NUCLEOPHILIC SUBSTITUTION AT TETRACOORDINATE SULFUR: AN EXAMPLE OF AN INTRAMOLECULAR ENDOCYCLIC REACTION

LINDA JEWELL YILDIZ

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NUCLEOPHILIC SUBSTITUTION AT TETRACOORDINATE SULFUR: AN EXAMPLE OF AN INTRAMOLECULAR ENDOCYCLIC REACTION

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NUCLEOPHILIC SUBSTITUTION AT TETRACOORDINATE SULFUR: 
AN EXAMPLE OF AN INTRAMOLECULAR ENDOCYCLIC REACTION

by

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B.A., Radcliffe College, 1961
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A THESIS
Submitted to the University of New Hampshire
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in
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The author dedicates this thesis to her children: David, Sara, and Suzan.
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2,2-Dimethylthietane 1-oxide was treated with phenyllithium. The products were shown to be 2,2-di-methylcyclopropyl phenyl sulfide and diphenyl sulfide. It appears that nucleophilic attack at sulfur and α-carbanion formation are two competing reactions.

An endocyclic intramolecular nucleophilic attack at tetracoordinate sulfur was demonstrated. 2'-Aminophenyl 4-toluenesulfonate when treated with four equivalents of n-butyllithium rearranged to N-(2'-hydroxyphenyl)-4-toluene-sulfonamide. This rearrangement is not reversible. The rearrangement did not occur when phenyllithium or methyllithium was used as the base. A variety of sulfonates of ortho aminophenols were found to undergo this rearrangement. However, 2'-amino-4'-methylphenyl 2,4,6-trimethylbenzene-sulfonate did not rearrange.

The rearrangement was shown to be intramolecular by a crossover experiment in which none of the possible intermolecular products were formed. The corresponding nitrogen protected sulfonimidate ester was synthesized. The aim was to synthesize the optically active tetracoordinate sulfur species in order to probe the stereochemistry of the substitution reaction and to determine if the rearrangement occurred with retention of configuration at sulfur as predicted.
HISTORICAL

Sulfur commonly exists in one of three oxidation states: dicoordinate divalent S(II), tricoordinate tetravalent S(IV), and tetracoordinate hexavalent S(VI). Nucleophilic substitution reactions at these different types of sulfur centers have been reviewed.1-7

**Dicoordinate Sulfur**

The nucleophilic reactions at dicoordinate sulfenyl sulfur that have been studied kinetically gave the rate expression: \[ \text{Rate} = k \ [RSX][Nu] \], which indicates that these reactions are bimolecular - perhaps with a linear transition state. A monomolecular S_N1 substitution reaction, which can occur at sp^3 carbon, does not appear to take place at sulfenyl sulfur. Nucleophilic substitution at dicoordinate sulfur has a rate that is many orders of magnitude faster than for the corresponding reaction at sp^3 carbon. In general, S_N2-like reactions at second row elements occur with much greater ease than for first row elements. This is due to the greater atomic radius and polarizability of second row elements, thus their greater ability to disperse a negative charge. Substitution reactions at dicoordinate sulfur occur about 500 times faster than at tricoordinate sulfur.
Little is known about the nature of intermediates in these substitution reactions. The large steric effects and small substituent effects which have been measured for a variety of reactions at dicoordinate sulfur have been taken as proof of a direct $S_N^2$ type of displacement with no intermediate. However, the reaction of sulfenyl derivatives with amines in benzene is catalyzed by added bases or the nucleophile itself and appears to proceed by an intermediate complex mechanism. Since sulfenyl sulfur cannot be chiral, nothing is known about the stereochemistry of the nucleophilic substitution reaction at sulfur(II).

**Tricoordinate Sulfur**

Most of the studies of nucleophilic substitution at sulfur have been with tricoordinate sulfur compounds because they are chiral. Optically active sulfur compounds were first reported by Pope and Peachey and Smiles, who isolated sulfonium salts as their D-camphorsulfonates or hexachloroplatinates.

The first investigation of the stereochemistry of nucleophilic substitution at sulfinyl sulfur was done by Phillips in 1925. He partially resolved ethyl and $n$-butyl $p$-toluenesulfinates by a kinetic resolution with $l$-$\beta$-octanol. Then he demonstrated that heating $n$-butyl alcohol with optically active ethyl $p$-toluenesulfinate gave $n$-butyl $p$-toluenesulfinate of opposite sign with inversion of configuration (eq. 1). He compared the mechanism of
this reaction to the Walden inversion of optically active carbon compounds.

\[
\text{n-BuOH} + \begin{array}{c}
\text{O} \\
p-\text{Tol}
\end{array} \xrightarrow{18 \text{ hrs}} \begin{array}{c}
\text{O} \\
\text{OEt}
\end{array} \xrightarrow{\text{V}} \text{EtOH}
\]

Hebrandson and Cusano\textsuperscript{12} separated the two diastereomers of (−)-menthyl p-iodobenzenesulfinate, 1 and 2, by fractional crystallization. They stated that because of extensive steric interaction between the aromatic ring and the isopropyl group, the thermodynamically less stable (−)-menthyl (−)-p-iodobenzenesulfinate possessed structure 2 and was of the S configuration.

Optically active sulfoxides were first conveniently synthesized by Andersen\textsuperscript{13,14} by the reaction of optically active (−)-menthyl (−)-p-toluenesulfinate (3) with Grignard reagents (eq. 2). The reaction occurs with inversion. The conversion of sulfinate 3 into the corresponding sulfinamide also goes with inversion\textsuperscript{15} (eq. 3).
Alkaline hydrolysis of the ethoxyxysulfonium salt, synthesized from cis-4-(p-chlorophenyl)thiane 1-oxide, by alkylation with triethyloxonium tetrafluoroborate, was shown by Johnson to occur with inversion (eq. 4).
Nucleophilic substitution at tetrahedral sulfur increases the number of ligands bonded to sulfur in the transition state, which is generally assumed to exist as a trigonal bipyramid, 5. The question of whether this trigonal bipyramid represents a transition state or an intermediate has not been settled. Sulfuranes such as 6, which possess this structure, have been isolated\textsuperscript{17,18} and this has been used to support the existence of trigonally bipyramidal sulfur species.

\begin{align*}
\text{a} &= \text{apical} \\
\text{e} &= \text{equatorial}
\end{align*}

\textbf{Trigonal Bipyramid}

\textbf{Sulfurane}
Inversion of Configuration

apical-apical  
equatorial-equatorial

Retention of Configuration

apical-equatorial

Figure 1. Stereochemical course of nucleophilic substitution at sulfur.
If the nucleophile and leaving group occupy both apical positions, one has a situation equivalent to an $S_N^2$ reaction at carbon and inversion of configuration will result (see Figure 1). One example of inversion, which possibly involves an equatorial-equatorial arrangement, has been reported by Cram (eq. 5). The conversion of

$$2 \text{TsN} = S = \text{NTs} + \text{O} \rightarrow \text{sulfoxide}$$

$$\text{TsN} = S = \text{NTs} + \text{CH}_3 \rightarrow \text{TsN} = S = \text{O}$$

sulfimide
sulfoxides to sulfimides with N,N'-bis(p-tosyl)sulfur
diimide, (TsN)$_2$S, or N-sulfinyl p-toluenesulfonamide,
TsN = S = 0, in pyridine proceeds with inversion of con­
figuration. The reaction is second order in sulfur diimide
and appears to occur via the six-membered ring, 7.

While most of the reactions involving nucleophilic
substitution at sulfur occur with inversion of configuration,
there are some examples in which retention has been demon­
strated. If the nucleophile and leaving group occupy apical-
equatorial positions (see Figure 1), retention of configura­tion will result.

The oxygen exchange reaction of optically active
sulfoxides with dimethyl sulfoxide occurs with retention (eq. 6), since the rate of exchange is much faster than the
rate of racemization.
The conversion of N-phthaloylmethionine sulfoxide to the corresponding sulfimide by N-sulfinyl-p-toluene-sulfonamide in benzene also occurs with retention\(^{21}\) (eq. 7). In this case anchimeric assistance, resulting in a double inversion, might account for the observed retention.

\[
\begin{align*}
\text{Me} & \quad \begin{array}{c}
S = 0 \\
\text{p-TolSO}_2N = S = 0 \\
\text{benzene}
\end{array} \\
\text{CH}_2 & \quad \text{S} = \text{NSO}_2\text{p-Tol} \\
\text{H} & \quad \text{C} \quad \text{NCOC}_6\text{H}_4\text{CO-} \\
\text{CO}_2\text{H} & \quad \text{H} \quad \text{C} \quad \text{NCOC}_6\text{H}_4\text{CO-} \\
\text{S} & \quad \text{S} = \text{NTs}
\end{align*}
\]

(7)

In a later study, Christensen\(^{22}\) demonstrated that both methyl tolyl and methyl butyl sulfoxide, when caused to react with N,N'-bis(p-tosyl) sulfur diimide in benzene, gave the sulfimide of retained configuration (eq. 8).

\[
\begin{align*}
\begin{array}{c}
\text{Me} \\
\text{Tol}
\end{array} & \quad \begin{array}{c}
S = 0 \\
+ \quad (\text{TsN})_2\text{S}
\end{array} \quad \begin{array}{c}
\text{benzene}
\end{array} \\
\begin{array}{c}
\text{Me} \\
\text{Tol}
\end{array} & \quad \begin{array}{c}
\text{S} = \text{NTs}
\end{array}
\end{align*}
\]

(8)
The reaction of p-tolyl methyl sulfoxide with p-toluenesulfinyl nitrene in acetonitrile yields the corresponding sulfimide of retained configuration \(^ {23}\) (eq. 9).

\[
\begin{align*}
\text{p-Tol} \rightleftharpoons \text{S} \rightleftharpoons \text{CH}_3 & + \text{p-TolSN}_3 \quad \overset{\text{CH}_3\text{CN}}{\xrightarrow{50^\circ\text{C}}} \text{p-Tol} \rightleftharpoons \text{S} \rightleftharpoons \text{CH}_3 \\
\text{NTs} & \\
\text{p-Tol} \rightleftharpoons \text{S} \rightleftharpoons \text{CH}_3 & + \text{p-TolSO}_2\text{NH}_2 & + \text{p-TolSMe} \\
& 15\% & 2.8\%
\end{align*}
\]

These retention reactions are consistent with a four-membered cyclic intermediate such as structure 8 (eq. 6). Maricich and Hoffman, \(^ {23}\) however, suggested an alternative mechanism (see Figure 2). The first step was attack of sulfoxide oxygen on the positive sulfur to give a dipolar adduct 9, which closed to a four-membered ring, and then underwent pseudorotation to expel the oxygen from an apical position. Pseudorotation is contradicted by the experiments of Mislow and Tang\(^ {24}\) with thietanium salts which demonstrated that pseudorotation in cyclic sulfurane intermediates is slow. However, Martin\(^ {25}\) synthesized spirosulfurane 10 which showed a temperature dependent \(^ {19}\text{F} \) NMR which could be explained by postulating a pseudorotation mechanism (eq. 10).
Figure 2. Reaction of p-tolyl methyl sulfoxide with p-toluenesulfinylnitrene
Reactions of Sulfoxides with Organometallics

The reactions of sulfoxides with Grignard or organolithium reagents can take a variety of paths and are frequently complex. The mechanism depends on the sulfoxide, the organometallic, solvent, and temperature. The possible mechanisms include: (i) ligand exchange, (ii) α-carbanion formation when an α-hydrogen is present, (iii) sulfurane formation followed by collapse to a sulfide and biaryl, (iv) aryne formation, and (v) simple $S_{N}^2$ type displacement.

The reactions of aromatic sulfoxides have been studied by Andersen (eq. 11). Initially this reaction was assumed to proceed via a triaryl sulfonium ion intermediate, which upon proton abstraction and then elimination...
\[
\begin{align*}
\text{CH}_3\text{C}_6\text{H}_4\text{S} \text{CH}_3 + \text{CH}_3\text{C}_6\text{H}_4\text{Li} & \rightarrow (\text{pTol})_3\text{Li}^+ \rightarrow (\text{pTol})_2\text{S} + \\
\text{CH}_3\text{C}_6\text{H}_4\text{S} \text{CH}_3 + \text{CH}_3\text{C}_6\text{H}_4\text{C}_6\text{H}_4\text{CH}_3 & \rightarrow 66\% \\
& \rightarrow 31\% \\
& \rightarrow 26\%
\end{align*}
\]

\[
11 + \text{pTol Li} \rightarrow (\text{pTol})_3\text{S}^+\text{OLi}^- \rightarrow (\text{pTol})_2\text{S} + \\
\text{CH}_3 + \text{C}_6\text{H}_4\text{Li} \rightarrow (\text{pTol})_3\text{Li}^+ \rightarrow (\text{pTol})_2\text{S} + \\
\text{CH}_3\text{C}_6\text{H}_4\text{C}_6\text{H}_4\text{CH}_3 + \text{CH}_3\text{C}_6\text{H}_4\text{C}_6\text{H}_4\text{CH}_3
\]

(11)
formed a diaryl sulfide and aryne (eq. 12). However, the reaction of sulfonium salts with organolithium reagents gave a different distribution of products, with aryne formation being a very minor pathway (eq. 13).

Consequently intermediate 12 was postulated (see Scheme I), which, depending on the nature of the leaving group, partitions between two pathways.

The existence of tetracoordinate intermediates like 12 was supported by Trost in studies of the reactions of aryl sulfonium salts with organolithium reagents (eq. 14). Trost ruled out the benzyne mechanism, the addition-elimination mechanism, and electron transfer to sulfur from

\[
\text{Ph}_3\text{S}^+\text{BF}_4^- + \text{Li} \rightarrow \text{PhSPh} + \text{PhCH} = \text{CH}_2 \quad (14)
\]
Scheme I. Reaction of p-tolyl sulfoxide with tolyllithium

11 + Tol Li

\[ \text{Tol} \quad \text{OLi} \quad \text{TolLi} \quad \text{OLi} \quad \text{Tol} \quad \text{Tol} \]

\[ \text{Tol} \quad \text{S} \quad \text{Tol} \quad \text{Tol} \quad \text{Tol} \]

\[ \text{CH}_3 \quad \text{C}_6 \text{H}_{4} \quad \text{C}_6 \text{H}_{4} \quad \text{C}_6 \text{H}_{4} \quad \text{C}_6 \text{H}_{4} \]

\[ \text{Tol}_3 \text{S}^+ \text{OLi}^- \quad \text{Tol}_2 \text{S} \]
the organolithium and proposed the formation of a tetra-coordinate intermediate $13$, which then collapsed to diphenyl sulfide and styrene in quantitative yields. The coupling reaction involves the overlap of the $\pi$ systems of two of the ligands with concurrent cleavage of the C - S bond. Coupling

\[
\begin{array}{c}
\text{CH} \\
\text{Ph} \\
\text{S} \\
\text{Ph} \\
\text{Ph} \\
\text{CH}_2
\end{array}
\]

of the vinyl-phenyl type is preferred over phenyl-phenyl coupling, which would require the destruction of aromaticity of two benzene rings in the transition state.

Trost$^{28}$ also investigated the reaction of dibenzothiophenium salts with aryl lithium reagents. The ratio of these two paths (see Scheme II) was found to be a function of the nature of the aryl groups. The data refuted an addition-elimination mechanism and supported the formation of a tetracoordinate intermediate. Electron withdrawing groups on the aryl rings weaken the C - S bond and favor path A, whereas electron donating groups favor path B.
Scheme II. Reaction of dibenzothiophenium salts with aryllithium reagents

\[
\text{Path A} \quad \text{Path B}
\]

Hori\textsuperscript{29,30} in a similar study of the mechanism for the formation of ring opening products in the reactions of organolithiums with dibenzothiophenium and thioxanthenium salts (14 and 15, respectively) concluded from the results that the reactions proceeded by a tetracoordinate intermediate which underwent pseudorotation before collapsing to products (eq. 15 and eq. 16).
However, Hori\textsuperscript{31} stated that the reaction between 9-phenylthioxanthene 10-oxide, 16, and organometallic reagents proceeded through the formation of 9-phenylthioxanthenyl radical because of the ESR spectra for the reactions (eq. 17).

In the reactions of organolithiums with sulfoxides with $\alpha$-hydrogens, two concurrent processes can occur: (i) the abstraction of the acidic $\alpha$-hydrogen to form a carbanion and (ii) the exchange of one of the alkyl groups of the sulfoxide for the alkyl group of the alkyllithium. The relative amounts of reactions (i) or (ii) will depend on the structure of the sulfoxide (the number of $\alpha$-hydrogens, their acidity, and the nature of the substituents) and on the organolithium used (its size and basicity).
Optically active aryl methyl sulfoxides were found by Mislow\textsuperscript{32} to partially racemize with methyllithium (eq. 18).
\[ \text{Ph-S-CH}_3 + \text{MeLi} \rightarrow \text{Ph-S-CH}_3 \] (18)

13.3% racemization

13CH3-enriched methyl phenyl sulfoxide on reaction with 12CH3Li gave recovered sulfoxide with no loss of 13C content. Thus the exchange mechanism, which occurs commonly for sulfoxides, can be ruled out in this instance as being the cause of racemization. Mislow\textsuperscript{32} proposed as an alternative mechanism the reversible cleavage of lithium arenesulfinylmethide into methylene sulfine and aryllithium (eq. 19). Methylene sulfine is an achiral intermediate and

\[ \text{Ar-S-CH}_3 + \text{MeLi} \rightarrow \text{S=CH}_2^-\text{Li}^+ \rightarrow \text{Ar-Li}^+ \] (19)

recombination with aryllithium would result in formation of racemic starting material. There are some alternative mechanisms, however, which can also lead to racemization and cannot be excluded from consideration. The arenesulfinylmethide ion \( \text{L}_7^\prime \) may undergo rapid pyramidal inversion and thus may racemize more readily than the corresponding
sulfoxides, which are normally resistant to pyramidal inversion at room temperature.

