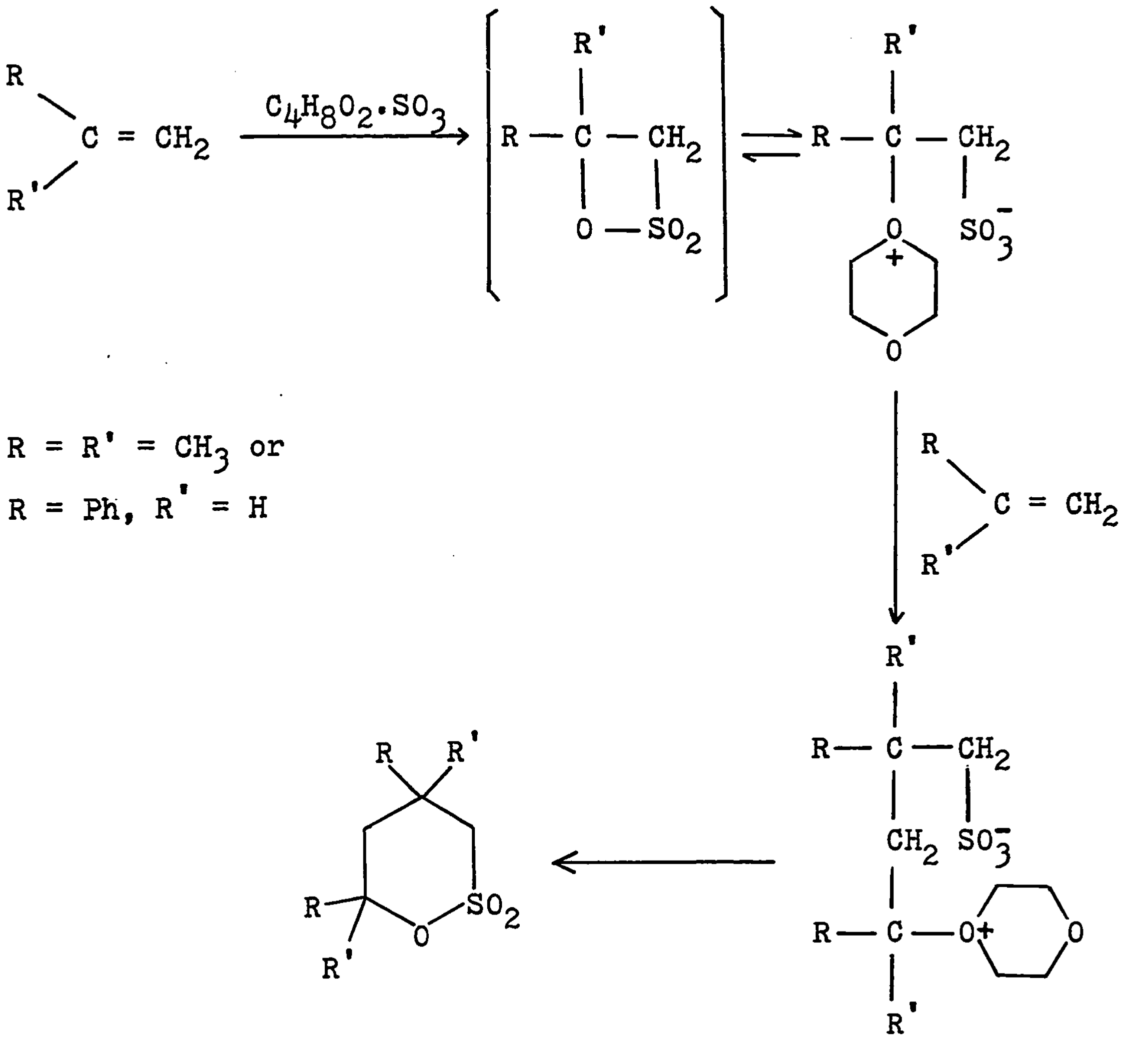
n = 1 or 2

The sulfonation of olefins yields sultones only when the olefin bears substituents capable of stabilizing the positively charged intermediate (See Scheme 1). In the case of 5-membered ring sultones only the 3,3-dialkyl substituted derivatives can be prepared by this route. The substitution pattern available by this route for the 6-membered series is also restricted. A brief description of other even more limited methods is given in reference 2.

Scheme 1



R = CH_3
R' = CH_3 or H

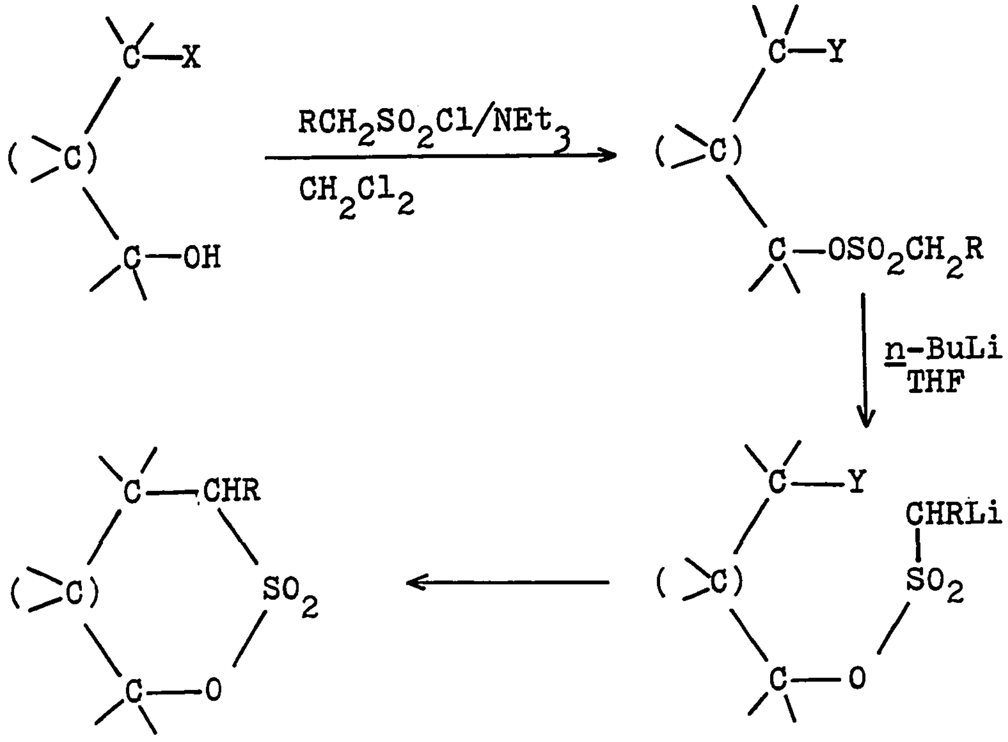


$R = R' = CH_3$ or
$R = Ph,\ R' = H$

Because of the lack of generality of the above syntheses especially with regard to control of the substitution pattern, a general synthesis from readily accessible starting materials seemed desirable.

Recent reports regarding the preparation of α-sulfonate ester carbanion (See below) suggested the synthesis of sultones according to equation 1. Such a route should have considerable scope because of the ready availability of the required starting materials such as diols and halohydrins. In addition this scheme held out the possibility of synthesizing 7 and possibly 8 membered ring sultones and sultones whose substitution pattern and stereochemistry could be predictably related to that of the starting materials.

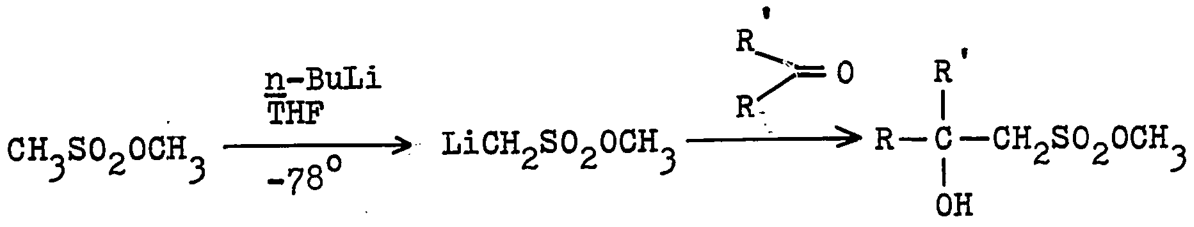
Equation 1



X = OH or halide

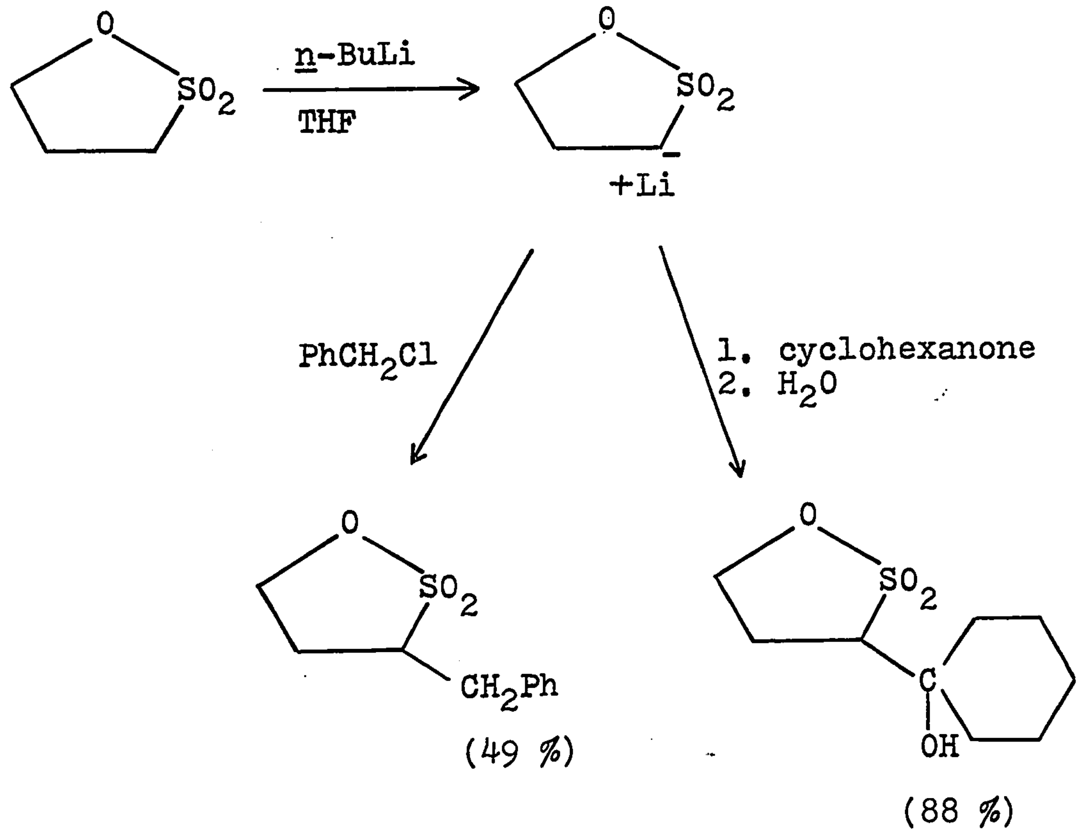
Y = sulfonate or halide

The first report of the preparation of α-sulfonate ester carbanions was made by Corey and Durst (4). These authors showed that the lithio derivative of methyl methanesulfonate was formed cleanly with n-butyllithium in THF at -78°, as evidenced by the isolation of adducts with benzophenone and cyclohexanone.

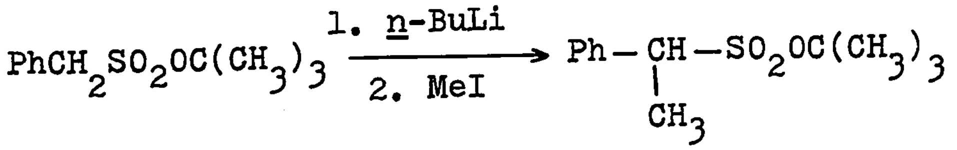


$R = R' = Ph$ (91 %)
$RR' = (CH_2)_5$ (76 %)

Other reports of the formation of α-lithio sulfonate esters have appeared (5 - 7). These are shown in the equations below. Of particular interest to us were the observations that these species could be readily alkylated with reactive alkylating agents.



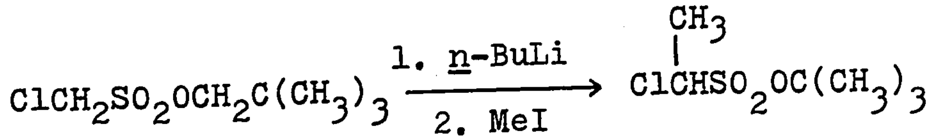
(5)



$$\mathrm{PhCH_2SO_2OC(CH_3)_3} \xrightarrow[\text{2. MeI}]{\text{1. } \underline{\text{n}}\text{-BuLi}} \mathrm{Ph{-}\underset{\displaystyle CH_3}{\underset{|}{CH}}{-}SO_2OC(CH_3)_3}$$

(6)

(79 %)



$$\mathrm{ClCH_2SO_2OCH_2C(CH_3)_3} \xrightarrow[\text{2. MeI}]{\text{1. } \underline{\text{n}}\text{-BuLi}} \mathrm{Cl\overset{\displaystyle CH_3}{\overset{|}{C}}HSO_2OC(CH_3)_3}$$

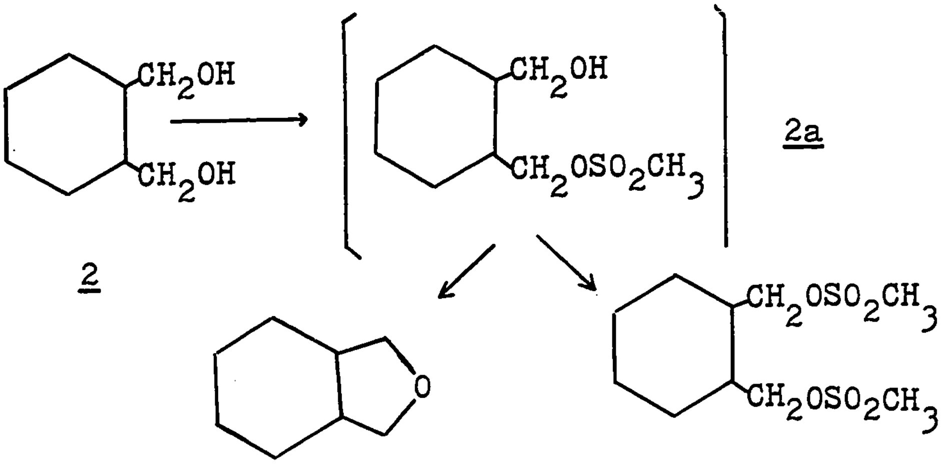
(7)

(100 %)

RESULTS AND DISCUSSION

A. Synthesis of the Sulfonate Esters:

Sulfonate esters are generally obtained by addition of a sulfonyl chloride to mixture of the alcohol and pyridine. Low yields are often obtained in the preparation of disulfonate esters of 1,2-, 1,3- and 1,4-diols due to the competing formation of cyclic oxides. For example, Haggis and Owen (8) have reported that mesylation of the cis diol 2 gave only 33 % of dimethane-sulfonate 3 together with 31 % of the cis oxide 4. The intermediate monosulfonate 2a can react in two ways, either with a second equivalent of methanesulfonyl chloride to form the disulfonate 3, or with loss of methanesulfonic acid under the influence of pyridine resulting in the oxide 4. When one equivalent of sulfonyl chloride is employed 1,4- and 1,5- diols are converted in good yields to tetrahydrofurans and tetrahydropyrans respectively. (9)



2 2a

(31 %) 4 (33 %) 3

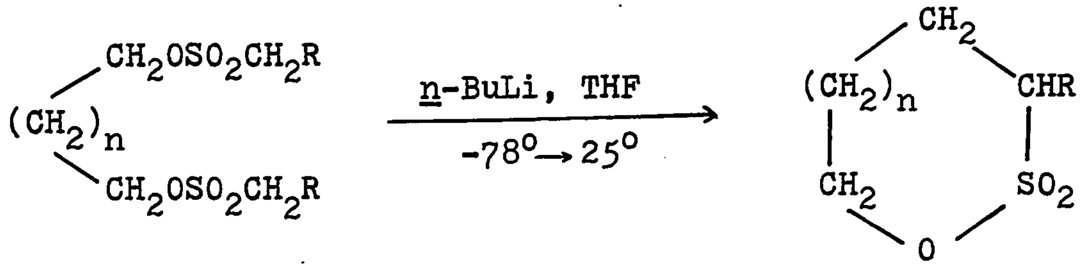
We have found that slow addition of triethylamine to a mixture of sulfonyl chloride and diol in methylene chloride at -78° or at 0° results in good yields of disulfonate esters with no significant amount of cyclic oxide. Sulfenes are known to be formed from methanesulfonyl chloride and triethylamine under these conditions (10). The high yields together with the advantages of simpler workup and shorter reaction time, make this procedure the better method for preparing various kinds of sulfonate esters. See Experimental Parts for details.

B. Cyclization from Symmetrical Disulfonate Esters.

Initial experiments were carried out on 1,2-ethylene dimethanesulfonate (5) and 1,3-propylene dimethanesulfonate (6). Treatment of either 5 or 6 in THF at -78° with one equivalent of *n*-butyllithium followed by warming to 0° for 30 minutes yielded the sultones 7 and 8 in 68 (11) and 88 % respectively. They were identified by comparison of t.l.c. behavior and i.r. spectra with authetic material (12). The cyclizations of the corresponding ethane- and phenylmethanesulfonate esters 9, 10, and 11 were carried out similarly except that longer reaction times were required. The crude products from these reactions were generally contaminated with up to 20 % of starting materials even when the reaction time was 2 days. The products were purified either by recrystallization, chromatography, or distillation under reduced pressure. The yields refer to purified products.

