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# SOME ASPECTS OF NUCLEOPHILIC SUBSTITUTION AT TRICOORDINATE SULFUR

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# SOME ASPECTS OF NUCLEOPHILIC SUBSTITUTION AT TRICOORDINATE SULFUR

by

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The author would like to take this opportunity to express his most sincere gratitude to Dr. Kenneth K. Andersen under whom this work was conceived and carried out. He was always ready when help, advice, or encouragement was needed; but more importantly he gave me the independence to pursue my own ideas to their logical and quite often disappointing conclusion.

Thanks are also extended to Dr. John L. Marshall and Dr. R. L. Caret for their valuable discussions and suggestions at various phases of this work. Special thanks are due to Professor Paul R. Jones who served as second reader.

Finally, the author would like to dedicate this thesis to his parents and his wife, Victoria.

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ABSTRACT

SOME ASPECTS OF NUCELOPHILIC SUBSTITUTION AT TRICOORDINATE SULFUR

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The reaction of dialkyl, diaryl and arylalkyl sulfoxides with fluorinated acid anhydrides followed by treatment with various nucleophilic reagents was studied.

Treatment of these sulfoxides with trifluoroacetic anhydride, trifluoromethanesulfonic anhydride, and fluorosulfonic anhydride at low temperatures followed by treatment with p-toluenesulfonamide gave the corresponding N-tosyl sulfimides in fair to good yields.

When optically active sulfoxides were employed in this procedure only racemic sulfimides were obtained.

A number of investigations concerning the racemization of these sulfoxides were undertaken.

When sulfoxides were treated with fluorosulfonic anhydride followed by treatment with sodium cyanoborohydride the corresponding sulfides were obtained.

Treatment of sulfoxides or sulfimide with diisobutylaluminum hydride also gave the corresponding sulfides in good yields.

The scope and limitations of both the sulfimide preparation procedures and the sulfide preparation procedures were explored.

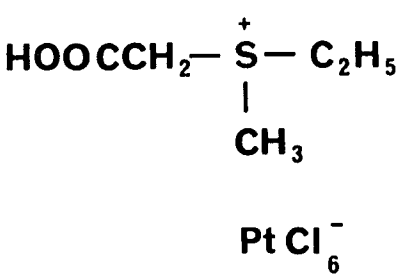
"The universe is a dissymmetrical whole . . . for, if the whole of the bodies which compose the solar system were placed before a mirror, moving with their individual movements, the image in the mirror could not be superposed to the reality."

Pasteur

# HISTORICAL

The study of the course of nucleophilic substitution at tricoordinate sulfur has been under way for well over fifty years,[1] and yet many basic questions remain unanswered. The existence of intermediates along the reaction coordinate is an intriguing possibility; and the timing and geometrical requirements of bond breakage and formation in rate-determining steps pose some questions whose answers have begun to illuminate the intricacies and nuances of nucleophilic substitution at tricoordinate sulfur.

The property of chirality in tricoordinate sulfur species was first demonstrated in 1900 by Pope and Peachy[2] and by Smiles,[3] when these investigators successfully resolved sulfonium salts 1 and 2. These salts were isolated as the hexachloroplatinate and the d-camphorsulfonate salts



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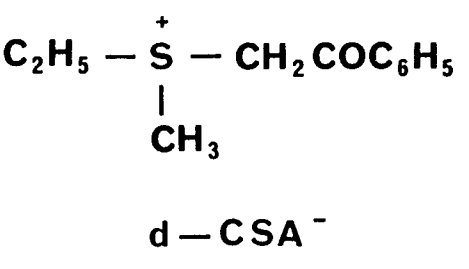

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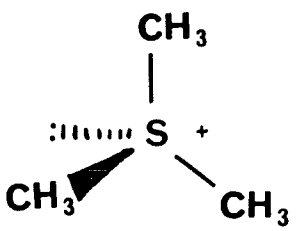
respectively, and this work established the nonplanar nature of the sulfur atom and its ligands. Subsequent X-ray work[4] on trimethyl and triethyl sulfonium iodide (3 and 4) confirmed a three-dimensional array of the sulfur atom and its substituents, and a pyramidal geometry was proposed. The chiral



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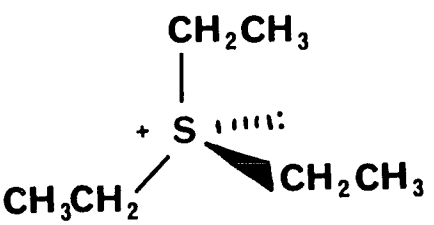

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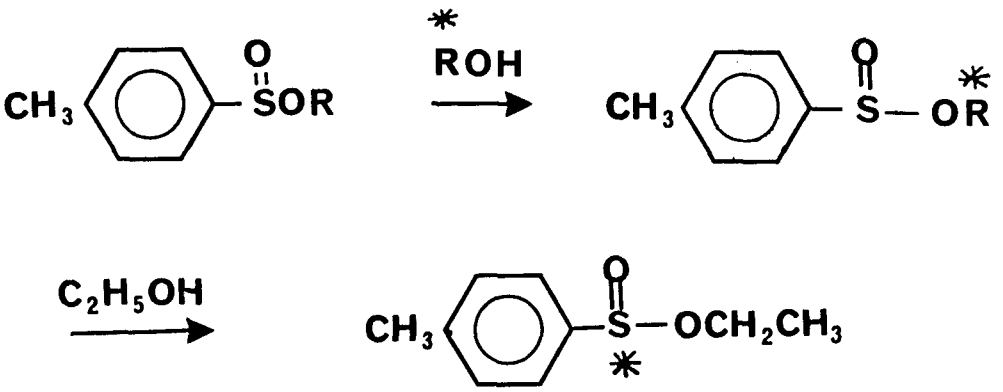
properties associated with sulfonium salts or any other appropriately substituted, tricoordinate sulfur species (e.g., sulfoxide; R-$\overset{O}{\overset{\|}{S}}$-R', sulfinate ester; R-$\overset{O}{\overset{\|}{S}}$-OR, etc.) has allowed a very subtle, but fundamental and revealing probe of the

stereochemical course of nucleophilic substitution at sulfur. Phillips[4] was the first to exploit this property of tricoordinate sulfur. He was able to partially resolve a number of sulfinate esters and determine their optical rotations. By studying the transformation of these esters into other alkyl sulfinate esters (Scheme 1) he found that treatment of

Scheme 1

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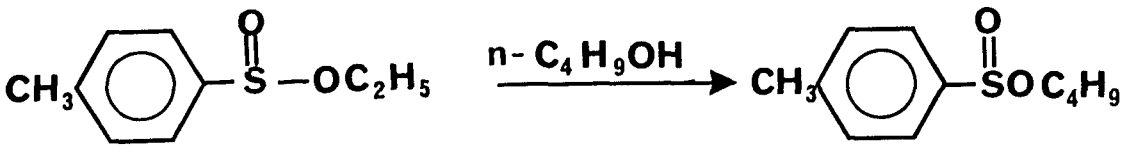


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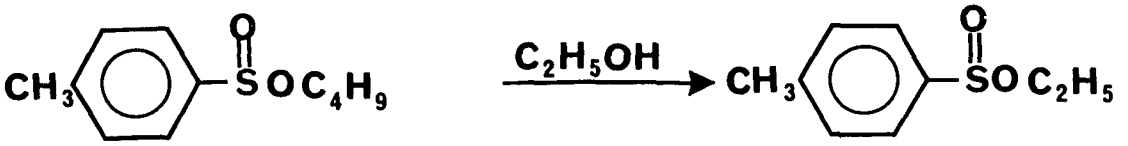
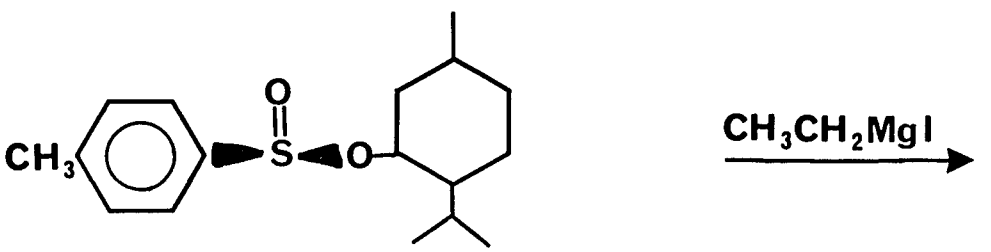



(+) (-)- 5

(-)-ethyl p-toluenesulfinate (5) with n-butanol gave (+)-n-butyl p-toluenesulfinate. Subsequent treatment of the butyl ester regenerated the original (-)-ethyl p-toluenesulfinate to complete the cycle. Phillips compared these transesterifications to Walden inversions at chiral carbon centers. This work strongly implicated a bimolecular substitution process, but this could not be stated unequivocally until much later.

In 1962 Andersen[5] reported that treatment of (-)-menthyl p-toluenesulfinate (6) with ethylmagnesium iodide gave (+)-ethyl p-tolyl sulfoxide (7) (Equation 1).

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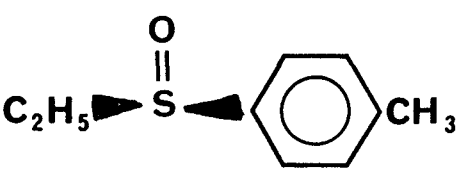


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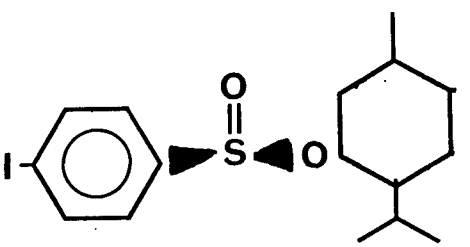
Herbrandson[6] had already assigned the S configuration to sulfur in (-)-menthyl p-iodobenzenesulfinate, an analog of

6, on the basis of kinetic and thermodynamic data. Andersen reasoned that one would not expect to observe much change in the amplitude or sign of rotation in going from p-iodo- to p-toluenesulfinate esters. Since Herbrandson had assigned the S configuration to sulfur in (-)-menthyl p-iodobenzenesulfinate (8), (-)-menthyl p-toluenesulfinate (6) should also

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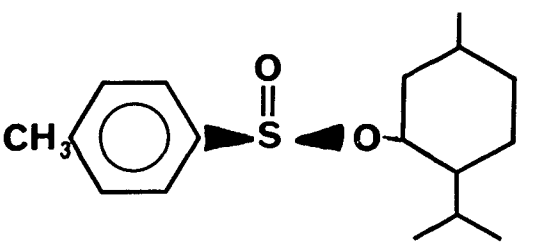
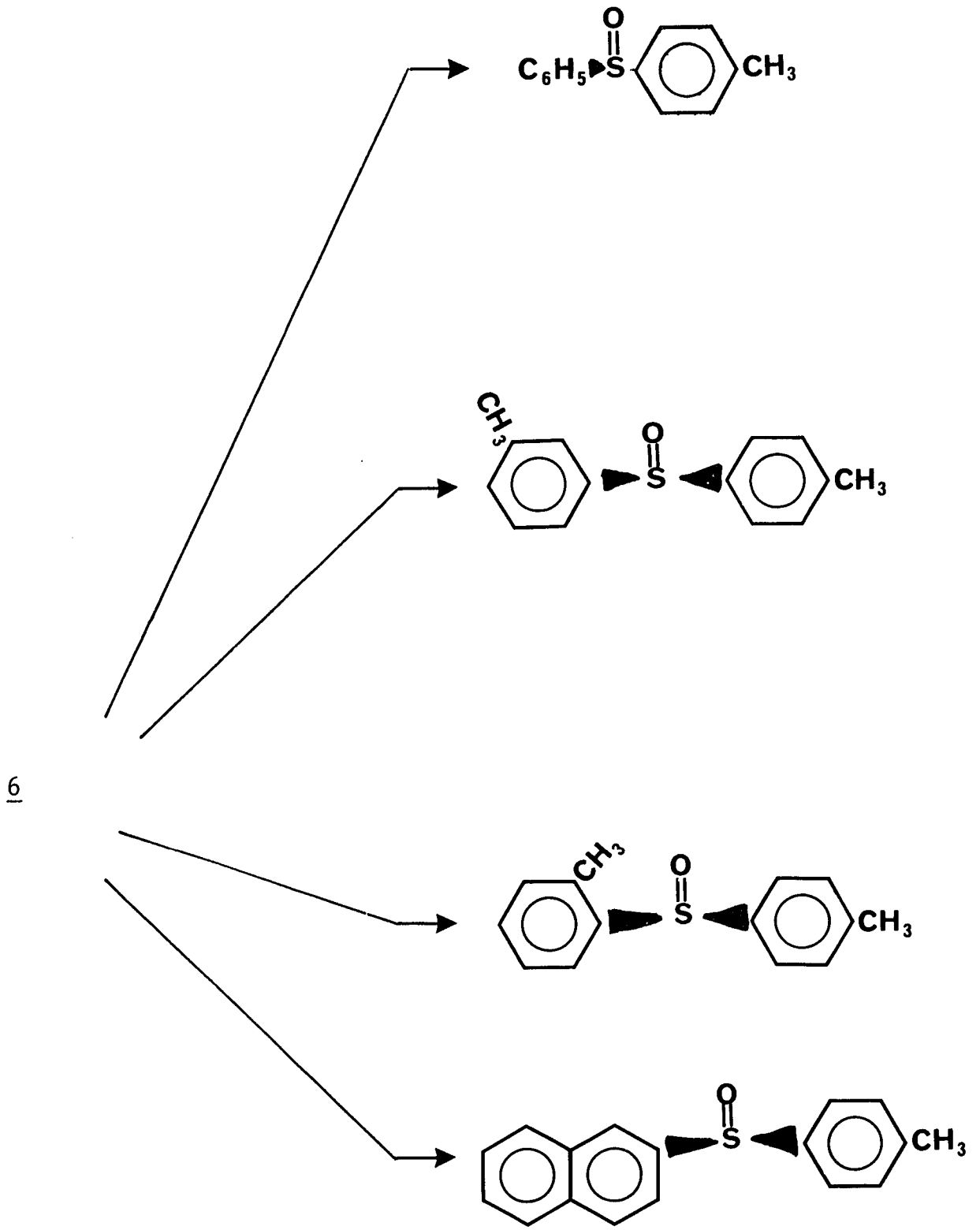



6

have the same (that is, the S) configuration at sulfur. Andersen also reasoned that, because the (-)- ester gave the (+) rotating sulfoxide, the process must occur with inversion of configuration at sulfur.

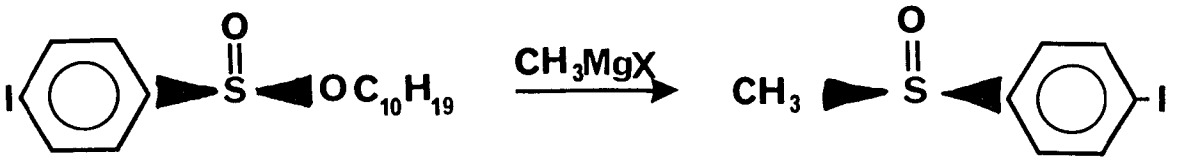
Andersen and coworkers[7] were able to prepare a variety of optically active sulfoxides in this manner (Scheme 2). Both R and S sulfoxides were accessible by this route by

Scheme 2



proper choice of sulfinate ester substrate and Grignard reagent as nucleophile. Finally, in 1968, Mislow and coworkers[8] were able to relate the absolute configurations of sulfinate esters (8, 9) and sulfoxide (10) (Scheme 3) through rigorous

Scheme 3

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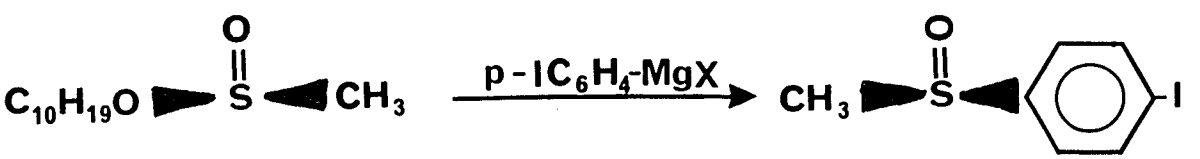


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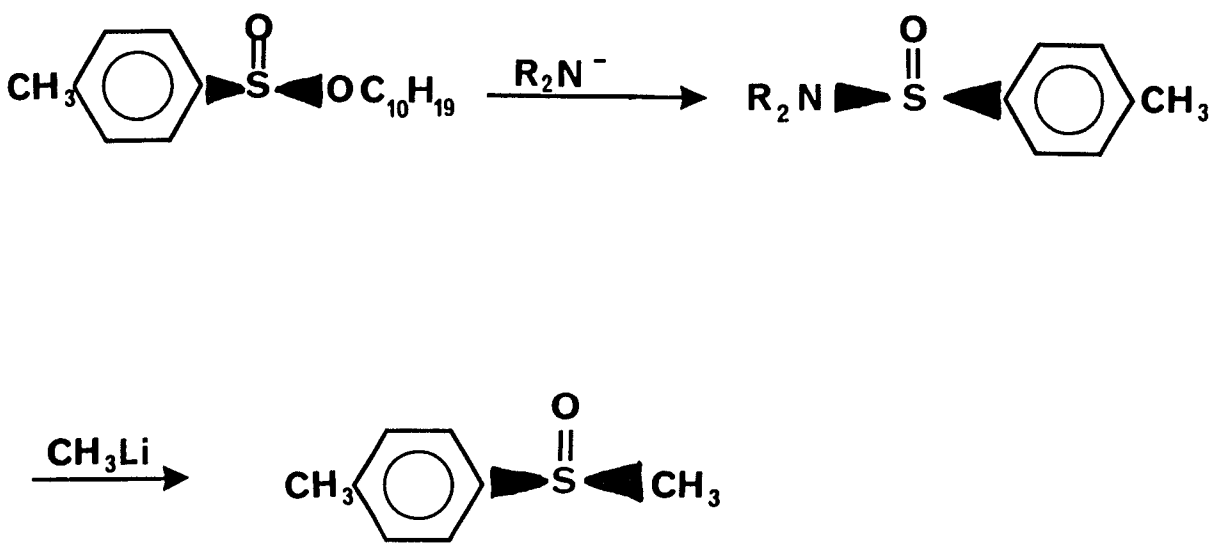
stereochemical reaction cycles and painstaking crystallographic analysis. It was now determined unequivocally that the reaction of Grignard reagents with sulfinate esters did proceed with inversion of configuration at sulfur.