Johnson\textsuperscript{33} showed that ligand exchange occurred with inversion of configuration (eq. 20).

\[
\begin{align*}
\text{p-Tol} & \quad \text{S} \quad \text{CH}_3 & + & \text{n-BuLi} & \quad \text{Et}_2\text{O} & \quad \text{CH}_3 & \quad \text{S} \quad \text{n-Bu} \\
(+)(R) & & & & & & (+)(S)
\end{align*}
\]

In an investigation of the alkyl group exchange reaction, Durst\textsuperscript{34} determined that the group which can best carry a negative charge is the one most readily displaced. Benzyl, -CH\textsubscript{2}Cl, and -CHClCH\textsubscript{3} are all displaced in preference to phenyl, which is displaced in preference to alkyl groups. His results indicate that the sulfine mechanism is not an important pathway for the exchange reaction of sulfoxides, but rather suggest a simple $S_N2$ displacement at sulfur similar to that observed in the reaction of sulfinate esters with Grignard reagents.

The reaction of sulfoxides with methyllithium gave mainly carbanion formation and very little ligand displacement. The stronger bases, \textit{tert}-BuLi and n-BuLi, gave 30 percent to 50 percent phenyl group displacement; and thus, these bases are not suitable for the generation of $\alpha$-sulfinyl carbanions. With methyllithium or n-butyllithium the displacement went with inversion. The racemization of \textit{tert}-butyl aryl sulfoxides with \textit{tert}-butyllithium cannot proceed via
a sulfine intermediate nor via $S_N^2$ displacement of the tert-
butyl group as an anion. Durst proposed a radical mechanism
involving one electron transfer from the tert-butyllithium
to the sulfoxide. He favored a simple $S_N^2$ type mechanism
for the displacement reaction of sulfoxides and stated
that there was no evidence for a sulfurane intermediate.

There has been one study of the reactions of
thietan-1-oxides with organometallics. Cis-2,4-diphenyl-
thietan-1-oxide (18) (eq. 22) and trans-2,4-diphenylthietan-
1-oxide (19) (eq. 23) were treated with methylmagnesium
iodide. The cis and trans thietanoxides 18 and 19 gave
the same products with phenylmagnesium bromide (eq. 24).
Dodson proposed that sulfides 20 and 21 were formed via
the sulfonium ylide 22.

\[
\begin{align*}
\text{H} & \quad \phi \\
\phi & \quad \text{H}
\end{align*}
\]

\[
\begin{align*}
\text{CH}_3\text{MgI} \
\rightarrow \
\begin{align*}
\phi & \quad \phi \\
\phi & \quad \text{H}
\end{align*}
\]

(22)
Trost\textsuperscript{36} found that thietanes when treated with \textit{n}-butyllithium did not give cyclopropanes. Thietanes proved to be poor substrates for desulfuration, but the corresponding thietanonium salt did give cyclopropanes on reaction with \textit{n}-butyllithium (eq. 25). The decrease in the electronegativity of sulfur facilitated nucleophilic attack at sulfur by the butyllithium. This reaction was found to
proceed with a high degree of stereospecificity. The proposed mechanism assumed the initial formation of a tetracoordinate sulfur species, followed by trimethylene formation and conrotatory closure to give cyclopropane and sulfide.

The nature of the mechanisms of the reaction of organolithiums with sulfoxides still remains confused and further investigation is necessary to clarify the nature of these reactions.
Tetracoordinate Sulfur

Information concerning nucleophilic substitutions at tetracoordinate hexavalent sulfur is limited. The first study of the stereochemistry of nucleophilic substitution at tetracoordinate sulfur was done by Andersen\(^{37}\) (eq. 26). (-)-Menthy1 phenylmethanesulfinate, 23, was oxidized to (-)-menthy1 phenylmethanesulfonate, 24. Since 16\(^{18}\)O-menthy1 £-TolMgBr in inversion (-)-(S)- 24, it is highly probable that reactions involving electrophilic attachment or removal from the nonbonding pair of electrons occur without configurational change at sulfur, the oxidation reactions 23 to 24 and 26 to 25 occurred with retention. Consequently, the reaction of the Grignard reagent with the sulfonate 24 must have gone with inversion.

Optically active sulfoximines 28 have been prepared from sulfoxides with retention of configuration\(^{38}\) (eq. 27).
Since the sulfimide $29$ was formed from the sulfoxide $27$ with inversion and was oxidized to the sulfoximide $28$ with retention, the formation of the sulfoximide $28$ from the sulfoxide $27$ had to have gone with retention.

Cram$^{19,39-41}$ has made an extensive study of the interconversion of sulfoxides, sulfinamides, and sulfoximides through the use of stereochemical reaction cycles in which all of the compounds in the cycle are chiral and all of the reactions are stereospecific (see Scheme III). From these cycles the stereochemical course of a new stereospecific reaction can be assigned. He used methyl $p$-tolyl sulfoxide ($30$) as starting material because it is easily prepared and also because its absolute configuration is known. In Scheme III, $p$-tolyl is the only ligand common to all the members. Conversion of sulfoxide $30$ with
N,N'-bis(p-tosyl)sulfur diimide, (TsN)$_2$S, in pyridine to the sulfimide 31 is known to go with inversion. Oxidation of sulfimide 31 to sulfoximide 32 goes with retention. Reactions 32 to 33 and 33 to 34 do not involve a change at sulfur. The reaction of sulfinamide 35 with Grignard reagent to give sulfoxide 30 is known to go with inversion. Thus, the only reaction whose stereochemical course is not known is the conversion of sulfoximide 34 to sulfinamide 35 with p-tosyl chloride and pyridine, and this is required to occur with retention if the cycle is to be consistent. This last reaction is in fact a nucleophilic attack at carbon with the configuration at the sulfur leaving group being preserved. Tosylation of the nitrogen causes sulfur to become a positively charged leaving group which is displaced from the methyl group by nucleophilic attack of the pyridine (and possibly chloride ion) (eq. 28). Since the electron pair from the methyl-sulfur bond remains with sulfur, the configuration at sulfur is preserved.

\[
\begin{align*}
\text{CH}_3\text{S} & \quad \text{Tol} \\
\text{NCH}_3 & \quad \text{TsO}_2\text{Cl} \\
\text{pyridine} & \quad \text{Cl}^- \\
\text{(-)-(R)-} & \quad 34
\end{align*}
\]
S-methylpyridinium chloride → 4-Tol
Scheme III. Stereochemical reaction cycle

\[ \text{Tol} = \text{p} \text{CH}_3 \text{C}_6 \text{H}_4 \quad ; \quad \text{Ts} = \text{pCH}_3 \text{C}_6 \text{H}_4 \text{SO}_2 \]
The phenomenon of ligand metathesis is illustrated in Scheme IV.

Scheme IV. Ligand metathesis.

Ligand metathesis involves the interchange of two ligands between two bonds, irrespective of the movement of the bonds themselves. In Scheme IV, there is one reaction with inversion and one with ligand metathesis, which is equivalent to two inversions.

Optically active sulfoximines, which possess a tetracoordinate sulfur, have been known for some time. However, derivatives of sulfonimidic acids have received
only slight attention. These compounds possess the potential of being chiral and, thus, can be used to study the stereochemistry of nucleophilic substitution at tetra-coordinate sulfur.

\[
\begin{align*}
\text{sulfoximide} & \quad \text{sulfonimidic acid} & \quad \text{sulfonimidoyl chloride} \\
R'\text{"} & \quad \text{R'--S--OH} & \quad \text{R'--S--Cl} \\
\text{NR} & \quad \text{NR} & \quad \text{NR}
\end{align*}
\]

Sulfonimidoyl chlorides have been previously prepared by the reaction of sulfinyl chlorides with a variety of chloramine derivatives including chloramine-T, N,N-dichloromethylamine, and the sodium salts of N-chloroamides (eq. 29).

\[
R\text{"}--S--Cl + \text{NaCl} \rightarrow R\text{"}--S--Cl + \text{NaCl} \quad (29)
\]

R' = arylsulfonyl, ethoxy carbonyl, or acetyl

Sulfonimidoyl bromides have been reported as unstable non-isolatable intermediates (eq. 30 and 31). There may be for the sulfonimidamide two tautomeric forms 37 and 38. Thus, the product of both reactions in (eq. 30) is because the phenyl group has a greater tendency to attract electrons.
\[
\phi \text{SNH}\phi + \text{NBS} \rightarrow \left[ \begin{array}{c}
\phi \\
\text{SBr} \\
\phi \\
\text{NH}_2
\end{array} \right] \\
\rightarrow \phi \text{SNH} \phi + 2 \text{NH}_2
\]

(30)

\[
\phi \text{SNH}_2 \phi + \text{NBS} + 2 \phi \text{NH}_2 \rightarrow \phi \text{SNH} \phi
\]

sulfonimidamide

(31)

\[
\phi \text{SNH}\phi + \text{NBS} + \text{NaO} \rightarrow \phi \text{SO} \phi
\]
N-alkoxybenzenesulfinamides are reported to rearrange via an O-alkylsulfonimidate intermediate to give the sulfonamide \[^{46}\] \text{(eq. 32)}, indicating that the sulfonimidate esters may be unstable if the nitrogen is unsubstituted.

\[
\begin{align*}
\text{Ph} - &\text{S} - \text{NHOCH}_3 \xrightarrow{\text{rm. temp} \ 2 \ wks} \\
&\text{Ph} - &\text{S} - \text{OCH}_3 \rightarrow \text{Ph} - &\text{S} - \text{NCH}_3
\end{align*}
\]

(32)

The first synthesis of an optically active sulfonimidoyl chloride was reported by Johnson \[^{47,48}\] (see Scheme V). Optically active N-methyl phenylsulfinamide \[^{39}\] was prepared with retention from optically active sulfoximide \[^{40}\] by a stereospecific reduction with aluminium amalgam. \[^{49}\] This sulfinamide \[^{39}\] was oxidatively chlorinated to give the optically active sulfonimidoyl chloride \[^{41}\] with retention. The nucleophilic substitutions of the sulfonimidoyl chloride \[^{41}\] by phenoxide to give the sulfonimidate \[^{42}\] and by diethylamine to give the sulfonimidamide \[^{43}\] can be assumed by analogy to have gone with inversion.

The chiral sulfonimidoyl chloride prepared by Johnson was unstable and was converted without characterization to the optically active sulfonimidate and sulfonimidamide. Cram \[^{50}\] has prepared the two optically pure crystalline diastereomers of N-carbomethoxy-p-toluenesulfonimidoyl chloride, \[^{44}\] (see Scheme VI), and has studied the stereochemistry of their reactions. By the preferred method,
Scheme V. Synthesis of sulfonimidoyl chloride.

\[
\begin{align*}
\text{Ph} &\quad \text{S} &\quad \text{NHCH}_3 \\
\text{Ph} &\quad \text{S} &\quad \text{NHCH}_3 \\
\text{Ph} &\quad \text{S} &\quad \text{NHCH}_3 \\
\text{Ph} &\quad \text{S} &\quad \text{NHCH}_3 \\
\end{align*}
\]

\[
\begin{align*}
(\cdot)-(\text{R})-39 &\quad \text{Al(Hg)} &\quad \text{ret.} &\quad (\cdot)-(\text{R})-43 \\
(\cdot)-(\text{S})-39 &\quad \text{Cl}_2 &\quad \text{Pyr. ret.} &\quad (\cdot)-(\text{R})-41 \\
(\cdot)-(\text{S})-40 &\quad \text{MeLi} &\quad \text{inv.} &\quad (\cdot)-(\text{S})-42 \\
\end{align*}
\]
Scheme VI. Synthesis of N-carbomethoxy-p-toluenesulfonimidoyl chloride.

\[
\text{Tol} = \text{pCH}_3\text{C}_6\text{H}_4; \quad \text{NCM} = \text{NCO}_2\text{(-)-menthyl}
\]

\[
\text{Ns} = \text{pNO}_2\text{C}_6\text{H}_4\text{SO}_2
\]
p-toluenesulfinyl chloride was caused to react with \((-\)\)-menthyl carbamate, $H_2NCM$, and pyridine to give the N-carbomenthoxy-p-toluenesulfinamide $45$, which was somewhat unstable and so was directly chlorinated to give the sulfonylimidoyl chloride $44$ as a mixture of diastereomers, which were separated by chromatography.

The reduction of sulfonylimidoyl chloride $44$ with methylmagnesium bromide to give sulfinamide $46$ went with retention. By contrast, reduction with hydrazine went with inversion. The reduction by Grignard reagent appears to involve nucleophilic attack by methyl on the chlorine (eq. 33). Since the bonding electron pair accompanies the leaving group, retention is expected. The inversion by hydrazine suggests the occurrence of nucleophilic substitution at sulfur (eq. 34).

$$
\begin{align*}
\text{Tol} &\text{S}^-\text{Cl} &\rightarrow &\text{Tol} &\text{S}^-\text{H}_2\text{O} &\rightarrow &\text{Tol} &\text{S}^- + \text{CH}_3\text{Cl} \\
&\text{O} & &\text{O} & &\text{O} & &
\end{align*}
$$

(eq. 33)
Cram also studied the reaction of nucleophiles with sulfonimidoyl chloride 44 (see Scheme VII), and he assigned the stereochemical course of these reactions. The sulfonimidoyl chloride 44 gave sulfonimidamides 47 and 48 on the addition of sodium amide and dimethylamine, respectively, and sulfonimidate 49 on the addition of potassium p-cresylate. That these reactions went with inversion is highly probable based on similar types of reactions.

### Intramolecular Reactions

The nucleophilic substitution reactions at sulfur discussed so far have all been intermolecular. There are very few examples of intramolecular nucleophilic substitution at sulfur reported.

Intramolecular substitution reactions fall into two main categories; exocyclic, in which the leaving group is lost from the ring, and endocyclic, in which the leaving group remains part of the ring.
Scheme VII. The reactions of N-carbomethoxy-p-toluenesulfonimidoyl chloride.
Eschenmoser attempted to demonstrate an intramolecular endocyclic reaction at saturated sp$^3$ carbon. S_N2 reactions at sp$^3$ carbon are generally assumed to involve a linear Nu . . . C . . . L transition state. If this required transition state cannot form, nucleophilic substitution should not occur. Eschenmoser designed a system that required the nucleophile to approach the carbon center at an approximate right angle to the leaving group in order for the intramolecular reaction to occur (see Scheme VIII). High-dilution crossover experiments with an equimolar mixture of 50a and deuterium labeled 50b were performed. If the reaction were intramolecular, one should obtain a $d_0:d_6$ ratio of 1:1. However, a ratio of $d_0:d_3:d_6$ equal to 1:2:1 was obtained which proved that the reaction was intermolecular.

When the leaving group was arranged so that a linear transition state was possible, the intramolecular substitution took place (see Scheme IX, 53).

Recently Baldwin formulated rules for ring closure reactions (see Figure 3). These rules are based on the stereochemical requirements of the transition state. Whether X and Y can attain the required transition state
Scheme VIII. Experiment by Eschenmoser: The intermolecular reaction

50a: R=H
50b: R=D
Scheme IX. Experiment by Eschenmoser: The intramolecular reaction

\[
\begin{align*}
\text{SO}_2 & \quad \text{CH}_2\text{I} \quad \text{B}^- \\
\text{SO}_2 & \quad \text{CH}_2 \quad \text{SO}_2 \\
\text{CH}_3 & \quad \text{CH}_3 \\
53 & \\
\to & \\
\text{SO}_2 & \quad \text{C} \equiv \text{CH}_2 \\
\text{SO}_2 & \quad \text{CH}_3
\end{align*}
\]
Figure 3. Rules for ring closure
geometry will depend on the nature and length of the chain connecting X and Y. For tetrahedral systems, three to seven-membered ring exocyclic reactions are favored and have many literature precedents, but five and six endocyclic processes are disfavored. Eschenmoser's endocyclic system would have had a six-membered ring transition state which is disfavored; and, as predicted, the intramolecular reaction did not occur. These results support the necessity for a linear transition state for S_N2 reactions at sp^3 carbon.

Baldwin does add that second row elements may not follow these rules because of their larger radii and bond distances. Sulfur, since it can form a trigonally bi-pyramidal transition state, may allow for geometries that are not possible for first row elements like carbon. It should be possible for the nucleophile and leaving group to be at right angles in an apical-equatorial arrangement for nucleophilic substitution reactions at sulfur, in which case, the reaction should go with retention of configuration at sulfur.

Only a few examples exist in the literature of endocyclic nucleophilic reactions at sulfur. In an attempt to demonstrate a nonlinear transition state for sulfinyl sulfur, 3-hydroxy-1-methylpropyl 2'-nitrobenzenesulfenate (54) was treated with sodium hydride in dioxane yielding a mixture of 3-Hydroxybutyl 2'-nitrobenzenesulfenate (55), starting material, butane-1,3-diyl bis(2-nitrobenzenesulfenate)
Treatment of the primary sulfenate $5^\circ$ under the same conditions gave only starting material and decomposition products.

\[
\begin{align*}
\text{MeCH} & \xrightarrow{\text{CH}_2\text{CH}_2\text{OH}} \text{NaH} & \text{MeCH} & \xrightarrow{\text{CH}_2\text{CH}_2\text{O}} \text{SAr} \\
\text{0} & \text{SAr} & \rightarrow & \text{OH} \\
54 & \sim & 55 & \sim \\
+ \text{MeCH} & \xrightarrow{\text{CH}_2\text{CH}_2\text{O}} \text{SAr} \\
\text{0} & \text{SAr} \\
56
\end{align*}
\]

(35)

If the trans-sulfenylation reaction was intramolecular, it would have required a non-linear transition state. However, if the rearrangement was intermolecular, a linear $S_N2$-type transition state would be possible. The authors stated that the observed reaction was most likely intermolecular, but they do not give definitive evidence for this conclusion.