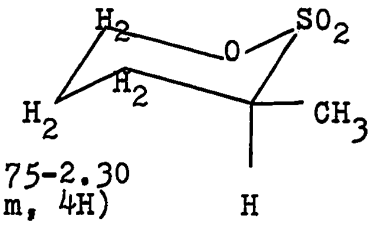
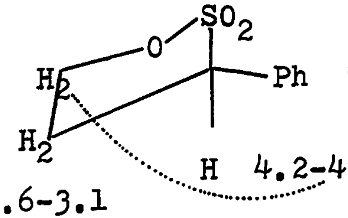
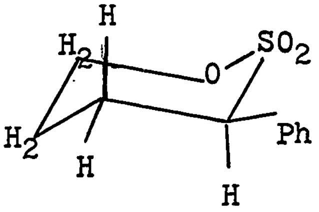
TABLE I

Preparation of Sultones from 1,2- and 1,3-Disulfonate Esters



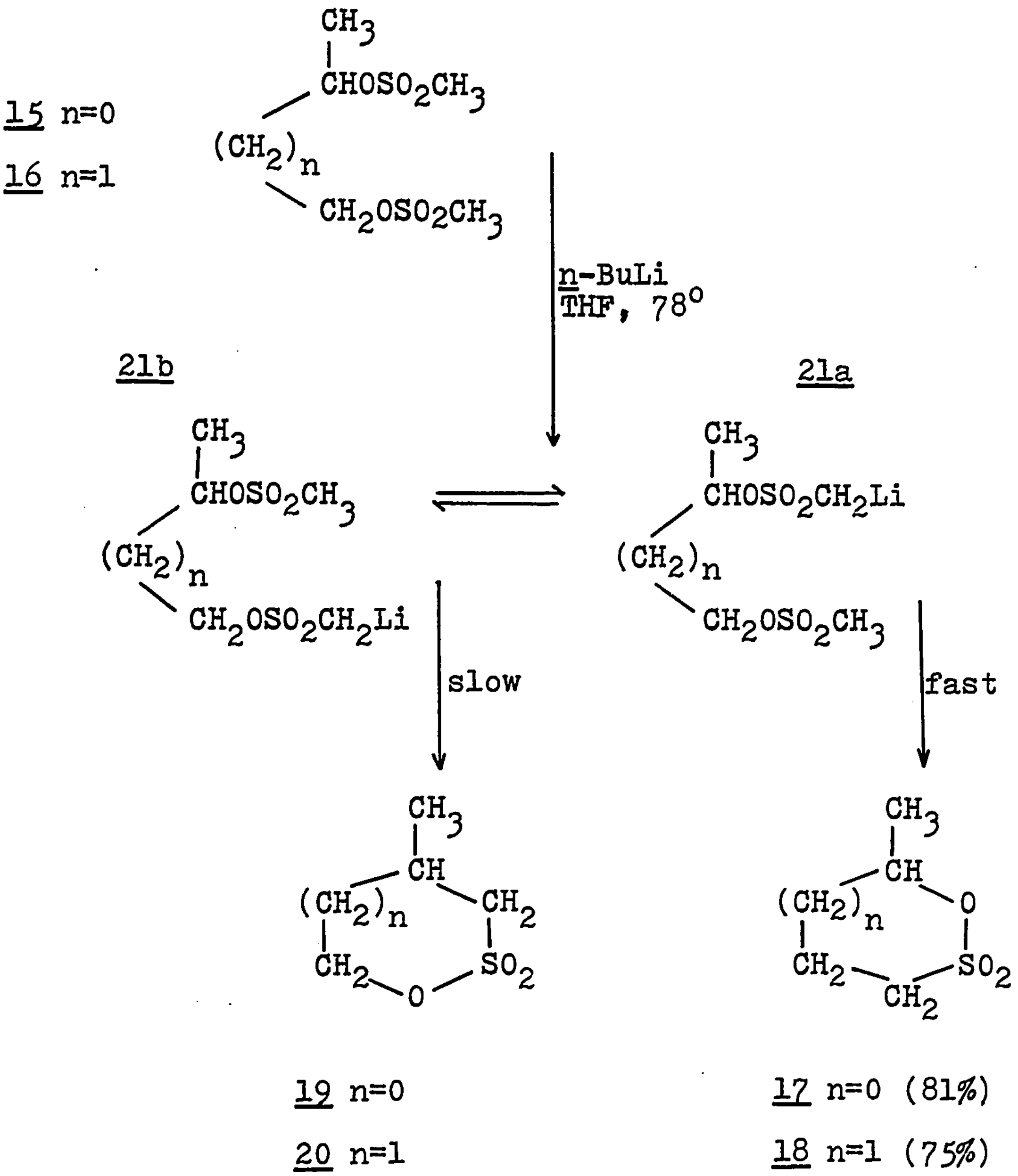
Sulfonate Ester	R	n	Sultone	Yield (%)
5	H	0	7	68
6	H	1	8	88
9	Me	1	12	74
10	Ph	0	13	47
11	Ph	1	14	51

The structures of sultones 12, 13 and 14 were based on analytical data and spectroscopic properties. In particular the infrared spectra showed strong bands in the regions 1350, 1150 and 925 cm^{-1} expected for the sultone grouping (13). The positions of the n.m.r. peaks were in good agreement with those reported by Bordwell *et al* (14) for similar sultones. Details are shown below.

Sultone	n.m.r. (δ)	i.r. (cm^{-1})
12	4.35-4.60 (m, 2H)  1.75-2.30 (m, 4H) 3.0-3.35 (m, 1H) CH_3 1.42 (d, 3H, J = 6.4Hz)	1345 1155 1010 925
13	 Ph 7.40 (s, 5H) H 4.2-4.7 (m, 3H) 2.6-3.1 (m, 2H)	1350 1160 990
14	4.3-4.8 (m, 2H)  Ph 7.3-7.6 (m,5H) 1.8-2.8 (m, 4H) 4.22 (d of d, J=4 and 12Hz 1H)	1350 1162 1010 925

C. Unsymmetrical Disulfonate Esters

Dimethanesulfonate esters of unsymmetrical diols e.g. 1,2-propane- or 1,3-butanediol, cyclized as expected with displacement occurring preferentially at the least substituted carbon. Thus the dimesylate 15 and 16 afforded the sultones 17 and 18 in 81 and 75 % respectively. The spectroscopic and physical properties of these materials were agreement with literature values (14, 15). Nuclear magnetic resonance inspection of the total crudes indicated the absence of significant amounts of the isomeric sultones 19 and 20 (14). Equilibration of the two possible isomeric lithio derivatives 21a and 21b is expected to be facile (16) thereby allowing the preferential production of the isomer resulting from the displacement of the less-hindered mesylate. Although the present experimental data is very limited, it seems reasonable to expect high selectivity in the cyclization of mono-lithio derivatives of other unsymmetrically substituted 1,2- and 1,3-disulfonate esters.



15 n=0

16 n=1

21b

21a

19 n=0

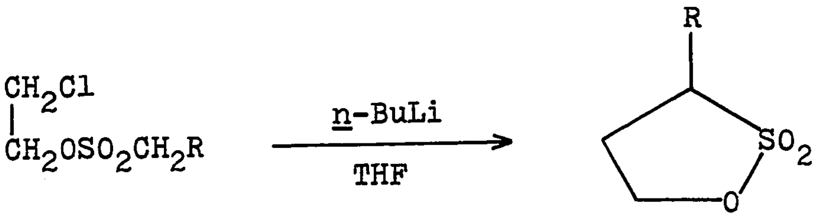
20 n=1

17 n=0 (81%)

18 n=1 (75%)

D. Halosulfonate Esters:

Several 5-membered ring sultones have been prepared from alkanesulfonate esters of 1,2-halohydrins. The yields of cyclized product from these compounds were considerably lower than those obtained from the disulfonate esters; in general they roughly parallel the ease of displacement of the leaving group ($\bar{O}SO_2R > Br^- > Cl^-$). For instance, ethylene chlorohydrin benzyl sulfonate 22 gave the sultone 13 in 30 % yield, while the mesylate of trans-2-bromocyclohexanol 23 afforded a 33 % yield of the cis-bicyclic sultone 24 (See below)

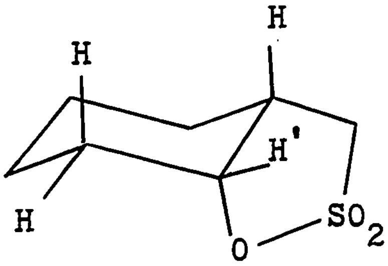


22   R = Ph   13 (30 %)

R = CH_3 (19 %)

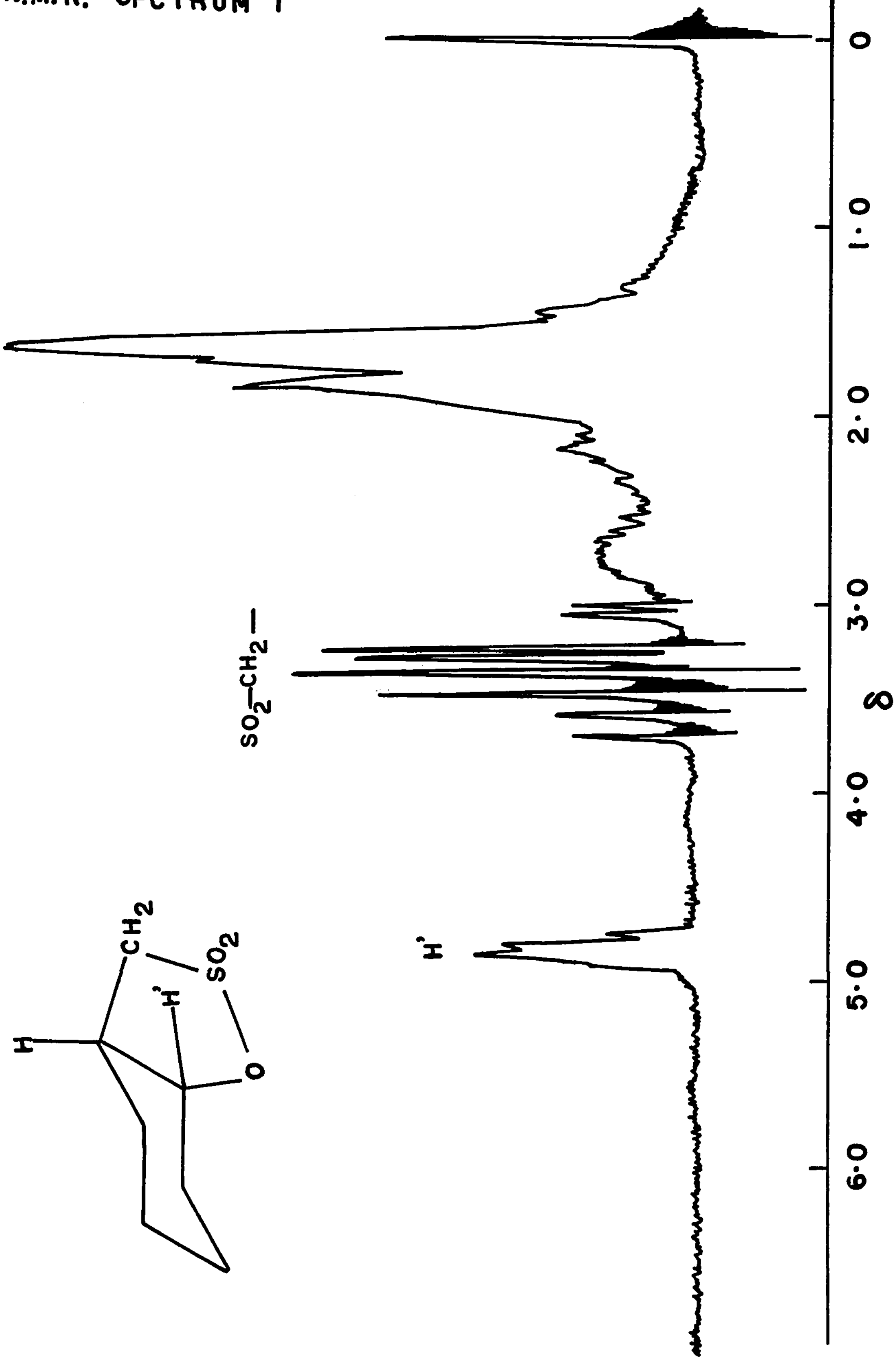
E. Bicyclic Sultones:

Trans-2-bromocyclohexanol methanesulfonate (23) was prepared by reaction of cyclohexene with n-bromoacetamide in aqueous dioxane (17) and followed by mesylation. Addition of n-BuLi to 23 and followed by storage at 5° for 2 days gave a mixture which was separated by preparative t.l.c.. The yield of pure cis-sultone 24, m.p. 54-55° (methylene chloride-pentane) was 33 %. The structure assignment of cis-bicyclic sultone 24 rests on its mode of synthesis, and is supported by spectroscopic data. The infrared spectrum showed strong bands at 1340, 1150 and 810 cm^{-1} which indicated that the sultone grouping had been retained. The n.m.r. spectrum showed the AB part of an ABX (an 8-line multiplet from δ= 3.0-3.8 (2H)) due to the methylene group α to the sultone with J_{gem} = 13.0Hz and J_{vic} 7.0 and 3.0 Hz. The hydrogen (H$'$) on carbon bearing oxygen occurred at δ= 4.8-5.0. The shape of the signal (the band width at half height was 7.0Hz) is in agreement with its assignment as an equatorial proton. (See also n.m.r. spectrum 1)

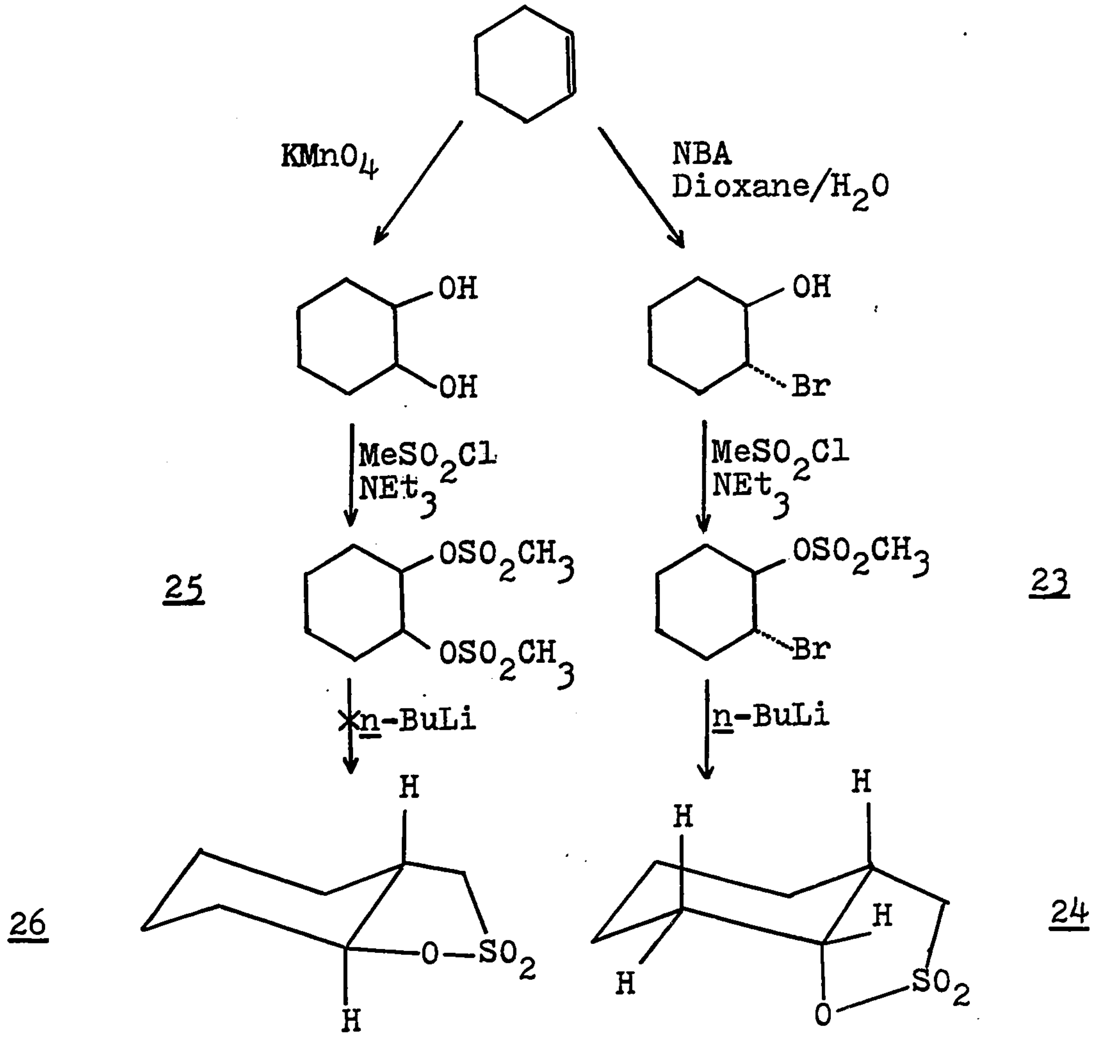


24

N.M.R. SPCTRUM I



Scheme 2



Attempt cyclization of the cis-dimesylate 25 gave no trans-sultone 26. Inspection of molecular models showed that the cyclization of cis-dimesylate 25 should be extremely difficult and thus the trans-sultone 26 is not accessible by this route.

We have however succeeded in preparing the cis- and trans-bicyclic sultones 28 and 30 starting from cyclooctene (Scheme 3). This illustrates that sultones having at least part of their stereochemistry uniquely defined can be synthesized from olefins of known stereochemistry. Treatment of trans-2-bromocyclooctyl methanesulfonate (27) and cis-dimesylate 29 with n-butyllithium at -78° followed by storage at 10° overnight gave the bicyclic sultones 28 and 30 in 36 and 17% yield respectively. The stereochemistry assignments are based solely on the mode of synthesis (cyclization requiring inversion at carbon bearing leaving group) and could in these particular cases not be verified by spectroscopic methods. The analytical and spectroscopic properties of this pair of geometrical isomers are compared in TABLE II .