Other workers[9] demonstrated that menthyl sulfinate esters would react with metalated amines to give the corresponding sulfinamides (11), which themselves could be converted to sulfoxides (Scheme 4). Both of these reactions were shown to proceed with inversion of configuration at sulfur. All the evidence compiled so far was compatible

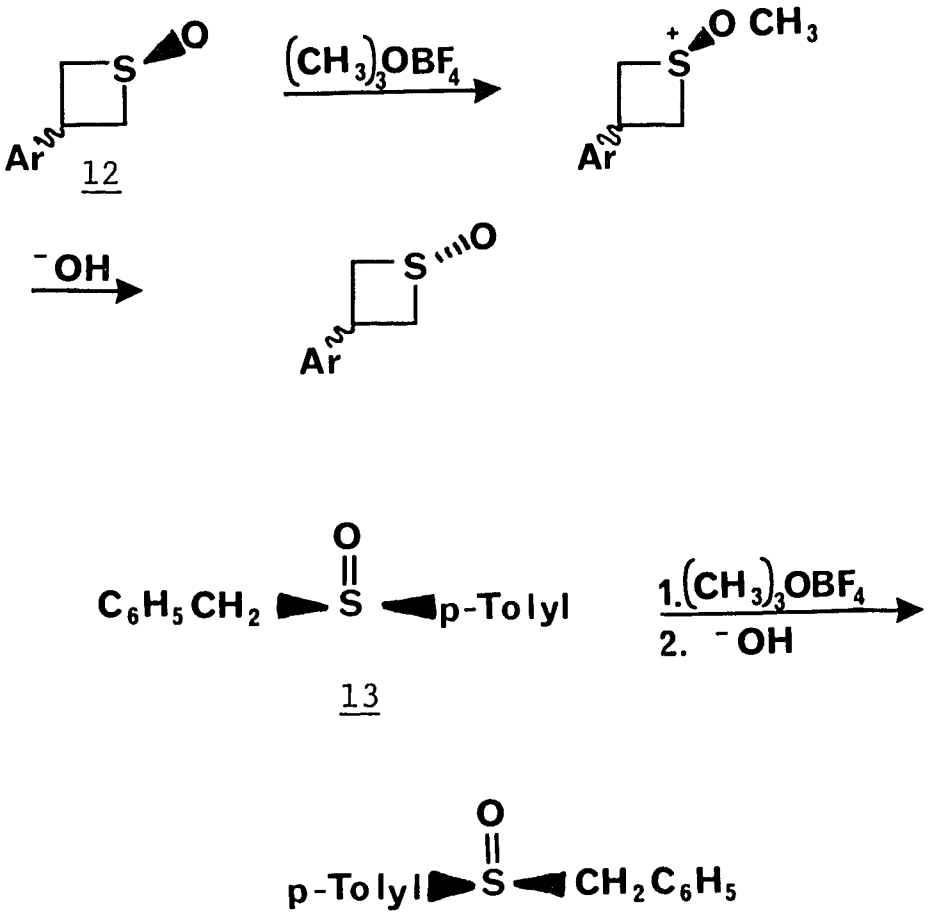
Scheme 4




with the normally accepted mechanism for bimolecular nucleophilic substitution.

From work in this laboratory[10] and that of Johnson and coworkers[11] it was shown that alkylated sulfoxides (12, 13) underwent inversion of configuration when subjected to alkaline hydrolysis (Scheme 5). However, a small (about 10%)

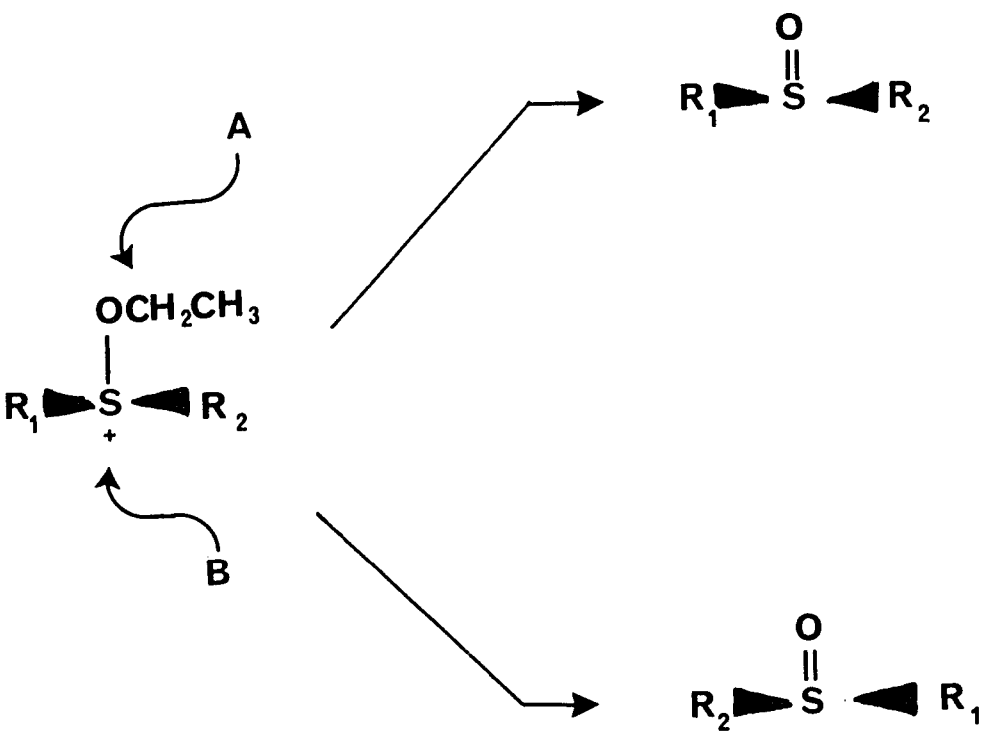
Scheme 5




but significant amount of racemization was observed in this process. This was attributed to the fact that any alkylated sulfoxide (14) has two electrophilic centers, each capable of reacting under the described conditions and each giving

sulfoxide as product (Scheme 6). Unfortunately, reaction at the alkyl group (site A) gives only starting sulfoxide (with retention of configuration) in about 10% yield. When reaction occurs at sulfur (site B) (the predominant reaction site) the sulfoxide of opposite configuration is produced; hence the observation of predominant inversion with some racemization is explained.

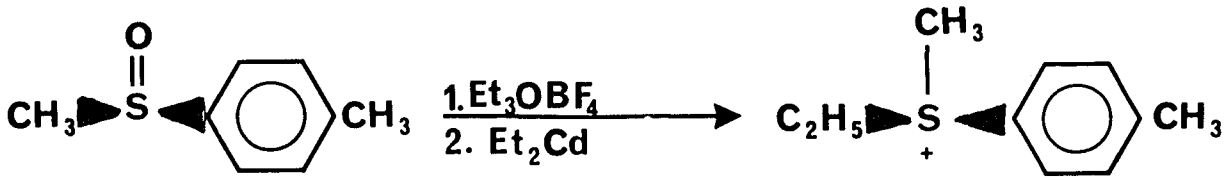
Scheme 6




In 1971, Andersen[12] showed that alkylated optically active sulfoxides could be treated with organocadmium reagents to give the corresponding aryl dialkyl sulfonium

salts (15, 16) (Scheme 7). Through further efforts by Andersen and coworkers[13] the reaction conditions were optimized

Scheme 7

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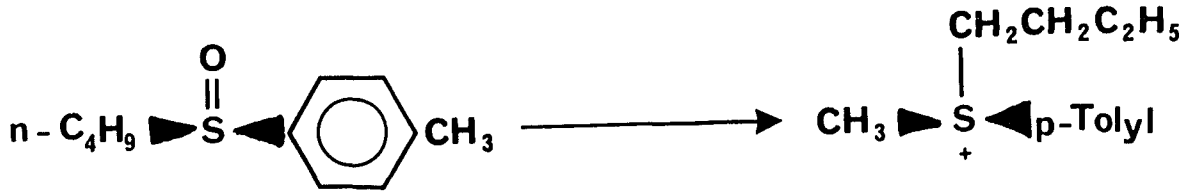


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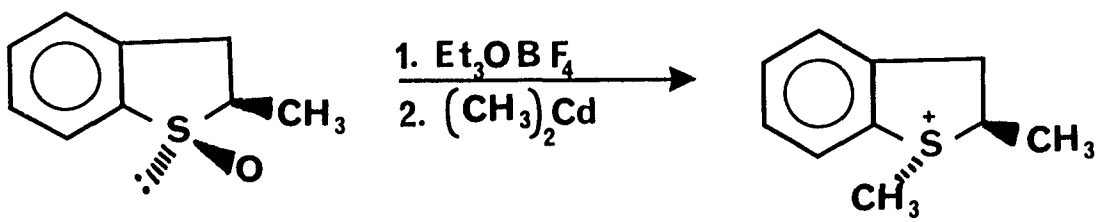
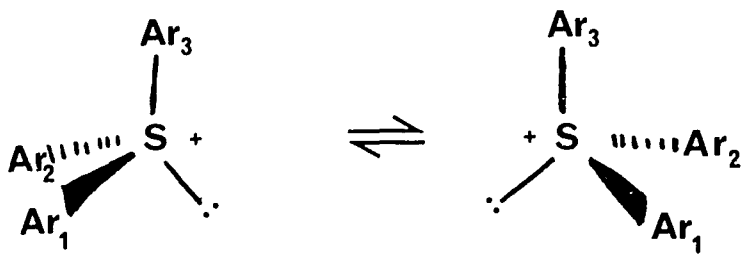
and it was determined that the process proceeded with inversion of configuration at sulfur (Equation 2).




2

This work also related the configurations of these aryl dialkyl salts to their Cotton effects in ORD spectra. It was determined that a positive Cotton effect in the 270-280 nm region in aryl dialkyl sulfonium salts corresponded to the R configuration at sulfur. It was also concluded that triaryl sulfonium salts would not be obtainable in an optically active state because of the low barrier to pyramidal inversion at sulfur (Equation 3).

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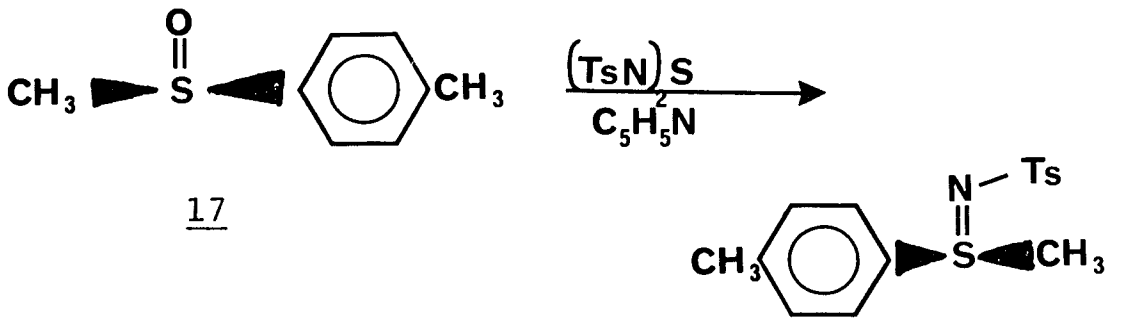
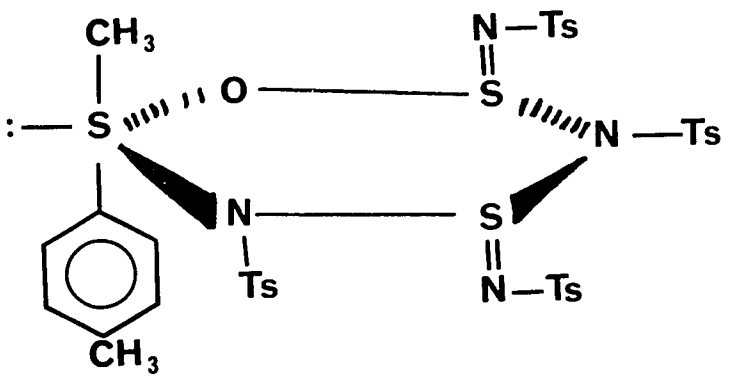
Several groups[14] investigating the conversion of sulfoxides to sulfimides have observed that, depending on the reaction conditions (the two most important considerations are the reagent and the solvent), this reaction can proceed with either retention or inversion of configuration at sulfur. Cram and his coworkers have shown through the use of rigorous stereochemical cycles that, when sulfoxide 17 is treated with di-N-tosylsulfurdiimide in pyridine, the sulfimide (18) of

inverted configuration is obtained (Equation 4). The kinetics of the conversion show a second-order dependence on the diimide under these conditions.




17 18 4

Cram[14] and Mislow[15] have discussed the possible transition states, and intermediates, focusing on their electronic and geometrical requirements. To explain the experimental observations they invoked a tetracoordinate sulfur species (19) with a trigonal bipyramidal geometry. Both the

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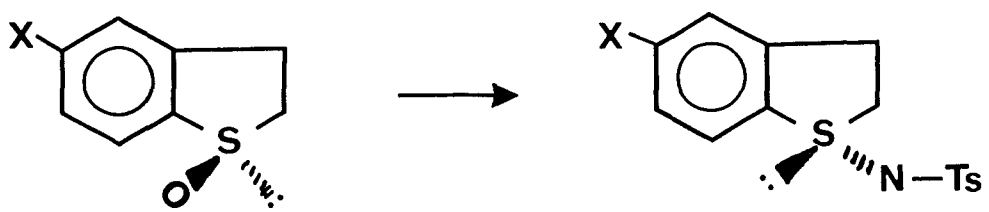
incoming group (N) and the leaving group are in equatorial positions. This equatorial arrangement is compatible with the kinetic data and the stereochemical results observed for the transformation. However, an apical-apical arrangement of these groups in the intermediate or transition state would also be consistent with the experimental observations. The conversion of cyclic sulfoxide 20 to sulfimide (Equation 5)

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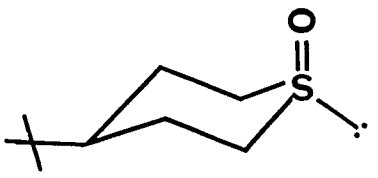
20

rules out this arrangement in the intermediate. This system would require the postulation of a highly strained intermediate; therefore, an apical-apical arrangement was precluded from consideration as a description of the transition state or intermediate. Johnson and Rigau[16] have reported quite similar stereochemical results with the thiane oxide system

(22) (Equation 6) and concluded that substitution at sulfur usually occurs with inversion of configuration.



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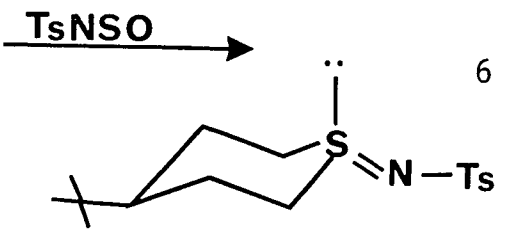
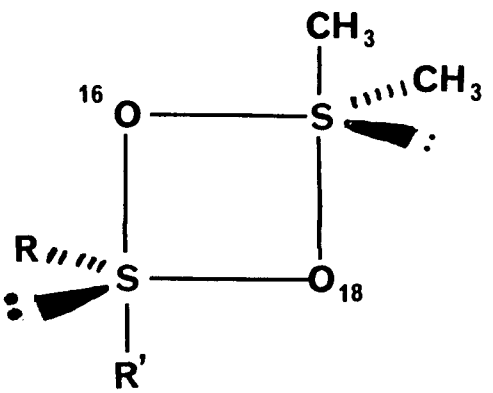
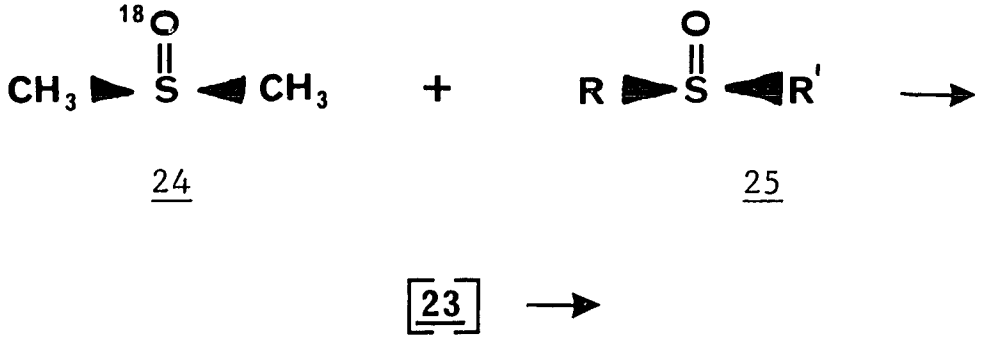



Although most of the work discussed so far supports substitution with inversion, a number of examples of substitution at tricoordinate sulfur that proceed with retention have been reported. Oxygen-18 exchange studies of alkyl aryl sulfoxides with DMSO O-18 by Oae[17] show that the exchange occurs with retention, for which a four-center transition state (23) has been postulated. In this case the incoming




23

group (O-18 of the DMSO 24) and the leaving group (O-16 of the sulfoxide 25) are in the equatorial-apical arrangement (Equation 7). Christensen[18] has also shown that both methyl



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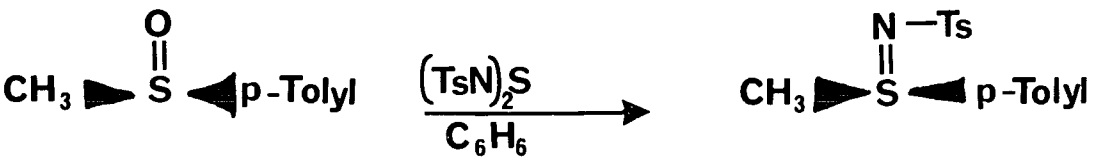
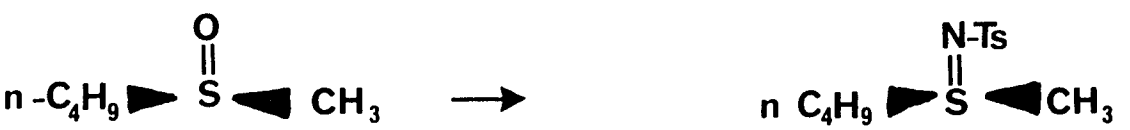
tolyl and methyl butyl sulfoxides (26, 27) when treated with $(TsN)_2S$ in benzene, are converted to the corresponding sulfimide of retained configuration (Scheme 8).