The treatment of arenesulfonamides such as $57$, which have a completely substituted nitrogen, with a strong base (phenyllithium, n-butyllithium, or methyllithium) resulted in a rearrangement to the sulfone $58$. If the nitrogen of the sulfonamide was not completely substituted, only metalation occurred and starting material was recovered. This reaction was shown to be intramolecular by crossover experiments. The first step was metalation at the acidic
ortho-sulfonyl hydrogen (eq. 37), followed by a transmetalation and then the rearrangement. If these ortho positions were blocked, such as with 59 and 60, no rearrangement occurred, but only a variety of cleavage reactions took place.
Neither Hellwinkel\textsuperscript{55} nor Shafer and Clossen\textsuperscript{54} commented on the geometry of the transition state for these rearrangements, which would be classified according to Baldwin as four-membered ring endocyclic.

There is only one investigation of the stereochemistry of an endocyclic reaction at sulfur.\textsuperscript{56} (R)-l-ephedrine-p-toluenesulfinate (61) rearranged to (S)-l-ephedrine-p-toluenesulfinamide (62) (eq. 38). At low concentrations (4.1 x 10\textsuperscript{-3}M) predominant retention of configuration took place, but at high concentrations mainly inversion occurred. Thus, at low concentrations intramolecular endocyclic sulfinyl transfer occurred via a proposed five-membered tetracoordinate intermediate 63 and retention was predicted.

\begin{equation}
\begin{array}{c}
\text{N} \quad \phi \\
\text{SO}_2 \\
\text{BuLi} \\
\Rightarrow \\
\text{N} \quad \phi \\
\text{H} \quad \text{Li} \\
\text{SO}_2 \\
\text{BuLi} \\
\Rightarrow \\
\text{NH} \\
\text{SO}_2 \\
\end{array}
\end{equation}

(37)
The purpose of this research is to investigate the stereochemistry of endocyclic nucleophilic reactions at sulfur.
RESULTS AND DISCUSSION

Part I

Reaction of Sulfoxides with Organolithium Reagents.
The original purpose of this research was to study the chemistry of sulfuranes by extending the previous investigation of the reaction of tricoordinate aromatic sulfoxides with aryllithium reagents. Thietane 1-oxides were of particular interest because they had been little studied and because the geometry of the four-membered ring might require an apical-equatorial arrangement in a trigonal bi-pyramid transition state. The only example of the reaction of thietane 1-oxide with organometallic reagents is the work of Dodson\textsuperscript{35} who used Grignard reagents as the base. We found that the addition of 2,2-dimethylthietane 1-oxide to phenyllithium resulted in the formation of 2,2-dimethylcyclopropyl phenyl sulfide in 44 percent yield and of diphenyl sulfide in 52 percent yield (eq. 39).

\[
\begin{align*}
\text{S} = 0 & \quad + \quad \text{PhLi} \quad \rightarrow \quad & \quad \text{A} \quad + \quad \text{PhSPh} \\
\text{71} & \quad \text{S} - \text{Ph}
\end{align*}
\]

2,2-Dimethylcyclopropyl phenyl sulfide was identified by its mass spectrum (see Appendix, Figure A). The major fragmentation paths are reported here (see Scheme X). Loss of
Scheme X. Fragmentation of 2,2-dimethylcyclopropyl phenyl sulfide.

\[ \begin{align*}
\text{CH}_3 & \quad \text{H} & \quad \text{H} & \quad -\text{e} & \quad \text{CH}_3 & \quad \text{H} & \quad \text{H} & \quad \text{M}^+_{178} \\
\text{CH}_3 & \quad \text{S} & \quad \phi & \quad \quad & \quad & \quad & \quad & \quad \\
\quad & \quad & \quad & \quad & \quad & \quad & \quad & \quad \\
\text{CH}_3 & \quad \text{H} & \quad \quad & \quad & \quad & \quad & \quad & \quad \\
\text{m/e 69} & \quad & \quad & \quad & \quad & \quad & \quad & \quad \\
\end{align*} \]
methyl group from the molecular ion (m/e+ 178) led to 64 (m/e 163). Cleavage of the S - C bond led to 65 (m/e 69) and 66 (m/e 109).

Table 1. m/e of major peaks (relative intensity, percent)

<table>
<thead>
<tr>
<th>m/e</th>
<th>relative abundance</th>
</tr>
</thead>
<tbody>
<tr>
<td>69</td>
<td>94.5</td>
</tr>
<tr>
<td>77</td>
<td>17.8</td>
</tr>
<tr>
<td>109</td>
<td>74.0</td>
</tr>
<tr>
<td>121</td>
<td>6.8</td>
</tr>
<tr>
<td>129</td>
<td>9.6</td>
</tr>
<tr>
<td>130</td>
<td>17.8</td>
</tr>
<tr>
<td>134</td>
<td>21.9</td>
</tr>
<tr>
<td>163</td>
<td>45.2</td>
</tr>
<tr>
<td>178</td>
<td>100.0 M+</td>
</tr>
<tr>
<td>179</td>
<td>12.3 (M+1)+</td>
</tr>
<tr>
<td>180</td>
<td>12.3 (M+2)+</td>
</tr>
</tbody>
</table>

This reaction might occur by an initial nucleophilic attack at sulfur to form sulfurane 67 which then reacted further by either of two pathways (see Scheme XI). In path A, sulfurane 67 formed sulfonium salt 68. On addition of a second phenyllithium, 68 gave sulfurane 69 which decomposed to diphenyl sulfide and an untrapped material. If the reaction proceeded along path B, the second phenyllithium abstracted an α-hydrogen to form carbanion 70 which rearranged to 2,2-dimethylcyclopropyl phenyl sulfide (71).

Dodson also obtained a cyclopropyl phenyl sulfide and diphenyl sulfide when 2,4-diphenylthietane 1-oxide was treated with phenylmagnesium bromide. It appears that nucleophilic attack at sulfur and carbanion formation are two competing reactions.
Scheme XI. Reaction of Sulfoxide with Phenyllithium.
That the diphenyl sulfide was formed via sulfonium salt 68 is supported by the work of Trost.\textsuperscript{36} He found that treatment of sulfonium salt 72 with n-butyllithium gave sulfide and cyclopropane (eq. 40). He proposed the formation of a tetracoordinate sulfur species similar to 69 which collapsed to produce the sulfide and cyclopropane. Since he did not obtain any cyclopropyl sulfide, it is unlikely that sulfide 71 was formed via a sulfonium salt intermediate but was formed more probably by another pathway. It would be valuable to treat sulfonium salt 68 with phenyllithium to determine if cyclopropyl sulfide 71 can form from this intermediate.

Our work was not continued and many interesting questions relating to the stereochemistry of the reaction, the effect of varying the ring size of the sulfoxide, or of varying the organolithium remain unanswered.
Part II

**Endocyclic Nucleophilic Substitution at Sulfur.** The aim of this research was to investigate the stereochemistry of nucleophilic substitution at tricoordinate sulfur (IV) and at tetracoordinate sulfur (VI). Endocyclic systems were used in order to determine the geometry of the substitution processes at sulfur. It was necessary to synthesize molecules in which the nucleophile N and leaving group L were arranged (as in 73) so that intramolecular endocyclic substitution would occur. If two of the carbons are part of an aromatic ring, the intramolecular process would be more favored entropically since rotation about the C-C bond would be impossible.

Since more is known about the stereochemistry of substitution at sulfinyl sulfur, such species were investigated first. Apical-apical (inversion), equatorial-axial (inversion), and apical-equatorial (retention) attack and departure on trigonally bipyramidal intermediates have been demonstrated for sulfinyl sulfur.

The first such molecule that we attempted to synthesize was p-toluenesulfinyl 2-(p-toluenesulfonyl)-methylbenzene sulfone (74) which when treated with a
non-nucleophilic base would be predicted to undergo an intramolecular endocyclic rearrangement (eq. 41). Sulfinyl sulfones such as $7_4$ can exist in optically active forms, and it was intended to make optically active $7_4$ so that the stereochemistry of the reaction could be probed.

Only symmetrical sulfinyl sulfones ($R$-$SO$-$SO_2$-$R$) are reported in the literature and there are no known methods for the synthesis of unsymmetrical sulfinyl sulfones. Sodium 2-(p-toluenesulfonyl)methylbenzenesulfinate ($7_5$) was added to p-toluenesulfinyl chloride but the isolated product was not the desired sulfinyl sulfone $7_4$ but rather p-tolyl 2-(p-toluenesulfonyl)methylbenzene thiosulfonate ($7_6$) (eq. 42). The structures of thiosulfonates $7_6$ and $7_9$ were determined by CHN analyses and by nmr. From the CHN analyses, $7_6$ could have had either structure $7_6$ or $7_9$. However, the nmr spectrum of $7_6$ had only one peak for the tolyl methyls
since 76 has two equivalent sulfonyl tolyl groups, whereas
the nmr for thiosulfonate 79 had two tolyl methyl peaks,
since 79 has one sulfonyl tolyl and one sulfenyl tolyl
group.

The reason that this thiosulfonate was formed may
be due to the fact that sulfinyl sulfones are thermally
unstable and are known to rearrange to thiosulfonates.58
They undergo unimolecular thermal decomposition apparently
by a homolytic dissociation of the S-S bond with subsequent
head-to-head recombination of the radical fragments to form
sulfenyl sulfonate.77 (eq. 43). The reaction of 77 with
sulfinic acid gave the thiosulfonate product.57 Inevitably
some water was present in the reaction mixture (eq. 42) since
the sodium sulfinate salt 75 exists as a hydrate and it is
difficult to dry it completely.

The formation of thiosulfinate 76 may also be
explained by an alternative route (eq. 44) in which the
Disulfoxide 78, which is unstable, disproportionates to give a thiosulfonate. Excess sulfinyl chloride was present in the reaction mixture (eq. 42).

\[
\text{Ar} - \text{S} - \text{S} - \text{Ar} + \text{ArSO}_2\text{H} \rightarrow \text{ArSO}_3\text{H} + \text{Ar} - \text{S} - \text{S} - \text{Ar}
\]

(43)

\[
\text{Ar} - \text{S} - \text{S} - \text{Ar} + \text{H}_2\text{O} \rightarrow 2 \text{ArSO}_2\text{H}
\]
sulfinic acid

\[
\text{Ar} - \text{S} - \text{O} - \text{SAr} + \text{ArSO}_2\text{H} \rightarrow \text{ArSO}_3\text{H} + \text{Ar} - \text{S} - \text{S} - \text{Ar}
\]

(44)

\[
\text{Ar} - \text{S} - \text{S} - \text{Ar} + \text{ArSCl} \rightarrow \text{Ar} - \text{S} - \text{Cl} + \text{Ar} - \text{S} - \text{S} - \text{Ar}
\]
disproportionation

(44)
Another route to the desired sulfinyl sulfone \(7^4\) was explored. An aqueous solution of sodium sulfinate \(7^5\) was mixed with a benzene solution of \(N-(p\text{-toluenethio})\)-succinimide to give \(p\text{-tolyl} 2-(p\text{-toluenesulfonyl})\)methylbenzene thiosulfonate \((7^9)\), which could then be oxidized, in principle, with \(m\text{-chloroperbenzoic acid to produce } 7^4\). However, the desired product was not formed by this oxidation, but rather, \(p\text{-tolyl} p\text{-toluenethiosulfinate (p-Tol-S-SO-p-Tol)}\) and other unidentified materials were obtained.
Among known compounds containing a single S-S linkage, the sulfinyl sulfone appears to be unique with regard to the extreme ease of dissociation of the S-S bond. Consequently, the attempt to synthesize sulfinyl sulfone 74 was abandoned.

Optically active thiosulfinates (R-S-SO-R') have been synthesized and they are relatively stable compounds. Therefore, we attempted to synthesize 2-(p-toluenesulfonyl)-methylbenzene p-toluenethiosulfinate (80) which when treated with a base should undergo an endocyclic nucleophilic reaction (eq. 46).

![Reaction Diagram](image)

\[
\begin{align*}
\text{80} & \xrightarrow{B^-} \text{80'} \\
\text{81} & \xrightarrow{\text{Et}_2\text{O}, \text{Pyr.}} \text{82}
\end{align*}
\]
2-(p-Toluenesulfonyl)methylbenzenethiol (81) was treated with p-toluenesulfinyl chloride. However, the desired thiosulfinate 80 was not formed; disulfide 82 was formed instead (eq. 47). The structure of 82 was determined by CHN analysis and by nmr. Also, 82 was reduced back to thiol 81 with zinc powder and sulfuric acid. Thiol 81 undergoes oxidation to the disulfide with extreme ease and this thiol, if dissolved in anhydrous ether and allowed to stand at room temperature for a few hours, will oxidize to the disulfide. The reaction might give the desired thiosulfinate 80 if peroxides and oxygen were rigorously excluded from the solution, but this was not attempted.

We also attempted to synthesize sulfonic anhydride 83 but were not successful (eq. 48) since only starting material was recovered. The intramolecular rearrangement of this anhydride would have been of interest, since it would have involved a six-membered endocyclic system (see structure 84).
Both O- and N-\(\text{p}\)-toluenesulfonyl derivatives of \(\text{o}\)-aminophenols can be prepared, since selectivity in the monotosylation is possible using tertiary amines of different basicity (see Scheme XII). \(\text{o}\)-Aminophenol and compounds 85, 86, and 87 can easily be distinguished by tlc since they possess different \(R_F\) values. The ir spectrum of sulfonamide 85 has a sharp NH peak and a strong broad OH peak; the ir spectrum of sulfonate 86 has two sharp NH peaks; and the ir spectrum of the ditosylate 87 has a single sharp NH peak in the 3200 to 3500 cm\(^{-1}\) region.

The selective O-tosylation with the stronger base (Et\(_3\)N) probably is due to the formation of phenoxide anion which acts as the nucleophile. When pyridine was used as the base, the tosylation product was N-(2'-hydroxyphenyl)-4-toluenesulfonamide (85), but if triethylamine was used, the tosylation product was 2'-aminophenyl 4-toluenesulfonate (86). Ditosylation with two equivalents of \(\text{p}\)-toluenesulfonyl chloride and two equivalents of triethylamine gave 2'-(4''-toluenesulfonylamido)phenyl 4-toluenesulfonate (87).

The addition of \(\text{n}\)-butyllithium to a very dilute solution of sulfonate 86 in THF resulted in the rearrangement of the sulfonate to the sulfonamide 85 (eq. 49). Two equivalents of \(\text{n}\)-butyllithium gave about 20 percent rearrangement; three equivalents gave about 60 percent rearrangement; four equivalents gave about 90 percent rearrangement; and five equivalents gave about 90 percent rearrangement (see
Scheme XII. Tosylation of \( o \)-Aminophenol.

\[
\begin{align*}
\text{p-Tol SO}_2\text{Cl} & \quad \text{pyridine} \\
\text{NH-SO}_2\text{-p-Tol} & \\
\text{NH}_2 & \\
\text{p-Tol SO}_2\text{Cl} & \quad \text{Et}_3\text{N} \\
\text{O-SO}_2\text{-p-Tol} & \\
\text{2 p-Tol SO}_2\text{Cl} & \quad \text{2 Et}_3\text{N} \\
\text{NH-SO}_2\text{-p-Tol} & \\
\text{O-SO}_2\text{-p-Tol} & 
\end{align*}
\]
Appendix. Figures B through E). The percent of rearrangement was determined by measuring the peak heights of the tolly methyl groups in the nmr. The tolly peak for sulfonate $86$ is at $\delta = 2.50$ and the tolly peak for sulfonamide $85$ is at $\delta = 2.41$ (see Appendix, Figures F and G).

Hellwinkel found that only one equivalent of organolithium was needed for sulfonamide $88$ to rearrange to the sulfone (eq. 50) in approximately 50 percent yield.
He used methyl lithium, phenyl lithium and n-butyl lithium as bases. Closson\textsuperscript{54} in a similar study with compound 88 (R = CH\textsubscript{3}) found it necessary to use 2.5 to 3 equivalents of base to effect the rearrangement. He found that n-butyl lithium, methyl lithium, phenyl lithium, and diisopropyl amide gave rearrangement. The bases which did not give rearrangement were sodium hydride, lithium hydride, sodium amide, lithium metal, and methyl magnesium iodide. Closson's yields varied from 45 percent to 89 percent depending on the base used and on the nature of R. Closson found that the addition of one equivalent or less of base gave a bright yellow solution, which when treated with methyl iodide gave ortho methylation (eq. 51). Thus, the first stage of the reaction is ortho metalation. Treatment of this yellow solution with additional base gave a red-brown solution which yielded the rearranged product.

\begin{equation}
\begin{array}{c}
\text{88} \\
\text{SO}_2\text{N}^\phi \\
\text{CH}_3
\end{array}
\xrightarrow{\text{equiv n-BuLi}}
\begin{array}{c}
\text{SO}_2\text{N}^\phi \\
\text{Li} \\
\text{CH}_3
\end{array}
\end{equation}

(51)
The rearrangement of sulfonate 86 required four equivalents of n-butyllithium and possible sites of lithiation are illustrated by structure 89 where the initial reaction was lithiation ortho to the sulfonyl group.

The addition of four equivalents of n-butyllithium to a dilute solution of sulfonamide 85 (eq. 49) gave only unchanged starting material as determined by nmr and tlc. None of the sulfonate 86 could be detected. Therefore, the rearrangement does not occur in the opposite direction.

The ditosylate 87 was treated with n-butyllithium and was found by nmr and tlc to remain unchanged (eq. 52). It is possible that the rearrangement failed because of steric crowding at the nitrogen.