Scheme 3

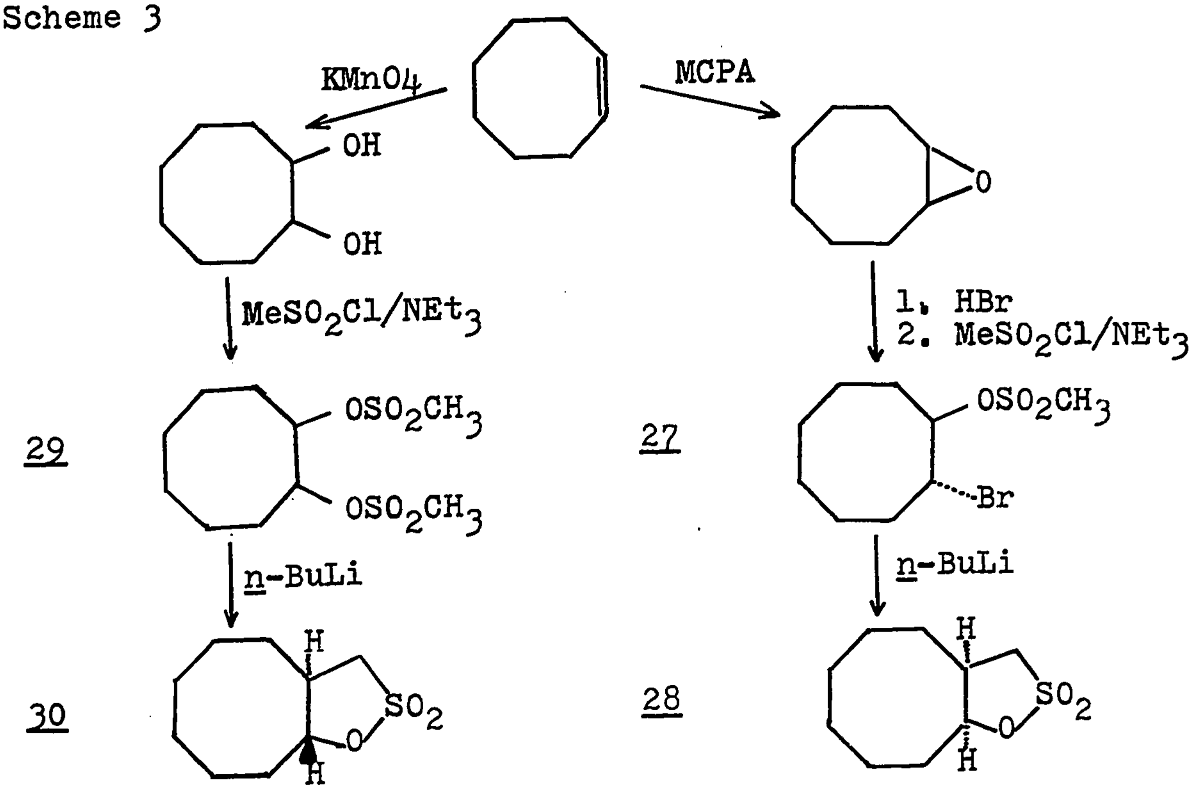
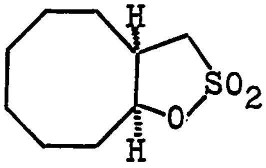
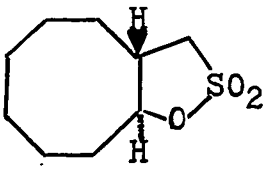


TABLE II

Comparison of cis-sultone 28 and trans-sultone 30

cis-sultone 28	trans-sultone 30
	
M.p. 56.5°-57.5°	56°-57°

mixed m.p. 35°-50°

Elemental Analysis

		Calcd. $C_9H_{16}O_3S$	
C	53.08	52.93	52.79
H	7.89	7.90	7.90
S	15.54	15.67	15.53

Infrared ($CHCl_3$) cm^{-1}

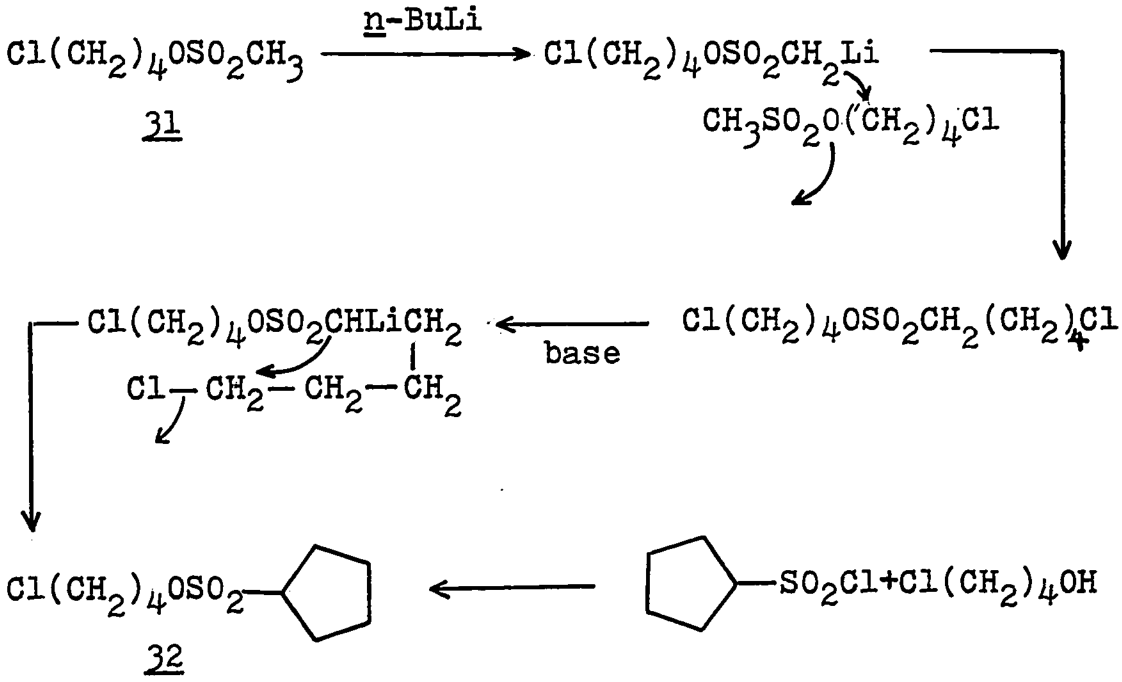
1340 (vs)	1340 (vs)
1155 (s)	1155 (s)
910 (s)	905 (m)
	880 (m)
	848 (m)

N.m.r. ($CDCl_3$) (δ)

1.2-2.3 (m, 12H)	1.2-2.4 (m, 12H)
2.8-3.6 (m, 3H)	2.6-3.7 (m, 3H)
4.8-5.0 (m, 1H)	4.5-4.8 (m, 1H)

F. Attempts to Prepare 7- and 8-Membered Ring Sultones

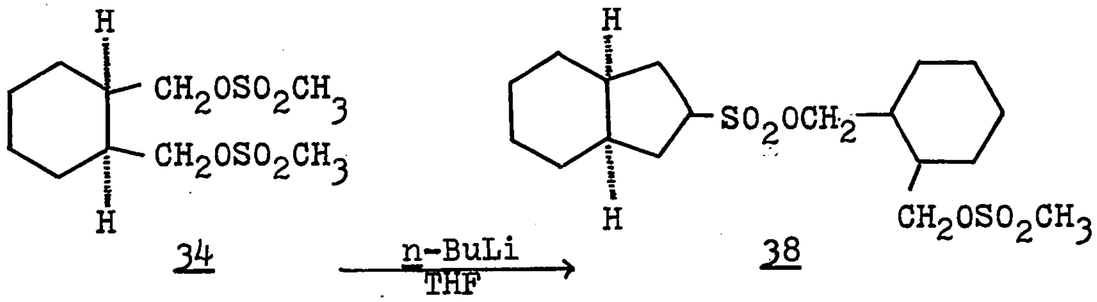
The success achieved in the formation of 5- and 6-membered ring sultones could not be duplicated for the 7- or 8-membered ring species. The failure to obtain 8-membered ring sultones was not completely unexpected because such rings are difficult to obtain via internal displacement reaction (18), but it was surprising that we were unable to obtain even small amounts of 7-membered ring series. Cyclization reactions were attempted with a number of sulfonate esters. The mesylate of 4-chlorobutanol 31 was investigated in greatest detail. The reaction mixture obtained from 31 and *n*-butyllithium was stored at room temperature for 2 days and the crude product was separated by preparative t.l.c.. In addition to significant amounts of starting meterial , 34% of a colorless oil was obtained which was identified by spectroscopic methods (i.r. strong bands at 1330, 1155, and 920 cm^{-1}; n.m.r. absorption at δ= 4.2-4.6 (m, 2H), 3.4-3.9 (m, 3H), and 1.5-2.4 (m, 12H)), and by independent synthesis as 4-chlorobutylcyclopentanesulfonate (32). The alternate synthesis of 32 and its probable mode of formation from 31 by intermolecular displacement and cyclization are shown in the following scheme.



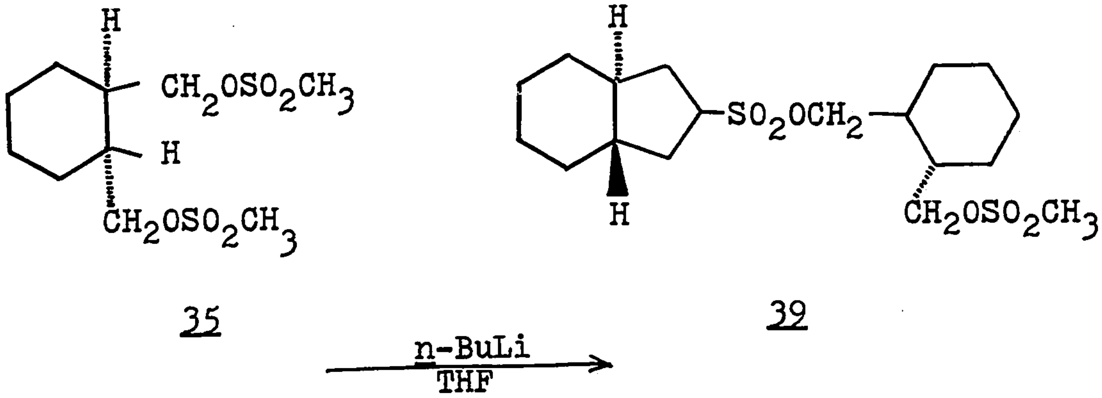
The products from other cyclization attempts were similarly separated and identified. Spectroscopic data in each case indicated that the products were analogous to 32, i.e. an ester of a cyclopentane sulfonic acid. These products which are listed in the following table have not been fully characterized. Available spectroscopic details are given in the Experimental Section.

TABLE III

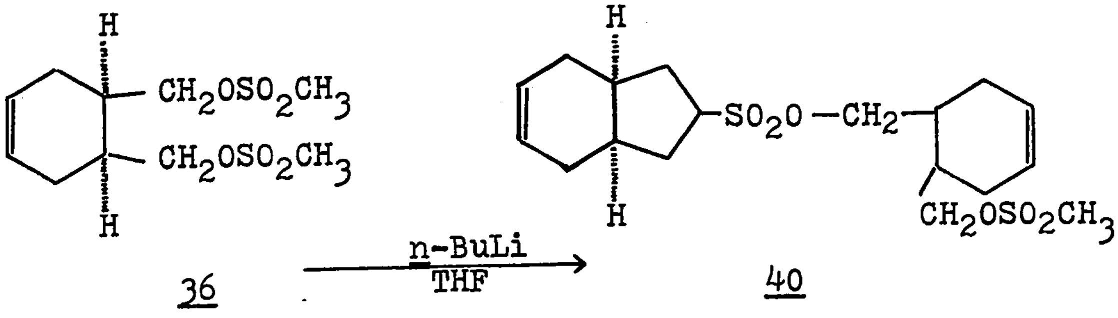
Attempts to Prepare 7-Membered Ring Sultones



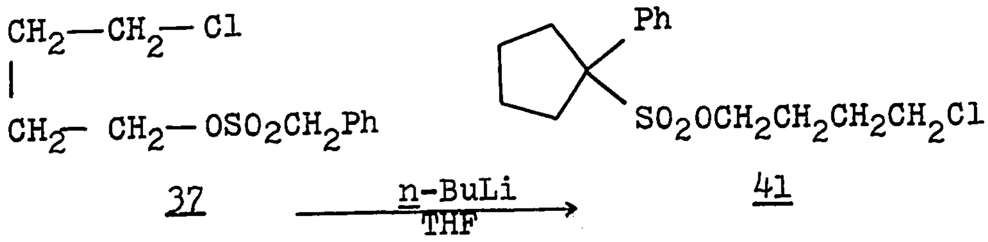
34 → 38



35 → 39

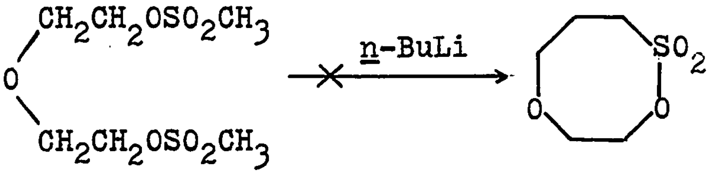


36 → 40



37 → 41

A single attempt to obtain an 8-membered ring sultone from 33 was unsuccessful and starting material was recovered.



33

EXPERIMENTAL

Melting points were determined with a Thomas Hoover apparatus and are not corrected; boiling points are also not corrected. Infrared spectra were recorded on Beckmann IR-8 or IR-20 Spectrophotometers. The n.m.r. spectra were obtained using Varian Associates HA-100 and T-60 Spectrophotometers. The chemical shifts are reported as p.p.m. downfield from internal tetramethylsilane. The mass spectra were recorded using a Hitachi-Perkin-Elmer RMU-6D Spectrometer. [illegible]. The drying of the organic extracts was carried over anhydrous magnesium sulfate. Alumina oxide pH (10-10.5) was supplied by McArthur Chemical Co. Ltd. (Montreal). The silica gel (0.05-0.20 mu) was from E. Merck, [illegible] Darmstadt (Germany). Thin layer chromatography (preparative t.l.c.) was carried out using MN-Kieselgel N/UV$_{254}$ from Machevey, Nagel & Co. (Germany). Methyllithium (1.5 M in ether) and n-butyllithium (1.6 M in hexane) were supplied by the Foote Mineral Co. Sulfuryl chloride was from Eastman Organic Chemicals and used as such except for the chlorination of sulfoxides where freshly distilled sulfuryl chloride was used. Heavy water (99.7% D_2O) was supplied by Atomic Energy of Canada Ltd. Dimethyl sulfoxide-d_6 was supplied by Merck Sharp and Dohme of Canada Ltd. Microanalyses were performed by Scandinavian Microanalytical Laboratories, Denmark; Dr. C. Daessle, Montreal; and National Research Council of Canada, Ottawa. Spectroscopic properties which have already been discussed in other parts of the thesis will not be repeated in the Experimental Section. All infrared and n.m.r. spectra were taken in chloroform and deuterochloroform solution unless otherwise specified. Because of the instablity of some of the new compounds prepared in this work, a number of them were not analyzed. Their structures were determined by n.m.r., i.r., mass spect., and by independent synthesis.

Some of the abbreviations used in this thesis are listed as following: i.r., infrared; n.m.r., nuclear magnetic resonance; t.l.c., thin layer chromatography; THF, tetrahydrofuran; MCPA, *m*-chloroperbenzoic acid; Py, pyridine; D.N.P., 2,4-dinitrophenylhydrazone derivative; MeLi, methyllithium; *n*-BuLi, *n*-butyllithium; M^+, parent molecular ion; *i.e.*, that is; l, liter; *vs*, versus; etc., and so forth.

PART I

Synthesis of Sulfoxides

Two General methods were employed for the oxidation of sulfides to sulfoxides.

a) m-Chloroperbenzoic Acid Oxidation: (MCPA)

To the sulfide (1 equivalent) dissolved in methylene chloride at 0° was added dropwise with stirring to a solution of 1 equivalent of MCPA (Aldrich Chemical, 85% purity) in methylene chloride. A colorless precipitate appeared after addition was complete. The mixture was stirred overnight and then washed with dilute sodium sulfite solution. The organic layer was dried and the solvent evaporated to give crude sulfoxide. Purification was by recrystallization or distillation.

b) Sodium Periodate Oxidation:

To the sulfide (1 equivalent) dissolved in 1:1 MeOH/H_2O at 0° was added dropwise with stirring a solution of 1 equivalent (0.5 Molar) of sodium periodate (44). A white precipitate appeared after addition. The mixture was stirred overnight and extracted with methylene chloride. The organic extracts were dried and the solvents evaporated to give crude sulfoxide. Purification was by recrystallization, distillation or chromatography.

Phenyl Methyl Sulfoxide

Obtained in 81% yield (b.p. $85-89^{\circ}/0.3$mm) by sodium periodate oxidation. The n.m.r. spectrum (CCl_4) showed peaks at δ=2.60 (s, 3H) and 7.38-7.78 (m, 5H). (44)

Phenyl Ethyl Sulfoxide

Obtained in 67% yield (b.p. $92^{\circ}/0.4$mm) by MCPA oxidation. The n.m.r. spectrum (CCl_4) had peaks at δ=1.10 (t, J=8Hz, 3H), 2.4-3.2 (m, 2H) and 7.3-7.7 (m, 5H). (45)

Phenyl Isopropyl Sulfoxide

Obtained in 83% yield by periodate oxidation and purification by column chromatography (basic alumina). The n.m.r. spectrum (CCl_4) had absorption at δ=1.08 (d, J=13Hz, 3H), 1.18 (d, J=14Hz, 3H), 2.72 (septulet, J=7Hz, 1H) and 7.38-7.64 (m, 5H). The sulfoxide bands in the infrared appeared at 1020, 1040 and 1080 cm^{-1}. (46)

n-Butyl Methyl Sulfoxide

Obtained in 60% yield by sodium periodate oxidation, b.p. $55-57^{\circ}/0.3$mm. The n.m.r. spectrum (CCl_4) had peaks at δ=0.78-1.20 (m, 3H), 1.2-2.0 (m, 4H), 2.40 (s, 3H) and 2.4-2.8 (m, 2H). The infrared spectrum (film) had sulfoxide band at 1020 cm^{-1}. (47)

Benzyl Methyl Sulfoxide

Available in these laboratories, m.p. 54-55°. The n.m.r. spectrum ($CDCl_3$) showed peaks at δ=2.42 (s, 3H), 3.98 (q, σ_A=4.05, σ_B=3.91, J=13Hz, 2H) and 7.37 (s, 5H). The sulfoxide showed absorption in the i.r. at 1030 cm^{-1}.(45)

Di-n-butyl Sulfoxide

Available from Aldrich Chemical Company Inc. The n.m.r. spectrum (CCl_4) had absorption at δ=0.8-2.0 (m, 14H) and 2.3-2.8 (m, 4H).

Di-n-propyl Sulfoxide

Available from Aldrich Chemical Co. Inc. The n.m.r. spectrum (CCl_4) had peaks at δ=0.9-1.3 (m, 6H), 1.4-2.2 (m, 4H) and 2.42-2.94 (m, 4H).

Thiane-S-oxide

Obtained by sodium periodate oxidation. The n.m.r. spectrum ($CDCl_3$) had peaks at δ=1.30-2.40 (m, 6H) and 2.40-3.20 (m, 4H). The sulfoxide absorption occurred at 1020 cm^{-1} in the i.r. (44)

α-Chlorination of Sulfoxides with Sulfuryl Chloride

General procedure:

Sulfuryl chloride (1.2 equivalent) was added dropwise to a solution of 1 equivalent sulfoxide in methylene chloride at -78°, 0° or 25° under anhydrous conditions. Thin layer chromatography (ether-pentane) indicated the reaction was generally complete within 15 min; as shown by the appearance of a faster moving spot i.e. α-chloro sulfoxide. The reaction mixture was then poured into a dilute KOH solution and extracted with methylene chloride. The organic layer was washed with water, dried with anhydrous magnesium sulfate and the solvents evaporated to give a crude α-chloro sulfoxide. (generally containing up to 10% sulfone as by-product) The crude product was purified by recrystallization, distillation or column chromatography to give pure α-chloro sulfoxide.

Chloromethyl Phenyl Sulfoxide

Sulfuryl chloride (3.5 mmole) was added to a solution of 420 mg (3 mmole) methyl phenyl sulfoxide in 25 ml methylene chloride at 25°. Column chromatography (basic alumina) elution with 2:1 ether-pentane gave 436 mg (83%) of chloromethyl phenyl sulfoxide. The n.m.r. spectrum ($CDCl_3$) showed peaks at δ=4.40 (s, 2H) and 7.32-7.78 (m, 5H) and was identical with the authentic sample prepared by oxidation of chloromethyl phenyl sulfide.

α-Chloroethyl Phenyl Sulfoxide

Sulfuryl chloride (300 mg) was added to a solution of 278 mg (1.7 mmole) ethyl phenyl sulfoxide at 0°. Column chromatography gave 287 mg (89%) α-chloroethyl phenyl sulfoxide. The n.m.r. spectrum (CCl_4) showed 6:1 mixture of diastereomers, the major isomer had peaks at δ=1.56 (d, J=6.5Hz, 3H), 4.80 (q, J=6.5Hz, 1H) and 7.3-7.8 (m, 5H). The minor isomer had the methyl doublet (J=5Hz) occurred at δ=1.66. (10)

α-Chloro-α-methylethyl Phenyl Sulfoxide

Sulfuryl chloride (9.7 mmole) was added to a mixture of 1.46 g (8.7 mmole) phenyl i-propyl sulfoxide and 4 g CaO in 50 ml methylene chloride at -78°. The crude product was purified by chromatography to give 1.24 g (71%) α-chloro sulfoxide, m.p. 64-65°, (Lit. (10) m.p. 64.5-65.5°). The n.m.r. spectrum ($CDCl_3$) has peaks at δ=1.56 (s, 3H), 1.82 (s, 3H) and 7.40-7.98 (m, 5H). The sulfoxide band occurred at 1035 cm^{-1} in the infrared.