Scheme 8

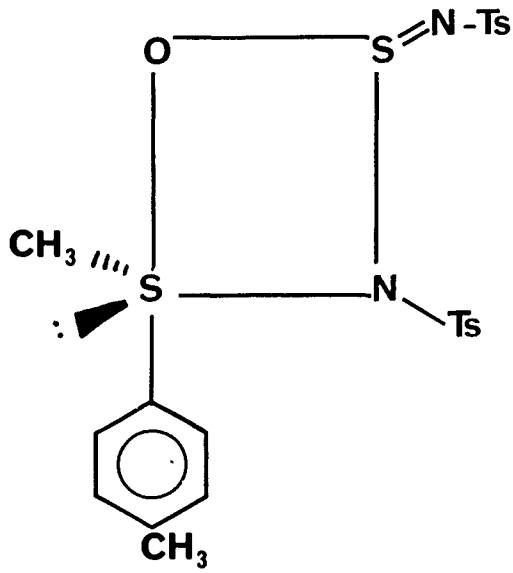



26 28




27 29

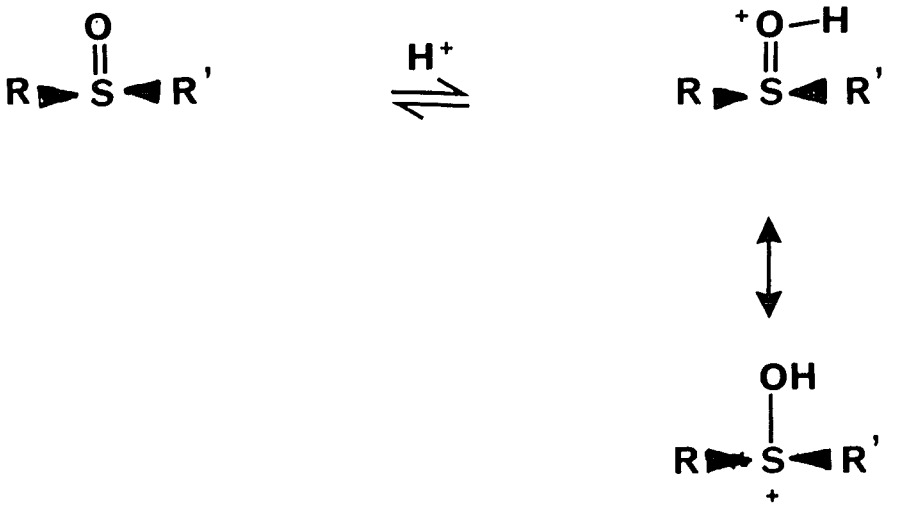
Again, a four-center transition state (30) was proposed with an apical-equatorial arrangement of incoming and leaving groups. Kinetic studies of the sulfimide synthesis in benzene showed a first-order dependence on TsNSO and supported this proposal. A four-center intermediate or transition state best explains the kinetics and stereochemical results (retention) in this case. When the solvent is changed to




30

pyridine and $(TsN)_2S$ is employed, the six-center mechanism is considered to be favored; indeed inversion at sulfur (due to an equatorial-equatorial arrangement of nucleophile and leaving group) is observed for the transformation.

Tetracoordinate sulfur species (sulfuranes) have also been invoked to explain the mechanistic implications of racemization and reduction of sulfoxides by halide ion in acid solution. These processes can and usually do occur simultaneously. Investigations[19, 20] by several groups support the view that the first step in either process is protonation of the sulfoxide (Equation 8). This could be



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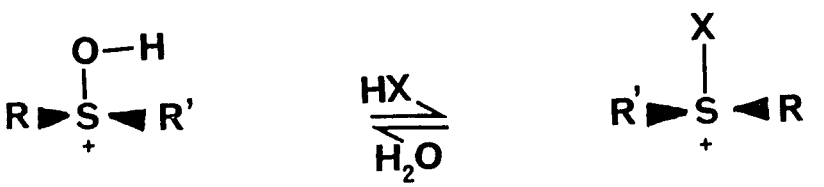
followed by displacement of water by halide ion to give a halosulfonium ion (31) (Equation 9). The intermediate 31



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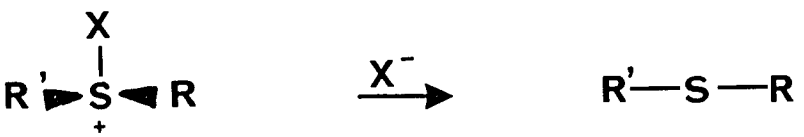
plays a key role in each process because it can be reduced to sulfide (Equation 10) or it can revert to inverted and

therefore racemized halosulfonium ion (Equation 11), depending on the rate of reaction 10 and on the position of the



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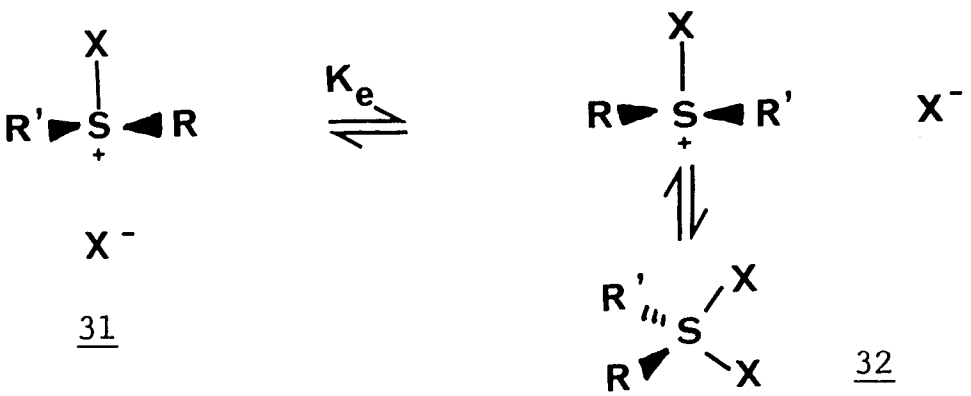

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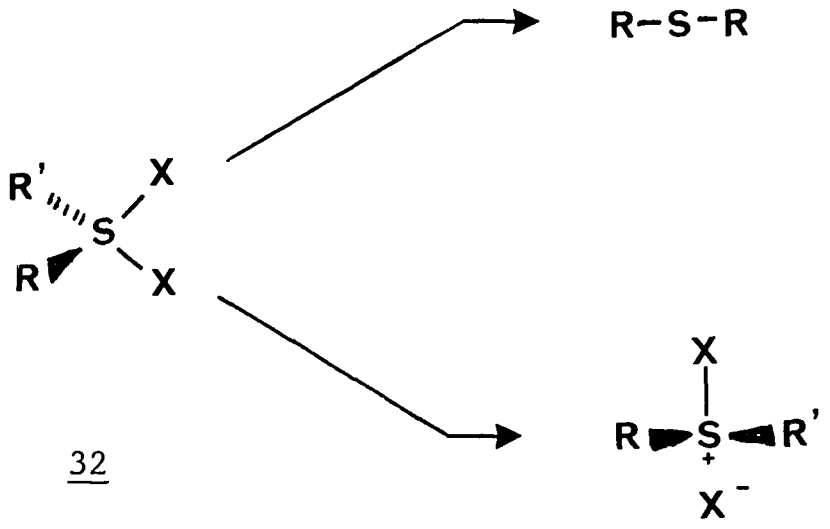
32

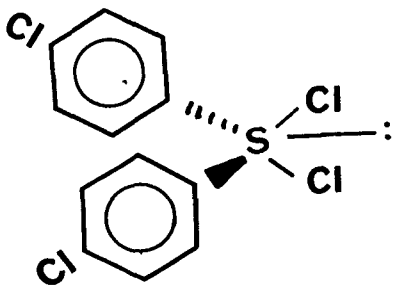
equilibrium. The equilibrium in turn is governed by the nature and the concentration of the halide ion (iodide will give reduction whereas chloride effects racemization). In the presence of a large excess of halide ion, formation of the dihalide (32) is also possible (Equation 11), and both racemized product (sulfoxide) and the reduced product (sulfide) could be accounted for from this intermediate (Scheme 9). Further support for the existence of a discrete

Scheme 9



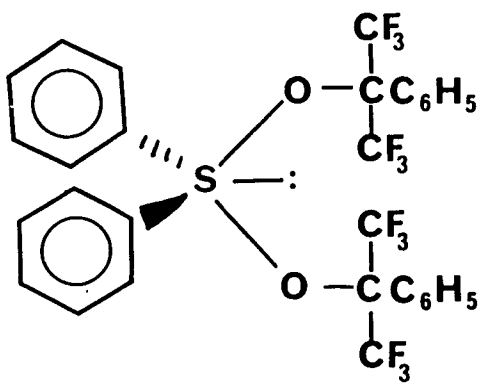

32

tetracoordinate dihalide intermediate is found in the X-ray work of Maner and coworkers,[21] who have found that chlorine complexes of sulfides (33) exist in distorted trigonal bipyramidal geometries at low temperatures.




33

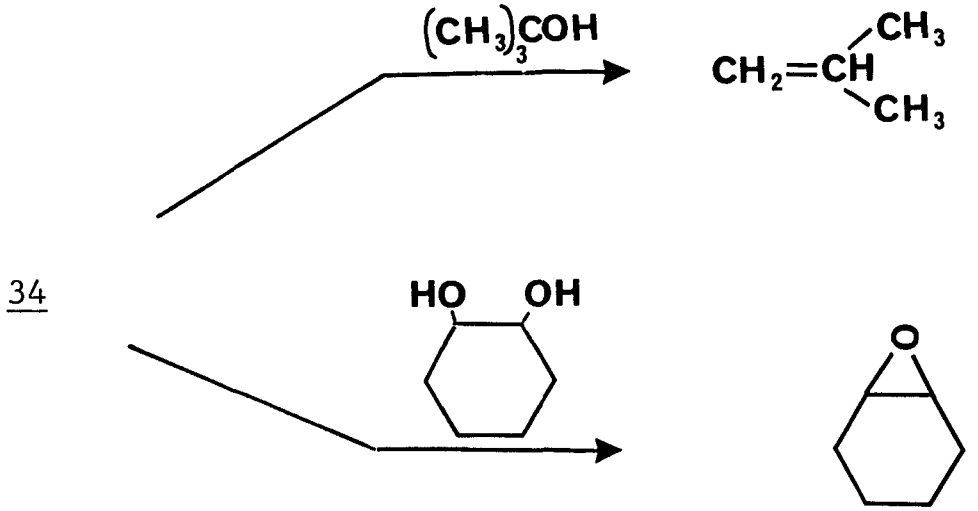
The most tangible evidence in favor of trigonal bipyramidal tetracoordinate sulfur species is found in the work of Martin et al.[22] In 1971 Martin and Arhart[23] reported the preparation and isolation of a sulfurane (34), which was



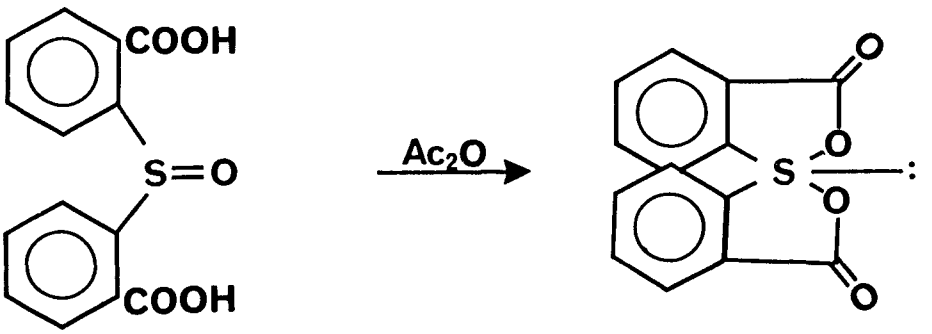
34

found to be stable indefinitely at room temperature under anhydrous conditions, but was subject to rapid hydrolysis when exposed to moisture. This oxysulfurane was the first of a new class of compounds to be characterized, and subsequent investigations showed it to be a powerful dehydrating agent for secondary and tertiary alcohols (Scheme 10).

Scheme 10



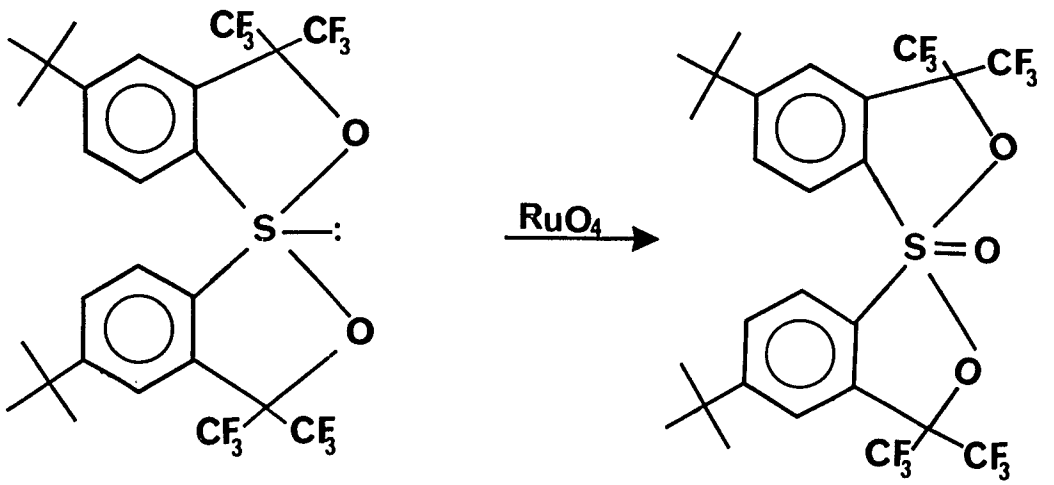

Kalman and Kapovits[24] independently showed that stable spiro oxysulfuranes (35) could be prepared directly from sulfoxides (Equation 12). Martin and Perozzi[25] were also able to prepare novel spiro analogs (36), which they found could be




12

35

oxidized easily to the corresponding spiro oxysulfurane oxide (37) (Equation 13), a hexacoordinate sulfur species.



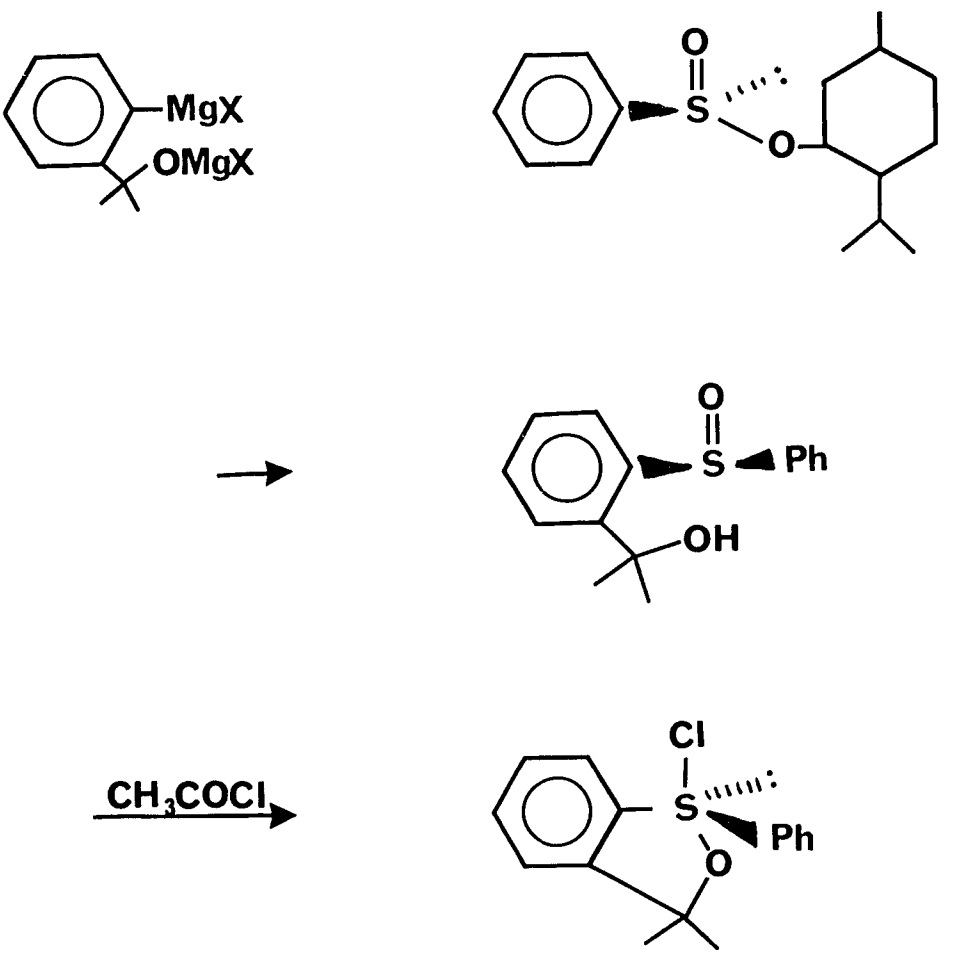

13

36 37

Considerable interest was generated in these oxysulfuranes, and physical and theoretical studies[26,27] probing their actual geometrics were undertaken. It is generally agreed that oxysulfuranes exist as trigonal bipyramids which are somewhat distorted; however, it was also shown that other geometrics are possible, and in some cases ligand reorganization (Berry pseudorotation) can be fast even at extremely low temperatures. Stabilization of the sulfuranes was possible by incorporation of the sulfur atom into a five-membered ring which would occupy one apical and one equatorial position in the trigonal bipyramid. This stabilization factor could account for the low chemical reactivity of 35 and 36 when

compared to 34. Similar observations[32] are common in phosphorus heterocyclic chemistry. Martin [22, 28] has also reported the synthesis of an optically active sulfurane (38) by a novel adaptation of the Andersen synthesis (Scheme 11),

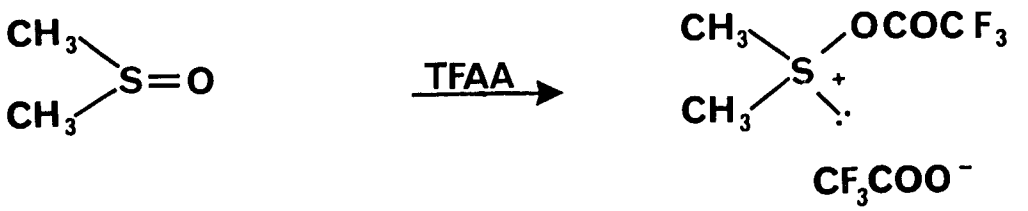
Scheme 11




38

and has presented convincing evidence in favor of a covalent S-Cl bond based on geometry, bond hybridization, and nmr shifts.