The following sulfonates were found to undergo this rearrangement to the sulfonamide (eq. 53). Each of the compounds in equation 53 was synthesized following the same general procedure used for making sulfonamide 85 and sulfonate 86.
87

\[
\text{[Reaction 52]}
\]

\[
R = \text{H or CH}_3
\]
However, 2'-amino-4'-methylphenyl 2,4,6-trimethyl-benzenesulfonate (90) did not undergo the rearrangement but formed a variety of decomposition products on reaction with n-butyllithium as determined by the large number of spots on tlc and by the nmr spectrum (eq. 54). The expected rearranged sulfonamide was synthesized according to the general method for making these sulfonamides. A comparison of the nmr spectrum of this compound with the nmr spectrum of the product of the reaction in equation 54 showed that none of this sulfonamide was produced. This is in agreement with the findings of Closson, who made N-methyl-N-2,6-dimethylphenyl-benzenesulfonamide (91) and N-methyl-N-phenyl 2,4,6-trimethylbenzenesulfonamide (92) and found that with these compounds the rearrangement failed. Instead, apparently a variety of cleavage reactions occurred. He stated that this failure was due to the blocking of the ortho positions by the methyl groups which prevented lithiation at these
positions. Blockage of these ortho positions in sulfonate 90 (eq. 54) to lithiation should not prevent the rearrangement so that the failure of 90 to rearrange is more likely due to the increased steric hindrance at the sulfur which prevented the attainment of the necessary transition state.

\[
\begin{align*}
\text{CH} & \text{CH} \\
\text{CH} & \text{CH} \\
\text{CH} & \text{CH}
\end{align*}
\]

91

\[
\begin{align*}
\text{CH} & \text{CH} \\
\text{CH} & \text{CH} \\
\text{CH} & \text{CH}
\end{align*}
\]

92

Mikolajczyk demonstrated that the presence of ortho methyl groups on the benzene ring did not retard the rate of nucleophilic displacement at sulfonyl sulfur in the chloride-radiochloride ion exchange between radioactive tetraethylammonium chloride and sulfonyl chloride (eq. 55).

\[
\begin{align*}
\text{CH}_3 & \text{SO}_2\text{Cl} + \text{Et}_4\text{NCl}^* \rightleftharpoons \text{CH}_3 & \text{SO}_2\text{Cl}^* \\
\text{CH}_3 & \text{SO}_2\text{Cl} + \text{Et}_4\text{NCl}
\end{align*}
\]

(55)
The ortho methyl groups may, in fact, accelerate nucleophilic substitution at the sulfonyl center. He attributed this acceleration in rate to the "relief of steric interactions between alkyl groups and the sulfonyl sulfur oxygen atoms upon transformation of a tetrahedral sulfonyl structure into a trigonal bipyramidal intermediate" (eq. 56).

That the rearrangement of sulfonate 90 does not occur supports the premise that the rearrangement of sulfonates to sulfonamides in eq. 49 occurs by an intramolecular mechanism. If the rearrangement were intermolecular, the nucleophile and leaving group would be located in an axial-axial arrangement, which molecular models (Corey-Pauling-Koltun or CPK) showed gave relief of strain between ortho methyls and the doubly bonded oxygens, and therefore the rearrangement of sulfonate 90 should occur more easily.

On the other hand, the intramolecular reaction forces the nucleophile and leaving group to be arranged in a
diequatorial position (see Scheme XIII, structure 93) in which case the two sulfonyl oxygen atoms would be located diaxially, which is not a favored arrangement for electron-rich groups, or in an axial-equatorial position as in 94 where the oxygens are all equatorial and the aromatic ring is axial. However, in this latter conformation there is a good deal of steric interaction between the three oxygen atoms and the ortho methyl groups. Therefore, the intramolecular rearrangement of sulfonate 90 probably cannot occur because the necessary intermediates 93 or 94 cannot form.

Other bases were also used to determine if they would effect the rearrangement of sulfonate 86 to sulfonamide 85 (eq. 49). When phenyllithium was used, the rearrangement did not occur. Instead the phenyllithium, which is a more nucleophilic base than n-butyllithium, gave nucleophilic attack at sulfur to yield phenyl p-tolyl sulfone and o-aminophenol (eq. 57). Methyllithium also did not cause the rearrangement to sulfonamide 85. By comparison with the tlc of an authentic sample of methyl p-tolyl sulfone, it was shown that this product was not produced. No rearrangement appears to have occurred since the starting material was recovered as demonstrated by tlc.

The possibility that the rearrangement in eq. 49 occurs by an intramolecular process was suggested by the work of Hellwinkel and of Closson. Closson was able to demonstrate by a crossover experiment that the rearrangement
Scheme XIII. Stereochemical course of the intramolecular endocyclic reaction of 2'-aminophenyl arylsulfonates
of sulfonamide 88 to sulfone (eq. 50) was intramolecular. Hellwinkel synthesized a cyclic sulfonamide 95, which underwent rearrangement to a cyclic sulfone by what could only be an intramolecular mechanism. If sulfonamide 95 is treated with only one equivalent of n-butyllithium, only unrearranged starting material is recovered. The rearrangement occurred on the addition of the second equivalent of n-butyllithium. The sulfonamide 95 is not able to undergo an intramolecular transmetalation as occurs in eq. 50
because of the steric constraints of the system. Also, intermolecular transmetalation apparently does not occur to any significant degree. Therefore, two equivalents of base are needed to effect the rearrangement.

If the rearrangement in eq. 49 occurs via an intermolecular mechanism, the formation of o-aminophenol and the ditosylate 87 as intermediates would be expected (see Scheme XIV). An equimolar mixture of o-aminophenol and the ditosylate 87 was treated with n-butyllithium. No new products were formed. Only starting material was detected by tlc and nmr. The addition of a small amount of sulfonate 86 to the mixture of o-aminophenol and ditosylate 87 did not change these results, so it seems unlikely that the rearrangement went by way of a chain-type mechanism with an anion of o-aminophenol as the chain carrier.

From this result it appears unlikely that the rearrangement occurs by an intermolecular mechanism and thus must occur by an intramolecular endocyclic mechanism with nucleophilic substitution at the tetracoordinate sulfur to form a sulfurane (96) intermediate or transition state, with the nucleophile and the leaving group in an apical-equatorial arrangement.

To establish more conclusively that the rearrangement is indeed intramolecular, a crossover reaction was performed (see Scheme XV).
Scheme XIV. The Intermolecular Mechanism.

\[
\text{NH}_2\text{-O-SO}_2\text{-p-Tol} + \text{NH}_2\text{-O-SO}_2\text{-p-Tol} \xrightarrow{\text{n-BuLi}} \left[ \begin{array}{c} \text{NH}_2\text{OLi} + \text{NH-SO}_2\text{-p-Tol} \end{array} \right] \xrightarrow{87} 2 \text{NH-SO}_2\text{-p-Tol} \text{OH} \xrightarrow{85}
\]
The possible products 99 through 102 were synthesized by the general method for preparing these compounds.

Equal amounts of 2'-amino-4'methylphenyl 4-tert-butylbenzenesulfonate (97) (1.5 g, 4.7 mmol) and 2'-amino-phenyl 4-methoxybenzenesulfonate (98) (1.5 g, 5.4 mmol) were dissolved in 800 ml of THF. This mixture was treated with four equivalents of n-butyllithium. The rearrangement occurred. The product mixture gave two spots on tlc for the sulfonamide products. A mixture of authentic samples of the four possible products gave three spots on tlc since compounds 100 and 102 have the same Rf (see Table 2). Comparison of this tlc with the product tlc demonstrated that none of sulfonamide 101 was present in the product mixture. Thus, crossover product 101 was not formed by the rearrangement.
Scheme XV. Crossover Experiment.

intramolecular products

intermolecular products
The reaction products were separated by column chromatography on silica gel. Fraction 18 was shown by tlc to contain the two sulfonamide products (two spots). The nmr of this fraction had only one aromatic ring methyl peak at $\delta = 2.12$. (see Appendix, Figure I). The nmr of a mixture of authentic samples of the intramolecular product 99 and the intermolecular product 102 had two peaks at $\delta = 2.12$ and $\delta = 2.20$. When a small amount of sulfonamide 102 was added to the nmr tube which contained fraction 18, a methyl peak appeared at $\delta = 2.20$ (see Appendix, Figure J). This demonstrated fairly conclusively that sulfonamide 102 was not formed during the rearrangement.

Integration of the methyl peak at $\delta = 2.12$ and the tert-butyl peak at $\delta = 1.32$ of the nmr spectrum of fraction 18 gave an exact 1:3 ratio which would not be the case if any of the intermolecular product 101 were present.

Fraction 24 showed a single spot on tlc for the p-methoxy substituted sulfonamide. The nmr of this fraction had no methyl peak at $\delta = 2.20$ (see Appendix, Figure K). Since both p-methoxy substituted products have the same Rf, any sulfonamide 102 that was formed in the rearrangement should be present in this fraction. However, since there is no peak at $\delta = 2.20$ for the intermolecular product, it can be concluded that it was not produced.

The rearrangement of sulfonates 97 and 98 occurs rapidly and probably at similar rates. For both compounds,
the addition of n-butyllithium results in the initial formation of a light yellow colored solution followed by a change to a red-brown color within a few minutes. Closson\textsuperscript{54} observed a similar phenomenon in his investigation and showed that the initial yellow color was due to ortho lithiation. When the red-brown color appeared, the rearrangement had occurred. Therefore, it can be concluded that the absence of crossover products is probably not due to differences in the rate of the two rearrangements. Similar rates are expected, since the two compounds are alike in structure.

Table 2. Results of the Crossover Experiment

<table>
<thead>
<tr>
<th>Compound</th>
<th>( R_f )</th>
<th>( 5% ) EtOAc</th>
<th>tBu</th>
<th>OMe</th>
<th>Ar-CH(_3)</th>
<th>Nature of the product</th>
</tr>
</thead>
<tbody>
<tr>
<td>101</td>
<td>0.28</td>
<td>1.36</td>
<td></td>
<td></td>
<td></td>
<td>intermolecular</td>
</tr>
<tr>
<td>99</td>
<td>0.32</td>
<td>1.32</td>
<td></td>
<td></td>
<td>2.12</td>
<td>intramolecular</td>
</tr>
<tr>
<td>100</td>
<td>0.18</td>
<td></td>
<td>3.84</td>
<td></td>
<td></td>
<td>intramolecular</td>
</tr>
<tr>
<td>102</td>
<td>0.18</td>
<td></td>
<td></td>
<td></td>
<td>3.90</td>
<td>2.20</td>
</tr>
</tbody>
</table>

101: \( \text{N-(2')-hydroxyphenyl)-4-tert-butylenesulfonamide} \)
99: \( \text{N-(2'-hydroxy-4'-methylphenyl)-4-tert-butylenesulfonamide} \)
100: \( \text{N-(2'-hydroxyphenyl)-4-methoxybenzenesulfonamide} \)
102: \( \text{N-(2'-hydroxy-4'-methylphenyl)-4-methoxybenzenesulfonamide} \)

From these results it can be concluded that the rearrangement of 2'-aminophenyl 4-toluenesulfonate (eq. 49) occurs by an intramolecular endocyclic mechanism. This is
in violation of Baldwin's rule for ring closure which states that five-membered ring endocyclic reactions are forbidden. However, Baldwin does say that his rules may not apply to second row elements because of the larger radii and bond distances of these elements.

From the work of Eschenmoser it is apparent that nucleophilic substitution at first row elements must occur *via* a linear transition state. But since sulfur can form sulfurane-type structures, it is possible for nucleophilic attack to occur at right angles to the leaving group as in structure 96. Our results demonstrate that this must indeed occur.

There is a possible alternative mechanism for this rearrangement (eq. 59). The intermediate 103 must resemble a tight-ion pair so that crossover products are not formed. This mechanism would result in partial or complete racemization at sulfur if a corresponding optically active compound could be made.

In order to investigate the mechanism of this intramolecular endocyclic rearrangement in more detail, it would be valuable to determine the stereochemistry of the reaction. If the rearrangement does proceed *via* a sulfurane, such as 96, retention of configuration at sulfur would be predicted. Optically active tetracoordinate sulfur species were needed for our study. Although sulfonates are not chiral, it is possible to replace one of the oxygens by a
nitrogen to give derivatives of sulfonimidic acids, which are chiral. Optically active sulfonimidoyl chlorides have been made by Johnson.\textsuperscript{46,47} Optically active sulfonimidoyl chlorides will react with oxygen nucleophiles to give sulfonimidates (eq. 60) with inversion of configuration at sulfur.

\[
\begin{align*}
\text{R'} - &\text{S} - \text{Cl} + \text{OAr}^- \rightarrow \text{R} - &\text{S} - \text{OAr}^+ + \text{Cl}^- \\
\end{align*}
\]
Our aim was to make the optically active sulfonimidate 104 and sulfonimidamide 105, both of known configuration, and then to determine the stereochemistry of the rearrangement (eq. 61).

![Chemical structures](attachment:image)

**Equation 61**

Synthesis of the desired sulfonimidoxy chloride required N-methyl p-toluenesulfinamide, which can be prepared from p-toluenesulfinyl chloride and methylamine (eq. 62).

\[
\begin{align*}
\text{p-Tol} - \text{S} - \text{Cl} + \text{NH}_2\text{CH}_3 & \quad \xrightarrow{\text{anhydrous ether}} \quad \text{p-Tol} - \text{S} - \text{NHCH}_3 \\
& \quad \xrightarrow{-78^\circ} \\
\end{align*}
\]

Equation 62

N-Methyl p-toluenesulfinamide was oxidatively chlorinated to give N-methyl p-toluenesulfonimidoyl chloride (106) (eq. 63). Sulfonimidoyl chloride 106 is unstable and is very moisture sensitive so it was used immediately without characterization.
The sulfonimidoyl chloride, dissolved in anhydrous ether, was added to a solution of o-aminophenol and triethylamine in DMF. Two products were isolated by column chromatography on silica gel. The sulfonimidamide 105 was the major product. Only a small amount of the sulfonimidate 104 was formed (eq. 64).
Because only a slight amount of the desired sulfonimidate was formed, ways of blocking the nitrogen were explored. Sulfonimidates are easily hydrolyzed under acidic conditions so that the nitrogen protecting group must be removable under non-acidic conditions. The first such group that was used was the acetyl group. Acetic anhydride was added to an acidic aqueous solution of 2-amino-4-methylphenol. 2-Acetamino-4-methylphenol (107) precipitated on the addition of sodium acetate to the solution (eq. 65).

\[
\begin{align*}
\text{CH}_3 \text{CONHCH}_3 + & \quad \text{NaOAc} \\
\text{CH}_3 \text{CONHCH}_3 + \text{CH}_3 \text{CONHCH}_3 & \quad \text{NaOAc} \\
\end{align*}
\]

Sulfonimidoyl chloride 106 in ether was added under nitrogen to a solution of 2-acetamino-4-methylphenol (107) and triethylamine in methylene chloride to yield N'-acetyl 2'-amino-4'-methylphenyl N-methyl 4-toluenesulfonimidate (108) (eq. 66).
Unfortunately, all efforts to hydrolyze the acetyl group resulted in nucleophilic attack at the sulfur atom which gave 2-acetamino-4-methylphenol (107) and N-methyl p-toluenesulfonamide (eq. 67).

The aminophenol was treated with trifluoroacetic anhydride to give 2-trifluoroacetamino-4-methylphenol (109).
(eq. 68). The trifluoroacetyl protecting group was used since it should be more easily removed than the acetyl group.

\[
\text{CH}_3\text{NHCOCF}_3 + \text{CH}_3\text{NH}_2\text{OH} \rightarrow \text{CH}_3\text{NHCOCF}_3\text{OH}
\]

(S8)

Sulfonimidoyl chloride 106 was treated with phenol 109, but the desired sulfonimidate did not form. Instead, phenol 109 and N-methyl p-toluenesulfonamide were recovered (eq. 69).

\[
\text{CH}_3\text{NHCOCF}_3 + \text{NCH}_3\text{SOCI} \rightarrow \text{CH}_3\text{NHCOCF}_3\text{OH} + \text{NCH}_3\text{SO}_{2}\text{NHCH}_3
\]

(69)
Since we have been unsuccessful in finding a suitable nitrogen protecting group, unprotected o-aminophenol can be used (eq. 64) and the two products separated by chromatography. A sufficient amount of sulfonimidate 104 could be obtained in this way in order to determine if the rearrangement occurs with retention as predicted. If so, the rearranged product 105b should have the same configuration as the unrearranged sulfonamide 105a (eq. 70).
To be certain that no rearrangement of 104 to 105a occurs in the reaction shown by eq. 64, the following sequence will be attempted with 105a (eq. 71). Compound 110 should have the same sign of rotation independent of its method of synthesis.

The optically active sulfonimidoyl chloride 106 can be synthesized as illustrated in Scheme XVI. p-Toluenesulfinyl chloride is added to an ether solution of (-)-menthol and pyridine. Two diastereomers are formed. The (-)-(S)-sulfinate (111) can be isolated by fractional crystallization since the (+)-(R)-sulfinate is a liquid. Treatment of (-)-(S)-(−)-menthyl p-toluenesulfinate (111) with methylmagnesium bromide yields the optically active (+)-(R)-menthyl p-tolyl sulfoxide (112). Relfuxing this sulfoxide in methanol with tosyl azide and copper powder will give (-)-(R)-N-(p-tosyl)methyl-p-tolylsulfoximide (113), which
when mixed with concentrated sulfuric acid forms \((-\)-(R)-methyl-\(p\)-tolylsulfoximide (114). Sulfoximide 114 on treatment with formic acid and formaldehyde gives \((-\)-(R)-methyl \(p\)-tolyl \(N\)-methyLSulfoximide (115). Aluminium amalgam reduction of sulfoximide 115 occurs with retention to give the optically active \((R)\)-\(N\)-methyl \(p\)-toluenesulfinamide (116). This reaction is reported\(^{49}\) to give a high degree of retention of optical activity. Chlorination of sulfinamide 116 then produces the optically active sulfonimidoyl chloride 106.