Chlorobenzyl Methyl Sulfoxide (3)

Prepared in 25% yield utilizing 1.0 g (6.7 mmole) benzyl methyl sulfoxide, 3 g CaO, and 8.5 mmole sulfuryl chloride. The crude product was purified by preparative t.l.c.; no chloromethyl benzyl sulfoxide was isolated. The n.m.r. spectrum ($CDCl_3$) showed mixture of diastereomer 3 and had peaks at δ=2.20 and 2.58 (2 singlets, 3H), 5.40 and 5.58 (2 singlets, 1H), and 7.2-7.5 (m, 5H). (8)

α-Chloro-n-butyl Methyl Sulfoxide (8)

To a mixture of 1.47 g (12.2 mmole) n-butyl methyl sulfoxide and 3 g CaO in 35 ml methylene chloride at -78° was added 16 mmole of sulfuryl chloride. The reaction mixture was stirred for 1 hr at -78°. Workup gave 2.01 g crude oil. Column chromatography (basic alumina) gave 1.42 g (75%) α-chloro sulfoxide 8. The n.m.r. spectrum showed the crude contained 1:1 ratio of the diastereomers which were separated on preparative t.l.c. (elution with ether). Each of the diastereomers was shown to be configurationally stable under the reaction conditions. (by stirring each of the diastereomers in HCl saturated methylene chloride for 1/2 hr at -78°) The physical properties of the diastereomers are recorded in TABLE III. The mass spectra of both of the diastereomers have parent molecular ions at m/e = 154 and 156 with the ratio of 3 to 1.

α-Chloro-n-butyl n-Butyl Sulfoxide (11)

Sulfuryl chloride (15 mmole) was added to a mixture of 1.25 g (7.7 mmole) n-butyl sulfoxide and 3 g CaO in 40 ml methylene chloride at -78°. Workup gave 1.87 g crude product which on column chromatography afforded 1.28 g (85%) of α-chloro sulfoxide <u>11</u>. The n.m.r. spectrum (CCl_4) had peaks at δ=0.8-1.2 (m, 6H), 1.2-2.4 (m, 8H), 2.5-3.2 (m, 2H) and 4.4-4.8 (m, 1H). The sulfoxide had absorption at 1048 cm^{-1} in the infrared. (10)

α-Chloro-<u>n</u>-propyl <u>n</u>-Propyl Sulfoxide

Sulfuryl chloride (2.4 mmole) was added to a mixture of 255 mg (1.78 mmole) <u>n</u>-propyl sulfoxide and 1 g CaO in 5 ml methylene chloride. Workup gave 245 mg (77%) of α-chloro-<u>n</u>-propyl <u>n</u>-propyl sulfoxide as diastereomeric mixtures. The n.m.r. spectrum (CCl_4) had peaks at δ=0.85-1.40 (m, 6H), 1.50-3.20 (m, 6H) and 4.35-4.72 (m, 1H). The i.r. had the sulfoxide band at 1045 cm^{-1}. The mass spectrum showed the parent molecular ions at m/e = 168 and 170 in a ratio of 3:1.

α-Chlorothiane-S-oxide

Sulfuryl chloride (5.5 mmole) was added to a mixture of 566 mg (4.79 mmole) thiane-S-oxide and 1 g CaO in 20 ml methylene chloride at -78°. Workup gave 464 mg (64%) of α-chlorothiane-S-oxide. The n.m.r. spectrum had peaks at δ=1.35-2.75 (m, 6H), 2.75-3.3 (m, 2H) and 4.8-5.1 (m, 1H). The sulfoxide absorption occurred at 1060 cm^{-1} in the infrared. The compound was identified by MCPA oxidation to the corresponding α-chloro sulfone (See page 115).

Dichloromethyl Phenyl Sulfoxide (10)

To a solution of 1.55 g (8.8 mm) chloromethyl phenyl sulfoxide at -78°, was added 1.6 g sulfuryl chloride. The reaction mixture was allowed to warm to room temperature overnight. Workup gave 1.32 g (72%) of 10. The n.m.r. spectrum (CCl_4) had peaks at δ=6.36 (s, 1H) and 7.30-7.90 (m, 5H). The i.r. had strong bands at 1070 and 1090 cm^{-1}.(32)

α,α-Dichloro-n-butyl n-Butyl Sulfoxide (12)

Sulfuryl chloride (6.7 mmole) was added to a solution of 1.0 g (5.1 mmole) of α-chloro sulfoxide 11 in 20 ml methylene chloride. T.l.c. showed the reaction was complete in 1/2 hr. Workup gave 828 mg (70%) of dichloro sulfoxide 12. The n.m.r. spectrum (CCl_4) had peaks at δ= 0.82-1.35 (m, 6H), 1.4-2.2 (m, 6H), 2.2 -2.6 (m, 2H) and 3.15 (m, 2H). The i.r. had sulfoxide band at 1090 cm^{-1}.

Anal. Calc'd for $C_8H_{16}OSCl_2$: C, 41.40; H, 6.89. Found: C, 41.94; H, 7.04

Chlorination of Methyl Phenyl Sulfoxide with Chlorine

To a mixture of 1.9 g sulfoxide and 3 g calcium oxide in 35 ml methylene chloride at -78° was added 1 g of chlorine. The reaction mixture was stirred at -78° for 1/2 hr. Workup gave 2.2 g crude product which was shown by n.m.r. to be a mixture of chloromethyl phenyl sulfoxide and the starting material in a ratio of 1:1.

Oxidation of α-Chloro Sulfoxides with m-Chloroperbenzoic Acid (MCPA).

α-Chlorothiane-S,S-dioxide

To a solution of 1.43 g (9.4 mmole) α-chlorothiane-S-oxide in 30 ml methylene chloride at 0° was added 2.1 g MCPA in 50 ml methylene chloride. Workup gave 1.47 g (83%) chloro sulfone as colorless needles, m.p. 74°. (methylene chloride-pentane) The n.m.r. spectrum ($CDCl_3$) had peaks at δ=1.4-2.7 (m, 6H), 2.7-3.5 (m, 2H) and 4.6-4.8 (m, 1H). The i.r. ($CHCl_3$) had strong bands at 1122, 1300, and 1326 cm^{-1}.

Anal. Calc'd for $C_5H_9ClO_2S$: C, 35.61; H, 5.34; Cl, 21.02. Found: C, 36.03; H, 5.50; Cl, 20.59.

α-Chloro-n-butyl n-Butyl Sulfone

MCPA (6.1 g) in 200 ml methylene chloride was added slowly to a solution of 5.6 g chloro sulfoxide 12 in 150 ml methylene chloride at 0°. The reaction mixture was allowed to warm to room temperature for 3 hr. The crude product was recrystallized from methylene chloride-pentane to give 5.1 g (84%) colorless granules m.p. 33-34°. N.m.r. spectrum (CCl_4) had peaks at δ=0.8-1.3 (m, 6H), 1.3-2.5 (m, 8H), 2.96-3.36 (m, 2H), and 4.44-4.80 (m, 1H). The i.r. (CCl_4) showed strong sulfone bands at 1135 and 1320 cm^{-1}.

Anal. Calc'd for $C_8H_{17}ClO_2S$: C, 45.18; H, 8.00;

Cl, 16.71. Found: C, 45.04; H, 8.04; Cl, 16.80.

Preparation of Hydroxy Sulfides

In general, equal amounts of hydroxy halide was added to a solution of 1 equivalent potassium mercaptide in methanol. The reaction mixture was generally stirred overnight at room temperature. Workup accomplished by adding water and extracting with methylene chloride and ether. The organic extracts were dried over magnesium sulfate and the solvents evaporated on a rotor evaporator. The crude colorless oils so obtained were distilled under reduced pressure.

2-Phenylmercaptoethanol (22a)

Prepared in 72% yield from 11 g (0.137 mole) of ethylene chlorohydrin, 15.1 g (0.137 mole) of thiophenol and 8 g KOH, b.p. 99-100°/0.25 mm. Lit. b.p. 136-7°/9 mm (33).

3-Phenylmercaptopropanol (23a)

Prepared in 58% yield from 0.2 mole of 3-bromopropanol, 0.2 mole of thiophenol and 15 g potassium hydroxide, b.p. 114-6°/0.3 mm. Lit. b.p. 134-5°/2 mm (33).

4-Phenylmercaptobutanol (24a)

Prepared in 83% yield from 0.2 mole thiophenol, 12 g KOH and 22 g 4-hydroxybutyl chloride, b.p. 118-120°/

0.3 mm. Reported m.p. 24° (34).

5-Phenylmercaptopentanol (48a)

Prepared in 92% yield from 11 g thiophenol, 12.2 g 5-chloropentanol and 8 g KOH in 150 ml methanol. The product recrystallized from ether-pentane was a colorless powder, m.p. 30-31°. Lit. m.p. 31.5° (34).

6-Phenylmercaptohexanol (49a)

Prepared in 60% yield from 14.1 g thiophenol, 17.5 g 6-chlorohexanol and 9 g KOH, m.p. 41-42°. (ether-pentane) Lit. m.p. 43° (34).

trans-2-Phenylmercaptocyclohexanol (41a)

Cyclohexene oxide 17 g (0.17 mole) was added slowly to a solution of 18.7 g thiophenol and 7.5 g NaOH in 200 ml aqueous methanol. The reaction mixture was stirred overnight and workup accomplished by extracting with methylene chloride, drying and evaporating the solvents under reduced pressure. Vaccum distillation gave 16.5 g (47%) colorless liquid, b.p. 124°/0.3 mm. Reported b.p. 207°/22 mm. (35)

Oxidation of Hydroxy Sulfides to Hydroxy Sulfoxides

Either *m*-chloroperbenzoic acid or sodium periodate was used to oxidize the hydroxy sulfides to sulfoxides. These methods have been described in page 107.

2-Hydroxyethyl Phenyl Sulfoxide (22)

Prepared in 78% yield from 10.2 g of hydroxy sulfide 22a and 14.2 g sodium periodate. The crude product was purified by column chromatography (basic alumina) elution with ether-methylene chloride. The n.m.r. spectrum ($CDCl_3$) had peaks at δ=2.8-3.2 (m, 2H), 3.9-4.3 (m, 2H) 7.4-7.8 (m, 5H) and the OH at 3.4-3.8. The i.r. had strong bands at 1033 and 3360 cm^{-1}.

Anal. Calc'd for $C_8H_{10}O_2S$: C, 56.46; H, 5.92. Found: C, 56.96; H, 5.88.

3-Hydroxypropyl Phenyl Sulfoxide (23)

Obtained in 83% yield by MCPA oxidation of 7.0 g of hydroxy sulfide 23a. The n.m.r. spectrum ($CDCl_3$) had peaks at δ=1.5-2.2 (m, 2H), 2.8-3.17 (m, 2H), 3.65 (t, J=6.2Hz, 2H), 3.76 (s, 1H) and 7.3-7.75 (m, 5H). The i.r. had strong bands at 3380 and 1070 cm^{-1}.

Anal. Calc'd for $C_9H_{12}O_2S$: C, 58.69; H, 6.57. Found: C, 58.19; H, 6.60.

4-Hydroxybutyl Phenyl Sulfoxide (24)

Prepared in 88% yield from 10.3 g of hydroxy sulfide 24a and 11.7 g MCPA. The n.m.r. spectrum ($CDCl_3$) had peaks at δ=1.4-2.1 (m, 4H), 2.65-3.05 (m, 2H), 3.4-3.65 (m, 2H), 3.78 (s, 1H) and 7.4-7.78 (m, 5H). The i.r. had strong bands at 3380 and 1022 cm^{-1}.

Anal. Calc'd for $C_{10}H_{14}O_2S$: C, 60.59; H, 7.12; Found: C, 58.98; H, 7.01.*

5-Hydroxypentyl Phenyl Sulfoxide (48)

Prepared in 82% yield by sodium periodate oxidation with 7.5 g of hydroxy sulfide 48a. The n.m.r. spectrum ($CDCl_3$) had peaks at δ=1.2-2.0 (m, 6H), 2.3-2.65 (broad peak, 1H), 2.65-3.0 (m, 2H), 3.38-3.76 (m, 2H) and 7.3-7.7 (m, 5H). The infrared had strong bands at 3380 and 1024 cm^{-1}.

Anal. Calc'd for $C_{11}H_{16}O_2S$; C, 62.25; H, 7.60. Found: C, 62.04; H, 7.62.

6-Hydroxyhexyl Phenyl Sulfoxide (49)

Prepared in 94% yield from 9.0 g hydroxy sulfide 49a and 9.18 g sodium periodate. The n.m.r. spectrum ($CDCl_3$) had peaks at δ=1.2-2.1 (m, 9H), 2.62-3.0 (m, 2H), 3.4-3.8 (m, 2H) and 7.4-7.8 (m, 5H). The infrared had strong bands at 3400 and 1027 cm^{-1}.

Anal. Calc'd for $C_{12}H_{18}O_2S$: C, 63.70; H, 8.02. Found: C, 63.57; H, 8.02.

trans-2-Phenylsulfinyl cyclohexanol (41)

Obtained in 67% yield from 8.88 g hydroxy sulfide 41a and 8.65 g MCPA, as colorless square plates (methylene

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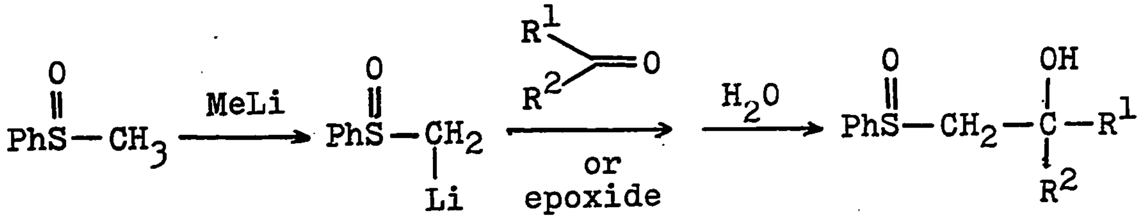
* The carbon analysis is lower than expected due to the hygroscopic nature of the compound.

chloride-ether-pentane) m.p. 155-6°. The n.m.r. spectrum ($CDCl_3$) had peaks at δ=0.9-2.4 (m, 8H), 2.5-3.1 (m, 1H), 3.7-4.3 (m, 1H), 4.7-5.2 (OH peak) and 7.4-7.8 (m, 5H).

Anal. Calc'd for $C_{12}H_{16}O_2S$: C, 64.27; H, 7.19; S, 14.27. Found: C, 64.18; H, 7.15; S, 14.09.

Synthesis of β-Hydroxy Sulfoxides by Metallation and Hydroxyalkylations of Methyl Phenyl Sulfoxide. General procedure:



To a solution of methyl phenyl sulfoxide in tetrahydrofuran (THF) at -78° under nitrogen atmosphere was added dropwise 1.2 equivalents of MeLi (1.5 M in ether; Foote Mineral Co.). The clear yellow solution was stirred for 15 minutes at -78° and then treated with the carbonyl compound (or epoxide), neat if liquid, or as a tetrahydrofuran solution if solid. The reaction mixture was stirred for 30 min and then quenched with water. Extraction, twice with methylene chloride, drying of the extracts and evaporation of the solvents yielded the crude product. Recrystallized from methylene chloride-pentane gave the analytical sample. Yields referred to purified products.

The i.r. spectra of each product (adduct) showed strong intramolecular OH stretching bands from 3600 to 3300 cm^{-1}; the characteristic sulfoxide absorption appeared in the range 1015-1050 cm^{-1} for the various compounds.

Reaction of Lithio Derivative of Methyl Phenyl Sulfoxide with

-Acetone 45

Available in these laboratories, m.p. 116°. Lit. m.p. 117-118° (36). The n.m.r. spectrum ($CDCl_3$) showed peaks at δ=1.40 (s, 3H), 1.60 (s, 3H), 2.92 (q, σ_A=2.80, σ_B=3.02, J=20Hz, 2H), 3.6-4.0 (m, 1H) and 7.4-7.8 (m, 5H).

-Cyclohexanone 46

A solution of 36.6 mmole of the lithio derivative of methyl phenyl sulfoxide and 3.68 g of cyclohexanone gave 6.8 g (77%) of 46 as colorless needles m.p. 95°. The n.m.r. spectrum ($CDCl_3$) had peaks at δ=1.0-2.2 (m, 10H), 2.94 (q, σ_A=2.80, σ_B=3.02, J=18Hz, 2H), 3.86 (s, 1H) and 7.42-7.84 (m, 5H).

Anal. Calc'd for $C_{13}H_{18}O_2S$: C, 65.53; H, 7.61; S, 13.43. Found: C, 65.29; H, 7.60; S, 13.49.

-Benzophenone 47

A solution of 28.4 mmole of the lithio derivative of methyl phenyl sulfoxide and 5.17 g of benzophenone gave 5.6 g

(61%) of 47 as colorless granules, m.p. 145°. N.m.r. spectrum ($CDCl_3$) had peaks at δ=3.6 (s, 2H), 5.78 (s, 1H) and 7.0-7.8 (m, 15H) was in agreement with an authentic sample (37).

-Benzaldehyde 44

A solution of 40 mmole of the lithio derivative of methyl phenyl sulfoxide and 4.25 g of benzaldehyde gave 6.5 g (67%) of 44 as colorless powder, m.p. 127-128°. The n.m.r. spectrum ($CDCl_3$) had peaks at δ=2.7-3.5 (m, 2H), 4.2-4.6(m, 1H), 5.15-5.48 (m, 1H), 7.30 (s, 5H) and 7.4-7.8 (m, 5H).

Anal. Calc'd for $C_{14}H_{14}O_2S$: C, 68.28; H, 5.73. Found: C, 67.77; H, 5.72.

-Cyclohexene oxide 39

To a solution of 15.7 mmole of lithio derivative of methyl phenyl sulfoxide in 35 ml THF at -78° was added 1.5 g of cyclohexene oxide. The reaction mixture was warmed to room temperature and refluxed for 1/2 hr. Workup as usual and purification by preparative t.l.c. gave 265 mg (7%) of 39 as colorless needles, m.p. 95-96°. The n.m.r. spectrum ($CDCl_3$) had peaks at δ=0.9-2.3 (m, 9H), 2.6-3.6 (m, 3H), 3.75 (s, 1H), and 7.4-7.8 (m, 5H). The i.r. spectrum had sulfoxide band at 1015 and broad O-H band at 3100-3600 cm^{-1}.

Anal. Calc'd for $C_{13}H_{18}O_2S$: C, 65.53; H, 7.61; S, 13.43. Found: C, 65.79; H, 7.36; S, 13.52.

Chlorination of Hydroxy Sulfoxides with Sulfuryl Chloride

To a solution of hydroxy sulfoxide in methylene chloride at -78° or 0° under nitrogen atmosphere was added dropwise 1.2 equivalents of sulfuryl chloride. The clear greenish yellow solution was stirred for 30 minutes and then quenched with water. Extraction twice, with methylene chloride, drying of the extracts and evaporation of solvent yielded the crude product (chloro sulfone). Recrystallization from ether-pentane gave pure chloro sulfone. When the crude product was passed through a basic alumina column, the corresponding unsaturated sulfone was generally obtained.