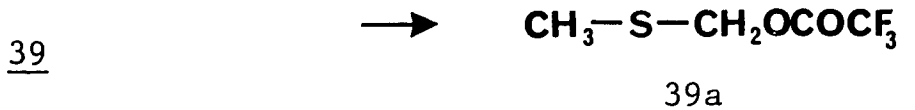
In 1974 Swern and Sharma[29] reported that DMSO reacts exothermically with trifluoracetic anhydride (TFAA) even at low temperatures to give a 1:1 adduct (39) which they represented as an ionic species (Equation 14). When warmed




14

39

this adduct undergoes a Pummerer rearrangement to give a thioether ester (39a) (Equation 15). The adduct also condensed with a number of amines and amides to give the corresponding sulfimides (Scheme 12).

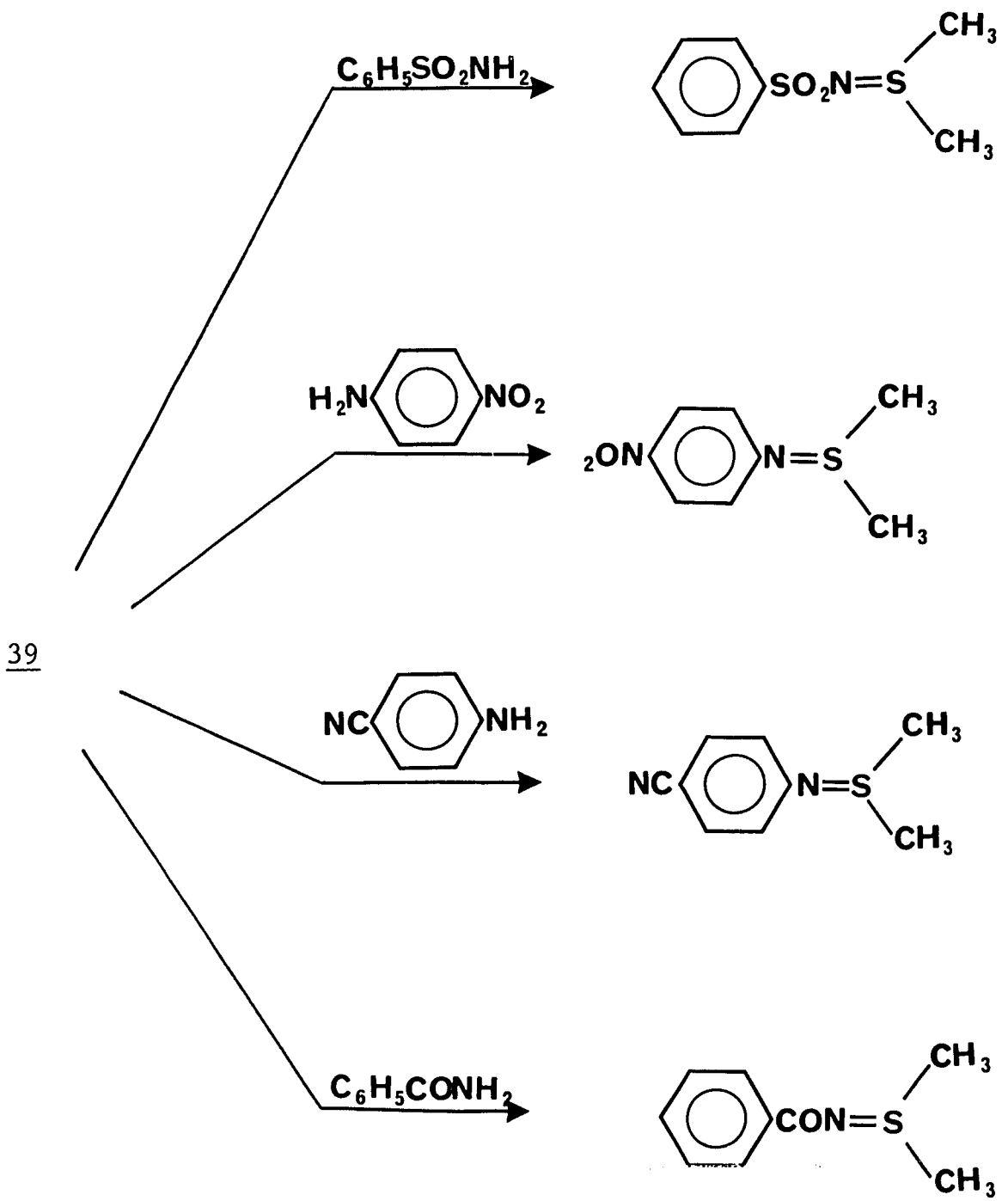



39

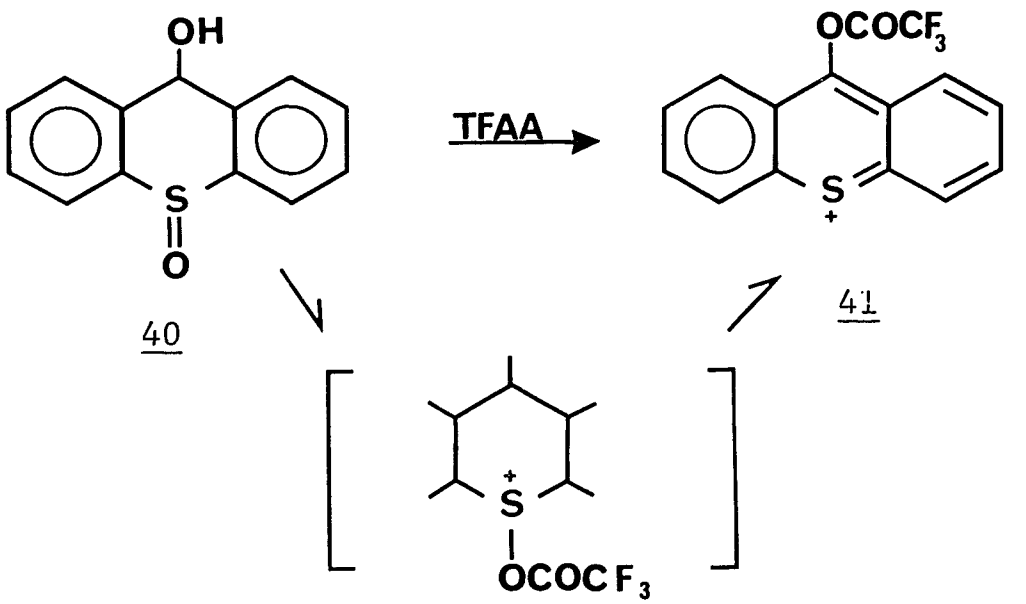
39a

15

Scheme 12



Previously, Ternay and Chasar[30] had reported that thioxanthenol oxides (40), when treated with TFAA, gave sulfonium salt (41), and proposed an intermediate (42) that was similar to the one later proposed by Swern (Equation 16).

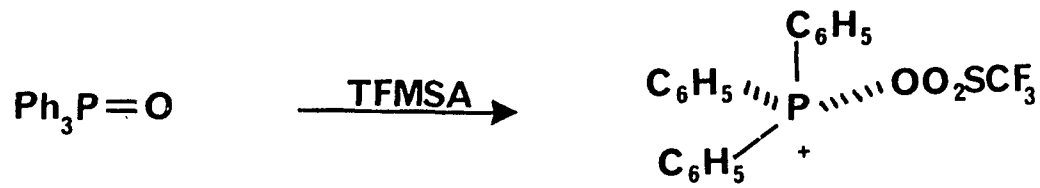



40 41 42 16

In 1975 Hendrickson[31] reported that both S-oxides and P-oxides react with trifluoromethanesulfonic anhydride (TFMSA). He proposed an adduct (43) for its reaction with DMSO similar to those previously proposed by Ternay (42) and Swern (39) (Scheme 13).

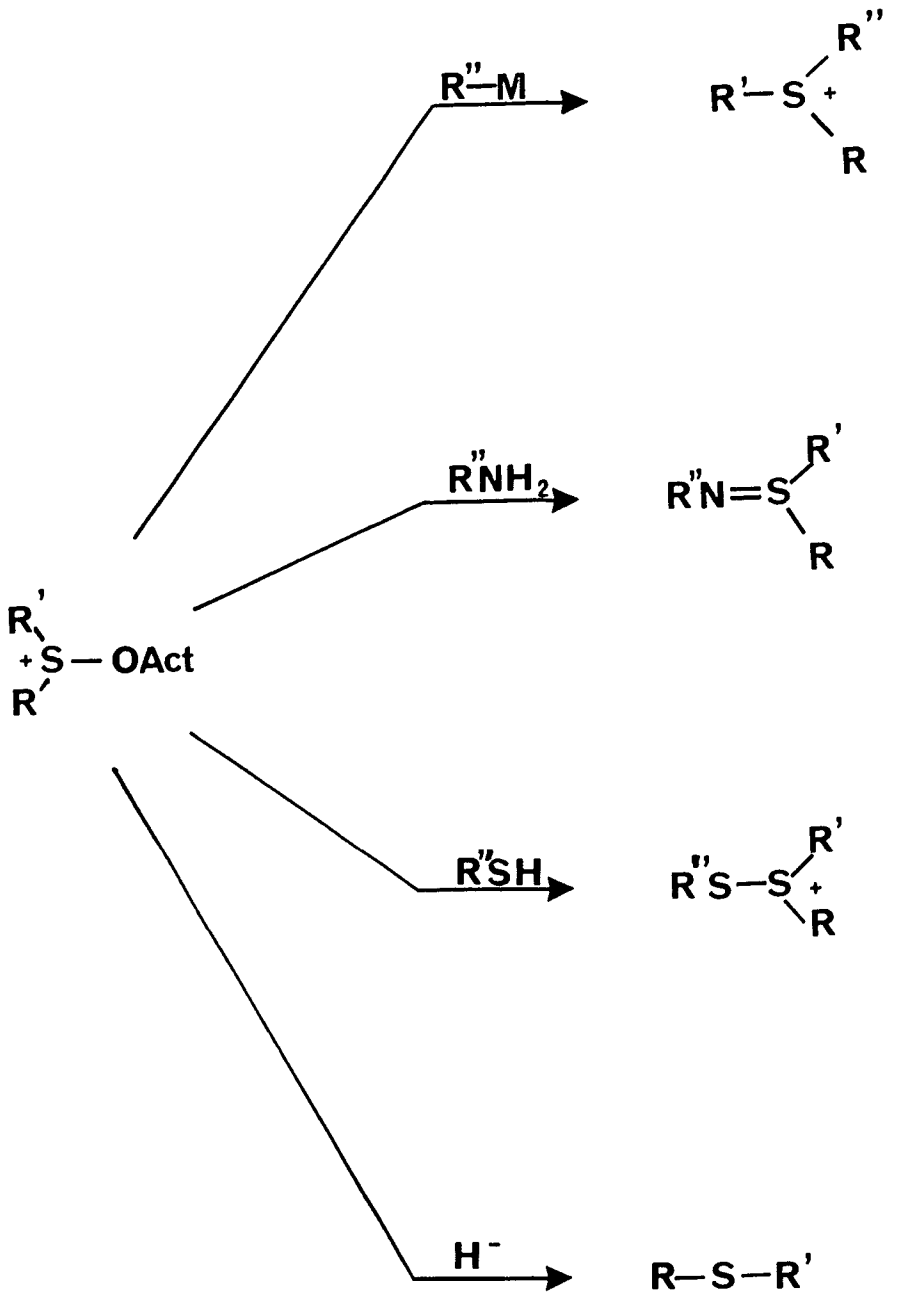
Scheme 13


43


Our own investigation into this area was prompted by the possibility that this type of reactive intermediate obtained from DMSO (39) (43) with active acid anhydrides could be obtained from other dialkyl, alkyl aryl, and diaryl sulfoxides as well. Reaction of these new intermediates with various nucleophilic reagents could provide novel routes to a number of classes of sulfur compounds (Scheme 14).

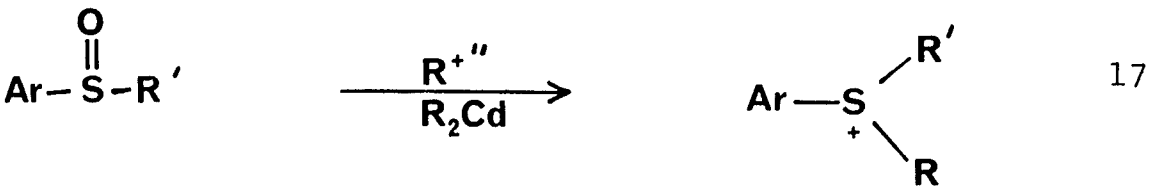
Scheme 14



The purpose of this research has been to investigate the generation of active sulfoxide derived intermediates, and to explore their reactivity with suitable nucleophilic reagents. In this work we have paid particular attention to the nature of the intermediate, and have focused on the relationship of structure and reactivity in the derived intermediates, as well as the scope and limitations of the reactions they will undergo.

## RESULTS AND DISCUSSION

At the outset of this research our primary interest was focused on the conversion of optically active alkyl aryl sulfoxides to the corresponding dialkylarylsulfonium salts. As previously mentioned, this was accomplished via alkylation of the sulfoxide followed by treatment with an organomagnesium or organocadmium reagent (Equation 17).




17

The optical and chemical yields for this conversion were inversely related. If a high optical yield (>80%) was desired, short reaction times were employed and low chemical conversions resulted. On the other hand, chemical yields were greatly increased by extending the reaction time.[13] However, when the alkylated sulfoxide (alkoxysulfonium salt) was exposed to the organometallic reagent for extended periods, racemization was unavoidable. Andersen and coworkers[33] had already shown that the alkylation of the sulfoxide produced a chemically and optically stable intermediate which underwent racemization only slowly. Further studies revealed that

extended exposure of the alkoxysulfonium salt to magnesium halide or methoxide not only increased the amount of racemization but also increased a number of undesired side reactions. The problem became one of finding conditions under which a sulfoxide-derived intermediate (not necessarily an alkoxysulfonium salt) could be cleanly and exclusively converted to a sulfonium salt after brief exposure to an organometallic reagent. In more general terms our goal was to find the least drastic reaction conditions under which sulfoxides could be converted to other tricoordinate sulfur species.

Any overall improvement of this procedure would obviously be due to improvement in the two individual steps of this process. That would mean optimization in the activation of the sulfoxide (by formation of the alkoxysulfonium salt or another electrophilic sulfur species) and in the nucleophilic displacement step at the electrophilic sulfur atom. Two methods to optimize sulfoxide conversions were envisioned. The first approach would simply be to employ a more potent nucleophile in the displacement step. The other approach would be to increase the reactivity (electrophilicity) of the oxysulfonium intermediate by appropriate O-substitution in the sulfoxide.

Though the first approach seems attractively straightforward, it was the less desirable of the two. Andersen and coworkers[13] had already shown that when more drastic reaction conditions were resorted to a number of undesirable side reactions became important (namely reduction and racemization).

As a result of this, the chemical and optical yields were reduced.

In contrast, the second approach would allow experiments to be carried out under less drastic conditions, if appropriate groups could be attached to the sulfoxide oxygen. This might minimize the undesired side reactions, and so increase the relative amount of the desired reaction pathway.

Analysis of the sulfoxide-sulfonium salt conversion leads one to conclude that there are a number of necessary conditions for displacement to occur:

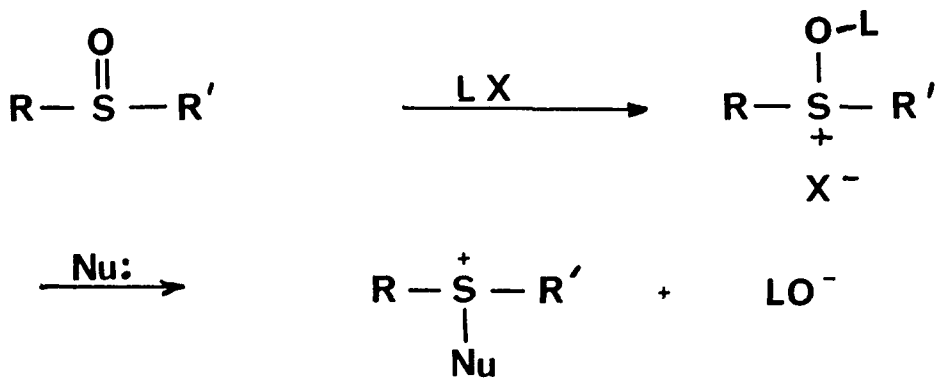
a. An electrophilic center must be created at the sulfoxide sulfur.

b. The electrophilic sulfur atom should have a good leaving group attached to it.

c. The acidity of the α-hydrogens should not be increased.

Scheme 15 outlines these requirements.

Scheme 15



Now the problem of optimizing conditions for sulfonium salt formation becomes one of choosing appropriate groups for electrophilic substitution of the sulfoxide oxygen (sulfonylation, alkylation, silylation, etc.). General requirements for any such reagent are:

a. It must be easily attached to the substrate molecule and the reaction should be quick and complete.

b. It should not racemize the starting material or product.