Work is continuing on this problem.
Scheme XVI. Synthesis of optically active sulfonimidoyl chloride.

\[ \text{p-TolSOCl} + \text{(-)-menthol} \xrightarrow{\text{PYR}} \text{(-)-(S)-111} \]

\[ \xrightarrow{\text{MeMgBr}} \text{inv.} \quad \xrightarrow{\text{p-TolSO}_2\text{N}_3} \text{ret.} \]

\[ \text{(-)-(R)-112} \quad \text{(-)-(R)-113} \]

\[ \xrightarrow{\text{H}_2\text{SO}_4} \quad \xrightarrow{\text{HCH}} \quad \xrightarrow{\text{HCO}_2\text{H}} \]

\[ \text{(-)-(R)-114} \quad \text{(-)-(R)-115} \]
Scheme XVI (continued).

\[
\begin{align*}
\text{H}_3\text{C} & \text{N}\text{S} \overset{\text{ret.}}{\rightarrow} \text{H}_3\text{C} & \text{N}\text{S} \\
\text{CH}_3 & & \text{CH}_3
\end{align*}
\]

\[
\begin{align*}
\text{(-)-(R)-115} & \text{ (R)-116} \\
\text{(R)-116} & \text{Cl}_2 \rightarrow \text{H}_3\text{C} & \text{N}\text{S} \\
\text{Cl} & & \text{Cl}
\end{align*}
\]
EXPERIMENTAL

Instrumentation. Nmr spectra, obtained on a Varian A-60, Jeolco HM-100, or Varian EM 360 spectrometer, are in ppm downfield from TMS. Optical rotations were taken on a Carl Zeiss 0.005° photoelectric precision polarimeter. Ir spectra were obtained on a Perkin-Elmer Model 337 grating infrared spectrophotometer. Melting points, determined on a Hoover capillary melting point apparatus, are uncorrected. Glpc analysis of reaction mixtures was performed on an Aerograph Model 90-P Gas Chromatograph. Mass spectra were recorded with a Hitachi-Perkin Elmer RMU-6E mass spectrophotomer with an ionization potential of 30 eV.

Materials. All chemicals were reagent grade. Methylene chloride, carbon tetrachloride and chloroform were distilled from phosphorus pentoxide and stored over oven-dried potassium carbonate. THF was refluxed and then distilled from calcium hydride just prior to use. Anhydrous ether was dried over sodium wire. Pyridine and triethylamine were dried by distillation from barium oxide and were stored over potassium hydroxide pellets. o-Aminophenol and 2-amino-4-methylphenol were decolorized with Norit and recrystallized from 20 percent methanol in water. The glassware was dried by heating in a 100° oven for 24 hours and was cooled under
Tlc was performed on glass pre-coated plates, silica gel 60 F-254 made by E. Merck.

2,2-Dimethyl-1,3-propyl di-p-toluenesulfonate.\textsuperscript{64} p-Toluene sulfonyl chloride (228.8 g, 20 percent excess) was dissolved in 300 ml pyridine (dried over potassium hydroxide pellets) in a 1-l round-bottomed flask, equipped with an addition funnel and placed in an ice bath. 2,2-Dimethyl-1,3-propanediol (53 g, 0.5 mol) dissolved in 50 ml of pyridine was added dropwise so that the temperature remained at 0°C. This mixture was stirred for 24 hr at room temperature. The reaction mixture was poured into 700 ml of ice water and the white solid was collected by filtration and washed with a small portion of ice water. The product was recrystallized from 2-l of isopropyl alcohol yielding 197.4 g (95.2 percent) of the desired product: mp 120-121.5°C (lit.\textsuperscript{64} mp 121-123°C).

3,3-Dimethylthietane.\textsuperscript{65} 2,2-Dimethyl-1,3-propyl di-p-toluenesulfonate (153.4 g, 0.37 mol) was intimately mixed with sodium sulfide nonahydrate (120 g, 0.5 mol) using a mortar and pestle and then was introduced in portions over a period of one hour to vigorously stirred dimethyl sulfoxide (300 ml) in a 1-l round-bottomed flask equipped with a magnetic stirrer and maintained at 80-90°C in an oil bath. On completion of this addition, 24 g (0.1 mol) of sodium sulfide nonahydrate was added and the flask was connected to a distillation apparatus. The temperature of the mixture
was raised to 130-140° and the liquids which distilled from
the reaction mixture were collected until the distillate
became nearly clear, about 65 ml. Sodium chloride was
added to the distillate and the two layers were separated.
The upper organic layer was dried over calcium chloride.
Distillation gave 21 g (55 percent) of 3,3-dimethylthietane:
bp 119-121° (lit. bp 116-117°). Nmr spectrum no. 2545
(CDC13): δ 2.9(s,2,SCH2), 1.26(s,3,CH3). The low yield
was due to a leak in the distillation apparatus.

3,3-Dimethylthietane 1-Oxide. 65 3,3-Dimethylthietane
(21 g, 0.2 mol) was dissolved in 56 ml of acetic acid in a
250-ml round-bottomed flask, equipped with a magnetic
stirrer and an addition funnel, and placed in an ice bath.
To this was added 31 percent hydrogen peroxide (22.5 g,
0.2 mol), dissolved in 14 ml of acetic acid, dropwise over
a period of 20 min. The mixture was stirred for one hour.
The excess solvent was removed under aspirator vacuum at
55°. The residue was dissolved in ether and this solution
was stirred over sodium hydroxide pellets until all excess
acetic acid was removed as determined by a basic reaction
with litmus paper. The sodium acetate was removed by
filtration. The ether solution was dried over anhydrous
magnesium sulfate. The ether was removed on a rotary
evaporator and the sulfoxide residue was distilled. Water
should not be run through the condenser during distillation
since the product solidifies at 30° and will collect in the
condenser. Distillation yielded 14.09 g (58 percent):
bp 70-79°C (5.0 mm), mp 30°C (lit mp 35-36°C).

The IR spectrum (no. 21187, neat) exhibited strong
S = 0 at 1080 cm⁻¹ and 2960 m, 1430 m, 1400 m, 1190 m cm⁻¹;
nmr spectrum no. 17,042 (CDCl₃): δ 3.52 (d of t, 2, trans OSCH),
3.00 (d of t, 2, cis OSCH), 1.30 (s, 3, cis CH₃), 1.24 (s, 3, trans
CH₃).

Phenyllithium²⁶ Lithium wire (1.8 g, 0.26 mol)
was hammered flat and cut into thin strips and placed in a
500-ml three-necked round-bottomed flask equipped with a
mechanical stirrer, an addition funnel, and a condenser.
All glassware was dried in an oven for 24 hr and assembled
while hot. The system was connected to a nitrogen outlet
and flushed with nitrogen. A positive nitrogen pressure
was maintained throughout the reaction by the use of a
mineral oil bubbler connected to the condenser. Anhydrous
ether (dried over sodium wire) (100 ml) was introduced and
then bromobenzene (13.15 ml, 0.125 mol) was added dropwise
to the vigorously stirring ether and lithium. The mixture
turned cloudy and then blackish. The stirring was continued
until all the lithium was dissolved.

Reaction of Phenyllithium and 3,3-Dimethylthietane
1-Oxide. The above flask of phenyllithium was cooled to 0°C
in an ice bath. A positive nitrogen pressure was maintained.
3,3-Dimethylthietane 1-oxide (3 g, 0.025 mol) was dissolved
in 15 ml of anhydrous ether and added dropwise to the
phenyllithium. The mixture was stirred for three hours at 0° and then for three hours at room temperature. It was hydrolyzed with 100 ml of 5 percent hydrochloric acid and the ether and water layers were separated. The water layer was extracted three times with 15 ml of ether and the ether layers were combined and dried over anhydrous magnesium sulfate. The ether was removed on the rotary evaporator and then by a vacuum pump, leaving 6.5 g of residue.

The composition of the residue was determined by gas-liquid chromatography using a column: 8 ft x 1/8 in, 10 percent Apiezon L on Chromosorb W 60/80, 230°. Four peaks were obtained. Three of the peaks were identified by comparison with the retention time of authentic samples as: bromobenzene, biphenyl, and diphenylsulfide. The remaining peak was isolated and identified as 2,2-dimethyl-66 cyclopropyl phenyl sulfide by mass spectrum. Nmr spectrum no. 3500 (CDCl₃) δ 6.90 (m, 5, ArH), 1.90 (q, 1, CH), 1.20 (s, 3, CH₃), 1.16 (s, 3, CH₃), 0.90 (q, 1, CH), 0.45 (t, 1, CH).
<table>
<thead>
<tr>
<th>Compound</th>
<th>Retention Time Min</th>
<th>Retention Volume Uncorrected ml</th>
<th>Relative Retention $\alpha$</th>
</tr>
</thead>
<tbody>
<tr>
<td>benzene</td>
<td>2.6</td>
<td>36.4</td>
<td>1.0</td>
</tr>
<tr>
<td>bromobenzene</td>
<td>4.0</td>
<td>56.0</td>
<td>1.5</td>
</tr>
<tr>
<td>2,2-dimethyl cyclopropyl phenyl sulfide</td>
<td>10.8</td>
<td>151.2</td>
<td>4.2</td>
</tr>
<tr>
<td>biphenyl</td>
<td>13.4</td>
<td>187.6</td>
<td>5.2</td>
</tr>
<tr>
<td>diphenyl sulfide</td>
<td>26.0</td>
<td>364.0</td>
<td>10.0</td>
</tr>
</tbody>
</table>

The flow rate was 14 ml/min and $\alpha$ was measured using benzene as the standard. The FID response factor was determined from a standard solution of benzene, bromobenzene, biphenyl, and diphenyl sulfide and then dividing $A/W$ of each peak by the $A/W$ of benzene. Since an authentic sample of

<table>
<thead>
<tr>
<th>Peak</th>
<th>W mmol</th>
<th>$A$ Area cm$^2$</th>
<th>F Correction Factor</th>
<th>Weight Calculated g</th>
</tr>
</thead>
<tbody>
<tr>
<td>benzene</td>
<td>12.8</td>
<td>11.23</td>
<td>1.0</td>
<td>.439</td>
</tr>
<tr>
<td>bromobenzene</td>
<td>6.4</td>
<td>6.04</td>
<td>1.08</td>
<td>1.02</td>
</tr>
<tr>
<td>2,2-dimethyl cyclopropyl phenyl sulfide</td>
<td>--</td>
<td>--</td>
<td>1.11</td>
<td>1.97</td>
</tr>
<tr>
<td>biphenyl</td>
<td>5.4</td>
<td>5.27</td>
<td>1.11</td>
<td>0.08</td>
</tr>
<tr>
<td>diphenyl sulfide</td>
<td>6.5</td>
<td>6.37</td>
<td>1.12</td>
<td>2.42</td>
</tr>
</tbody>
</table>
2,2-dimethylcyclopropyl phenyl sulfide was not available, its correction factor was assumed to be 1.11. Using the formula \[ W_b = \frac{W_a \cdot A_b}{F_b \cdot A_a} \] where \( W_a \) is the moles of benzene and \( A_a \) is the area of the benzene peak, the amount \( W_b \) of each component was calculated. The yield of 2,2-dimethylcyclopropyl phenyl sulfide was 44 percent and of diphenyl sulfide was 52 percent.

1,1-Dioxy-3-Chloro-3H-2,1-Benzoxathiole. Benzaldehyde sulfonic acid, sodium salt (21 g, 0.1 mol) was placed in a 250-ml round-bottomed flask equipped with a magnetic stirrer. To this was added phosphorus oxychloride (31 g, 18.5 ml, 0.2 mol) and then phosphorus pentachloride (21 g, 0.1 mol). A reflux condenser was attached and the mixture heated in an oil bath at 120° for one hour. The excess phosphorus oxychloride was removed under reduced pressure. The residue was added carefully to ice water to destroy any unreacted phosphorus pentachloride and to dissolve the inorganic salts. Filtration yielded 20 g of white product (100 percent), which was recrystallized from benzene: mp 115°, nmr spectrum no. 4450 (CDCl\textsubscript{3}): \( \delta \) 7.5-8.0 (m, 4, ArH), 7.28 (s, 1, CHCl).

o-Tolyl Sultone. The crude 1,1-dioxy-3-chloro-3H-2,1-benzoxathiole (100 g, 0.49 mol) was suspended in 1-l of ether in a 2-l three-necked round-bottomed flask provided with a mechanical stirrer, an addition funnel, and a reflux condenser. To the suspension was added zinc powder (150 g,
2.3 g-atom). Then conc hydrochloric acid (60 ml, 0.72 mol) was added slowly with vigorous stirring. The ether boiled, and, as the reaction progressed, the chlorosultone dissolved. Stirring was continued for one to three hours with the progress of the reaction followed by tlc or nmr. Over-reduction results in significant lowering of yield and should be avoided. After filtration of the zinc powder, the ether filtrate was placed in a beaker and 300 ml ice water added. The product precipitated and was collected by suction filtration. Reduction of the volume of ether layer under reduced pressure allowed the remainder of the product to precipitate. Recrystallization from benzene gave 11.6 g (68 percent): mp 111-112° (lit66 mp 112.5°). Nmr spectrum no 5869 (CDCl₃): δ 7.4-8.0 (m, 4 ArH), 5.67 (s, 2 CH₂).

Sodium p-Toluenesulfinate Dihydrate. In a 4-l beaker (a porcelainized metal bucket is a convenient alternative) equipped with a mechanical stirrer and thermometer was placed anhydrous sodium sulfite (600 g, 4.76 mol), sodium bicarbonate (420 g, 5.0 mol) and water (2.4 l). The mixture was heated on a hot plate at 70-80° and was maintained at this temperature by switching the hot plate off occasionally, while p-toluenesulfonyl chloride (484 g, 2.54 mol) was added in portions of 5 to 10 g with stirring over a period of three hours. When the addition was complete the mixture was heated and stirred at
70-80° for one hour. If the volume exceeded 2.4 l after this period, the excess water was allowed to evaporate by continued heating. The mixture was then removed from the hot plate and allowed to stand for ten hours. The solid sodium p-toluenesulfinate crystallized and was collected by filtration. It was recrystallized from water to give 493 g (91 percent).

Sodium 2-(p-Toluenesulfonyl)methylbenzenesulfonate. 51 o-Toly sultone (23.8 g, 0.14 mol) in a 500-ml three-necked round-bottomed flask equipped with a mechanical stirrer and a reflux condenser was dissolved in 300 ml acetone. Sodium p-toluenesulfinate (27 g, 0.14 mol) and sodium iodide (1 g, 6.7 mmol) were added. The suspension was stirred and refluxed for four days. The white precipitate, which was not soluble in acetone, was filtered by suction and washed with fresh acetone to remove excess iodine. The product was air-dried to yield 47.06 g (96.5 percent).

Sodium 2-(p-Toluenesulfonyl)methylbenzenesulfonate Chloride. 51 Sodium 2-(p-toluenesulfonyl)methylbenzenesulfonate (40 g, 0.115 mol) was put into a 500-ml round-bottomed flask provided with a magnetic stirrer. Chloroform (200 ml) was added to form a suspension to which was added phosphorus pentachloride (48 g, 0.23 mol). A reflux condenser was added and the mixture was refluxed for eight hours and then allowed to stand for 12 hours. This mixture was then
carefully poured over ice water to destroy the excess phosphorus pentachloride. The chloroform layer was dried over anhydrous sodium sulfate, reduced in volume on the rotary evaporator until a solid began to appear, and allowed to stand at 0° until crystallization was complete. The product was collected by suction filtration and recrystallized from benzene to give 31.6 g (79.8 percent): mp 126-128°.

The ir spectrum (no. 22720) exhibited strong O = S = O bands at 1320, 1300, 1180, 1150 cm⁻¹. Moderate bands appeared at 1090, 830, 820, 773, 718, and 608 cm⁻¹. Nmr spectrum (no. 4625) (CDCl₃): δ 7.2-8.2 (m, 8, ArH), 4.93 (s, 2, CH₂), 2.20 (s, 3, CH₃).


Sodium 2-(p-Toluenesulfonyl)methylbenzenesulfinate (75) Distilled water (162 ml) was placed in a 500-ml beaker provided with a mechanical stirrer and rubber tubing for passing steam directly into the water. Steam was passed into the water until the temperature reached 70°. The steam was shut off and zinc dust (24 g, 0.37 g-atom) was added. The 2-(p-toluenesulfonyl)methylbenzenesulfonyl chloride (31.58 g, 0.09 mol) was added in small portions by means of a porcelain spoon over a period of ten minutes. Stirring was continued for ten minutes after the addition was completed.
Steam was passed into the mixture until the temperature reached 90°. The steam was shut off and 12 N aqueous sodium hydroxide solution (18 ml) was added. Then powdered sodium carbonate (9 g, 8 mmol) was carefully added to avoid frothing. The mixture was filtered by suction on a sintered glass filter.

The cake of unchanged zinc dust and zinc compounds was transferred back to the beaker and distilled water (50 ml) was added, the stirrer was started, and the steam was passed in until the mixture started to froth violently. The steam was shut off, but stirring was continued for ten minutes. The mixture was filtered and the filtrate was added to the main solution in a large evaporating dish. The solution was evaporated to one liter by means of a gas burner, cooled to room temperature, and then to 0°. The mixture was filtered and the white crystals were air-dried. The product according to the literature is the dihydrate salt. The yield was 29.9 g (83.1 percent).

**p-Toluenesulfonyl Chloride.** Thionyl chloride, which had been purified by distillation from quinoline (10 ml quinoline per 50 ml thionyl chloride) and then from boiled linseed oil (20 ml linseed oil per 50 ml thionyl chloride), (500 ml, 755 g, 6.35 mol) was placed in a 2-l round-bottomed flask provided with a magnetic stirrer. Powdered sodium
p-toluenesulfinate dihydrate (150 g, 0.701 mol) was added in several small portions over a 30-minute period with stirring. The temperature rose at first but soon dropped as the addition proceeded. Throughout the addition, rapid gas evolution was observed. When the evolution of gas slowed, a drying tube was attached and the mixture was stirred at room temperature for one hour. The mixture was treated with 100 ml of anhydrous ether, then filtered under nitrogen through a sintered glass filter, and the collected solid was washed with one 50-ml portion of dry ether. The ether solutions were combined and excess thionyl chloride was removed under aspirator vacuum at 50°. The last traces of thionyl chloride were removed by the addition and removal of several small portions of dry ether. This yielded 74 g (0.42 mol) (61 percent) of the sulfinyl chloride which was used undistilled.