2-Hydroxyethyl Phenyl Sulfoxide (22)

Sulfuryl Chloride (6.9 mmole) was added to a solution of 978 mg (5.75 mmole) of 22 in 25 ml methylene chloride at 0°. Workup gave 1.14 g (95%) 2-chloroethyl sulfone (27) as colorless crystals, m.p. 54-55°; lit. m.p. 54-55° (38). The n.m.r. spectrum ($CDCl_3$) had peaks at δ=3.4-4.0 (m, 4H) and 7.5-8.1 (m, 5H). The i.r. ($CHCl_3$) showed strong sulfone bands at 1337, and 1162 cm^{-1}.

3-Hydroxypropyl Phenyl Sulfoxide (23)

Sulfuryl chloride (5.9 mmole) was added to a solution of 905 mg (4.92 mmole) of <u>23</u> in 25 ml methylene chloride at -78°. Workup gave 1.03 g (96%) of 3-chloropropyl sulfone <u>28</u>. (39) The n.m.r. spectrum ($CHCl_3$) had peaks at δ=1.90-2.44 (m, 2H), 3.08-3.42 (m, 2H), 3.57 (t, J=6Hz, 2H), and 7.42-8.02 (m, 5H). The strong sulfone bands occurred at 1312 and 1158 cm^{-1} in the i.r.

4-Hydroxybutyl Phenyl Sulfoxide (<u>24</u>)

Sulfuryl chloride (6.0 mmole) was added to a solution of 996 mg (5 mmole) of <u>24</u> in 25 ml methylene chloride at -78°. Workup gave 1.01 g (88%) of chloro sulfone <u>29</u> as colorless plates m.p. 56° (39). The n.m.r. spectrum ($CDCl_3$) had peaks at δ=1.70-2.10 (m, 4H), 2.92-3.38 (m, 2H), 3.38-3.67 (m, 2H) and 7.58-8.08 (m, 5H). The i.r. spectrum had strong sulfone absorption at 1305 and 1147 cm^{-1}.

5-Hydroxypentyl Phenyl Sulfoxide (<u>48</u>)

Sulfuryl chloride (3 mmole) was added to a solution of 565 mg (2.66 mmole) of <u>48</u> in 25 ml CH_2Cl_2 at -78°. Workup gave 720 mg of colorless oil which decomposed at room temperature to a black oil. Purification of the crude product was not successful.

6-Hydroxyhexyl Phenyl Sulfoxide (<u>49</u>)

Sulfuryl chloride (9 mmole) was added to a solution of 1.7 g (7.5 mmole) of 49 in 25 ml CH_2Cl_2 at 0°. Workup gave 2.09 g of colorless oil which turned brown on standing at room temperature. Purification by column chromatography gave a colorless oil 50. Spectroscopic properties are recorded on page 37.

trans-Hydroxy Sulfoxide (39)

To a solution of 250 mg (1.05 mmole) sulfoxide 39 in 20 ml methylene chloride at -78° was added 1.26 mmole of sulfuryl chloride. The reaction mixture was stirred for 30 minutes at -78°. Workup gave 303 mg crude product which was purified by preparative t.l.c. (ether-pentane) to give 224 mg (77%) of cis-chloro sulfone 40. The n.m.r. spectrum ($CDCl_3$) had peaks at δ=1.0-2.2 (m, 8H), 2.2-2.7 (m, 1H), 2.8-3.6 (8 line multiplet, J_{gem}=14Hz, J_{vic}=5.8 and 6Hz, 2H), 4.53 (m, 1H) and 7.5-8.1 (m, 5H). The i.r. spectrum ($CHCl_3$) had strong sulfone bands at 1150 and 1307 cm^{-1}. The mass spectrum showed the parent molecular ions at m/e=274 and 272 with a ratio of 1 : 3.

trans-Hydroxy Sulfoxide (41)

Sulfuryl chloride (3.3 mmole) was added to a mixture of 618 mg (2.8 mmole) of sulfoxide 41 in 25 ml methylene chloride at -78°. Workup as usual gave a crude oil (578 mg) containing at least 5 components which have not been separated.

β-Hydroxy Sulfoxide 44

Procedure 1

Sulfuryl chloride (470 mg) (3.5 mmole) was added to a solution of 723 mg (2.94 mmole) sulfoxide 44 in 45 ml methylene chloride at -78°. Usual workup followed by recrystallization (CH_2Cl_2-ether-pentane) gave 642 mg (78%) of β-chloro sulfone 44a as a colorless flaky powder m.p. 86°. The n.m.r. spectrum ($CDCl_3$) had peaks at δ=3.94 (d, J=7Hz, 2H), 5.37 (t, J=7Hz, 1H), 7.25 (s, 5H) and 7.4-7.9 (m, 5H). The i.r. ($CHCl_3$) had strong sulfone bands at 1320 and 1150 cm^{-1}.

Anal. Calc'd for $C_{14}H_{13}ClO_2S$: C, 59.68; H, 4.61. Found: C, 59.97; H, 4.75.

Procedure 2

Sulfuryl chloride (2.2 mmole) and sulfoxide 44 460 mg, 1.87 mmole) gave 463 mg of crude product. This material was eluted through basic alumina column (ether-pentane) to give 363 mg (80%) of α,β-unsaturated sulfone 44b as colorless needles m.p. 63°. The n.m.r. spectrum ($CDCl_3$) had peaks at δ=6.7 (s, 1H), 6.98 (s, 1H) and 7.2-8.1 (m, 10H). The infrared spectrum ($CHCl_3$) had sulfone bands at 1316 and 1153 cm^{-1} (48).

β-Hydroxy Sulfoxide 46

Procedure 1

Sulfuryl chloride (255 mg) was added to a solution of 375 mg (1.57 mmole) of sulfoxide 46 in 10 ml methylene chloride. Workup and purification by preparative t.l.c. gave 310 mg (73%) β-chloro sulfone 46a as colorless needles m.p. 95-97° (ether-pentane). The n.m.r. spectrum ($CDCl_3$) had peaks at δ=1.2-2.4 (m, 10H), 3.65 (s, 2H), and 7.48-8.1 (m, 5H). The i.r. ($CHCl_3$) had sulfone bands 1150 and 1320 cm^{-1}. The mass spectrum showed the parent molecular ions at m/e=272 and 274 with a ratio of 3 : 1.

Procedure 2

Sulfuryl chloride (2.9 mmole) and sulfoxide 46 (2.45 mmole) gave 522 mg (92%) of β,γ-unsaturated sulfone 46b as colorless needles, m.p. 73-74° (ether-pentane). The i.r. ($CHCl_3$) had strong sulfone bands at 1150 and 1303 cm^{-1}. The n.m.r. spectrum ($CDCl_3$) had peaks at δ=1.3-2.3 (m, 8H), 3.62 (s, 2H), 5.4 (s, 1H) and 7.4-8.0 (m, 5H).

Anal. Calc'd for $C_{13}H_{16}O_2S$: C, 66.08; H, 6.83. Found: C, 65.68; H, 6.74.

β-Hydroxy Sulfoxide 45

Procedure 1

Sulfuryl chloride (2.96 mmole) was added to a solution of 350 mg of sulfoxide 45 in 15 ml methylene chloride at -78°. Workup and purification by preparative t.l.c. gave 168 mg (41%) of chloro sulfone 45a as a colorless powder m.p. 45° (reported m.p. 44-45° (36)) and 115 mg (34%) of β,γ-unsaturated sulfone 45b as a colorless liquid. The n.m.r.

spectrum ($CDCl_3$) of 45a had peaks at δ=1.85 (s, 6H), 3.65 (s, 2H) and 7.4-8.1 (m, 5H). The i.r. spectrum (CCl_4) of 46a had sulfone bands at 1148 and 1320 cm^{-1}.

Procedure 2

Sulfuryl chloride (3.9 mmole) and sulfoxide (660 mg) gave 528 mg (81%) of the β,γ-unsaturated sulfone 45b. The n.m.r. spectrum ($CDCl_3$) had peaks at δ=1.85 (s, 3H), 3.8 (s, 2H), 4.75 (s, 1H) 5.50 (m, 1H) and 7.4-8.1 (m, 5H). The infrared spectrum ($CHCl_3$) had sulfone bands at 1150 and 1310 cm^{-1}. The mass spectrum showed the parent molecular ion at m/e=196.

β-Hydroxy Sulfoxide 47

Sulfuryl chloride (1.7 mmole) was added to a solution of 470 mg (1.46 mmole) of sulfoxide 47 in 25 ml methylene chloride at -78°. The mixture was stirred for 15 minutes at low temperature. Workup gave 417 mg (89%) of α,β-unsaturated sulfone 47a as a colorless powder m.p. 105-107°. (41) The n.m.r. spectrum ($CDCl_3$) had peaks at δ=6.84 (s, 1H), and 6.9-7.6 (m, 15H). The i.r. spectrum ($CHCl_3$) had strong bands at 1320, 1164, 1150 and 1096 cm^{-1}.

Bromination of γ-Hydroxy-n-propyl Phenyl Sulfoxide (23) in the presence of Pyridine

Bromine (8.8 mmole) was added to a solution of 1.38 g (7.5 mmole) of sulfoxide 23 and 1.5 g pyridine in

40 ml carbon tetrachloride at 0°. The reaction mixture was yellow in color and a considerable amount of yellow precipitate was formed within an hour. The mixture was allowed to warm to room temperature and stirred for 2 hr. The yellow precipitate was isolated by filtration to give 2.32 g (62%) of 38. Recrystallization from MeOH/H_2O gave the analytical sample, m.p. 137°. The residue was washed with dilute acid and water and extracted with methylene chloride. The extracts were dried and the solvents were evaporated to give 315 mg (16%) of γ-bromo-*n*-propyl phenyl sulfone (37). The mass spectrum of 37 had parent molecular ions at m/e=262 and 264 with a ratio of roughly 1 : 1. (See also page 31 for i.r. and n.m.r. data)

Anal. Calc'd for 38 $C_{14}H_{16}O_2SNBr_3$: C, 33.48; H, 3.21; N, 2.79; S, 6.49; Br, 47.75. Found: C, 33.46; H, 3.19; N, 2.80, S, 6.51; Br, 47.71.

Chlorination of 4-Hydroxy-*n*-butyl Phenyl Sulfide (51)

With 1 Equivalent of Sulfuryl Chloride

Sulfuryl chloride (3.16 mmole) was added to a solution of 521 mg of hydroxy sulfide 51 in 25 ml methylene chloride at -78°. An intermediate formulated as cyclic chloro-oxosulfonium 52 was stable enough to be observed by n.m.r. at room temperature (See page 37). The reaction mixture was stirred for 20 min at -78°. Workup accomplished by adding water, extracting with methylene chloride, drying and evaporating the solvent to give a colorless oil. N.m.r. and t.l.c. behavior showed the product was identical with the authentic sample of 4-hydroxy-n-butyl phenyl sulfoxide (24).

With 2 Equivalents of Sulfuryl Chloride

To a solution of 500 mg (2.74 mmole) of 51 in 25 ml methylene chloride at -78°, was added slowly 7 mmole of sulfuryl chloride. The reaction mixture was stirred for 1 hr at -78° and workup as usual gave 570 mg (88%) colorless crystals, m.p. 56°. The n.m.r. and t.l.c. behavior was identical with the authentic sample of 4-chloro-n-butyl phenyl sulfone (29).

Synthesis of Acid Sulfides

In general, a solution of the appropriate thiol dissolved in methanol containing 2.5 equivalents of potassium hydroxide was added dropwise to a solution of 1 equivalent of halo-acid. A white precipitate appeared immediately. The reaction mixture was stirred overnight and water was added to dissolve the precipitate. Acidifying the solution with hydrochloric acid, extracting with methylene chloride, drying and evaporating the solvents gave the acid sulfide. Recrystallization from CH_2Cl_2-pentane gave the pure sample.

Phenylmercaptoacetic Acid (53a)

Prepared in 68% yield from 19.4 g (0.176 mole) of thiophenyl, 22 g of potassium hydroxide and 16.6 g (0.176 mole) of chloroacetic acid, m.p. 62°. (Lit. m.p. 63.5°) (40) The n.m.r. spectrum ($CDCl_3$) had peaks at δ=3.61 (s, 2H), 7.1-7.6 (m, 5H) and 9.24 (s, 1H).

Phenylmercaptopropionic Acid (54a)

Prepared in 42% yield from 3-chloropropionic acid, thiophenol and KOH, m.p. 60° (Lit. m.p. 60-61°) (31). The n.m.r. spectrum ($CDCl_3$) had peaks at δ=2.4-2.8 (m, 2H), 2.9-3.3 (m, 2H), 7.1-7.5 (m, 5H) and 11.0 (s, 1H).

Phenylmercaptobutyric Acid (55a)

Prepared from thiophenol, 4-chlorobutyric acid and potassium hydroxide, m.p. 68° (Lit. (42) m.p. 68-69°). The n.m.r. spectrum ($CDCl_3$) had peaks at δ=1.65-2.2 (m, 2H), 2.35-2.7 (m, 2H), 2.97 (t, J=7Hz, 2H), 7.1-7.5 (m, 5H) and 11.5 (s, 1H).

o-Methylmercaptobenzoic Acid (62a)

Obtained in 53% yield from 11.2 g of methyl iodide, 12 g of *o*-mercaptobenzoic acid and 10 g potassium hydroxide, m.p. 169° (Lit. (43) m.p. 168-169°). The n.m.r. spectrum ($CDCl_3$) had peaks at δ=2.42 (s, 3H), 7.0-7.6 (m, 3H), 7.95-8.2 (m, 1H) and 9.46 (s, 1H).

Synthesis of Acid Sulfoxides

To the acid sulfide dissolved in aqueous methanol at 0° was added dropwise with stirring a solution of 1 equivalent of sodium periodate in water. The mixture was stirred overnight and then extracted with methylene chloride. The organic layer was dried and the solvents evaporated to give the crude acid sulfoxide. Purification by recrystallization from methylene chloride-pentane gave the pure acid sulfoxide.

2-Phenylsulfinylacetic Acid (53)

Obtained in 81% yield from 10 g of 53a and 12.6 g of sodium periodate, as colorless needles m.p. 118°(Lit. (44) m.p. 118-119°). The n.m.r. spectrum ($CDCl_3$) had peaks at δ=3.82 (s, 2H), 7.4-7.8 (m, 5H), and 9.5 (s,1H).

3-Phenylsulfinylpropionic Acid (54)

Prepared in 90% yield from 6.0 g of 54a and 7.1 g of sodium periodate, as colorless crystals m.p. 98° (Lit. (31) m.p. 97-99°). The n.m.r. spectrum ($CDCl_3$) had peaks at δ=2.2-2.98 (m, 2H), 3.0-3.6 (m, 2H), 7.4-7.8 (m, 5H) and 10.92 (s, 1H).

4-Phenylsulfinylbutyric Acid (55)

Prepared in 79% yield from 1.4 g of 55a and 1.53 g of sodium periodate, m.p. 122-124°, colorless granules. The n.m.r. spectrum ($CDCl_3$) had peaks at δ=1.7-2.3 (m, 2H), 2.3-2.7 (m, 2H), 2.92 (t, J=7.5 Hz, 2H), 7.3-7.7 (m, 5H) and 9.35 (s, 1H).

Anal. Calc'd for $C_{10}H_{12}O_3S$: C, 56.60; H, 5.70. Found: C, 56.39; H, 5.70.

o-Methylsulfinylbenzoic Acid (62)

Prepared in 48% yield from 6.0 g of 62a and 7.64 g of sodium periodate, m.p. 173-174° (Lit. (43) m.p. 178-180°) The n.m.r. spectrum ($CDCl_3$) had absorption at δ=2.94 (s, 3H) and 7.4-8.4 (m, 5H).

Chlorination of Acid Sulfoxides with Sulfuryl Chloride

Phenylsulfinylacetic Acid (53)

Sulfuryl chloride (3.5 mmole) was added to a heterogeneous mixture of 595 mg (3.2 mmole) of acid sulfoxide 53 in 25 ml methylene chloride at -78°. The reaction was complete in 1/2 hr as indicated by the formation of colorless fine powder. The solvents were evaporated under reduced pressure to give 670 mg (97%) a mixture of the distereomeric α-chloro sulfoxide acid 57. Recrystallization from methylene chloride-pentane gave the major isomer as a colorless powder m.p. 93-95°. (See page 41 for n.m.r. and i.r. data)

Anal. Calc'd for $C_8H_7ClO_3S$: C, 43.96; H, 3.20. Found: C, 44.61; H, 3.63.

3-Phenylsulfinylpropionic Acid (54)

Sulfuryl Chloride (5 mmole) was added to a mixture of 905 mg (4.6 mmole) of acid sulfoxide 54 in 20 ml methylene chloride at -78°. Workup by evaporating the solvents under reduced pressure and recrystallization from ether-pentane gave 882 mg (83%) 2-phenylsulfonylpropionyl chloride (60) as a colorless powder m.p. 68-70°. Hydrolysis of 60 gave the corresponding acid sulfone as a colorless powder, m.p. 124-126° (31). (See also page 39-40)

4-Phenylsulfinylbutyric Acid (55)

Sulfuryl chloride (3.5 mmole) was added to a mixture of 610 mg (2.88 mmole) of acid sulfoxide 55 in 20 ml methylene chloride at -78°. The reaction mixture was allowed to warm to room temperature for 30 minutes and the solvents were evaporated under vaccum. The crude solid product was recrystallized from CH_2Cl_2-ether-pentane to give 587 mg (83%) α-chloro sulfoxide acid 58, as a colorless powder m.p. 111°. (See also page 40-41)

Anal. Calc'd for $C_{10}H_{11}ClO_3S$: C, 48.68; H, 4.49; Cl, 14.38; S, 12.90. Found: C, 48.49; H, 4.52; Cl, 14.54; S, 12.90.

o-Methylsulfinylbenzoic Acid (62)

Sulfuryl chloride (5.4 mmole) was added to a heterogeneous mixture of 827 mg of acid sulfoxide 62 in

25 ml methylene chloride at 25°. The reaction proceeded as indicated by the disappearing of the solid acid sulfoxide. The mixture was stirred for an hour and followed by evaporating the solvent under vaccum to give 1.0 g, a quantitative yield of o-methylsulfonylbenzoyl chloride (64) as colorless needles m.p. 60°. (See page 40 for i.r. and n.m.r.) Hydrolysis of 64 gave the corresponding o-methylsulfonylbenzoic acid as colorless needles m.p. 130-132°(ether-pentane) (49).

3-Phenylmercaptopropionamide (65a)

3-Chloropropionamide 0.1 mole was added to a mixture of 11 g (0.1 mole) of thiophenol and 7 g of potassium hydroxide in 150 ml methanol. The reaction mixture was stirred overnight at room temperature. The usual workup afforded a crude colorless solid. Recrystallization from ether-pentane gave 16.7 g (92%) colorless flaky plates, m.p. 114°. The n.m.r. spectrum ($CDCl_3$) had peaks at δ=2.5 (t, J=7Hz, 2H), 3.2 (t, J=7Hz, 2H), 5.2-6.2 (broad peak, 2H) and 7.1-7.38 (m, 5H). The i.r. spectrum ($CHCl_3$) had characteristic bands at 3540, 3510 (free N-H), 3420 (bonded N-H), 1680 (amide I) and 1590 cm^{-1} (amide II).

Anal. Calc'd for $C_9H_{11}NOS$: C, 59.67; H, 6.08. Found: C, 59.66; H, 6.10.