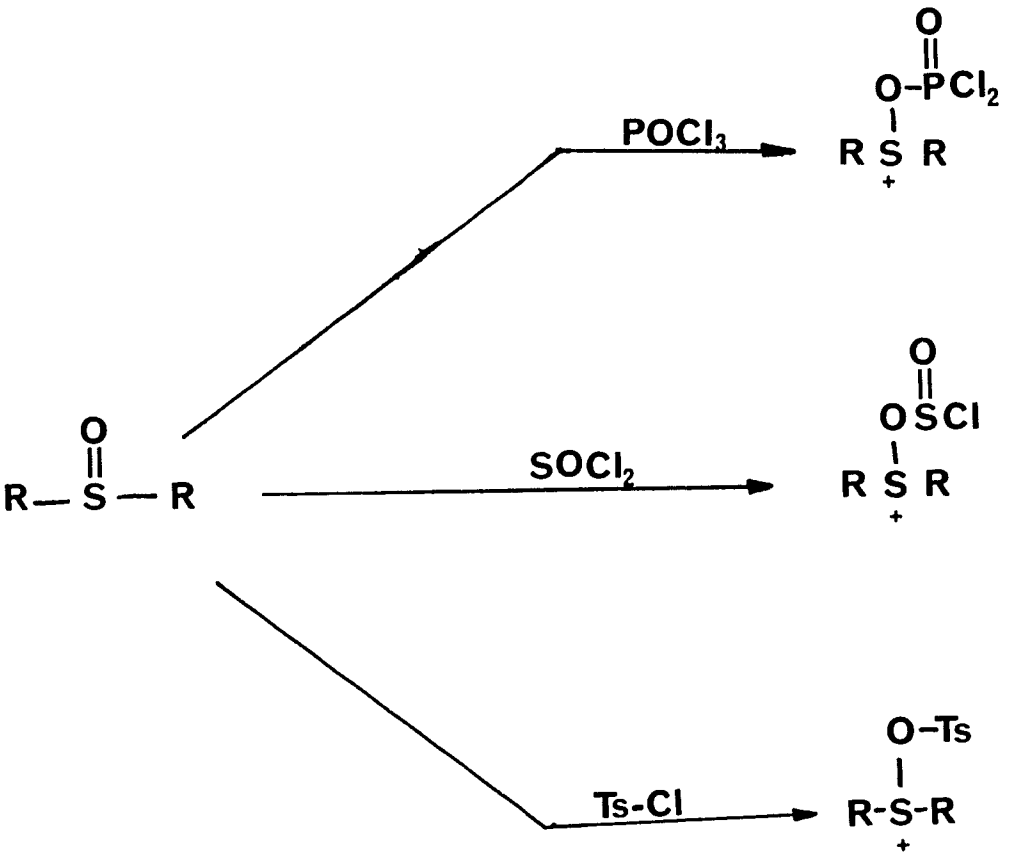
c. It must be a good leaving group, capable of being displaced easily under mild conditions.

d. It should not cause any side reactions.

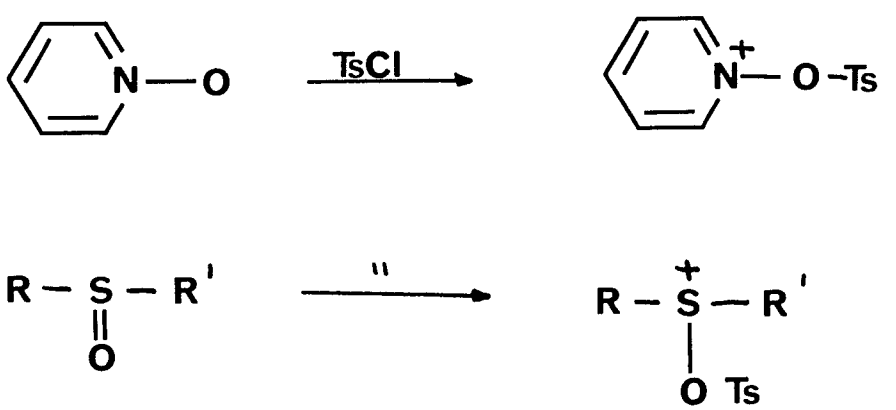
Obviously, a large number of organic compounds could meet these requirements (Scheme 16). In our initial experiments we explored the possibility of activating a sulfoxide toward displacement by attachment of a tosyl group to the sulfoxide oxygen. Analogous experiments with aromatic N-oxides[34] have shown that tosylation can occur under mild conditions and that the tosylation increases the rate of nucleophilic substitution in these systems (Scheme 17). Unfortunately, all of our attempts to tosylate a number of sulfoxides under a wide variety of conditions met with very little success. Dialkyl and diaryl sulfoxides were inert to treatment with either tosyl iodide or tosyl bromide. In the case of tosyl iodide, decomposition in solution was noticeable after short periods.

Tosyl perchlorate[35] (43), derived from tosyl chloride and silver (I) perchlorate was similarly inert in the presence

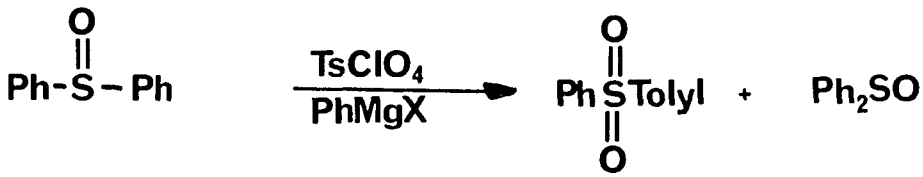
Scheme 16




Scheme 17



of sulfoxides. When diphenyl sulfoxide was treated sequentially with tosyl perchlorate and phenylmagnesium halide, the major product recovered was unreacted sulfoxide along with a trace of sulfone which would arise from coupling of the organometallic and tosyl perchlorate (Equation 18).



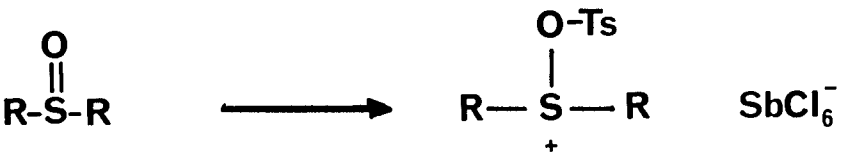

18

Work[36] in the preparation of novel aromatic systems has shown $SbCl_5$ to be an efficient complexing agent for halide ion in carbocation preparations from alkyl halides. Thus, one might expect an active halogen compound such as tosyl chloride would give tosyl hexachloroantimonate (44) (Equation 19). Treatment of an appropriate sulfoxide with 44 could be expected to give the O-toluenesulfonyloxysulfonium salt (45) (Equation 20).

This approach also proved fruitless for the preparation of intermediates such as 45. Subsequent work by Olah


44

19

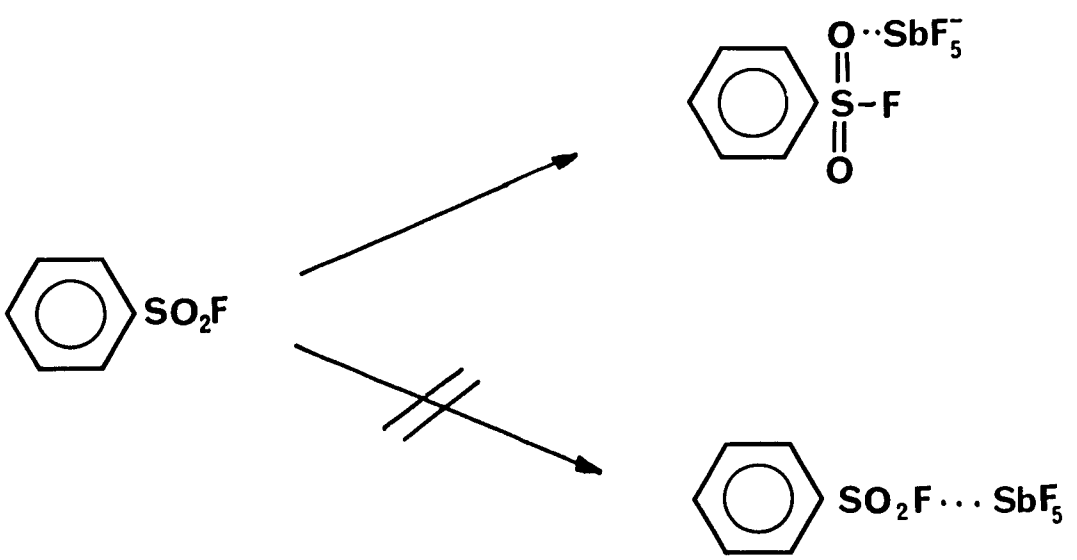



20

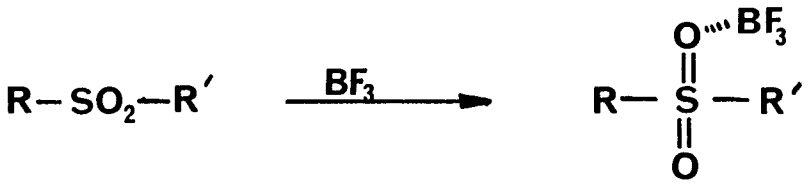
45

and coworkers[37] provided a rationalization of these results. They examined the reaction of $SbF_5$ with various aromatic sulfonyl flourides by $^{19}F$ nmr and showed that complexation occurred with the sulfonyl oxygen rather than with the halogen. They also showed that this complexation is not very strong (Scheme 18). Previous work by Laughlin[38] had shown

Scheme 18



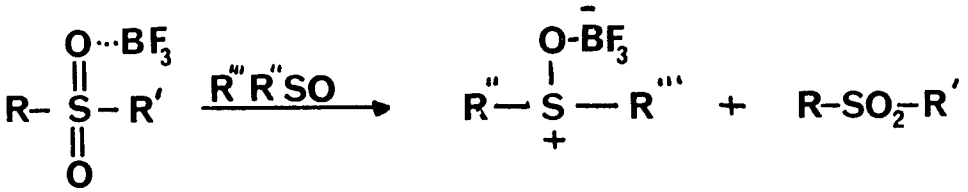
that even though sulfones were weak Lewis bases, they could complex with certain Lewis acids (Equation 21).



21

This work also showed sulfoxides to be more basic than either sulfides or sulfones. The basicity of sulfoxides has also been demonstrated by many others.[39] On the basis of these findings, one might expect that when a sulfonyl halide-antimony (V) halide complex (46) was treated with sulfoxide, the sulfoxide would be able to compete with the sulfonyl halide for the available Lewis acid (Scheme 19) to give the more stable sulfoxide complex (47).[38] Subsequent treatment

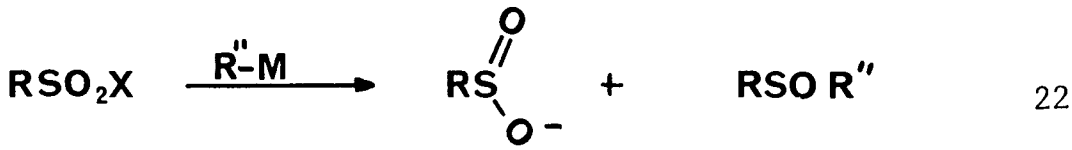
Scheme 19



46 R = Cl 47

of this mixture with an organometallic reagent would be expected to give three products, sulfone and sulfinate salt

arising from reaction of the organometallic and sulfonyl halide (Equation 22), and a stibonium salt arising from reaction of the organometallic with the antimony pentahalide-sulfoxide complex (Equation 23).[50] This indeed is what was observed.



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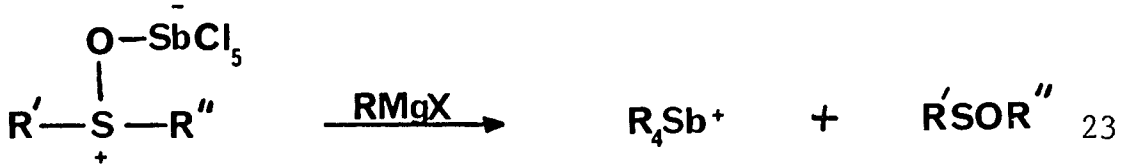
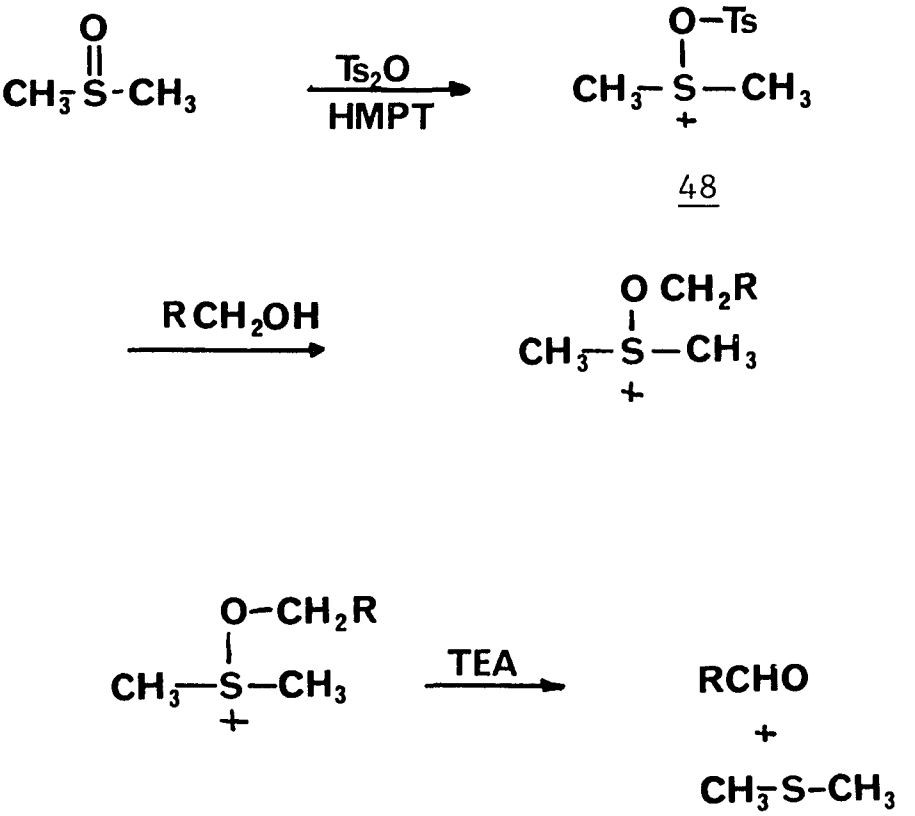


23

In 1974, Albright[40] reported that treatment of dimethyl sulfoxide with methanesulfonic anhydride, toluenesulfonic anhydride, or tosyl chloride in hexamethylphosphoric triamide at -20° gave an intermediate, which he represented as the ionic structure (48) (Scheme 20). When this intermediate was treated with various and secondary alcohols followed by addition of triethyl amine, the corresponding carbonyl compounds were obtained. Our own observations led us to conclude that indeed DMSO could be tosylated under these conditions. However, treatment of 48 with organo-

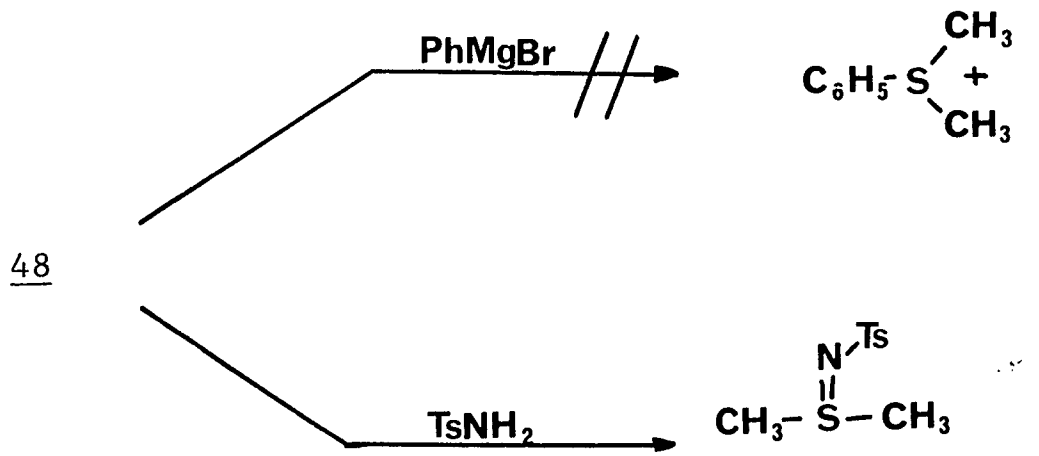
Scheme 20



48

metallic reagent gave no trialkyl- or aryldialkysulfonium salt (Scheme 21). The result came as no surprise in as much as Andersen and coworkers[13, 33] had already shown that it was not possible to obtain trialkylsulfonium salts from

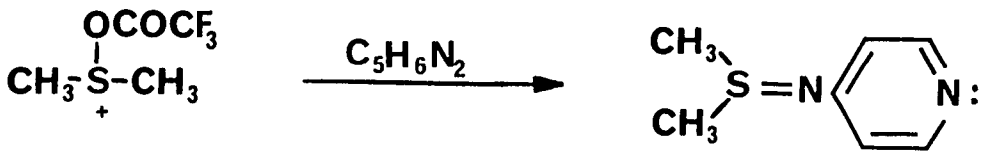
Scheme 21




dialkyl sulfoxides. We did observe that the intermediate (48) would react with toluenesulfonamide to give the corresponding sulfimide in good yield. Unfortunately, all attempts to carry out these reactions with other dialkyl, diaryl, and alkyl aryl sulfoxides under these conditions failed. This reaction appeared to be unique for DMSO; it was the only sulfoxide for which any evidence supported a tosylated sulfoxide intermediate.

Swern and coworkers'[29] initial report on dimethyl sulfoxide activation by trifluoroacetic anhydride for nucleophilic substitution raised an old question. Could a reaction of DMSO, the simplest sulfoxide, be considered general behavior for all other types of sulfoxides, or was it a unique and anomalous case? Swern did not address himself to this question but studied the reactions of the DMSO-TFAA adduct

with a wide variety of nitrogen nucleophiles (Equation 24).




24

We were interested in whether or not the scope of this reaction could be expanded to other dialkyl, diaryl, and aryl alkyl sulfoxides. We found that trifluoroacetic anhydride would react quite readily with various sulfoxides and was a useful reagent for the preparation of sulfimides from sulfoxides.[51] Table I contains a summary of these results.