Attempted Synthesis of p-Toluenesulfinyl 2-(p-Toluene-
sulfonyl)methylbenzene Sulfone (74). To a flame-dried 100-ml round-bottomed flask provided with a magnetic stirrer was added p-toluenesulfinyl chloride (17.8 g, 0.1 mol) dissolved in 20 ml anhydrous ether. A drying tube protected the flask from moisture. Sodium 2-(p-toluenesulfonyl)methylbenzenesulfinic (18.5 g, 0.1 mol) was added to the mixture in small portions with stirring. Several glass spheres were added to this suspension and the mixture was stirred for two days. It was then poured over ice water and the solid
product filtered. Trituration of the product with a little water and then twice with a small portion of ether yielded after recrystallization from benzene 1.12 g (26 percent): mp 181-181.5°.

The ir (spectrum no. 22251) exhibited peaks at 1320(s), 1290(s), 1140(s), 1080(s) cm⁻¹. Nmr spectrum (no. 4789) (CDCl₃): δ 7.20-7.50 (m, 12, ArH), 4.30 (s, 2, CH₂), 2.40 (s, 6, CH₃).


Thus the product was identified as p-toly 2-(p-toluenesulfonyl)methylbenzene thiosulfonate (7f).

**p-Toluenesulfenyl Chloride.** Thiocresol (62.1 g, 0.5 mol) was dissolved in 300 ml of pentane in a 1-1 round-bottomed flask provided with a magnetic stirrer. The flask was placed in an ice bath. Chlorine (39 g, 0.6 mol), which had been condensed in a tared flask placed in an acetone-Dry Ice bath and then allowed to warm slowly, was bubbled into the thiocresol solution via a glass tube placed below the surface of the solution. The resulting solution of sulfenyl chloride was used directly in the following reaction.

**N-(p-Toluenethio)phthalimide.** Phthalimide (73.5 g, 0.5 mol), triethylamine (60 g, 0.6 mol), and 200 ml of DMF were added to a 1-1 round-bottomed flame-dried flask
equipped with a magnetic stirrer and an addition funnel. The flask was placed in an ice bath and the system was flushed with nitrogen. Under an atmosphere of nitrogen, the solution of p-toluenesulfenyl chloride, made above, was placed in the addition funnel and added dropwise to the stirred phthalimide solution. The reaction mixture was stirred for 30 minutes at 0° and then transferred to a 4-l beaker to which two liters of ice water were added. The product precipitated and was collected by suction filtration to give 121 g (95 percent) of the colorless sulfenimide, which was recrystallized from ethanol to give white needle-shaped crystals: mp 201-202° (lit74 191-194°). The ir spectrum (no. 22383) exhibited strong carbonyl bands at 2000 and 1980 cm⁻¹ and strong bands at 1390, 1280, and 1155 cm⁻¹. Nmr spectrum (no. 4834) (CDCl₃): δ 7.10-8.00 (m,8,ArH), 2.40 (s,3,CH₃).

Attempted Synthesis of p-Tolyl p-Toluenethiosulfonate.75

N-(p-Toluenethio)phthalimide (2.69 g, 0.01 mol) was dissolved in benzene (100 ml) and placed in a 250-ml separatory funnel. Sodium p-toluenesulfinate (2.12 g, 0.01 mol) was dissolved in water (50 ml) and also added to the separatory funnel. This two-phase system was vigorously shaken for ten minutes at room temperature. The two layers were separated, the benzene layer was dried over anhydrous sodium sulfate, and then evaporated under reduced pressure. The resulting residue was found to be starting material, N-(p-toluenethio)phthalimide.
Di-p-Tolyl Disulfide.\textsuperscript{76} p-Thiocresol (12.4 g, 0.1 mol) was placed in a 250-ml round-bottomed flask, provided with a magnetic stirrer, and was dissolved in dimethyl sulfoxide (50 g, 45.5 ml). A reflux condenser was added and the flask was placed in an oil bath and heated at 80-90° for eight hours. The solution was decolorized with Norit and allowed to cool to room temperature. The reaction mixture was poured into a ten-fold volume of ice water and after three hours the precipitated disulfide was collected by suction filtration, washed twice with water, and dried in vacuo. The product was recrystallized from 95 percent ethanol to give 10.8 g (87.8 percent): mp 46-47° (lit\textsuperscript{76} mp 48°.)

N-(p-Toluenethio)succinimide.\textsuperscript{78} Di-p-tolyl disulfide (6.16 g, 0.025 mol) was dissolved in 25 ml of dry carbon tetrachloride in a dry 100-ml round-bottomed flask provided with a magnetic stirrer. To this was added benzoyl peroxide (0.1 g) and N-bromosuccinimide (4.45 g, 0.025 mol). This mixture was heated at 60° with stirring till the N-bromosuccinimide dissolved (about three hours). During this period, moisture was excluded by means of a calcium chloride drying tube. Upon cooling the mixture to 0°, in an ice bath, the solid product was filtered and then washed with a small portion of ice-cold carbon tetrachloride. Recrystallization from 95 percent ethanol yielded 3.2 g (58 percent):
mp 109-110° (lit mp 85.5-86°). The ir (spectrum no. 22631) exhibited a strong carbonyl peak at 1730 cm⁻¹ and strong bands at 1295 and 1140 cm⁻¹. Nmr spectrum (no. 5066) (CDCl₃): δ 7.0-7.6 (m,4,ArH), 2.75 (s,4,CH₂), 2.30 (s,3,CH₃).

**p-Tolyl 2-((p-Toluenesulfonyl)methylbenzene Thiosulfonate (79).** Sodium 2-((p-toluenesulfonyl)methylbenzenesulfinate (1.75 g, 0.005 mol) in 50 ml of water and N-((p-toluenethio)succinimide (0.89 g, 0.005 mol) in 100 ml of benzene were placed in a 250-ml round-bottomed flask equipped with a mechanical stirrer. The two phases were mixed by vigorous stirring for 30 minutes at room temperature. The layers were separated and the aqueous layer was washed twice with 50 ml of methylene chloride. The benzene and methylene chloride layers were combined and dried over anhydrous magnesium sulfate and the solvent was removed on the rotary evaporator. Recrystallization from absolute ethanol gave 0.38 g (26 percent): mp 100-100.5°. The ir (spectrum no. 22632) exhibited peaks at 1321(s), 1300(m), 1145(s), and 1133(m) cm⁻¹. Nmr spectrum (no. 5122) (CDCl₃): 7.1-8.0 (m,12,ArH), 4.65 (s,2,CH₂), 2.40 (s,3,CH₃), 2.32 (s,3,CH₃).

**Anal.** Calcd for C₂₁H₂₀O₄S₃; C,58.31; H,4.66.

Found: C,58.28; H,4.66.

**2-(p-Toluenesulfonyl)methylbenzenethiol (81).** Cracked ice (92 g) and conc sulfuric acid (16.6 ml, 30.54 g,
0.31 mol) were placed in a 500-ml three-necked round-bottomed flask, equipped with a mechanical stirrer and a reflux condenser. The mixture became very cold and was kept at -5° to 0° by means of an ice-salt bath. Mechanical stirring was started and 2-((p-toluenesulfonyl)methylbenzenesulfonyl chloride (15 g, 0.04 mol) was gradually added over a 30-minute period. Then zinc dust (15.35 g, 0.23 g-atom) was introduced in portions as rapidly as possible without allowing the temperature to rise above 0° over a 30-minute period. The contents of the flask were stirred for one hour at 0°. The ice bath was removed, the reaction mixture was allowed to warm to room temperature, and then it was heated to reflux for 12 hours while being stirred vigorously. Methylene chloride (25 ml) was added to the flask at room temperature to dissolve the organic product. The mixture was then filtered through a fritted glass funnel to remove the zinc. The two layers were separated and the water layer was washed with 25 ml of methylene chloride. The zinc cake was also washed with 25 ml of methylene chloride and this solution was filtered. The methylene chloride solutions were combined, dried over anhydrous magnesium sulfate, and the solvent was removed under reduced pressure. Recrystallization from isopropyl alcohol yielded 7.16 g (59 percent): mp 147-148°. The ir (spectrum no. 22888) exhibited a moderate S - H peak at 2540 cm⁻¹ and strong SO₂ peaks at 1286 and 1135 cm⁻¹. Nmr spectrum (no. 5759) (CDCl₃): δ 7.3-7.9 (m,8,ArH), 4.7 (s,2,CH₂), 3.65 (s,1,SH), 2.24 (s,3,CH₃).
A white powdery solid, which was not very soluble in isopropyl alcohol, was isolated: mp 190-191°. The ir (spectrum no. 22925) exhibited strong peaks at 1315, 1290, 1145 cm\(^{-1}\) and a moderate peak at 1085 cm\(^{-1}\). Nmr spectrum (no. 5834) (CDCl\(_3\)): \(\delta\) 7.20-7.70 (m, 8, ArH), 4.41 (s, 2, CH\(_2\)), 2.42 (s, 3, CH\(_3\)).

**Anal.** Calcd for C\(_{28}\)H\(_{26}\)O\(_4\)S\(_4\): C, 60.61; H, 4.72.

Found: C, 60.28; H, 4.75.

This product was identified as di-2-(p-toluenesulfonyl)-methylphenyl disulfide (8\(_8\)).

**p-Tolyl p-toluenethiosulfinate.**\(^80\) p-Thiocresol (6.2 g, 0.05 mol), dissolved in 5 ml of anhydrous pyridine and 96 ml of anhydrous ether, was put into a 250-ml round-bottomed flask provided with a magnetic stirrer and maintained at 0° in an ice bath. An addition funnel, which had been flamed dry, was added to the flask and the system was flushed with nitrogen. p-Toluenesulfinyl chloride, dissolved in 56 ml of anhydrous ether, was added to the addition funnel under a nitrogen atmosphere. The sulfinyl chloride was added dropwise to the vigorously stirring p-thiocresol so that the temperature stayed at 0°. A heavy white precipitate formed. After the addition was completed, the reaction mixture was stirred for an additional 15 minutes at 0° and then was treated with two ml of ice-cold 1 M sulfuric acid. Extraction three times with 10-ml portions of ice-cold 1 M sulfuric acid and then six times with 20-ml portions of ice water gave an ether.
layer which was dried over anhydrous magnesium sulfate and concentrated on the rotary evaporator to give a yellow oil which crystallized in the refrigerator. Recrystallization from benzene-hexane gave 9.96 g (76 percent): mp 104° (lit73 88-89°). The ir (spectrum no. 22907) exhibited strong peaks at 1089, 1070, 805 cm⁻¹ and a moderate peak at 1300 cm⁻¹. Nmr spectrum (no. 77691) (CDCl₃): δ 7.1-7.6 (q,8,ArH), 2.31 (s,3,CH₃), 2.27 (s,3,CH₃).

**Anal.** Calcd for C₁₄H₁₄O₃S₂: C,64.08; H,5.38. Found: C,63.85; H,5.45.

**Silver(I) Oxide.** ⁸¹ To avoid exposing the reaction mixture to light a 500-ml Erlenmeyer flask was covered with aluminum foil. The flask was equipped with a magnetic stirrer. Sodium hydroxide (1 M, 200 ml, 0.2 mol) was mixed with silver nitrate (34 g, 0.2 mol) with stirring for one hour in the stoppered flask. The dark brown precipitate was filtered by suction. After washing the filter-cake well in turn with deionized water, acetone, and anhydrous ether, it was dried in a vacuum desiccator at 0.5 mm to give 26.1 g (100 percent).

**Silver Tosylate.** ⁸² In an oven dried 100-ml round-bottomed flask provided with a magnetic stirrer and covered with aluminum foil to protect the reaction mixture from light, silver oxide (20 g, 0.086 mol) and p-toluenesulfonic acid (15 g, 0.086 mol) were mixed in 20 ml of dry acetonitrile. The flask was stoppered, and the mixture was stirred for one hour. The
silver, which precipitated, was filtered, the acetonitrile was removed on the rotary evaporator, and the product was dried in vacuo (0.4 mm) at 65° to yield 19.74 g (88.3 percent).

2-(p-Toluenesulfonyl)methylbenzenesulfonyl Hydrazine. Hydrazine hydrate (3.2 g), which had been diluted by one half with water to form a 50 percent aqueous solution, was put in a 500-ml Erlenmeyer flask equipped with a magnetic stirrer and an addition funnel. About 2.5 moles of hydrazine hydrate per mole of sulfonyl chloride were used. 2-(p-Toluenesulfonyl)-methylbenzenesulfonyl chloride (8.62 g, 0.025 mol) was dissolved in 200 ml of benzene, placed in the addition funnel, and was added dropwise to the vigorously stirring solution of hydrazine hydrate. A heavy white precipitate formed. The mixture was stirred for 30 minutes and then set in an ice bath for one hour. The product was filtered and air-dried to yield 8.5 g (100 percent): mp 103.5-106°. Nmr spectrum (no. 6099) (CDCl₃): δ 7.3-8.4 (m, 10, ArH, NH₂), 7.0 (bs, 1, NH), 5.1 (s, 2, CH₂), 2.52 (s, 3, CH₃).

2-(p-Toluenesulfonyl)methylbenzenesulfonyl Bromide. 2-(p-Toluenesulfonyl)methylbenzenesulfonyl hydrazine (8.5 g, 0.025 mol) and 100 ml of 10 percent hydrochloric acid were placed in a 250-ml Erlenmeyer flask provided with a magnetic stirrer and an addition funnel. Sodium bromide (1.05 g, 0.01 mol) and sodium bromate (3.05 g, 0.02 mol) dissolved in 18 ml of water were added dropwise to this turbid mixture.
At the end of the addition, the yellow color of the bromine persisted. The evolution of nitrogen transformed the white precipitate into a thick persistent froth that was filtered immediately, washed with ice water, and dried in vacuo. The sulfonyl bromide was kept from heat and light. Recrystallization from 1:1 petroleum ether-benzene gave 6.24 g (64 percent): mp 145-147°. The nmr spectrum (no. 6098) (CDCl₃): δ 8.3-7.3 (m,8,ArH), 5.1 (s,2,CH₂), 2.47 (s,3,CH₃).

Attempted Synthesis of 2-(p-Toluenesulfonyl)methylbenzene p-Toluene Sulfonic Anhydride. 2-(p-Toluenesulfonyl)methylbenzenesulfonyl bromide (1.95 g, 0.005 mol) was dissolved in 40 ml freshly distilled acetonitrile in a 100-ml round-bottomed flask equipped with a magnetic stirrer and covered with aluminum foil. Silver tosylate (1.4 g, 0.005 mol) in 20 ml of dry acetonitrile was added to the flask, which was then stoppered and vigorously stirred for two hours at 50°. The desired anhydride did not form. Starting material was recovered.

2'-Aminophenyl 4-Toluenesulfonate. o-Aminophenol (1.09 g, 0.01 mol) was suspended in 20 ml methylene chloride in a 50-ml Erlenmeyer flask equipped with a magnetic stirrer. The flask was placed in an ice bath and triethylamine (1.01 g, 0.01 mol) was added with stirring. Then p-toluenesulfonyl chloride (1.905 g, 0.01 mol) was added. The reaction mixture was stirred for one hour at room temperature. The solution was washed with 15 ml of water, the organic layer
dried over anhydrous magnesium sulfate, and the solvent was evaporated under reduced pressure to give 2.84 g (94 percent) of slightly yellow crystals. Recrystallization from benzene-hexane: mp 99-100° (lit 100-101°). The ir (spectrum no. 23107) exhibited NH2 peaks at 3420 and 3510 cm⁻¹, and also strong peaks at 1315, 1192, 1175, 1150, 1120, and 1084 cm⁻¹. Nmr spectrum (no. 6095) (CDCl₃):  δ 8.0-6.6 (m,8,AH), 3.85 (bs,2,NH₂), 2.50 (s,3,CH₃).

This general method was used to prepare the following sulfonates:

2'-Amino-4'-methylphenyl 4-Toluenesulfonate. mp 76-78°. Nmr spectrum (no. 6054) (CDCl₃):  δ 7.9-7.3 (q,4,AH), 6.8-6.3 (m,3,AH), 3.8 (s,2,NH₂), 2.42 (s,3,CH₃), 2.20 (s,3,CH₃). This is the presumed compound since CHN analysis was not done.

2'-Aminophenyl 4-tert-Butylbenzenesulfonate. mp 63-64°. Nmr spectrum (no. 6210) (CDCl₃):  δ 8.0-7.5 (q,4,AH), 7.1-6.5 (m,4,AH), 3.78 (s,2,NH₂), 1.36 (s,9,tBu). Anal. (acetyl derivative) mp 131°. Calcd for C₁₉H₂₁NO₄S: C,62.22; H,6.09; N,4.03. Found: C,62.0; H,6.28; N,4.41.

2'-Amino-4'-methylphenyl 4-tert-Butylbenzenesulfonate (95). mp 114-116°. The ir (spectrum no. 2310) exhibited strong peaks for NH₂ at 3410 and 3510 cm⁻¹ and for SO₂ at 1300 and 1175 cm⁻¹, and strong peaks at 1375, 1200, 1150, 1109, 1080, and 845 cm⁻¹. Nmr spectrum (no. 6070) (CDCl₃):  δ 8.1-7.6 (q,4,AH), 6.9-6.4 (m,3,AH), 3.82 (bs,2,NH₂), 2.22 (s,3,CH₃), 1.36 (s,9,tBu).
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**Anal.** Calcd for C_{17}H_{21}NO_{3}S: C, 63.92; H, 6.52; N, 4.39. Found: C, 63.44; H, 6.52; N, 4.40.

**Anal.** (tosyl derivative). mp 146°. Calcd for C_{24}H_{17}-NO_{5}S_{2}: C, 62.18; H, 3.70; N, 3.02. Found: C, 62.2; H, 4.19, N, 3.90.