3-Phenylsulfinylpropionamide (65)

To the amide sulfide 65a (7.1 g) dissolved in 250 ml methylene chloride at 0° was added with stirring a solution of 7.9 g m-chloroperbenzoic acid in methylene chloride. The reaction mixture was stirred overnight and then washed with saturated sodium carbonate solution. The organic layer was dried and the solvent evaporated to give 1.01 g amide sulfoxide 65 as a colorless powder, m.p. 132-3°. The n.m.r. spectrum ($CDCl_3$) had peaks at δ=2.1-3.5 (m, 4H), 5.4-6.5 (broad peak, 2H), and 7.3-7.65 (m, 5H). The i.r. spectrum had sulfoxide band at 1135 cm^{-1} and amide bands at 1682 and 1595 cm^{-1}.

Anal. Calc'd for $C_9H_{11}NO_2S$: C, 54.82; H, 5.55. Found: C, 54.56; H, 5.55.

Reaction of Amide Sulfoxide 65 with Sulfuryl Chloride

Sulfuryl chloride(257 mg)was added to a heterogeneous mixture of 318 mg of amide sulfoxide 65 in 20 ml methylene chloride at -78°. The reaction mixture was stirred at -78° for 2 hr and then washed with saturated sodium carbonate solution and extracted with methylene chloride. The organic layer was dried and the solvent evaporated to give 298 mg (95%) of sulfonyl nitrile 67 as colorless plates m.p. 92° (methylene chloride-pentane).

Anal. Calc'd for $C_9H_9NO_2S$: C, 55.38; H, 4.60. Found: C, 55.19; H, 4.64.

PART II

Reaction of α-Chloro Sulfoxides and Sulfones with Alkyllithiums Followed by Addition of Carbonyl Compounds.

General Procedure:

To a rapidly stirred solution of α-chloro sulfoxide (or sulfone) in dry tetrahydrofuran (THF) at -78° under nitrogen atmosphere was added dropwise 1.2 equivalents of methyllithium (1.5 M in ether) or n-butyllithium (1.6 M in hexane). The clear bright yellow or greenish yellow solution was stirred for 15 minutes at -78° and then treated with the carbonyl compound, neat if liquid, or as a tetrahydrofuran solution if solid. The reaction mixture was stirred for 30 minutes at low temperature and water was then added to quench the reaction. Extraction, twice with 100 ml of methylene chloride, drying and evaporation of solvents yielded the crude products. The products were purified by recrystallization or column chromatography.

α-Chloroethyl Phenyl Sulfoxide (3)

1. with Cyclohexanone

MeLi (14.2 mmole) was added to a solution of 2.22 g (11.88 mmole) of sulfoxide 3 in 50 ml of THF at -78°. The yellow colored reaction mixture was stirred for 15 minutes after which time was added 1.77 g of cyclohexanone. Workup gave a crude colorless solid (3.57 g). Fractional recrystallization from methylene chloride-pentane gave the chlorohydrin sulfoxide 4 (1.53 g, 45%) as colorless plates m.p. 163-164°. (See TABLE I for i.r. and n.m.r. data)

Anal. Calc'd for $C_{14}H_{19}ClO_2S$: C, 58.64; H, 6.63. Found: C, 58.52; H, 6.79.

From the mother liquor was obtained on recrystallization from ether-pentane the hydroxy sulfoxide 5 (1.55 g, 55%) as colorless needles m.p. 95°, identical with that of the sample described on page 121.

2. with Acetone

To a solution of the lithio sulfoxides prepared from 3.1 g (16.5 mmole) of sulfoxide 3 and 19.8 mmole MeLi was added excess acetone. Workup gave 2.67 g of colorless solid. Column chromatography (basic alumina) afforded on elution with ether-pentane initially the chlorohydrin sulfoxide 6 (1.36 g, 34%) as a colorless powder, m.p. 105-107°. The mass spectrum showed the parent molecular ions at m/e = 246 and 248 in a ratio of 3 : 1. (See TABLE I for i.r. and n.m.r. data)

Further elution with increasing proportions of ether in pentane gave 0.58 g (18%) of the hydroxy sulfoxide 7, m.p. 116°, identical with that of the sample described on page 121.

3. with Benzophenone

Benzophenone (2.35 g) in 15 ml of THF was added to a solution of the lithio sulfoxides obtained by reacting 15.7 mmole of MeLi and 2.47 g (13.1 mmole) of α-chloroethyl phenyl sulfoxide. Column chromatography (basic alumina) of the crude product afforded on elution with ether-pentane initially the epoxy sulfoxide 8 (2.73 g, 69%) as a colorless oil which was not analyzed. The mass spectrum showed the parent molecular ion at m/e = 334. The infrared (CCl_4) had bands at 3060, 1442, 1078, 1098 and 690 cm^{-1}. (See TABLE III for n.m.r. data)

Further elution with increasing proportions of ether in pentane gave 1.33 g (31%) of the hydroxy sulfoxide 9, m.p. 145°, identical with that of the hydroxy sulfoxide described on page 121-122.

α-Chloro-n-butyl n-Butyl Sulfoxide (10)

1. with Cyclohexanone

MeLi (3.36 mmole) was added to a solution of 550 mg (2.8 mmole) of sulfoxide 10 in 15 ml THF at -78°. The reaction mixture was stirred for 15 minutes and then 294 mg (3.0 mmole) of cyclohexanone was added. Workup gave 843 mg of crude product. Purification by column chromatography (basic alumina) gave on elution with ether-pentane 585 mg (71%) of the chlorohydrin sulfoxide 11, as a colorless powder, m.p. 88-90° (ether-pentane). (See TABLE I for i.r. and n.m.r. data)

Anal. Calc'd for $C_{14}H_{27}ClO_2S$: C, 57.06; H, 9.17. Found: C, 57.21; H, 9.25.

Further elution with increasing proportions of ether in pentane gave 107 mg (14%) of the hydroxy sulfoxide 12 as a colorless powder, m.p. 59-60° (ether-pentane). The mass spectrum showed the parent molecular ion at m/e = 218. The n.m.r spectrum ($CDCl_3$) had peaks at δ=0.8-1.2 (m, 3H), 1.2-2.05 (m, 14H), 2.56-3.03 (m, 4H) and 3.74 (s, 1H). The infrared spectrum ($CHCl_3$) showed strong bands at 3430, 2982, 2948, 1450 and 1008 cm^{-1}.

2. with Acetone

MeLi (24.6 mmole) was added to a solution of 4.03 g (20.2 mmole) of α-chloro sulfoxide 10 in 70 ml THF at -78°. Addition of excess acetone (4 ml) followed by usual workup gave 4.1 g (66%) of the chlorohydrin sulfoxide 13 as a colorless oil which was not analyzed. The n.m.r. and i.r. data given in TABLE I are in agreement with its designated structure. The mass spectrum showed the parent molecular ions at m/e = 254 and 256 with a ratio of 3 : 1.

3. with Benzophenone

MeLi (15.8 mmole) was added slowly to a solution of 2.61 g (13.5 mmole) of chlorosulfoxide 10 in 50 ml THF at -78°. Addition of benzophenone (2.35 g) followed by the usual workup and column chromatography (basic alumina) gave on elution with ether-pentane 1.82 g (34%) of the α,β-epoxy-sulfoxide 14 as a colorless powder, m.p. 74-75° (ether-pentane). The infrared spectrum ($CHCl_3$) had strong bands at 2980, 2965, 1448 and 1024 cm^{-1}. (See TABLE III for n.m.r.)

Anal. Calc'd for $C_{21}H_{26}O_2S$: C, 73.66; H, 7.66. Found: C, 73.63; H, 7.46.

Further elution with increasing proportions of more ether in pentane gave 520 mg (11%) of the hydroxy sulfoxide 15 as colorless needles, m.p. 118-120° (28). The infrared spectrum ($CHCl_3$) had strong bands at 3370, 2992, 2942, 1448, 1110 and 1005 cm^{-1}. The n. m.r. spectrum ($CDCl_3$) had peaks at δ=0.7-1.05 (m, 3H), 1.05-1.95 (m, 4H), 2.54-2.82 (m, 2H), 3.52 (q, σ_A=3.39, σ_B=3.65, J=15.5Hz, 2H), 5.7 (s, 1H) and 7.15-7.64 (m, 10H). The infrared spectrum ($CHCl_3$) had strong bands at 3370, 2992, 2942, 1448, 1110 and 1005 cm^{-1}.

α-Chloromethyl Methyl Sulfoxide (16)

1. with Cyclohexanone

n-Butyllithium (9.2 mmole) was added to a solution of 867 mg (7.7 mmole) of the sulfoxide 16 in 35 ml THF at -78°. The mixture was stirred for 30 minutes and then 830 mg of cyclohexanone was added. Usual workup gave 1.36 g of a crude yellow oil. Recrystallization from ether-pentane gave 238 mg (15%) of a colorless powder, m.p. 144-146°. (See TABLE I for n.m.r. and i.r. data)

Anal. Calc'd for $C_8H_{15}ClO_2S$: C, 45.60; H, 7.18; Cl, 16.83; S, 15.22. Found: C, 45.73; H, 7.23; Cl, 16.80; S, 15.05.

2. with Benzophenone

Benzophenone (1.31 g) was added to a solution of the lithio sulfoxide obtained by reacting 8.3 mmole of n-BuLi and 807 mg of sulfoxide 16. Usual workup followed by recrystallization from ether-pentane gave 345 mg (17%) of the epoxy sulfoxide 18 as colorless hard crystals m.p. 102.5-104°. The infrared spectrum ($CHCl_3$) showed bands at 3042, 2985, 1440, 1160 and 1035 cm^{-1}. The n.m.r. spectrum ($CDCl_3$) showed peaks at δ=2.58 (s, 3H), 4.60 (s, 1H), and 7.38-7.44 (m, 10H). The mass spectrum showed the parent molecular ion at m/e = 258.

α-Chloromethyl Methyl Sulfone (19)

1. with Cyclohexanone

To a solution of the lithio sulfone prepared from 722 mg of sulfone 19 and 6.5 mmole MeLi was added 555 mg cyclohexanone. Workup gave 1.15 g crude oil. Recrystallization from ether-pentane gave 990 mg (78%) of the chlorohydrin sulfone 21 as colorless flaky plates, m.p. 73-74°. Spectroscopic properties in agreement with the structure are reported in TABLE I. The mass spectrum showed the parent molecular ions at m/e = 226 and 228 in a ratio of 3 : 1.

2. with Benzophenone

Benzophenone (5.5 mmole) in 10 ml THF was added to a solution of lithio sulfone obtained by reacting 7.0 mmole of MeLi and 5.68 mmole of sulfone 19. Usual workup followed by recrystallization from ether-pentane gave 892 mg (52%) of the chlorohydrin sulfone 20 as colorless solid granules, m.p.

120-122°. The mass spectrum showed the parent molecular ions at m/e = 310 and 312 in a ratio of 3 : 1.

Reaction of α-Chloro-β-hydroxy Sulfoxides and Sulfones with Base.

General Procedure:

The chlorohydrin sulfoxide (or sulfone) was dissolved in a solution of 10% potassium hydroxide in methanol. The reaction mixture was generally stirred at room temperature for 30 to 60 minutes and then diluted with water. Workup accomplished by extracting with methylene chloride, drying and evaporating the solvents. The n.m.r. data of the α,β-epoxy sulfoxides and sulfones thus prepared are reported in TABLE III and V.

Chlorohydrin Sulfoxide 4

Sulfoxide 4 (127 mg) was dissolved in 5 ml of methanolic KOH. Workup gave 109 mg (99%) of the epoxy sulfoxide 42 as colorless granules, m.p. 60-62° (CH_2Cl_2-pentane). The n.m.r. and i.r. data are reported in page 65.

Anal. Cal'd for $C_{14}H_{18}O_2S$: C, 67.18; H, 7.25. Found: C, 67.05; H, 7.32.

Chlorohydrin Sulfoxide 6

Sulfoxide 6 (630 mg) was dissolved in 50 ml of methanolic KOH. The reaction mixture was stirred for 1/2 hr at room temperature. Workup gave 514 mg (96%) of the epoxide 41 as a colorless oil. The infrared spectrum ($CHCl_3$) showed absorption at 3010, 1387, 1108, 1090 and 1040 cm^{-1}. The mass spectrum showed the parent molecular ion at m/e = 210.

Chlorohydrin Sulfoxide 11

Sulfoxide 11 (388 mg) was dissolved in 10 ml of methanolic KOH. Workup gave 304 mg (92%) of the epoxy sulfoxide 43 as a colorless liquid. The infrared spectrum ($CHCl_3$) had bands at 2990, 1458, 1380 and 1025 cm^{-1}. The mass spectrum showed the parent molecular ion at m/e = 218.

Chlorohydrin Sulfoxide 17

Sulfoxide 17 (169 mg) was dissolved in 20 ml of methanolic KOH solution and stirred for an hour at room temperature. Workup gave 133 mg (96%) of the epoxy sulfoxide 44 as a colorless oil. The infrared ($CHCl_3$) showed the sulfoxide band at 1035 cm^{-1}. α,β-Epoxy sulfoxide 44 was identified by m-chloroperbenzoic acid oxidation to the corresponding epoxy sulfone 49.

Chlorohydrin Sulfone 21

Sulfone 21 (176 mg) was dissolved in 20 ml of methanolic KOH solution and stirred for an hour. Workup gave 138 mg (94%) of the epoxy sulfone 49 as a colorless liquid. N.m.r. peaks ($CDCl_3$) occurred at δ=1.38-2.32 (m, 10H), 3.02 (s, 3H) and 3.86 (s, 1H) was identical with those obtained from the oxidation of epoxy sulfoxide 44. The infrared ($CHCl_3$) had sulfone bands at 1145 and 1320 cm^{-1}.

Chlorohydrin Sulfone 45

Sulfone 45 (355 mg) was dissolved in a solution of 2 g KOH in 10 ml methanol. Usual workup gave a crude colorless solid (228 mg). The n.m.r. spectrum showed the crude product was a 9 : 1 mixture of chloromethyl phenyl sulfone and α,β-epoxy sulfone 47.

Chlorohydrin Sulfone 46

Sulfone 46 (206 mg) was dissolved in a solution of 2.5 g KOH in 10 ml methanol. Workup gave a crude solid (152 mg). The n.m.r. spectrum showed the crude product was a 6 : 4 mixture of chloromethyl phenyl sulfone and epoxy sulfone 48.

Oxidation of α,β-Epoxy Sulfoxides to α,β-Epoxy Sulfones with m-Chloroperbenzoic Acid. (MCPA)

To a solution of α,β-epoxy sulfoxide in methylene chloride at 0° was added dropwise excess amount of MCPA in methylene chloride. The reaction mixture was allowed to warm to room temperature and stirred overnight. Workup was accomplished by washing with 5% sodium carbonate solution, drying and evaporating the solvents. (See TABLE V for n.m.r. data of these α,β-epoxy sulfones)

Epoxy Sulfone 47

Epoxy sulfoxide 47a (1) (24.8 mmole) was oxidized with 5.24 g of MCPA in 100 ml of methylene chloride. Workup gave 5.29 g (95%) of α,β-epoxy sulfone as colorless granules m.p. 72-74° (ether-pentane). The infrared ($CHCl_3$) had strong sulfone bands at 1145 and 1305 cm^{-1}.

Anal. Calc'd for $C_{10}H_{12}O_3S$: C, 56.60; H, 5.70. Found: C, 56.83; H, 5.56.

Epoxy Sulfone 48

Epoxy sulfoxide 48a (1) (200 mg) was oxidized with 195 mg of MCPA to give 202 mg (93%) of epoxy sulfone 48 as a colorless powder m.p. 56° (ether-pentane). The infrared ($CHCl_3$) had strong sulfone bands at 1152 and 1324 cm^{-1}.

Anal. Calc'd for $C_{13}H_{16}O_3S$: C, 61.89; H, 6.39. Found: C, 62.51; H, 6.53.

Epoxy Sulfone 49

Epoxy sulfoxide 44 (133 mg) was oxidized with 180 mg of MCPA to give 104 mg (72%) of epoxy sulfone 49 as a colorless oil. N.m.r. peaks ($CDCl_3$) occurred at δ=1.38-2.32 (m, 10H), 3.02 (s, 3H) and 3.86 (s, 1H) was identical with that obtained from the base treatment of the halohydrin sulfone 21.

Treatment of Halohydrin Sulfoxide 50 with Base

Sulfoxide 50 (180 mg) was added to a mixture of 15 ml water, 5 ml methanol and 1 g potassium hydroxide. The reaction mixture was warmed to affect solution and then allowed to cool. The colorless needles which precipitated were filtered and dried. Yield 134 mg (95%) of benzhydryl phenyl sulfoxide (51) m.p. 132-133° (methylene chloride-pentane). Major bands in the infrared ($CHCl_3$) were at 1085 and 1045 cm^{-1}. The n.m.r. spectrum ($CDCl_3$) showed peaks at δ=4.81 (s, 1H), and 7.2-7.45 (m, 15H).

Anal. Calc'd for $C_{19}H_{16}OS$: C, 78.06; H, 5.52; S, 10.96. Found: C, 77.63; H, 5.52; S, 10.80.

Thermal Rearrangement of Epoxy Sulfone 47

Epoxy sulfone 47 (203 mg) was heated to 130° for 15 minutes under nitrogen atmosphere. The resultant dark brown oil was separated by preparative t.l.c. (elution with ether-pentane) to give 78 mg (38%) of the aldehyde sulfone 58, as colorless needles, m.p. 100.5-101.5° (ether-pentane). N.m.r. and i.r. data are reported on page 73-74.

Anal. Calc'd for $C_{10}H_{12}O_3S$: C, 56.60; H, 5.70; S, 15.08. Found: C, 56.36; H, 5.69; S, 14.91.

Acid-Catalyzed Rearrangement of Epoxy Sulfone 47

To a solution of 122 mg of epoxy sulfone 47 in 25 ml ether was added 0.2 ml of BF_3 etherate. The reaction mixture was stirred for 15 minutes at room temperature. Workup was accomplished by washing with 5% potassium bicarbonate solution, extraction with methylene chloride, drying and evaporating the solvents. The yield of the aldehyde sulfone 58 was 88 mg (72%). N.m.r. ($CDCl_3$) peaks occurred at δ=1.46 (s, 6H), 7.6-8.1 (m, 5H) and 9.8 (s,1H) was identical with that of the aldehyde sulfone obtained from the thermal rearrangement of epoxy sulfone 47.

Treatment of Aldehyde Sulfone 58 with Base

Aldehyde sulfone 58 (48 mg) was dissolved in 25 ml of 5% KOH in methanol. The reaction mixture was stirred overnight at room temperature. Usual workup gave 39 mg (93%) of the phenyl *i*-propyl sulfone (29). The n.m.r. spectrum (CCl_4) had peaks at δ=1.23 (d, J=7Hz, 6H), 3.10 (septulet, J=7Hz, 1H) and 7.5-8.0 (m, 10H). The infrared spectrum ($CHCl_3$) had strong sulfone bands at 1300 and 1140 cm^{-1}.

Acid-Catalyzed Rearrangement of Epoxy Sulfoxide 39

To a solution of 416 mg of sulfoxide 39 in 20 ml of ether was added 0.45 ml of $BF_3\cdot$etherate. The reaction mixture was allowed to stir at room temperature for 2 hours. Workup was accomplished by washing with saturated salt solution, extracting with methylene chloride, drying and evaporating the solvents. The crude product was separated by preparative t.l.c. (ether-pentane) to give

149 mg (36%) of the aldehyde sulfoxide 61 as a colorless oil. The n.m.r. spectrum (CCl_4) had peaks at δ=0.7-2.4 (m, 10H), 7.4-7.6 (m, 5H) and 9.36 (s, 1H). The infrared spectrum (CCl_4) had strong bands at 2960, 1700, 1435, 1075, 1045 and 1030 cm^{-1}. m-Chloroperbenzoic acid oxidation of aldehyde sulfoxide 61 gave the corresponding aldehyde sulfone 63 which was identical with that obtained from the rearrangement of epoxy sulfone 48.