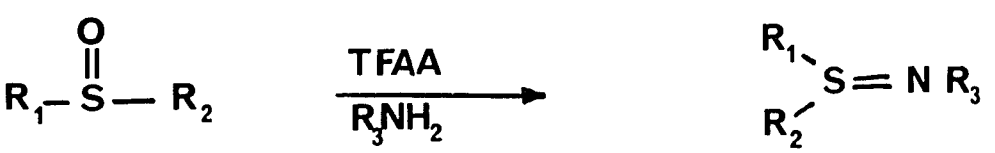


TABLE I

Conversion of Sulfoxides to Sulfimides Using TFAA

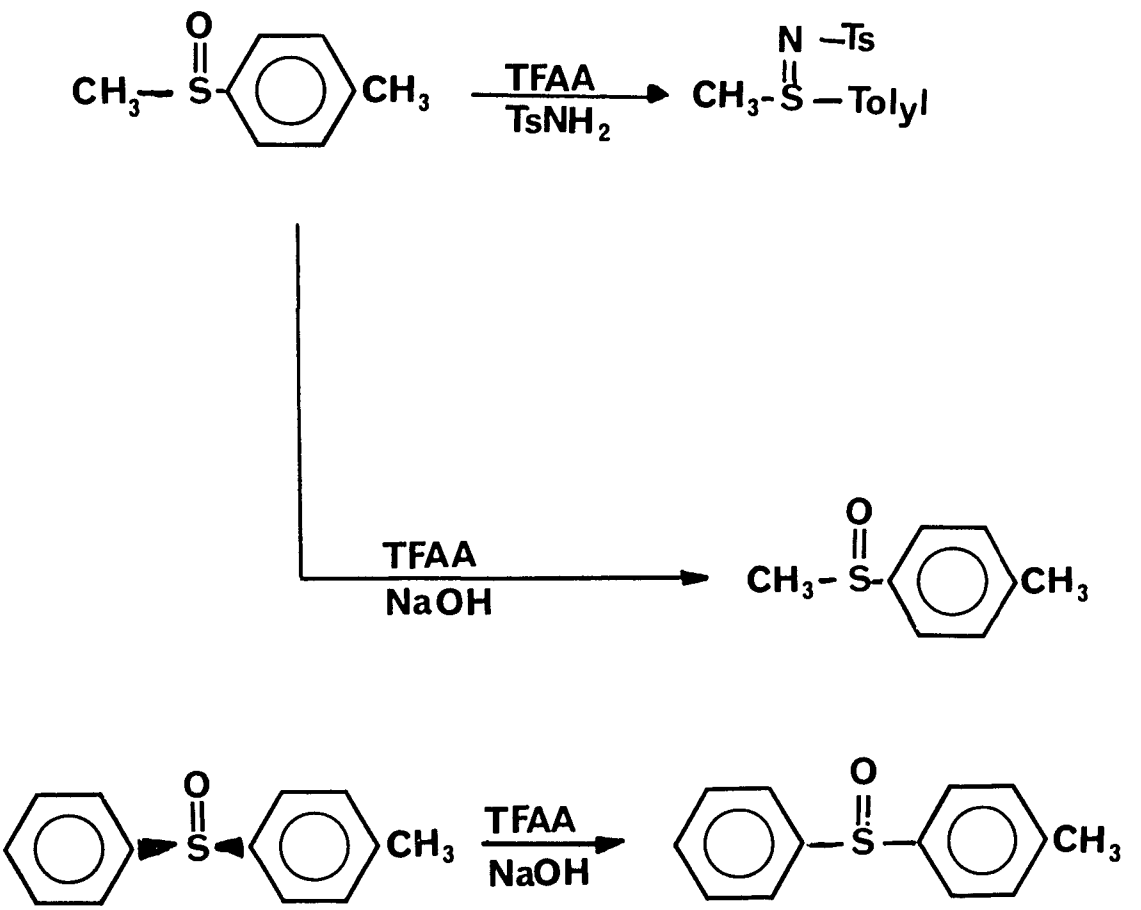
| Compound | $R_1$ | $R_2$ | $R_3$ | Yield (%) |
|---|---|---|---|---|
| Ia | $CH_3$ | $CH_3$ | Ts | 85 |
| Ib | Ph | Ph | Ts | 83 |
| Ic | Ph | Ph | Ts | 76[a] |
| Id | $CH_3$ | p-Tolyl | Ts | 65 |
| Ie | R-(+)-$CH_3$ | p-Tolyl | Ts | 56[b] |
| If | $-CH_2-(CH_2)_2-$ | $-CH_2-$ | Ts | 67 |
| Ig | $CH_3$ | Allyl | Ts | 77 |
| Ih | $PhCH_2$ | $PhCH_2$ | Ts | 81 |
| Ii | p-ClPh | p-ClPh | Ts | 0 |
| Ij | Mesityl | Mesityl | Ts | 0 |

[a]Reaction run at 0°C

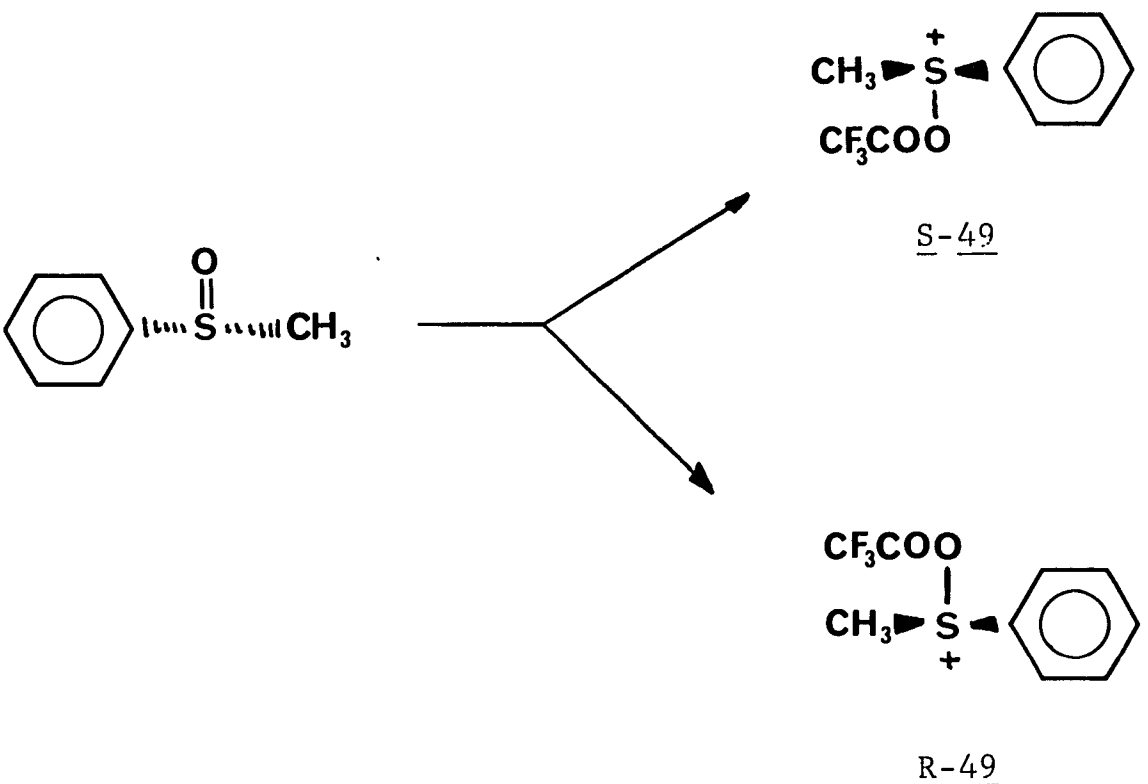
[b] $[\alpha]_D^{25} = 0.0°$

When optically active alkyl aryl sulfoxides were treated under these conditions, only racemic sulfimides were recovered. Also, when optically active alkyl aryl sulfoxides were treated with TFAA at -78° and hydrolysed, only racemic sulfoxide was recovered. Repetition of this experiment with optically active phenyl p-tolyl sulfoxide at 0° gave analogous results (Scheme 22). Sulfimide preparation and sulfoxide inversion

Scheme 22



are both well studied processes,[41] and it is known in both cases that the displacement step at the activated sulfur atom occurs with a high degree of stereoselectivity for both nucleophiles. Because total racemization is observed, it must occur before this displacement; that is, when the optically active substrate is treated with TFAA (Equation 25). If one represents the intermediate (49) as an ionic structure,

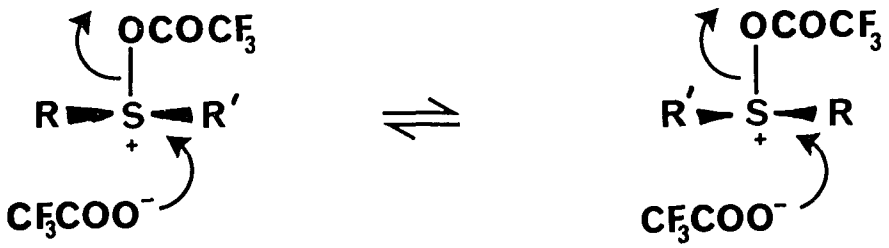


S-49

25

R-49

the mode of racemation can be further elaborated. Given an ionic intermediate (R-49), one could envision a series of discrete nucleophilic displacements by the counterion to give an equilibrating mixture of both activated enantiomers (Equation 26). Another interpretation is possible. Martin[23, 25] and Kapovits[24] have shown that treatment of sulfoxides can, in some cases, result in the formation of an oxysulfurane

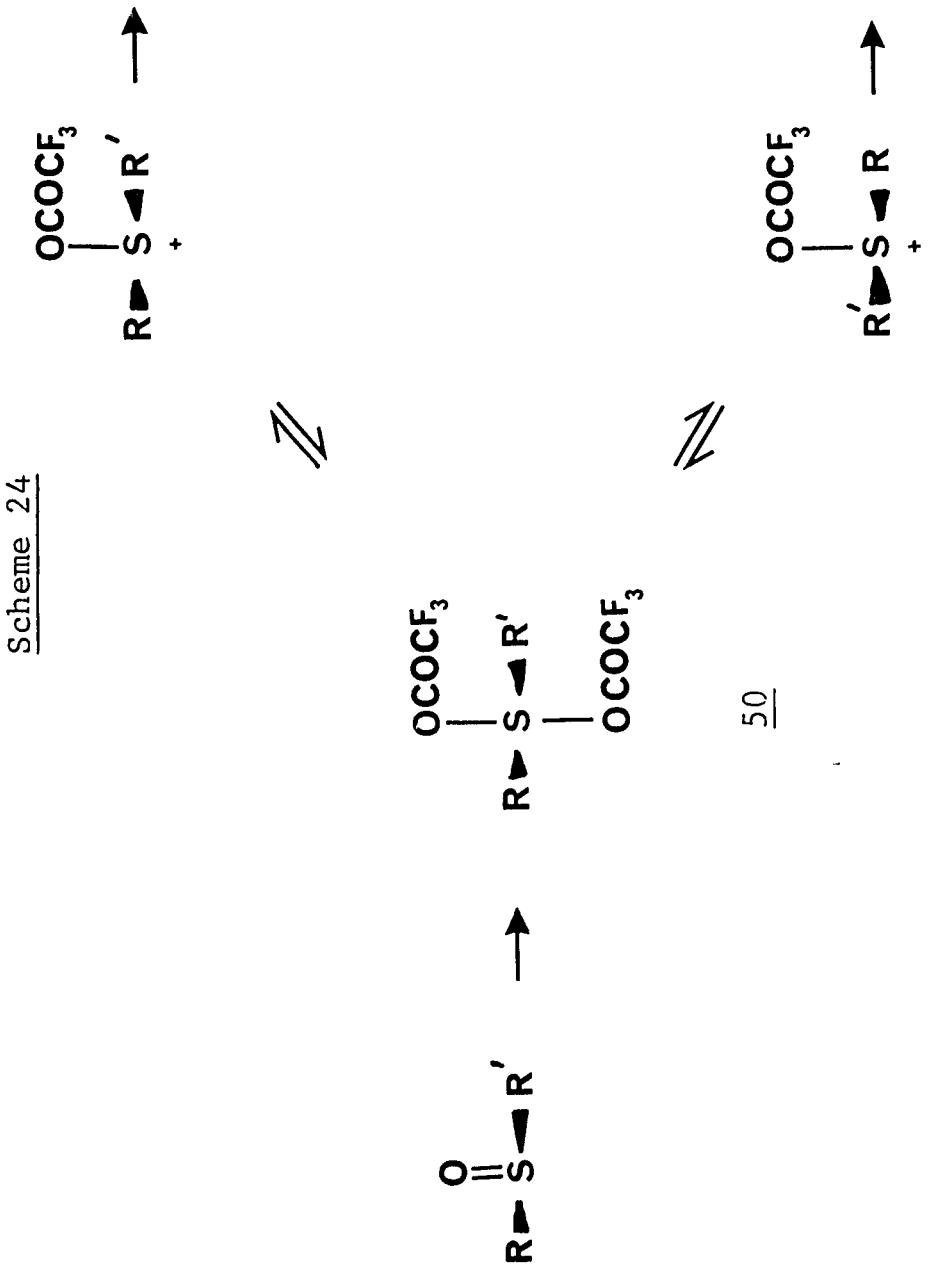


26

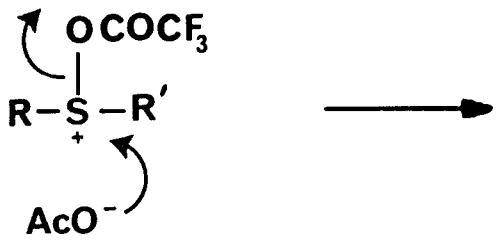
which was quite stable. Formation of a bis-(trifluoroacetyl) oxysulfurane from an optically active sulfoxide would give an achiral intermediate (50) which would also explain the observed racemization (Scheme 24). Dissociation followed by substitution could account for all experimental observations. This interpretation is more favorable, because trifluoroacetate is a poor nucleophile. Work by Tanakaga and coworkers[42] lends credence to this argument. Treatment of acetoxy sulfonium salts (51) with trifluoroacetate ion resulted in no observable change in the intermediate. However, when trifluoroacetoxysulfonium salts (52) were treated with acetate ion, an intermediate identical to 51 resulted (Scheme 25). Therefore, one could argue that under our experimental conditions, racemization by rapid displacement at sulfur by trifluoroacetate would be unfavorable.

Further experiments were undertaken to develop other suitable groups for sulfoxide activation in nucleophilic substitutions at sulfur. Canonical structures for sulfoxides

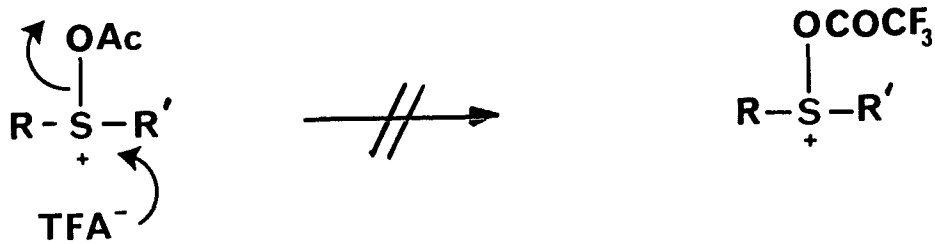
Scheme 24



Scheme 25

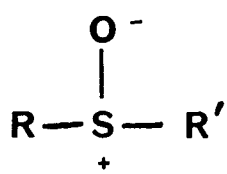


52 51



51 52

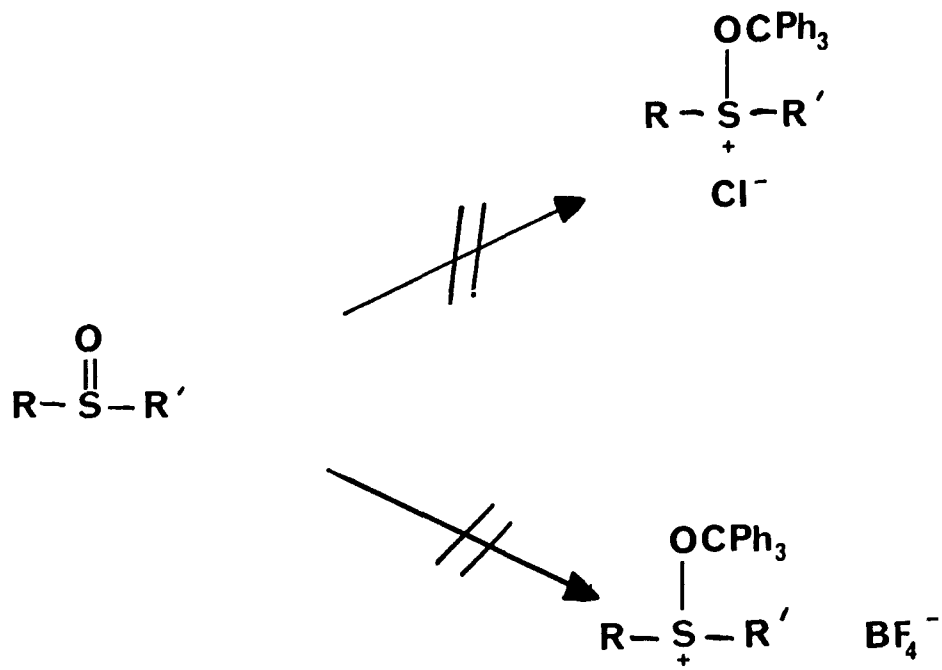
such as 53 can be drawn, and one would predict from these structures that sulfoxides would be nucleophilic enough to



53

react like other nucleophilic oxygen atoms. However, when dimethyl sulfoxide or diphenyl sulfoxide is treated with a number of electrophilic agents such as trityl chloride and ethyl chloroformate, no observable reaction occurs. When these sulfoxides were treated with triphenylmethyl chloride under a variety of reaction conditions, no isolable ionic intermediate was observed. Treatment of the sulfoxides with trityl fluoroborate likewise failed to give any evidence of reaction (Scheme 26). Since the trityl group is such a large

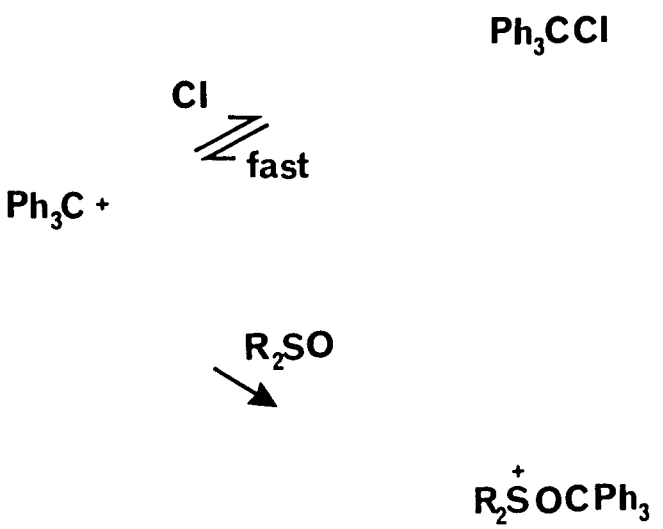
Scheme 26




and sterically hindered group, the rate of reaction with a similarly hindered diaryl sulfoxide would probably be retarded compared to most other substrates that react with trityl

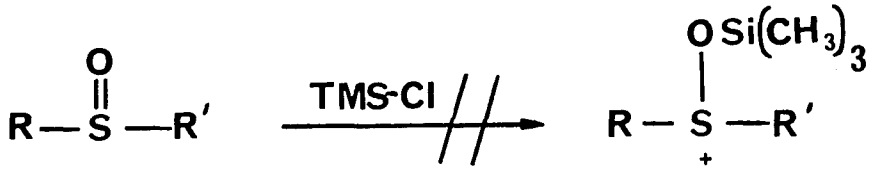
chloride. In addition, the trityl carbocation is known to be quite stable, and one would not necessarily predict that it would be reactive under the conditions examined. This carbocation would have a finite lifetime, and thus might recombine with chloride ion more readily than it would react with a sulfoxide (Scheme 27).