**2'-Aminophenyl 4-Methoxybenzenesulfonate (96).** mp 93-94°. The ir (spectrum no. 23101) exhibited strong peaks for NH_{2} at 3400 and 3500 cm^{-1} and strong peaks at 1310, 1260, 1195, 1172, 1150, 1090, 1020 cm^{-1}. Nmr spectrum (no. 6198) (CDCl_{3}): δ 8.0-6.5 (m, 8, ArH), 3.92 (s, 5, OCH_{3} and NH_{2}).

**Anal.** Calcd for C_{13}H_{13}NO_{4}S: C, 55.90; H, 4.69; N, 5.02. Found: C, 55.4; H, 4.5; N, 4.90.

**Anal.** (acetyl derivative). mp 135-136°. Calcd for C_{15}H_{15}NO_{5}S: C, 56.06; H, 4.71; N, 4.36. Found: C, 56.0; H, 4.84; n, 4.85.

**2'-Amino-4'-methylphenyl 4-Methoxybenzenesulfonate.** mp 79-82°. Nmr spectrum (no. 6197) (CDCl_{3}): δ 8.0-6.4 (m, 7, ArH), 3.91 (s, 3, OCH_{3}), 3.80 (bs, 2, NH_{2}), 2.21 (s, 3, CH_{3}).

**Anal.** (acetyl derivative): mp 133-134°. Calcd for C_{16}H_{17}NO_{5}S: C, 57.29; H, 5.11; N, 4.18. Found: C, 57.46; H, 5.25; N, 4.22.

**2'-Amino-4'-methylphenyl 2,4,6-Trimethylbenzenesulfonate.** mp 83-84°; the ir (spectrum no. 23443) exhibited NH_{2} peaks at 3500 and 3400 cm^{-1} and strong peaks for SO_{2} at 1350 and 1170 cm^{-1}. Nmr spectrum (no. 7747) (CDCl_{3}): δ 6.83 (s, 2, ArH), 6.41 (s, 1, ArH), 6.15 (s, 2, ArH), 3.68 (s, 2, NH_{2}), 2.52 (s, 6, CH_{3}), 2.24 (s, 3, CH_{3}), 2.14 (s, 3, CH_{3}).

**Anal.** (acetyl derivative). mp 138°. Calcd for C_{18}H_{21}NO_{4}S: C, 62.22; H, 6.09; N, 4.03. Found: C, 62.70; H, 6.12; N, 3.68.
These sulfonates were analyzed by the acyl or p-tosyl derivatives.

**Acyl Derivative.** The sulfonate (0.005 mol) was put into a 25 ml round-bottomed flask equipped with a reflux condenser and a magnetic stirrer. Acetic anhydride (0.51 g, 0.5 ml), glacial acetic acid (0.5 ml) and zinc dust (0.005 g) were added. The mixture was refluxed for thirty minutes and then poured into ten ml of ice water. The product crystallized and was collected by vacuum filtration and purified by recrystallization from alcohol-water and then benzene-hexane.

**Tosyl Derivative.** The sulfonate (0.005 mol) was dissolved in 20 ml of methylene chloride in a 50 ml Erlenmeyer flask equipped with a magnetic stirrer. The solution was cooled to 0° in an ice bath. Pyridine (0.5 ml) was added and then p-toluenesulfonyl chloride (0.005 mol, 0.95 g). The mixture was stirred for two hours at room temperature, washed with ten ml of water, and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure to yield a solid which was re-crystallized from alcohol-water and then benzene-hexane.

**N-(2-Hydroxyphenyl)-4-toluenesulfonamide (85).** o-Aminophenol (1.09 g, 0.01 mol) was suspended in 20 ml of methylene chloride in a 50-ml Erlenmeyer flask provided with a magnetic stirrer. The flask was placed in an ice bath and the suspension was stirred. Pyridine (1 ml, 0.01 mol) was
added and then p-toluenesulfonyl chloride (1.905 g, 0.01 mol). The reaction mixture was stirred for one hour at room temperature. The solution was washed with 10 ml of water. The methylene chloride layer was dried over anhydrous magnesium sulfate, and then evaporated under reduced pressure to give 2.5 g (95 percent). Recrystallization from benzene: mp 138-139° (lit87 138-139°). The ir (spectrum no. 23108) exhibited a broadened strong peak at 3410 cm⁻¹ for the O-H, a sharp peak at 3280 cm⁻¹ for N-H, strong peaks at 1320 and 1160 cm⁻¹ for SO₂, and strong peaks at 1285, 1212, 1086, 911, 763, and 675 cm⁻¹. Nmr spectrum (no. 6096) (CDCl₃): δ 7.9-6.8 (m,10,ArH,NH,OH), 2.41 (s,3,CH₃).

This general method was used to prepare the following sulfonamides:

N-(2'-Hydroxy-4'-methylphenyl)-4-Toluenesulfonamide. mp 147-148°. Nmr spectrum no. 6064 (CDCl₃): δ 7.8-6.5 (m,8,ArH and OH), 6.2 (bs,1,NH), 2.41 (s,3,CH₃), 2.16 (s,3,CH₃). This is the presumed compound since CHN analysis was not done.

N-(2'-Hydroxyphenyl)-4-tert-Butylbenzenesulfonamide (99). mp 184.5-185°. Nmr spectrum (no. 6200) (CDCl₃): δ 8.0-6.4 (m,10,ArH,NH,OH), 1.36 (s,9,tBu).

Anal. Calcd for C₁₆H₁₉NO₃S: C,62.92; H,6.27; N,4.59. Found: C,63.11; H,6.50; N,4.84.

N-(2'-Hydroxy-4'-methylphenyl-4-tert-Butylbenzenesulfonamide (97). mp 138.5-139.5°. The ir (spectrum no. 23102) exhibited a strong broad peak at 3420 cm⁻¹ for O - H, a strong peak at 3280 cm⁻¹ for N - H, and strong peaks at 1400, 1320, 1278, 1160, and 1105 cm⁻¹. Nmr spectrum (no. 6088) (CDCl₃): δ 7.9-7.5 (q,4,ArH), 7.0-6.6 (m,3,ArH), 6.65 (s,1,OH), 6.28 (bs,1,NH), 2.12 (s,3,CH₃), 1.32 (s,9,tBu).

Anal. Calcd for C₁₇H₂₁NO₃S: C,63.92; H,6.63; N,4.39. Found: C,64.64; H,6.45; N,4.48.


N-(2'-Hydroxyphenyl)-4-Methoxybenzenesulfonamide (98). mp 118-119°; the ir (spectrum no. 23104) exhibited a strong broad peak at 3500 cm⁻¹ for O - H, strong peak at 3300 cm⁻¹ for N - H, and strong peaks at 1330, 1260, 1150, 980, 912, 830, 750, and 670 cm⁻¹. Nmr spectrum (no. 6614) (CDCl₃): δ 7.8-6.8 (m,10,ArH,NH,OH), 3.84 (s,3,OCH₃).

Anal. Calcd for C₁₃H₁₃NO₄S: C,55.90; H,4.69; N,5.02. Found: C,54.9; H,4.9; N,5.1.


N-(2'-Hydroxy-4'-methylphenyl)-4-Methoxybenzenesulfonamide (100). mp 102-104°; nmr spectrum no. 6191 (CDCl₃): δ 8.0-6.8 (m,10,ArH,NH,OH), 3.90 (s,3,OCH₃), 2.20 (s,3,CH₃).
**Anal.** (acetyl derivative). mp 122-123°. Calcd for
C_{16}H_{17}NO_{5}S: C, 57.29; H, 5.11; N, 4.18. Found: C, 57.2; H, 5.10; N, 4.33.

N-(2'-Hydroxy-4'-methylphenyl)-2,4,6-Trimethylbenzene-
sulfonamide. mp 129-130°; the ir (spectrum no. 23444)
exhibited a broad strong peak at 3450 cm\(^{-1}\) for O - H and
N - H and strong peaks at 1318, 1145, and 1105 cm\(^{-1}\). Nmr
spectrum (no. 7728) (CDCl\(_3\)): \(\delta\) 6.68 (s,2,ArH), 6.58 (s,2,ArH),
6.48 (s,1,NH), 6.39 (s,1,ArOH), 6.20 (s,1,OH), 2.42 (s,6,CH\(_3\)),
2.18 (s,3,CH\(_3\)), 2.0 (s,3,CH\(_3\)).

**Anal.** (acetyl derivative). mp 135°. Calcd for
C_{18}H_{21}NO_{4}S: C, 62.22; H, 6.09; N, 4.03. Found: C, 62.0; H, 6.16;
N, 4.20.

These sulfonamides were analyzed with the acetyl or
tosyl derivatives.

**Acetyl Derivative.** One gram of the sulfonamide was
dissolved in 5 ml of 3 N sodium hydroxide solution in a
50-ml Erlenmeyer flask. Ten to twenty grams of crushed ice
were added and then acetic anhydride (1.5 g, 1.5 ml) was
added. The mixture was shaken vigorously for two minutes.
The acetate precipitated out of solution and was collected by
vacuum filtration. It was purified by recrystallization
from alcohol-water and then benzene-hexane.

**Tosyl Derivative.** The sulfonamide (0.005 mol) was
dissolved in 20 ml of methylene chloride in a 50-ml
Erlenmeyer flask equipped with a magnetic stirrer. The
solution was cooled to 0° in an ice bath. Triethylamine
(0.5 g, 0.005 mol) was added and then p-toluenesulfonfonyl chloride (0.95 g, 0.005 mol). The mixture was stirred for two hours at room temperature, washed with ten ml of water, and dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure to yield a solid which was recrystallized from alcohol-water and then benzene-hexane.

2'- (4"-Toluenesulfonyl)phenyl 4-Toluenesulfonate. 

o-Aminophenol (1.09 g, 0.01 mol) was suspended in 20 ml of methylene chloride in a 50-ml Erlenmeyer flask equipped with a magnetic stirrer. The flask was placed in an ice bath and stirring was begun. Triethylamine (2.02 g, 0.02 mol) and then p-toluenesulfonfonyl chloride (3.8 g, 0.02 mol) were added. The reaction mixture was stirred for one hour at room temperature and then was washed with 10 ml of water. The methylene chloride layer was dried over anhydrous magnesium sulfate, concentrated under reduced pressure, to give the product which recrystallized from benzene-hexane to give white crystals: mp 138-140.5° (lit mp 143°).

The ir (spectrum no. 23109) exhibited a strong peak at 3280 for N - H and strong peaks at 1380, 1340, 1200, 1170, 1090 cm⁻¹. Nmr spectrum (no. 6097) (CDCl₃): δ 7.90-6.80 (m,13,ArH and NH), 2.50 (s,3,CH₃), 2.40 (s,3,CH₃).

This general method was used to prepare the following sulfonates.
4'-Methyl-2'-(4''-Toluenesulfonamido)phenyl 4-Toluenesulfonate. mp 137-139°; nmr spectrum (no. 6080) (CDCl₃): δ 7.9-6.6 (m, 12, ArH and NH), 2.50 (s, 3, CH₃), 2.39 (s, 3, CH₃), 2.30 (s, 3, CH₃).

2'-(4''-Methoxybenzenesulfonamido)phenyl 4-Methoxybenzenesulfonate. mp 120.5-122°; nmr spectrum (no. 6199) (CDCl₃): δ 8.0-6.9 (m, 13, ArH and NH), 3.94 (s, 3, OCH₃), 3.85 (s, 3, OCH₃).

Anal. Calcd for C₂₀H₁₉NO₇S₂: C, 53.44; H, 4.26; N, 3.12. Found: C, 53.3; H, 4.2; N, 3.4.

4'-Methyl-2'-(4''-Methoxybenzenesulfonamido)phenyl 4-Methoxybenzenesulfonate. mp 114-116°; nmr spectrum (no. 6087) (CDCl₃): δ 7.9-6.6 (m, 12, ArH and NH), 3.96 (s, 3, OCH₃), 3.86 (s, 3, OCH₃), 2.31 (s, 3, CH₃).

4'-Methyl-2'-(2'',4'',6''-Trimethylbenzenesulfonamido)-phenyl 2,4,6-Trimethylbenzenesulfonate. mp 157.5-159°; nmr spectrum (no. 7751) (CDCl₃): δ 7.17 (s, 1, NH), 7.10-6.18 (m, 7, ArH), 2.48 (s, 6, CH₃), 2.42 (s, 6, CH₃), 2.26 (s, 3, CH₃), 2.18 (s, 6, CH₃).

4-tert-Butylbenzenesulfonyl Chloride. tert-Butylbenzene (67 g, 0.5 mol) and 150 ml of chloroform (dry) were placed in a 1-l round-bottomed flask equipped with a magnetic stirrer and an addition funnel. The flask was placed in an ice bath. Chlorosulfonic acid (175 g, 1.5 mol) was added to the addition funnel and slowly dropped into the stirring solution. After the addition was complete,
the stirring was continued and the reaction mixture was allowed to warm slowly, over a 12-hour period, to room temperature. The solution was poured carefully over ice and the resulting organic and aqueous layers were separated. The aqueous layer was extracted with chloroform and the chloroform layers were combined and washed once with water. The volume of the organic layer was reduced under reduced pressure, and the remaining solution was allowed to crystallize in an ice bath to give 93.5 g (81 percent): mp 78-80°. Recrystallization from low-boiling petroleum ether and drying in vacuo gave mp 80-82° (lit 81-83°). Nmr spectrum (no. 6061) (CDCl₃): δ 8.14 (d, 2, ArH), 7.78 (d, 2, ArH), 1.40 (s, 9, tBu).

Rearrangement of 2'-Aminophenyl 4-Toluenesulfonate to N-(2'-Hydroxyphenyl)-4-Toluenesulfonamide. 2'-Aminophenyl 4-toluenesulfonate (0.04 g, 0.17 mmol) was placed in a dry 100-ml round-bottomed flask equipped with a magnetic stirrer. Dry THF (60 ml) was added and then the flask was capped with a rubber septum, flushed with nitrogen, and placed in an ice bath. 1.6 M n-Butyllithium (0.42 ml, 0.68 mmol), a four-fold excess, was introduced into the flask with a dry syringe. The reaction mixture was stirred for eight hours at room temperature and then hydrolyzed with 10 ml of 5 percent hydrochloric acid. The organic layer (THF) was removed under reduced pressure and the remaining aqueous layer was extracted three times with
20 ml of ether. The ether layers were combined, dried over anhydrous magnesium sulfate, and removed on the rotary evaporator and then in vacuo (0.3 mm) for two hours to give a brown liquid which contained the rearranged sulfonamide as shown by tlc (5 percent EtOAc, 95 percent CHCl₃) and by nmr. The nmr spectrum (no. 6105), (CDCl₃), exhibited a tolyl methyl peak at δ 2.41 for the sulfonamide and only a small peak at 2.50 for the sulfonate. It was estimated that the rearrangement went to 88 percent completion from measuring the peak heights.

Reaction of N-(2'-Hydroxyphenyl)-4-Toluenesulfonamide with n-Butyllithium. The procedure was the same as for the preceding rearrangement except that N-(2'-hydroxyphenyl)-4-toluenesulfonamide (0.04 g, 0.17 mmol) was dissolved in 60 ml of dry THF. The reaction product was identified by tlc (5 percent EtOAc, 95 percent CHCl₃) and by nmr. The nmr spectrum (no. 6120), (CDCl₃), showed a single tolyl methyl peak at δ 2.41 for the sulfonamide and no peak at 2.50 for the sulfonate. Thus, the rearrangement did not occur.

Reaction of 2'(4''-Toluenesulfonamido)phenyl 4-Toluenesulfonate with n-Butyllithium. The procedure was the same as above except that 2'(4''-toluenesulfonamido)phenyl 4-toluenesulfonate (0.17 g, 0.4 mmol) was dissolved in 80 ml of dry THF and n-butyllithium (1 ml, 1.6 mmol) was added. The reaction product was identified as unreacted starting material by tlc (5 percent EtOAc, 95 percent CHCl₃) and by
nmr. The nmr spectrum (no. 6137), (CDCl₃), matched identically with the nmr of the starting material.

**Reaction of 2'-(4"-Toluenesulfonamido)phenyl 4-Toluenesulfonate and o-Aminophenol with n-Butyllithium.**

The procedure was the same as above except that equivalent amounts of o-aminophenol (0.05 g, 0.458 mol) and 2'-(4"-toluenesulfonamido)phenyl 4-toluenesulfonate (0.19 g, 0.458 mol) were placed in a 250-ml flask with 160 ml of dry THF. n-Butyllithium (2.3 ml, 3.66 mmol) was added. The product was identified by tlc (5 percent EtOAc, 95 percent CHCl₃) and nmr. The nmr spectrum (no. 6063), (CDCl₃), showed that none of the N-(2'-hydroxyphenyl)-4-toluene-sulfonamide was formed.

**Crossover Experiment.** 2'-Amino-4'-methylphenyl 4-tert-butylbenzenesulfonate (1.5 g, 4.7 mmol) and 2'-aminophenyl 4-methoxybenzenesulfonate (1.5 g, 5.4 mmol) were placed in a dry 1-l round-bottomed flask provided with a magnetic stirrer. To this was added 800 ml of dry THF. The flask was capped with a rubber septum, placed in an ice bath, and flushed with dry nitrogen. 1.6 M n-Butyllithium (26 ml, 0.04 mol) was introduced with a dry syringe, the reaction mixture was stirred for six hours at room temperature, and then hydrolyzed with 100 ml of 5 percent hydrochloric acid. The THF was removed under reduced pressure. The aqueous layer was extracted three times with 50 ml of ether, the ether layers were combined, and dried over
anhydrous magnesium sulfate. The ether was removed by the rotary evaporator and then in vacuo (0.3 mm) for three hours. Tlc (5 percent EtOAc, 95 percent CHCl₃) showed that no N-(2'-hydroxyphenyl)-4-tert-butylbenzenesulfonamide (one of the possible products of the intermolecular reaction) was present.