Thermal Decomposition of Epoxy Sulfoxide 39

The experiment was carried out by heating 822 mg (3.48 mmole) of epoxy sulfoxide 39 in a micro-distillation apparatus. The sulfoxide decomposed at about 190°and Δ-1-cyclohexene carboxaldehyde (62) (260 mg, 68%) was collected as a colorless oil. The n.m.r. spectrum ($CDCl_3$) had peaks at δ=1.4-2.0 (m, 4H), 2.0-2.58 (m, 4H), 6.7-6.95 (m, 1H) and 9.48 (s, 1H). The infrared spectrum (neat) had strong bands at 2970, 1685, 1645 and 1180 cm^{-1}. The 2,4-dinitrophenylhydrazone of aldehyde 62 was obtained as red needles, m.p. 213-216° (reported m.p. 213-214°) (30).

Acid-Catalyzed Rearrangement of Epoxy Sulfone 48

To a solution of 300 mg of epoxy sulfone 48 in 25 ml of ether was added 0.4 ml of boron trifluoride etherate. No reaction was observed after stirring at room temperature for one hour. The reaction mixture was then refluxed for one hour and worked up in the usual manner. The crude product was separated by preparative t.l.c. to give 102 mg (34%) of aldehyde sulfone 63 as colorless plates, m.p. 66-67.5° (ether-pentane). The n.m.r. spectrum ($CDCl_3$) had peaks δ=0.7-2.5 (m, 10H), 7.3-7.9 (m, 5H) and 9.67 (s, 1H). The infrared spectrum ($CHCl_3$) showed strong sulfone bands at 1142 and 1310 cm^{-1} and the aldehyde band at 1717 cm^{-1}.

Anal. Calc'd for $C_{13}H_{16}O_3S$: C, 61.89; H, 6.39; S, 12.68. Found: C, 61.82; H, 6.40; S, 12.68.

The crude n.m.r. spectrum had peaks in addition to those due to 63. These were a multiplet at δ=6.7-6.9 and a singlet at 9.48; thus showing that the unsaturated aldehyde 62 was also formed in this reaction.

Metallation of Thiane-S,S-dioxide and Addition of Benzophenone

MeLi (15 mmole) was added to a solution of 1.53 g of thiane-S,S-dioxide in 60 ml dry tetrahydrofuran at -78°. Benzophenone (2.34 g), in 20 ml of tetrahydrofuran, was added after 15 minutes and the reaction mixture was stored at -20° overnight. The crude product, obtained by the usual workup, was recrystallized from ether-pentane and gave 3.24 g (90%) of the adduct 67a as colorless fluffy plates m.p. 112-114°. The n.m.r. spectrum ($CDCl_3$) had peaks at δ=1.0-2.5 (m, 6H), 2.8-3.17 (m, 2H), 3.90-4.34 (m, 1H), 4.64 (s, 1H) and 7.0-7.75 (m, 10H). The infrared spectrum ($CHCl_3$) had strong bands at 3235, 1310, 1280, 1120 and 890 cm^{-1}.

Anal. Calc'd for $C_{18}H_{20}O_3S$: C, 68.34; H, 6.37. Found: C, 68.85; H, 6.04.

Dehydration of the Benzophenone Adduct of Thiane-S,S-dioxide 67a

A solution of 1.53 g of 67a and 150 mg of *p*-toluenesulfonic acid in 50 ml of benzene was refluxed overnight. Workup gave 1.42 g (98%) of the unsaturated sulfone 67 as a colorless powder, m.p. 207° (methylene chloride-pentane). The n.m.r. spectrum ($CDCl_3$) had peaks at δ=1.42-2.52 (m, 4H), 2.62-2.98 (m, 2H), 2.98-3.32 (m, 2H) and 7.04-7.60 (m, 10H). The infrared spectrum ($CHCl_3$) showed bands at 1585, 1435, 1305, 1277 and 1115 cm^{-1}.

Anal. Calc'd for $C_{18}H_{18}O_2S$: C, 72.46; H, 6.08. Found: C, 72.16; H, 6.08.

Ring Expansion of Exo-α,β-unsaturated Sulfone 67 via *m*-Chloroperbenzoic Acid Oxidation

To a solution of 120 mg (0.4 mmole) of sulfone 67 in 50 ml benzene was added a large excess of *m*-chloroperbenzoic acid (0.5 g, 3 mmole). The reaction mixture was refluxed overnight. The crude product was filtered through a basic alumina column to give 115 mg (91%) of the 7-membered ring sulfone 68 as colorless granules m.p. 108° (methylene chloride-pentane). The n.m.r. spectrum ($CDCl_3$) had peaks at

δ=1.08-3.2 (m, 8H) and 7.04-7.66 (m, 10H). The infrared spectrum ($CHCl_3$) had strong bands at 1725, 1315 and 1123 cm^{-1}. Mass spectrum showed the parent molecular ion at m/e = 314.

Anal. Calc'd for $C_{18}H_{18}O_3S$: C, 68.78; H, 5.77. Found: C, 68.70; H, 5.90.

Ring Expansion of Exo-α,β-unsaturated Sultone 71 via Trifluoroperacetic Acid Oxidation (31)

To a solution of 882 mg of sultone 71 in 25 ml methylene chloride was added a solution of 20 mmole of trifluoroperacetic acid in 25 ml of methylene chloride. The resulting mixture turned cloudy and was refluxed for 1/2 hr. The crude black oil obtained on workup was purified by column chromatography (basic alumina, elution with ether-pentane) to give 215 mg (24%) of 7-membered ring sultone 72 as a colorless powder m.p. 150-151°. The n.m.r. and i.r. data have been reported on page 80.

Anal. Calc'd for $C_{17}H_{16}O_4S$: C, 64.55; H, 5.10. Found: C, 64.38; H, 5.38.

Thermal Decomposition of Lithio Chloromethyl Phenyl Sulfoxide

n-BuLi (5.1 mmole) was added dropwise to a solution of 752 mg (4.3 mmole) of chloromethyl phenyl sulfoxide in 25 ml of dry tetrahydrofuran at -78°. The greenish-yellow reaction mixture was allowed to warm slowly to room temperature. The color of the reaction mixture changed to brown at about -20° and finally to black at 0°. It was then stored for 5 hr at room temperature. The crude black oil was filtered through basic alumina column to give 366 mg of a brown oil which was purified by column chromatography to give 80 mg (22%) of diphenyl disulfide and 20 mg of n-butyl sulfoxide. The n.m.r. and i.r. spectra of these compounds were identical with those of authentic samples.

Thermal Decomposition of Lithio Chloromethyl Phenyl Sulfone

To a solution of 842 mg (4.4 mmole) of chloromethyl phenyl sulfone in 25 ml of dry tetrahydrofuran at -78° was added dropwise 3.2 ml (5.1 mmole) of n-BuLi. The yellow reaction mixture changed to brown at -20° and became dark red at room temperature. The reaction mixture was kept for 5 hr at room temperature. Workup gave a dark colored oil which was purified by column chromatography (basic alumina, elution with ether-pentane). The yield was 105 mg (10.4%) of dichloromethyl phenyl sulfone (34), 156 mg (19%) of chloromethyl phenyl sulfone (2) and 63 mg (9%) of methyl phenyl sulfone (33). The n.m.r. spectra of these sulfones were identical with the authentic samples available in these laboratories.

In another experiment where only 1/2 equivalent of n-BuLi was used, the products 34, 2 and 33 were formed in a ratio of 1 : 4.5 : 1 as indicated by the crude n.m.r. spectrum.

Treatment of Methyl Phenyl Sulfone(33) with 2.4 Equivalents of n-Butyllithium

To a solution of 1.03 g (6.45 mmole) of sulfone 33 in 30 ml tetrahydrofuran at -78° was added dropwise 15.5 mmole (2.4 equivalents) of n-BuLi. The resulting solution was orange in color and was stored at -20° overnight and then allowed to warm to room temperature. Addition of a mixture, prepared by hydrolyzing 2.5 ml acetyl chloride with 8 ml of D_2O, to the reaction mixture discharged the yellow color. Workup afforded a crude yellow solid which was purified by basic alumina column yielding 0.91 g of phenyl methyl sulfone. The mass spectrum showed the relative abundance of the deuterated and the nondeuterated sulfones in the following percentages: m/e = 156 ($PhSO_2CH_3$), 25%; 157 ($PhSO_2CH_2D$), 57% and 158 ($PhSO_2CHD_2$), 18%. These percentages have been corrected for other isotopic distributions.

PART III

Preparation of the Sulfonate Esters

In general the diol was dissolved in dry methylene chloride containing 2.2 equivalents of alkanesulfonyl chloride. The solution was cooled in an acetone-Dry Ice bath and treated with dropwise addition of 2.2 equivalents of triethylamine in methylene chloride. After the addition of the triethylamine was complete the reaction mixture was allowed to warm to room temperature and poured into water. The methylene chloride layer was separated, dried over magnesium sulfate and the solvent evaporated. The products were purified either by recrystallization, column chromatography or distillation under reduced pressure. The yields refer to purified products. The monosulfonate esters of the halohydrins were similarly prepared except that for each equivalent of halohydrin only 1.1 equivalents of sulfonyl chloride and triethylamine were employed.

1,2-Ethylene Dimethanesulfonate

Prepared in 38% yield, m.p. 45-46°. Lit. (19) m.p. 45-46°.

1,2-Ethylene Diphenylmethanesulfonate

From 3.1 g of ethylene glycol was obtained

11.2 g (74%) of diester m.p. 141° (methylene chloride-pentane). The i.r. spectrum ($CHCl_3$) showed strong bands at 1352, 1160 and 905 cm^{-1}. N.m.r. absorptions ($CDCl_3$) were at δ=4.23 (s, 2H), 4.44 (s, 2H) and 7.40 (s, 5H).

Anal. Calc'd for $C_{16}H_{18}O_6S_2$: C, 51.89; H, 4.90. Found: C, 51.79; H, 4.93.

1,2-Propylene Dimethanesulfonate

Prepared in 61% yield from 3.80 g of glycol, 11.45 g of methanesulfonyl chloride and 10.1 g of triethylamine. M.p. 51-52°. Lit.(20) m.p. 53°.

1,3-Propylene Dimethanesulfonate

Prepared in 33% yield, m.p. 38-39°. Lit.(19) m.p. 38-39°.

1,3-Propylene Diethanesulfonate

Propane-1,3-diol (3.80 g, 0.05 mole), ethanesulfonyl chloride (11.55 g, 0.09 mole) and 12.0 g (0.11 mole) of triethylamine gave 11.5 g of crude diester as an oil. Chromatography on basic alumina gave on elution with 1:1 ether-pentane 6.20 g (53%) of pure material. The n.m.r. spectrum ($CDCl_3$) showed absorption at δ=1.42 (t, J=7.5, 6H), 2.18 (quint., J=6.0, 2H), 3.16 (quart., J=7.5, 4H) and 4.36 (t, J=6.0, 4H). Infrared peaks occurred at 1340(vs), 1158(s) and 920(s) cm^{-1}.

Anal. Calc'd for $C_7H_{16}O_6S_2$: C, 32.29, H, 6.57. Found: C, 32.28; H, 6.17.

1,3-Propylene Diphenylmethanesulfonate

From 2.45 g of diol, 13.2 g of benzylsulfonyl chloride and 10.7 g of triethylamine was obtained 6.80g(55%) of product m.p. 109-110° (methylene chloride-pentane). N.m.r. absorption ($CDCl_3$) occurred at δ=1.90 (quint., J=6Hz, 2H), 4.05 (t, J=6Hz, 2H), 4.32 (s, 2H) and 7.37 (s, 5H), while i.r. peaks ($CHCl_3$) were at 1350(vs), 1160(s) and 922(s) cm^{-1}.

Anal. Calc'd for $C_{17}H_{20}O_6S_2$: C, 53.12; H, 5.25. Found: C, 53.08; H, 5.32.

1,3-Butylene Dimethanesulfonate

Prepared in 68% yield utilizing 5.0 g of 1,3-butanediol, 13.95 g methanesulfonyl chloride and 11.4 g triethylamine. M.p. 39-41°, after recrystallization from methylene chloride-pentane. Lit.(21) m.p. 40-41°.

β-Chloroethyl Methanesulfonate

Prepared in 67% yield, b.p. 73°-76°/0.2 mm. Lit.(22) b.p. 130°/11 mm.

β-Chloroethyl Phenylmethanesulfonate

From 5.0 g of ethylene chlorohydrin, 13.0 g benzylsulfonyl chloride and 6.9 g triethylamine was obtained 4.25 g (29%) of sulfonate ester as colorless granules m.p. 46-47°. Lit.(22) m.p. 47°. The n.m.r. spectrum ($CDCl_3$) showed absorption at δ=3.60 (t, J=6Hz, 2H), 3.92 (t, J=6Hz, 2H) and 7.40 (s,5H).

Anal. Calc'd for $C_9H_{11}ClO_3S$: C, 46.06; H, 4.72; Cl, 15.10. Found: C, 46.10; H, 4.76; Cl, 15.05.

cis-1,2-Cyclohexene Dimethanesulfonate

Prepared in 50% yield, m.p. 84-85°, Lit.(23) m.p. 85.5°.

trans-2-Bromocyclohexyl Methanesulfonate

trans-2-Bromocyclohexanol was prepared in 72% yield from cyclohexene according to the following procedure: Solid N-bromoacetamide (8.3 mmole) was added in portions to a stirring solution of 4.9 g (60mmole) cyclohexene in 50 ml aqueous dioxane containing a few drops of $HClO_4$ as catalyst. The reaction mixture was stirred overnight and extracted with methylene chloride. The organic extracts were dried and the solvents evaporated. Distillation of the crude product gave 7.7 g of a colorless oil b.p. 60-65°/1.8 mm. Lit.(17) b.p. 60-61°/1 mm.

To a solution of 7.7 g trans-2-bromocyclohexanol and 5.0 g methanesulfonyl chloride in 150 ml methylene chloride at -78° was added 4.5 g of triethylamine.

Recrystallization of the crude product from methylene chloride-pentane gave 5.5 g (50%) of ester m.p. 59°. The i.r. spectrum ($CHCl_3$) showed strong bands at 1350, 1160, 960, 895, 867 and 817 cm^{-1}. N.m.r. peaks ($CHCl_3$) were at δ=1.1-2.7 (m, 8H), 3.10 (s, 3H), 3.9-4.3 (m, 1H) and 4.4-4.8 (m, 1H).

Anal. Calc'd for $C_7H_{13}BrO_2S$: C, 32.69; H, 5.09; S, 12.46; Br, 31.76. Found: C, 32.71; H, 5.04; S, 12.33; Br, 31.24.

trans-2-Bromocyclooctyl Methanesulfonate

Cyclooctene oxide was prepared in 80% yield from MCPA oxidation of cyclooctene b.p. 98-105°/60 mm. Lit.(24), b.p. 90-93°/37 mm. Hydrobromination of cyclooctene oxide to give trans-2-bromocyclooctanol was carred out according to procedure used by Cope and Johnson (25). The yield was 60% and b.p. 80-88°/0.2 mm was the same as reported.

To a solution of 4.15 g (20 mmole) of trans-2-bromocyclooctanol and 2.52 g (22 mmole) methanesulfonyl chloride in 100 ml methylene chloride was added dropwise 2.2 g (22 mmole) of triethylamine. The usual workup gave 5.60 g (96%) of crude product (pale yellow oil) which was at least 90% pure as judged by its n.m.r. spectrum ($CHCl_3$) δ=1.2-2.4 (m, 12H), 3.02 (s, 1H, exchangeable with D_2O), 4.1-4.5 (m, 1H) and 4.6-5.1 (m,1H). The crude product failed to crystallize and could not be distilled without decomposition. It was considered sufficiently pure for the cyclization reaction.

<u>cis</u>-1,2-Cyclooctylene Dimesylate

<u>cis</u>-1,2-cyclooctanediol was prepared in 24% yield from <u>cis</u>-cyclooctene according to the following procedure: A solution of 40 g $KMnO_4$ and 30 g anhydrous $MgSO_4$ in 800 ml water was added over 2 hr to a vigorously stirred mixture of 28 ml <u>cis</u>-cyclooctene in 1 l. of 95% ethanol. The reaction mixture was cooled in a Dry-Ice acetone bath throughout the addition. The brown (MnO_2) precipitate was filtered and the clear solution concentrated under reduced pressure to about 100 ml which was then saturated with sodium chloride and extracted with several 50 ml portions methylene chloride. The organic extracts were dried and the solvent evaporated. Recrystallization of the crude product from methylene chloride-pentane gave 9.4 g of <u>cis</u>-1,2-cyclooctanediol m.p. 76-78°. Reported m.p. 76-78° (24).

To the above diol (3.1 g, 20.8 mmole) and 5.07 g (44.3 mmole) methanesulfonyl chloride in methylene chloride was added 4.5 g (44 mmole) of triethylamine. Recrystallization of the crude product from methylene chloride gave 4.72 g (75%) of dimesylate as colorless granules m.p. 69-70°. The i.r. spectrum ($CHCl_3$) showed bands at 1350 (s), 1160(s) and 890(s) cm^{-1}. N.m.r. absorption ($CDCl_3$) occurred at

δ=1.2-2.4 (m, 12H), 3.10 (s, 6H), 4.9-5.2 (m, 2H).

Anal. Calc'd for $C_{10}H_{20}O_6S_2$: C, 40.00; H, 6.71; S, 21.32. Found: C, 39.76; H, 6.73; S, 20.85.

4-Chlorobutyl Methanesulfonate

Prepared by adding 12.5 g of triethylamine to a -78° solution of 10.9 g (0.1 mole) of 4-chlorobutanol and 12.6 g (0.11 mole) of methanesulfonyl chloride in 50 ml of methylene chloride. Distillation gave 13.9 g (74%) of sulfonate ester b.p. 100-103°/1.5 mm.

Anal. Calc'd for $C_5H_{11}ClO_3S$: C, 32.19; H, 5.90. Found: C, 32,29; H, 5.96.

4-Chlorobutyl Phenylmethanesulfonate

From 7.97 g of 4-chlorobutanol was obtained 11.2 g (59%) of 37 m.p. 50° (methylene chloride-ether-pentane). The i.r. spectrum ($CHCl_3$) showed strong bands at 1345, 1160 and 935 cm^{-1}. N.m.r. absorptions ($CDCl_3$) were at δ=1.7-1.9 (m, 4H), 3.4-3.6 (m, 2H), 3.98-4.15 (m, 2H), 4.35 (s, 2H) and 7.38 (s, 5H).