Scheme 27




Silyl chlorides are also known to react cleanly and quickly with nucleophiles, especially alcohols and alkoxides. Accordingly the preparation of a sulfoxide analog of a silyl ether was undertaken. DMSO and phenyl sulfoxide were treated with trimethylsilyl chloride under a variety of experimental conditions, but no sulfoxide-silane adduct was observed either directly (by nmr) or by examination of the reaction mixture

and products (Equation 27). It was concluded that a more reactive and less hindred silane derivative was needed. Reaction of DMSO with dimethyldichlorosilane, even at 0°, was

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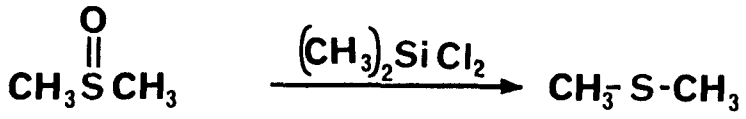
exothermic, and the odor of dimethyl sulfide was apparent as soon as the reagents were mixed. Treatment of the reaction mixture with toluenesulfonamide followed by normal work-up revealed no sulfimide, but glpc analysis did confirm the presence of dimethyl sulfide as the major product of the reaction. Reduction was indeed taking place, although starting material

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was still a major component of the reaction mixture (Equation 28). This result was not unexpected. Mislow and coworkers[43] and other investigators have shown that perchlorosilanes are efficient reducing agents for phosphine oxides, and one would expect sulfoxides to be more easily reduced than phosphine oxides. Methyltrichlorosilane was also found to be a fair reducing agent for sulfoxides by us. Results for both of these reducing agents are summarized in Table II. It should be noted in both cases, the reduction proceeded more efficiently when a large excess of silane was employed.

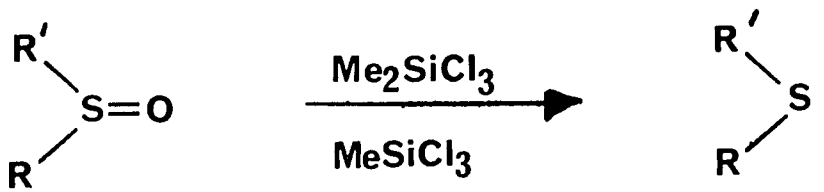


TABLE II

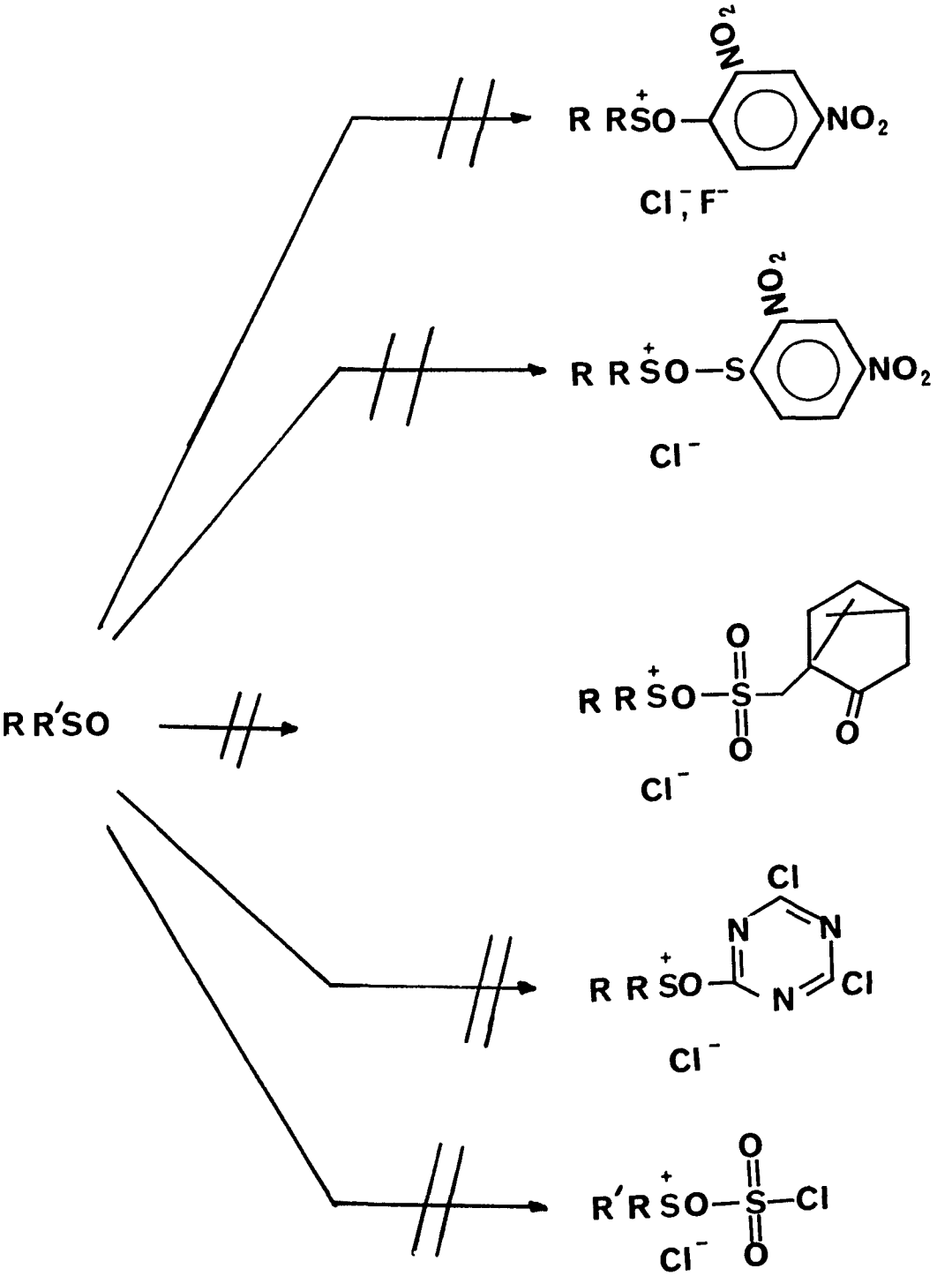
Reduction of Sulfoxides Using Chlorosilanes

| Compound | $R_1$ | $R_2$ | Silane | Yield (%) |
|---|---|---|---|---|
| IIa | Ph | Ph | dimethyldichloro | 62[a] |
| IIb | Ph | Ph | methyltrichloro | 41 |
| IIc | Ph | $CH_3$ | methyltrichloro | 37 |
| IId | Ph | $CH_3$ | methytrichloro | 65[a] |
| IIe | $CH_3$ | $CH_3$ | dimethyldichloro | 49 |

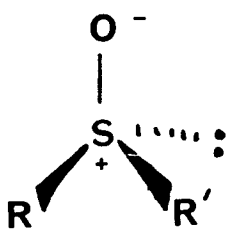
[a]two equivalents of silane present

A number of other groups were examined as potential sulfoxide activating groups, but none was found to be satisfactory (Scheme 28).

Scheme 28



The failure of most sulfoxides to undergo reaction with the reagents of varying electrophilicity is undoubtedly due to the low nucleophilicity of sulfoxides and their steric bulk. Even though canonical structures such as 53 can be drawn, it should be emphasized that other effects such as electron delocalization and electronegativity differences between S and O dramatically decreases the nucleophilicity of the sulfoxide oxygen atom.[44]



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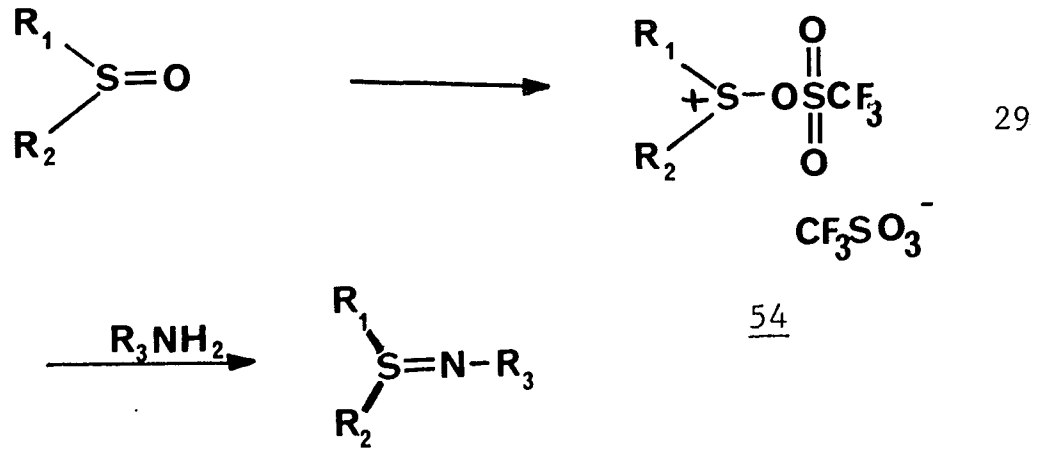
Hendrickson's[31] report that triphenylphosphine oxide as well as DMSO react with trifluoromethanesulfonic anhydride (TFMSA) was of special interest. He found that both of these substrates were easily sulfonylated under mild conditions. Our own exploration into the scope of these reactions focused on nucleophilic substitutions of the sulfoxide trifluoromethanesulfonate. Because one might expect S-oxides and P-oxides to behave in an analogous fashion on the basis of $pK_a$ considerations, exploration of the possibility of substitution at phosphorus in phosphine oxide triflates was in order.[39, 49] We found that a wide variety of sulfoxides would react with TFMSA. When the intermediate (54) was treated with toluene-

sulfonamide, the corresponding sulfimide was formed in good yield (Equation 29).



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These results are summarized in Table III, and are analogous to the results obtained with TFAA.[51]

Again, it should be noted that when an optically active sulfoxide was treated under these conditions, only racemic sulfimide was isolated. Basic hydrolysis of the reaction mixture of optically active sulfoxide treated with TFMSA gave only racemic material (Scheme 29). Rationalization of these observations involves arguments and reasoning similar to those presented for racemization with TFAA. Loss of optical activity due to a series of nucleophilic displacements by $CF_3SO_3^-$ would not seem to be a favorable pathway at $-78^{\circ}$. Postulation of an achiral sulfurane intermediate could account for the racemization. Random dissociation of the oxysulfurane (55) would be expected to give a racemic modification of enantiomeric sulfoxide triflates which could then go on to give the observed reaction products (Schemes 29, 30).

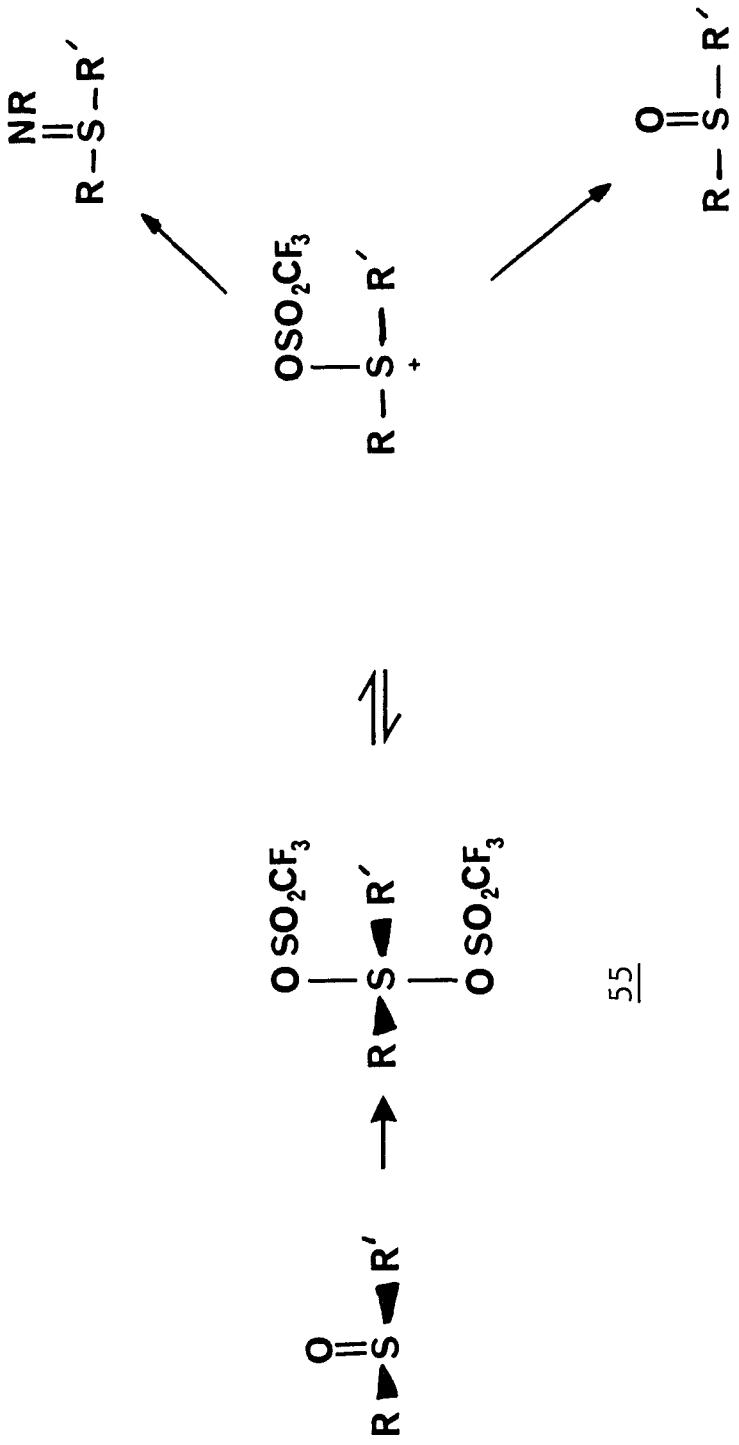
TABLE III

Conversion of Sulfoxides to Sulfimides Using TFMSA

| Compound | $R_1$ | $R_2$ | $R_3$ | Yield (%) |
|---|---|---|---|---|
| IIIa | $CH_3$ | $CH_3$ | Ts | 80 |
| IIIb | Ph | Ph | Ts | 83 |
| IIIc | p-Tolyl | p-Tol | Ts | 80 |
| IIId | p-Tolyl | $CH_3$ | Ts | 73 |
| IIIe | R-(+)-p-Tolyl | $C_2H_5$ | Ts | 79[a] |
| IIIf | $PhCH_2$ | $PhCH_2$ | Ts | 82 |
| IIIg | Ph | n-propyl | Ts | 79 |
| IIIh | p-Tolyl | n-propyl | Ts | 83 |
| IIIi | p-ClPh | p-ClPh | Ts | 0 |
| IIIj | Mesityl | Mesityl | Ts | 0 |

[a] $[\alpha]_D^{25} = 0.0^o$

Scheme 29

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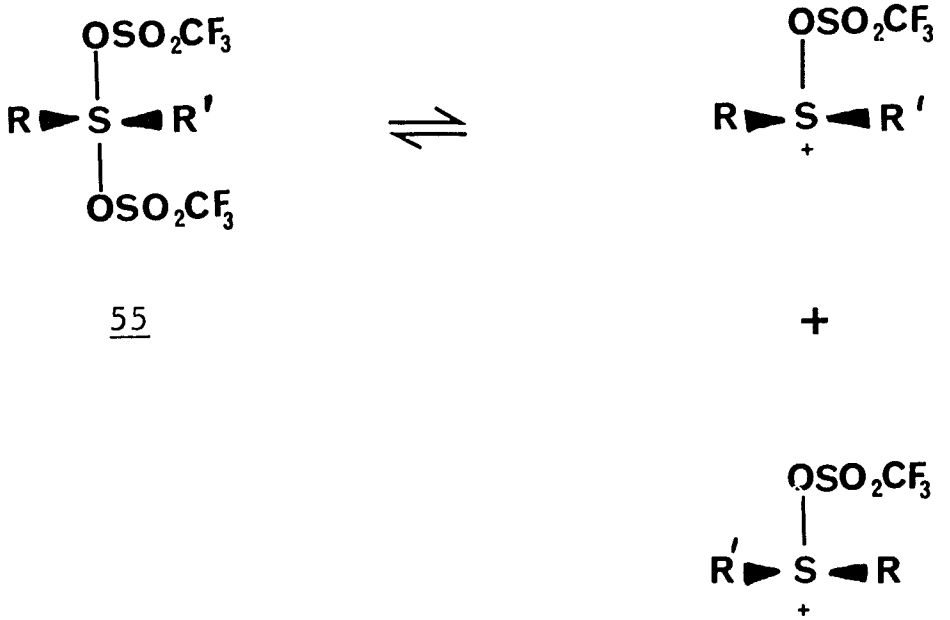
Scheme 30



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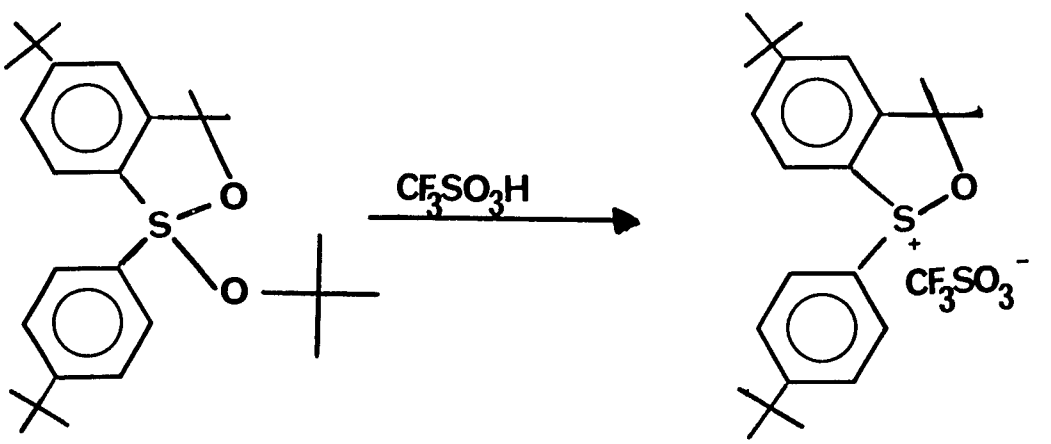
Martin[28] has shown that oxysulfonium triflates exist as ionic solids when isolated, and that the sulfur atom bears a full positive charge (Equation 30). It should be emphasized



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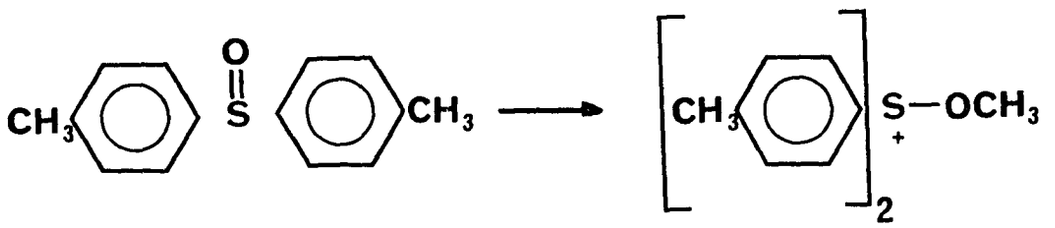
that the ionic nature of these isolated salts would not necessarily preclude small equilibrium concentrations of the oxysulfurane in solution, thereby effecting racemization of the substrate.