The products were separated by column chromatography (silica gel column, 12" x 1"; 60-200 mesh; J. T. Baker; 5 percent EtOAc, 95 percent CHCl₃) to give two products which were identified by nmr. The nmr spectrum (no. 6256), (CDCl₃), of fraction 18, containing the two sulfonamide products, exhibited only one peak at δ 2.08 for the 4'-methyl. Integration of the peaks at δ 2.08 and 1.30 gave an exact 1:3 ratio. An authentic sample of N-(2'-hydroxy-4'methylphenyl)-4-methoxybenzenesulfonamide was added to this nmr tube and the nmr spectrum (no. 6266), (CDCl₃), now had a previously absent peak at 2.14, demonstrating that this compound was not formed in the rearrangement. Fraction 24 from the column contained a single compound, as shown by tlc, which was identified as N-(2'-hydroxyphenyl)-4-methoxybenzenesulfonamide by nmr (spectrum no. 6259), (CDCl₃): δ 7.8-6.5 (m, 9, ArH, NH), 3.90 (s, 3, OCH₃).

**The Rearrangement with Phenyllithium.** 2'-Aminophenyl 4-toluenesulfonate (8g) (0.1 g, 0.38 mmol) was dissolved in 70 ml of THF in a dried 100-ml round-bottomed flask equipped with a magnetic stirrer. The flask was capped with a septum,
flushed with nitrogen, and placed in an ice bath. Freshly prepared phenyllithium in ether (1.52 mmol) was added to the flask by means of a syringe. The mixture was stirred at room temperature for six hours and then hydrolyzed with ten ml of 5 percent hydrochloric acid. The THF was removed under reduced pressure and the remaining aqueous layer was extracted thrice with 20 ml of ether. The ether extracts were combined, dried over anhydrous magnesium sulfate, and the ether was evaporated under reduced pressure. The residue was analyzed by tlc (5 percent EtOAc, 95 percent CHCl₃). None of the rearrangement product 85 could be detected. Four spots were present on tlc which were identified by comparison with authentic samples as starting material, o-aminophenol, and phenyl p-tolyl sulfone and a fourth unidentified material.

The Rearrangement with Methyllithium. The procedure was the same as for the rearrangement with phenyllithium except that 1.52 mmol of methyllithium were added. The residue was analyzed by tlc (5 percent EtOAc, 95 percent CHCl₃). Mostly starting material was present. None of the rearrangement product 85 could be detected. No methyl tolyl sulfone was present as demonstrated by comparison with a tlc of an authentic sample.

Methyllithium. Methyllithium must be prepared from methyl iodide because the presence of iodine is essential.
Lithium wire (0.8 g) which had been flattened and cut into thin strips was added to a dried 250-ml three-necked round-bottomed flask equipped with a mechanical stirrer, a reflux condenser, and an addition funnel. The flask was flushed with nitrogen and a positive pressure of nitrogen was maintained throughout the reaction. Anhydrous ether (50 ml) was added to the flask. Methyl iodide (0.05 mol, 3.2 ml) was added with stirring at a rate adequate to maintain a gentle reflux. The mixture was stirred for 24 hours and was used immediately.

**N-Methyl p-Toluenesulfinamide.** Anhydrous ether (200 ml) was added to a 500-ml dried round-bottomed flask equipped with a magnetic stirrer. The flask was weighed and then was placed in an acetone-Dry Ice bath. Methylamine was bubbled into the flask by means of a gas dispersion tube placed below the liquid surface. When the weight of the flask had increased by about 10 g, which occurred fairly rapidly, a dried addition funnel was added and the system was flushed with nitrogen at -78°. Under an atmosphere of nitrogen, p-toluenesulfinyl chloride (24 g, 0.137 mol) dissolved in 100 ml of anhydrous ether was added to the addition funnel. The system was protected from moisture with a calcium chloride drying tube. The sulfinyl chloride was added dropwise to the rapidly stirring ether solution. After the addition was complete, the flask was removed from
the acetone-Dry Ice bath and allowed to warm to room temperature with stirring. After one hour at room temperature, the white precipitate was filtered with a sintered glass funnel. The ether solution was washed with water and dried over anhydrous magnesium sulfate. The ether was removed on the rotary evaporator and then in vacuo (0.3 mm) to give a yellow waxy solid. This solid was washed with pentane and dissolved in a minimum amount of carbon tetrachloride. Pentane was added until the solution became cloudy, and a seed crystal was added. Crystallization gave 14.02 g (60.5 percent): mp 57-58°. The ir spectrum (no. 23043) exhibited strong peak at 3240 cm⁻¹ for N - H and a strong peak at 1042 cm⁻¹ for S = O, at 885 cm⁻¹ for S - N and at 1085 cm⁻¹. The nmr spectrum (no. 6305), (CDCl₃): δ 7.55-7.48 (d, 2, ArH), 7.30-7.20 (d, 2, ArH), 5.12 (bs, 1, NH), 2.50 (d, 3, NCH₃), 2.40 (s, 3, CH₃).

**N-Methylp-Toluenesulfonimidoyl Chloride.** N-Methyl p-toluenesulfinamide (1.69 g, 0.01 mol) was dissolved in 60 ml anhydrous ether in a dried 100-ml three-necked round-bottomed flask equipped with a magnetic stirrer and a gas inlet tube. Dry pyridine (1 ml) was added and the flask was flushed with nitrogen and placed in an acetone-Dry Ice bath. Dry chlorine was bubbled into the ether solution until the yellow color of chlorine persisted. The flask was removed from the acetone-Dry Ice bath and allowed to warm to room temperature. The white precipitate was removed by
filtration under a nitrogen atmosphere with a sintered glass funnel. The excess chlorine and ether were removed under reduced pressure to give a yellow moisture-sensitive oil which was used immediately.

**Reaction of 2-Aminophenol and N-Methyl p-Toluene-sulfonimidoyl chloride.** 2-Aminophenol (1.09 g, 0.01 mol) was dissolved in 40 ml of dry DMF in a 100-ml round-bottomed flask equipped with a magnetic stirrer. The flask was placed in an ice bath and triethylamine (1.10 g, 0.01 mol) was added with stirring. A dry addition funnel was added to the flask and the system was flushed with nitrogen. The N-methyl p-toluenesulfonimidoyl chloride (0.01 mol) was added to the addition funnel under nitrogen and then was added dropwise to the flask. The reaction mixture was stirred for one hour at room temperature. The solvent was washed with water, dried over anhydrous magnesium sulfate, and removed under reduced pressure. The two products were separated by column chromatography, (silica gel; 12" x 1"; 60-200 mesh; J. T. Baker; 15 percent EtOAc, 85 percent CHCl₃). The first fraction (Rf 0.80) was 2'-aminophenyl N-methyl 4-toluenesulfoniminate. Nmr spectrum (no. 6359) (CDCl₃): δ 7.6-7.1 (m,8,ArH), 2.40 (s,3,CH₃), 2.36 (s,3,CH₃), 1.24 (s,2,NH₂). The major second fraction was N-(2'-hydroxyphenyl)-N-methyl-4-toluenesulfonimidamide. Nmr spectrum (no. 6360) (CDCl₃): δ 7.77 (d,2,ArH), 7.2 (d,3,ArH), 6.9-6.5 (m,3,ArH), 5.9 (bs,1,NH), 2.50 (s,3,NCH₃), 2.34 (s,3,CH₃).
2-Acetamino-4-methylphenol. 2-Amino-4-methylphenol (12.32 g, 0.1 mol) was placed in a 500-ml Erlenmeyer flask equipped with a magnetic stirrer. Water (230 ml) and conc hydrochloric acid (8.4 ml) were added and the solution was decolorized with Norit. Acetic anhydride (9.5 ml, 0.1 mol) was dissolved in the vigorously stirring solution. A solution of sodium acetate (15 g, 0.18 mol) in 46 ml of water was added immediately. A white precipitate formed which was collected by suction filtration and air-dried to give 11.04 g (67 percent): mp 151.5-152.5° (lit mp 159-160°). The ir spectrum (no. 23280) exhibited a strong peak at 3280 cm\(^{-1}\) for N - H, at 3100 cm\(^{-1}\) for O - H, and at 1650 cm\(^{-1}\) for C = O.

N' - Acetyl 2'-Amino-4'-methylphenyl N-Methyl 4-Toluenesulfonimidate. 2-Acetamino 4-methylphenol (1.7 g, 0.01 mol) dissolved in 80 ml of methylene chloride was placed in a 250-ml round-bottomed dried flask equipped with a magnetic stirrer. The flask was put in an ice bath and triethylamine (2.5 ml, 0.01 mol) was added with stirring. The mixture was stirred for 15 minutes at 0° and then a dried addition funnel was added. The system was flushed with nitrogen. N-Methyl-p-toluenesulfonimidoyl chloride (0.01 mol) was added to the addition funnel under nitrogen and was then added dropwise to the vigorously stirring solution at 0°. After the addition was complete, the reaction mixture was stirred for one hour at room temperature.
The mixture was washed with 5 percent hydrochloric acid, with water, and dried over anhydrous magnesium sulfate. The methylene chloride was removed on the rotary evaporator and then in vacuo (0.3 mm) to yield a brown oil which crystallized after two weeks in the refrigerator. The product was recrystallized from CCl₄-hexane: mp 89-89.5°.

The ir spectrum (no. 23353) exhibited strong peaks at 3300 cm⁻¹ for N-H, 1780 cm⁻¹ for C=O, and at 1290 and 1170 cm⁻¹ for O=S=N. Nmr spectrum (no. 7556) (CDCl₃): δ 7.82-7.08 (m,5,ArH), 7.48 (bs,1,NH), 6.66 (s,2,ArH), 2.97 (s,3,NCH₃), 2.37 (s,3,CH₃), 2.25 (s,3,CH₃), 1.92 (s,3,COCH₃).


Methyl p-Tolyl Sulfide.92 p-Thiocresol (50 g, 0.4 mol) and 20 percent aqueous sodium hydroxide (35 ml) were added to a 250-ml round-bottomed flask equipped with a magnetic stirrer and an addition funnel. A 20 percent excess of base was used since an excess of alkali was helpful in breaking down any sulfonium salts which formed. The flask was placed in an ice bath. Dimethyl sulfate (58 g, 44 ml; 0.45 mol) was added slowly to avoid a vigorous reaction, which would occur on too fast an addition. After the addition was complete, the reaction mixture was removed from the ice bath and was heated at reflux for two to three hours. The reaction mixture was extracted thrice with ether, the ether layers were combined, washed once with a small amount of water, dried over anhydrous magnesium sulfate, and
concentrated on the rotary evaporator. The residue was distilled at 44-46° (0.2 mm) to give 38.95 g (78 percent): (lit^92 bp 104-105°, 20 mm). The ir spectrum (no. 23207) exhibited strong peaks at 2940, 1500, 1450, 1095, and 805 cm\(^{-1}\). Nmr spectrum (no. 6885) (CDCl\(_3\)): \(\delta\) 7.08 (q,4,ArH), 2.36 (s,3,SCH\(_3\)), 2.23 (s,3,CH\(_3\)).

Methyl p-Tolyl Sulfoxide.\(^{65}\) Methyl p-tolyl sulfide (8.7 g, 0.063 mol) was dissolved in 18 ml of glacial acetic acid in a 250-ml round-bottomed flask equipped with a magnetic stirrer and an addition funnel. The flask was placed in an ice bath. To the ice cold solution was added dropwise 31 percent hydrogen peroxide (7.1 g, 0.063 mol) dissolved in 5 ml acetic acid. The mixture was stirred for one hour at 0°. The excess acetic acid was removed under aspirator vacuum at 42°. The residue was dissolved in ether and stirred over sodium hydroxide pellets until all the excess acetic acid had been removed. The solution was filtered and the ether was dried over anhydrous sodium sulfate and concentrated under reduced pressure. The sulfoxide was distilled at 98° (0.35 mm) to yield 7.57 g (87 percent): mp 46-48° (lit\(^93\) mp 50-54°). The ir spectrum (no. 23233) exhibited a strong peak at 1040 cm\(^{-1}\) for S \(=\) 0 and peaks at 1500(m), 1420(m), 1290(m), 1085(s), 1010(m), 950(m), and 805(m) cm\(^{-1}\). Nmr spectrum (no. 6708) (CDCl\(_3\)): \(\delta\) 7.36 (q,4,ArH), 2.68 (s,3,SCH\(_3\)), 2.34 (s,3,CH\(_3\)).
Methyl p-Tolyl Sulfoximide.\textsuperscript{94} Methyl p-tolyl sulfoxide (39.79 g, 0.258 mol), sodium azide (22.7 g, 0.35 mol), and 250 ml of chloroform were put into a 1-l three-necked round-bottomed flask equipped with a mechanical stirrer, reflux condenser, and an addition funnel. The mixture was cooled to 0° in an ice bath. Conc sulfuric acid (65 ml) was added over a 15-minute period with stirring. The mixture was carefully warmed to 45° and maintained at this temperature until the evolution of nitrogen subsided. Then it was stirred for an additional 24 hours at 45°. After being cooled to room temperature, 90 ml of ice water were added to dissolved the inorganic salts. The layers were separated and the aqueous layer was extracted with 30 ml of chloroform. The aqueous layer was made slightly alkaline with 20 percent sodium hydroxide and then was extracted twice with 20 ml of chloroform. The chloroform layers were combined, dried over anhydrous magnesium sulfate, and concentrated under reduced pressure to give a pale yellow oil which crystallized after one week in the refrigerator: mp 58-66°, 73-74° (CCl\textsubscript{4})(\textit{lit}\textsuperscript{95} mp 71-72°). The ir spectrum (no. 23247) exhibited peaks at 3270 cm\textsuperscript{-1} for N - H and at 1220, 1090, and 995 cm\textsuperscript{-1} for N = S = O. Nmr spectrum (no. 7125)(CDC\textsubscript{3}): \(\delta\) 7.62 (d,2,ArH), 7.10 (d,2,ArH), 3.0 (s,3,SCH\textsubscript{3}), 2.72 (s,1,NH), 2.40 (s,3,CH\textsubscript{3}).
(-)-Menthyl (-)-(S)-p-Toluenesulfinate (111).  

p-Toluenesulfinyl chloride (38.2 g, 0.22 mol) and 1-menthol (34.4 g, 0.22 mol) were dissolved in 250 to 300 ml of anhydrous ether in a 2-l two-necked, round-bottomed flask equipped with a magnetic stirrer, an addition funnel, and a 40 cm Vigreaux column. Pyridine (dried over potassium hydroxide pellets) (35.4 ml, 0.44 mol) was added at room temperature to the well stirred solution within 15 seconds. One minute after the addition was complete, a drying tube was placed on the Vigreaux column. After having stirred overnight, the reaction mixture was filtered with suction to remove pyridinium hydrochloride. The ether filtrate was washed with four 50-ml portions of water, four 50-ml portions of 10 percent hydrochloric acid followed by 100 ml of water, and then the ether was dried over anhydrous magnesium sulfate. The ether was evaporated at reduced pressure until crystals began to form, and then the solution was cooled to -20° until crystallization was complete (three to four hours). Recrystallization from acetone yielded 27.27 g (40.5 percent): mp 105-106° (lit mp 105-106°), [α]_D^{20} -196.3° (c.2.0, acetone) (lit [α]_D^{100} -198° (c.2.0, acetone).

Methyilmagnesium Bromide.  

A 250-ml three-necked round-bottomed flask containing 40 ml of anhydrous ether was fitted with a stopper bearing an inlet tube extending below the surface of the ether and an outlet tube protected by a calcium chloride drying tube. The flask was cooled
to -78° in a Dry Ice-acetone bath, then placed on a balance, and methyl bromide was introduced through the inlet until the gain in weight was 8 g (0.084 mol). The flask was then returned to the Dry Ice-acetone bath until needed.

Oven-dried magnesium turnings (2.1 g) were placed in a 1-l three-necked round-bottomed flask equipped with a mechanical stirrer, reflux condenser, and an addition funnel. The flask was flame-dried and then protected from moisture with a calcium chloride drying tube. Anhydrous ether (350 ml) and a small crystal of iodine were added to the flask. The cold methyl bromide solution was transferred to the addition funnel and slowly added with stirring. The reaction started spontaneously, and the remainder of the methyl bromide was added at a rate such that the solution refluxed. Stirring was continued until all the magnesium was dissolved.

(+)-(R)-Methyl p-Tolyl Sulfoxide (112).100 The above flask of methylmagnesium bromide was placed in an ice bath. (-)-Menthyl (-)-(S)- p-toluenesulfinate (25 g, 0.084 mol), dissolved in 100 ml of anhydrous ether, was added slowly to the flask. The mixture was stirred at room temperature for one hour and then was hydrolyzed with saturated aqueous ammonium chloride (100 ml). The ether layer was separated and extracted twice with 20-ml portions of water. The combined aqueous extracts were saturated with sodium chloride and extracted twice with 50 ml of chloroform.
The combined organic layers were dried over anhydrous magnesium sulfate. The solvent was evaporated under reduced pressure. The sulfoxide was recrystallized from acetone-hexane to yield 8.59 g (66 percent): mp 75-77°C (lit: mp 73.0-74.5°C), [α]$_D^{21}$ +156.98 (c 0.795, acetone) (lit: [α]$_D^{100}$ +145.5 (c 0.795, acetone).
REFERENCES


Figure A. Mass spectral data for 2,2-dimethylcyclopropyl phenyl sulfide.
Figure B. Rearrangement of sulfonate 86 with 2 equiv. of n-butyllithium.
Figure C. Rearrangement of sulfonate 86 with 3 equiv. of n-butyllithium.
Figure D. Rearrangement of sulfonate 86 with 4 equiv. of n-butyllithium.
Figure E. Rearrangement of sulfonate 86 with 5 equiv. of n-butyllithium.
Figure F. Nmr of 2'-aminophenyl 4-toluenesulfonate (86).
Figure G. Nmr of N-(2'-hydroxyphenyl)-4-toluenesulfonamide (85).
Figure H. Nmr of crossover reaction (unseparated products).
Figure I. Nmr of fraction 18.
Figure J. Nmr of fraction 18 and added sulfonamide.
Figure K. Nmr of fraction 24.