Anal. Calc'd for $C_{11}H_{15}O_3SCl$: C, 50.28; H, 5.75. Found: C, 49.87; H, 5.57.

cis-1,2-Bishydroxymethylcyclohexene-4 Dimethanesulfonate (36)

To the diol (2.98 g, 21 mmole) prepared in 55% yield by $LiAlH_4$ reduction of the corresponding Δ^4-cyclohexene anhydride in 35 ml dry pyridine at 0°, was added slowly

7.2 g (63 mmole) methanesulfonyl chloride. The reaction mixture was stored overnight at 10°. Water was added and extracted with methylene chloride, dried and the solvents evaporated. Recrystallization of the crude from CH_2Cl_2-ether-pentane gave 4.8 g (77%) of the *cis*-dimesylate m.p. 84-86°. The i.r. spectrum ($CHCl_3$) has strong bands at 1354, 1165 and 942 cm^{-1}. N.m.r. ($CDCl_3$) showed peaks at δ=1.6-2.6 (m, 6H), 3.04 (s, 6H), 4.24 (m, 4H) and 568 (m, 2H).

Anal. Calc'd for $C_{10}H_{18}O_6S_2$: C, 40.27; H, 6.08. Found: C, 40.14; H, 6.07.

cis-1,2-Bishydroxymethylcyclohexane Dimethanesulfonate (34)

Prepared in 84% yield by hydrogenation (10% Pd/C; 60lb/in^2) of 36 in a mixed solvent of methanol and ethyl acetate for 1.5 hr. Recrystallization from methylene chloride-pentane gave colorless granules m.p. 75-76°. Lit.(26) m.p. 75-76°.

trans-1,2-Bishydroxymethylcyclohexane Dimethanesulfonate (35)

Methanesulfonyl chloride (4.4 g) was added slowly to a stirring mixture of 1.8 g (12.7 mmole) diol in 20 ml pyridine at 0°. The reaction mixture was stored overnight and water was added. The product was extracted with methylene chloride, dried and the solvents evaporated. Recrystallization of the crude product from methylene chloride gave 2.8 g (9.3 mmole 73%) trans-dimesylate m.p. 91°. Reported m.p. 92° (26).

Formation of the Lithio Derivatives of the Sulfonate Esters and Subsequent Cyclization. General Procedure.

To a tetrahydrofuran solution of disulfonate ester or β-halo-sulfonate ester at -78° under nitrogen atmosphere was added via syringe 1.05-1.10 equivalent of n-butyllithium (Foote Mineral Co., 1.6M in hexane). The reaction mixture was allowed to warm to -20°, 0° or room temperature for the times specified. It was then poured into water and extracted with methylene chloride. The organic extracts were dried over magnesium sulfate and the solvent evaporated. The crude products were usually purified by preparative thin layer chromatography (t.l.c.) yields refer to purified materials.

1,3-Propane Sultone (7)

a) From 1,2-Ethylene Dimethanesulfonate

Ethylene glycol dimesylate (1.00 g, 4.6 mmole) was dissolved in 30 ml of tetrahydrofuran at -78° and then treated with 3.0 ml (4.8 mmole) of n-butyllithium. The reaction mixture was warmed to -20° for 30 min during which time a colorless precipitate was formed. Workup gave 380 mg (68%) of 1,3-propane sultone, identified by comparison of t.l.c. behavior and i.r. spectrum with authentic commercial material (12). The i.r. spectrum ($CHCl_3$) showed strong bands at 1345, 1152 and 960 cm^{-1}.

b) From β-Chloroethyl Methanesulfonate

To a solution of 1.28 g (6.6 mmole) of the ester in 50 ml of tetrahydrofuran at -78° was added dropwise 7.2 mmole of n-butyllithium. The reaction mixture was stored for 24hr. The crude product (316 mg) was separated by preparative t.l.c. and yield 155 mg (19%) of 1,3-propane sultone.

1,4-Butane Sultone (8)

To a solution of 780 mg (3.36 mmole) of 1,3-propylene dimesylate in 30 ml of tetrahydrofuran at -78° was added 2.2 ml (3.5 mmole) n-butyllithium. Workup of the reaction mixture after it had been stored at -20° for 30 min gave 400 mg (88%) of 1,4-butane sultone whose i.r. was identical with that of authentic material (12).

3-Hydroxy-1-Phenylpropanesulfonic Acid 1,3-Sultone (13)

a) From 1,2-Ethylene Diphenylmethanesulfonate

1,2-Ethylene diphenylmethanesulfonate (255 mg, 0.69 mmole) was dissolved in 10 ml of tetrahydrofuran at -78° and treated with 0.70 mmole of n-butyllithium. The reaction mixture was stored at 0° for 3 days. Workup gave 129 mg of crude material whose n.m.r. spectrum indicated approximately 85% product and 15% starting material; n.m.r.

yield approximately 80%. Purification by preparative t.l.c. gave 64 mg (47%) of sultone m.p. 93.5-96° (methylene chloride-pentane). The i.r. spectrum ($CHCl_3$) showed strong bands at 1350, 1160 and 990 cm^{-1}. N.m.r. peaks occurred at δ=2.6-3.1 (m, 2H), 4.2-4.7 (m, 3H) and 7.40 (s, 5H).

Anal. Calc'd for $C_9H_{10}O_3S$: C, 54.54; H, 5.09; S, 16.15. Found: C, 54.15; H, 5.16; S, 16.19.

b) From β-Chloroethyl Phenylmethanesulfonate

Sulfonate ester (1.50 g, 6.4 mmole) was converted into its lithio salt in the usual manner at -78°. The reaction mixture was stored at 5° for 3 hr. An n.m.r. spectrum of the crude product (674 mg) indicated a 30% yield of the sultone 13.

3-Hydroxy-3-methylpropanesulfonic Acid 1,3-Sultone (17)

1,2-Propylene dimesylate (1.57 g, 6.8 mmole) was dissolved in 40 ml tetrahydrofuran at -78° and reacted with 7.5 mmole n-butyllithium. The reaction mixture was kept at 10° for 12 hr during which time a colorless precipitate was formed. Workup, followed by flash distillation of the crude product gave 0.75 g (81%) of sultone 17. N.m.r. peaks ($CDCl_3$) at δ=1.50 (d, J=6Hz, 3H), 2.0-3.0 (m, 2H), 3.2-3.55 (m, 2H) and 4.6-5.15 (m, 1H) was in agreement with that given by Bordwell et al. (14) The i.r. spectrum ($CHCl_3$) showed strong bands at 1340, 1150, 1020 and 900 cm^{-1}.

4-Hydroxy-1-phenylbutanesulfonic Acid 1,4-Sultone (14)

A solution of 2.01 g (5.2 mmole) of 1,3-propylene diphenylmethanesulfonate in 30 ml of tetrahydrofuran at -78° was treated with 5.5 mmole of *n*-butyllithium, and then stored at room temperature overnight. Workup gave 1.22 g of crude product from which 0.56 g (51%) of pure sultone, m.p. 157-158.5°, was obtained after two recrystallizations from methylene chloride-pentane. Spectroscopic properties were as follows: I.r. ($CHCl_3$), 1350(vs), 1162(s), 1010(s) and 925(s) cm^{-1}; n.m.r. peaks ($CDCl_3$),δ=1.8-2.8 (m, 4H), 4.22 (d of d, J=4 and 12Hz, 1H), 4.3-4.8 (m, 2H) and 7.3-7.6 (m, 5H).

Anal. Calc'd for $C_{10}H_{12}O_3S$: C, 56.60; H, 5.70; S, 15.08. Found: C, 56.53; H, 5.72; S, 15.24.

4-Hydroxy-1-methylbutanesulfonic Acid 1,4-Sultone (12)

To a solution of 1.74 g (6.7 mmole) of 1,3-propylene diethanesulfonate in 40 ml of tetrahydrofuran at -78° was added dropwise 7.5 mmole of *n*-butyllithium. The reaction mixture was stored at 10° for 2 hr. Distillation of the crude product gave 0.74 g (74%) of sultone 12. The n.m.r. spectrum ($CDCl_3$) showed absorptions at δ=1.35-1.50 (d, J=6.4Hz, 3H), 1.75-2.30 (m, 4H), 3.00-3.35 (m, 1H) and 4.35-4.60 (m, 2H). I.r. spectrum ($CHCl_3$) has strong bands at 1345, 1155 and 925 cm^{-1}.

4-Hydroxy-4-methylbutanesulfonic Acid-1,4-Sultone (18)

n-Butyllithium (6.7 mmole) was added to a solution of 1.55 g (6.3 mmole) of 1,3-butylene dimesylate in 35 ml of tetrahydrofuran at -78°. The reaction mixture was stored at -20° for 2 hr (colorless precipitate) then at 5° for a further 12 hr. Distillation of the crude product gave 0.71 g (75%) of sultone 18, n_D^{20}=1.460. Lit.(15) n_D^{25}=1.4586. The i.r. spectrum ($CHCl_3$) showed strong bands at 1352, 1162 and 890 cm^{-1}. N.m.r. absorptions (CCl_4) occurred at δ=1.40 (d, J=6Hz, 3H), 1.6-2.6 (m, 4H), 2.8-3.3 (m, 2H) and 4.4-5.0 (m, 1H).

Sultone 24

A solution of 1.03 g (4.0 mmole) of trans-2-bromocyclohexyl methanesulfonate in 35 ml tetrahydrofuran was treated with 4.8 mmole of n-butyllithium and then stored at 5° for 48hr. Workup gave 0.672 g of crude material from which was obtained by preparative t.l.c. 0.232 g (33%, 39% based on recovered starting material) of sultone 15, m.p. 54-55° (methylene chloride-pentane). The i.r. spectrum ($CHCl_3$) showed bands at 1338(s), 1150(s), 959(m), 908(m), 887(m) and 810(s) cm^{-1}. N.m.r. absorption occurred at δ = 1.0-2.5 (m, 8H), 2.5-2.9 (m, 1H), 3.18 (q, J=14 and 4Hz, 1H), 3.47 (q, J=14 and 7Hz, 1H) and 5.7-5.0 (m, 1H) p.p.m.

Anal. Calc'd for $C_7H_{12}O_3S$: C, 47.72; H, 6.87; S, 18.16. Found: C, 47.73; H, 6.93; S, 18.01.

cis-Sultone 28

n-Butyllithium (4.7 mmole) was added dropwise to a solution of 1.13 g (3.9 mmole) of trans-2-bromocyclooctyl methanesulfonate in 30 ml of tetrahydrofuran which had been cooled to -78°. The reaction mixture was kept at 10° for 18 hr. Workup gave 830 mg of crude product as a yellowish oil whose n.m.r, spectrum indicated a 1:1 mixture of starting material and sultone 17. The sultone was isolated by preparative t.l.c. (3:2 pentane-ether). The yield was 294 mg (36%, 64% based on recovered starting material). Recrystallization from methylene chloride-pentane gave colorless flakes m.p. 56.5-57.5°. The spectroscopic and analytical data of cis-sultone 28 and trans-sultone 30 were compared in the Discussion Section (See p.p.100).

trans-Sultone 30

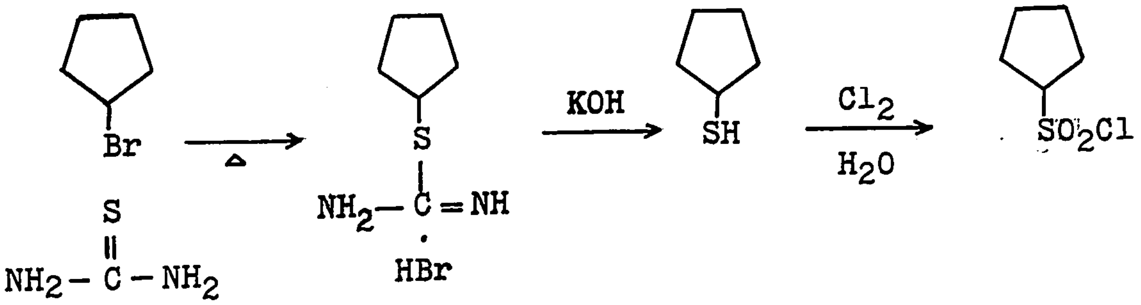
To a solution of 2.80 g (9.0 mmole) of cis-dimesylate 29 in 50 ml of tetrahydrofuran at -78° was added dropwise 9.9 mmole of n-butyllithium. The reaction mixture was kept at 10° overnight. Workup gave 2.30 g of crude product whose n.m.r. spectrum indicated a 3:1 mixture of starting material and product. Separation by preparative t.l.c. (3:2 pentane-ether) gave 304 mg (17%, 48% based on consumed starting material) of the trans-sultone 19 as colorless needles m.p. 56-57°.

Reaction of 4-Chlorobutyl Methanesulfonate with n-Butyllithium

n-Butyllithium (7 ml, 11.2 mmole) was added dropwise to a solution of 2.01 g (10.7 mmole) of 4-chlorobutyl methanesulfonate in 50 ml of tetrahydrofuran at -78°. The reaction mixture was stored at room temperature for 48 hr. The crude product (1.04 g) was purified by preparative t.l.c. and gave 475 mg (34%) of the ester 32 whose n.m.r. and i.r. spectra were identical to those obtained by reacting cyclopentanesulfonyl chloride with 4-chlorobutanol in methylene chloride in the presence of triethylamine. (See below).

Preparation of Cyclopentanesulfonyl Chloride

Cyclopentanesulfonyl chloride was prepared in the following scheme (27).



A solution of 29.8 g (0.2 mole) cyclopentyl bromide and 15.2 g (0.2 mole) thiourea dissolved in 250 ml methanol was refluxed for 10 hr. The solvent was removed under reduced pressure to give 42 g colorless solid (isothiouronium salt). 250 ml conc. potassium hydroxide solution was added to the salt and thiocyclopentanol was formed as evidenced by the onion odor. Extracted with methylene chloride and evaporation of the solvent gave the crude thiol. Acetic acid (50 ml) and 25 g crushed ice was added to the crude thiol. Chlorine gas was passed through the mixture for 1/2 hr. The crude product was dissolved in ether and washed with 5% sodium bisulphite and water. The organic extracts were dried and solvent evaporated. Distillation of the crude oil gave 6.7 g (5%) of the cyclopentanesulfonyl chloride b.p. 69°/0.75 mm.

Reaction of Cyclopentanesulfonyl Chloride with 4-Chlorobutanol

Cyclopentanesulfonyl chloride (5.35 g, 32 mmole) and 3.8 g (35 mmole) of 4-chlorobutanol were dissolved in 45 ml of methylene chloride at -78° and treated with dropwise addition of 3.5 g (35 mmole) of triethylamine. The reaction mixture was warmed to room temperature and worked up in the usual manner. Two distillations of the crude product gave a slightly yellowish oil 4.25 g (57%), b.p. 145-150/0.75 mm. The i.r. spectrum showed bands at 1330(s), 1155(s) and 920(s) cm^{-1}. N.m.r. peaks were at δ=1.5-2.4 (m, 12H), 3.5-3.9 (m, 3H) and 4.2-4.6 (m,2H).

<u>Anal</u>. Calc'd for $C_9H_{17}ClO_3S$: C, 44.91; H, 7.12; O, 19.92; S, 13.28. Found: C, 44.96; H, 6.91; O, 20.18; S, 13.49.

Diester 38

To a solution of 2.04 g (6.7 mmole) of dimethanesulfonate 34 in 40 ml of tetrahydrofuran at -78° was added dropwise 7.3 mmole of n-butyllithium. Workup gave 1.47 g of crude product from which 0.50 g of starting material was obtained by recrystallization. The remainder was purified by preparative t.l.c. and yielded 311 mg (23%) of the diester 23. Spectroscopic properties were in agreement with the proposed structural assignment. The i.r. spectrum (neat) has strong bands at 1335, 1170 and 950 cm^{-1}. The n.m.r. spectrum has absorption at δ=1.1-2.4 (m, 24H), 3.0 (s, 3H), 3.5-3.9 (m, 1H) and 4.1-4.3 (m, 4H). The compound tended to decompose and was not analyzed.

Diester 39

To a solution of 0.72 g (2.4 mmole) of dimethanesulfonate 35 in 25 ml tetrahydrofuran at -78° was added dropwise 2.7 mmole of n-butyllithium. The reaction mixture was kept at 10° overnight and workup gave 0.44 g of crude product from which 97 mg of diester 39 was isolated by preparative t.l.c. The spectroscopic properties were similar to the isomeric diester 38. The i.r. spectrum ($CHCl_3$) has strong bands at 1330, 1165 and 945 cm^{-1}. The n.m.r. spectrum showed absorptions at δ=0.8-2.4 (m, 24H), 3.0 (s, 3H), 3.4-3.8 (m, 1H) and 4.0-4.4 (m, 4H).

Diester 40

To a solution of 2.0 g (6.7 mmole) of dimesylate 36 in 40 ml tetrahydrofuran at -78° was added dropwise 7.4 mmole of *n*-butyllithium. The reaction mixture was kept at 10° overnight and workup gave 1.51 g of crude product. The diester 40 was isolated by preparative t.l.c. and the n.m.r. spectrum was in agreement with its structure. N.m.r. peaks at δ=1.5-2.6 (m, 16H), 3.0 (s, 3H), 4.0-4.4 (m, 4H) and 5.4-5.8 (m, 4H).

Ester 41

To a solution of 1.00 g (3.8 mmole) of sulfonate 37 in 30 ml of tetrahydrofuran at -78° was added dropwise 4.3 mmole of *n*-butyllithium. The reaction mixture was warmed to room temperature overnight. Workup gave 0.32 g of crude oil which was purified by preparative t.l.c. to give the ester 41. The n.m.r. spectrum ($CDCl_3$) has absorptions at δ=1.50-3.10 (m, 12H), 3.34-3.58 (m, 2H), 3.60-3.88 (m, 2H) and 7.20-7.60 (m, 5H), which was in good agreement with the structure of 41.

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CLAIMS TO ORIGINAL RESEARCH

1. The reaction of sulfuryl chloride with sulfoxides constitutes a simple and economical method for the preparation of α-chloro sulfoxides. It is suggested that the chlorination involves a chloro-oxosulfonium ion and an oxosulfenium ion as intermediates.

2. Reaction of β,γ, and δ-hydroxy sulfoxides with sulfuryl chloride gave the corresponding chloro sulfones. Stereochemical evidence is presented that cyclic alkoxyoxosulfonium salts are intermediates in these transformations.

3. Reaction of acid sulfoxides with sulfuryl chloride gave the corresponding α-chloro sulfoxide acids (new compounds) except when a 5-membered ring acyloxyoxosulfonium ion can be formed. In these cases, an acid chloride sulfone is obtained.

4. Reaction of a primary amide sulfoxide with sulfuryl chloride afforded the corresponding nitrile sulfone; thus intramolecular attack by oxygen on the chloro-oxosulfonium ion was preferred over attack by nitrogen.

5. A number of α-chloro sulfoxides and sulfones (dialkyl and aralkyl) were metallated with alkyllithiums at -78° and reacted with various ketones to give the corresponding α-chloro-β-hydroxy sulfoxides and sulfones. It was found that in addition to the metallation the reaction of

α-chloro sulfoxides with alkyllithiums resulted in considerable displacement of the chloroalkyl group by the alkyllithium.

6. Various α,β-epoxy sulfoxides and sulfones have been synthesized.

7. The thermal and acid-catalyzed rearrangements of α,β-epoxy sulfoxides and sulfones have been studied. The rearrangement involves fission of the oxirane ring and followed by the migration of the sulfinyl or sulfonyl group.

8. Two examples of an 6- to 7-membered ring expansion involving an α,β-epoxy sulfone and sultone have been observed.

9. A new route to 5- and 6-membered ring sultones via α-sulfonate ester carbanions has been reported. The route can yield sultones in which stereochemistry of the product can be related to that of the starting materials.

10. A total of more than one hundred new sulfur compounds have been synthesized and identified in this work.

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