The low reactivity of both p-chlorophenyl and mesityl sulfoxide in the sulfimide preparation using both TFAA and TFMSA presented interesting questions. Were the sulfoxides reacting with the anhydrides to give intermediates inert to nucleophilic displacement, or were the sulfoxides inert to treatment with the anhydrides? An nmr study of a number of electron deficient aryl alkyl sulfoxides and sterically hindered sulfoxides was undertaken to address these questions. Because of the nature of the substrates, they were expected to show relatively low reactivity with TFAA and TFMSA, so that the reaction process could be monitored by nmr spectroscopy (Scheme 31). The nmr spectra of both p-tolyl sulfoxide (56) and methyl p-tolyl sulfoxide (57) were recorded. A small amount of Magic Methyl (methyl fluorosulfonate) was added to both tubes and the spectra were recorded again (Scheme 31).

An intermediate shift of the resonance for the tolyl methyl group from δ 2.30 to δ 2.38 was observed for 56. The resonance for the S-methyl group in 57 was also shifted downfield from 2.44 to δ 2.58. These model compounds provided us with much useful information. They showed that Magic Methyl reacts immediately with sulfoxides ("immediately" would mean the time required to add the reagent and record the spectrum) since only the shifted downfield resonances were observed.

Scheme 31



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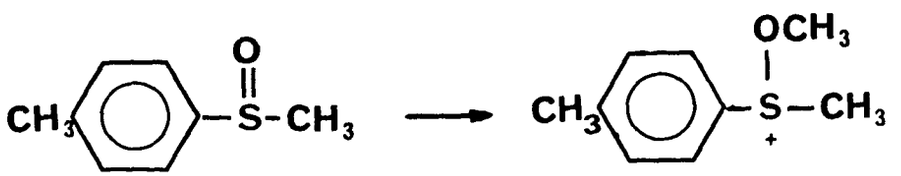

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These models also gave a rough approximation of the magnitude of the change in shift and their relative positions. Table IV lists the sulfoxides employed in this study and presents the changes in chemical shifts observed when the substrates were treated with TFAA or TFMSA.

TABLE IV

Nmr Parameter for Activated Sulfoxides

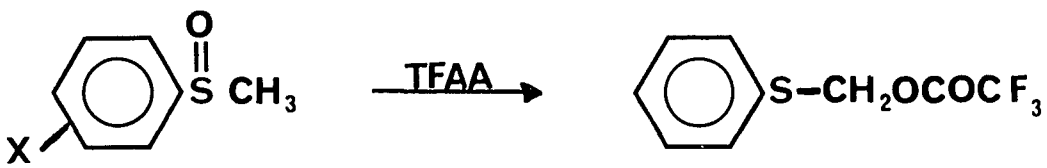
| Sulfoxide | δ Ar-$CH_3$ | δ S-$CH_3$ | Δ δ |
|---|---|---|---|
| p-Tolyl | 2.30 | | |
| p-Tolyl + MM* | 2.38 | | 0.08 |
| Mesityl | 2.25 | | |
| Mesityl + TFAA | 2.25 | | 0 |
| p-Nitrophenyl Methyl | | 2.80 | |
| p-Nitrophenyl Methyl + TFAA | | 2.93 | 0.13 |
| m-Nitrophenyl Methyl | | 2.85 | |
| m-Nitrophenyl Methyl + TFAA | | 3.00 | 0.15 |
| m-Trifluoromethylphenyl Methyl | | 2.78 | |
| m-Trifluoromethylphenyl Methyl + TFAA | | 3.04 | 0.26 |

| Sulfoxide | δ Ar-$CH_3$ | δ S-$CH_3$ | Δ δ |
|---|---|---|---|
| p-Tolyl | 2.30 | | |
| p-Tolyl + TFMSA | 2.46 | | 0.16 |

*MM = methyl fluorosulfonate (Magic Methyl)

From these observations it is evident that aryl sulfoxides with powerful electron-withdrawing groups in the m- and p- positions react more slowly with electrophiles such as TFAA and TFMSA than unsubstituted sulfoxides. Aryl sulfoxides with electron donating groups in the m- or p- positions reacted quite rapidly. It has also become clear that hindered sulfoxides such as mesityl sulfoxide or phenyl tert-butyl sulfoxide react very sluggishly, if at all, at room temperature. When mesityl sulfoxide in deuteriochloroform was treated with TFAA and warmed, there was no observable change in chemical shifts even after two days.

During the course of this study the aryl alkyl sulfoxides treated with TFAA or TFMSA were observed to undergo Pummerer rearrangements (Equation 30). Again, in the case of

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sulfoxides with electron deficient aryl groups the reaction proceeded quite slowly and could be observed by nmr spectroscopy. In the case of m-nitrophenyl methyl sulfoxide the nmr spectrum showed that the reaction mixture was still about 33% activated sulfoxide after twenty minutes.

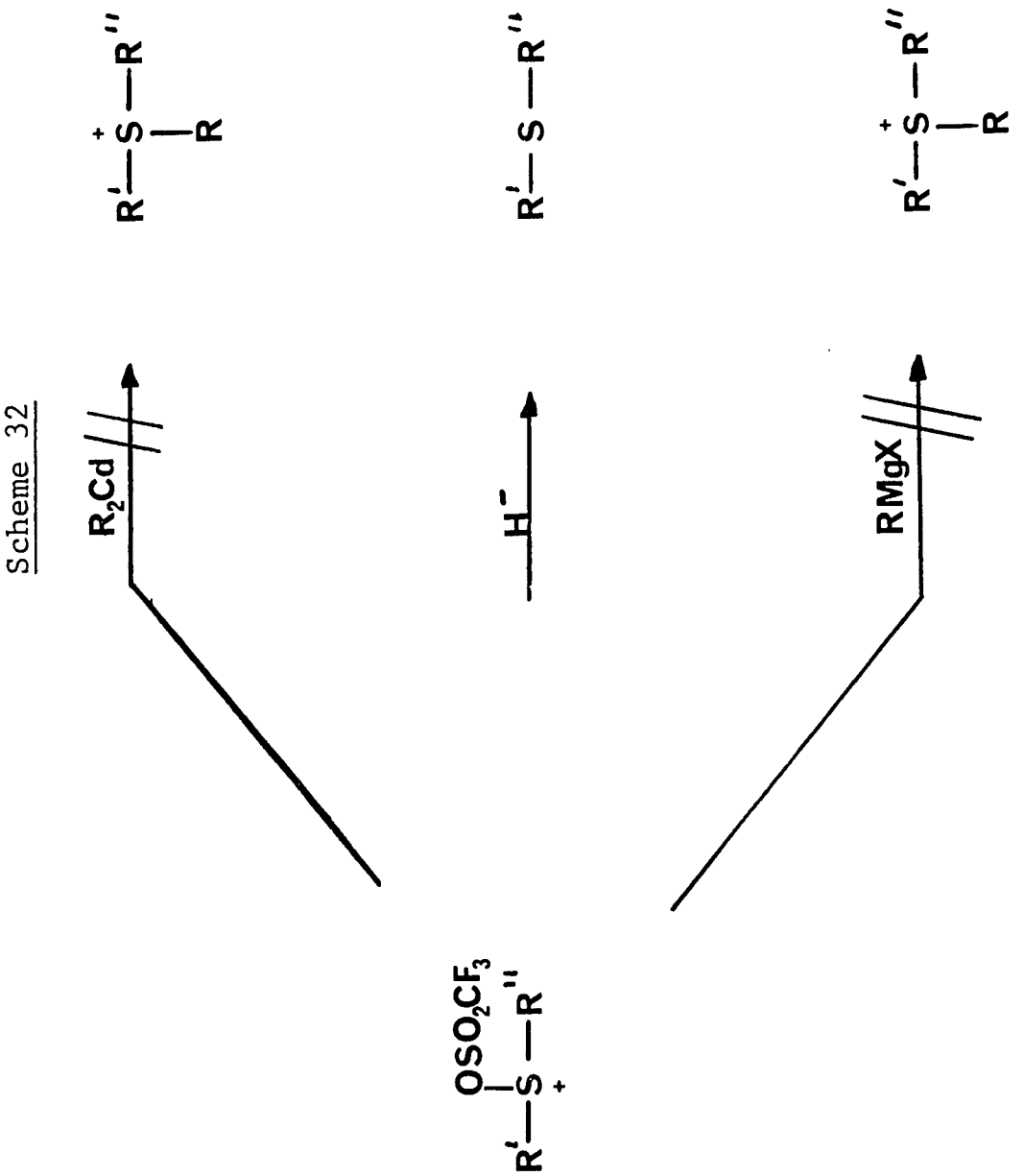
Treatment of sulfoxide triflates with organomagnesium halides or organocadmium reagents under a variety of conditions

results in recovery of starting sulfoxide. When the triflate was treated with lithium alanate or sodium cyanoborohydride, the corresponding sulfide was obtained in fair yield (Scheme 32).

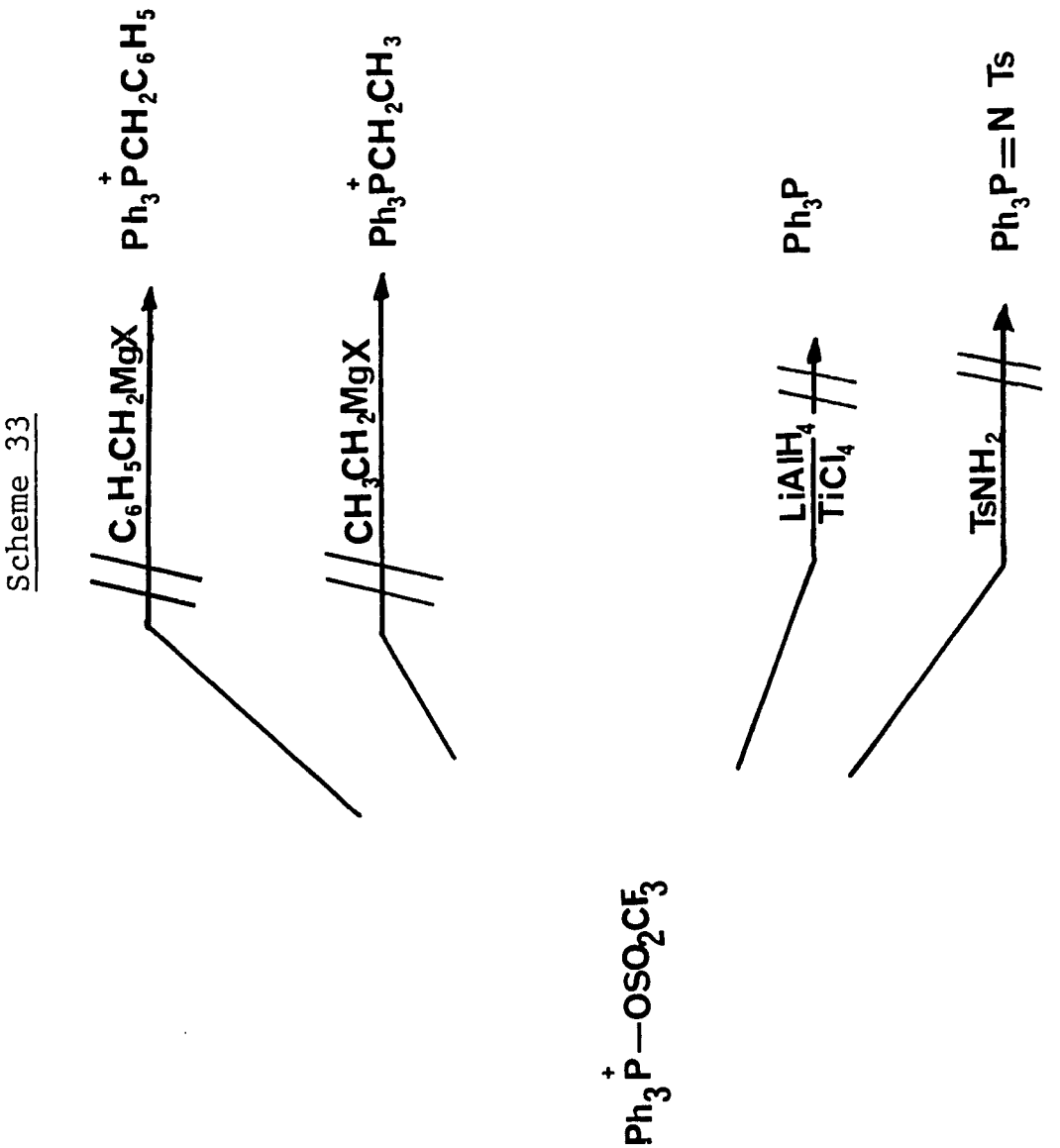
Similarly, treatment of triphenylphosphine ditriflate (58) with various Grignard reagents gave no evidence for the formation of phosphonium salts. When 58 was treated with lithium alanate-$TiCl_4$ reagent, only trace amounts of triphenyl phosphine were detected (tlc) along with recovery of triphenyphosphine oxide (Scheme 33).

Other acid anhydrides remained to be explored as nonracemizing activating groups for sulfoxides in nucleophilic substitutions. Our attention was focused on fluorosulfonic anhydride and its potential to function in this capacity.[45] Indeed, fluorosulfonic anhydride did react readily with sulfoxides even at temperatures as low as -70° to -100°. Reaction in most cases was instantaneous and exothermic. When reaction mixtures were warmed above -40°, normal Pummerer rearrangement products were observed in the case of sulfoxides with α-hydrogens. When diaryl sulfoxide fluorosulfonates were warmed above 0°, decomposition was noticeable after short periods of time. Most sulfoxide fluorosulfonates readily underwent substitution with p-toluenesulfonamide to give the corresponding sulfimide which were usually isolated as oil that could be purified by column chromatography on silica gel (Scheme 34). Again, as observed with other activating groups, mesityl sulfoxide was not converted to sulfimide.

Scheme 32

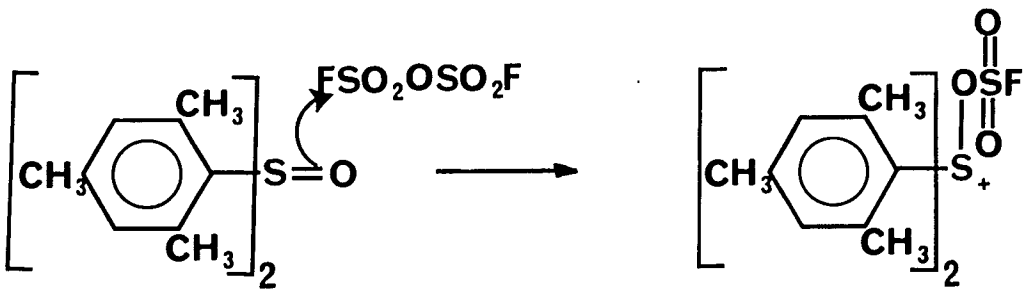


Scheme 33



Scheme 34


However, it appeared as if the anhydride did react with the sulfoxide. Because the reaction with anhydride occurs at sulfoxide oxygen, one might expect that the high reactivity of the anhydride might make the system less sensitive to the steric factors that would ordinarily limit reaction (Equation 31). The displacement at sulfur by toluenesulfonamide on the other hand occurs at an extremely hindered

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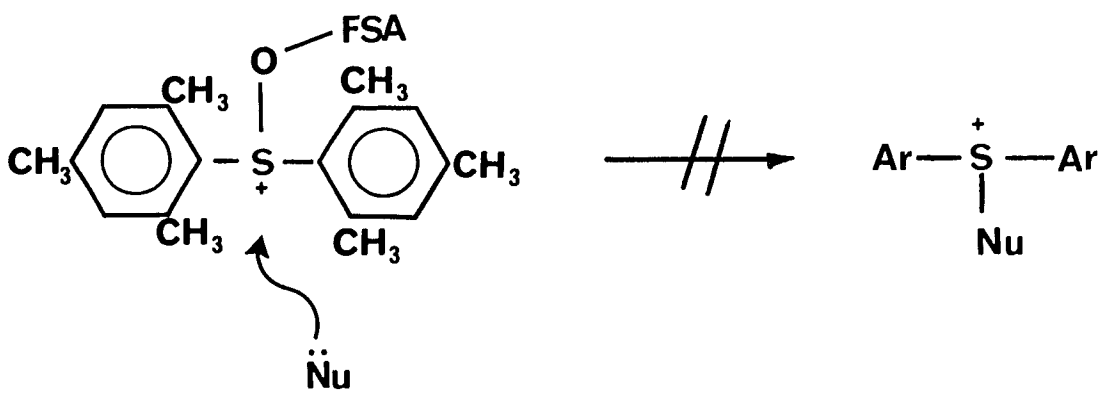
electrophilic site and the bulk of the substituted aryl groups is enough to inhibit reaction (Equation 32). These observations are consistent with findings in related systems such as mesitoic acid ester hydrolyses.[46]




32

Steric hindrance as the inhibiting factor in the substitution step could be tested. A smaller nucleophile would be less effected by steric factors. It was decided to examine the reaction of mesityl sulfoxide fluorosulfonate with a hydride ion source. Treatment of the activated sulfoxide with sodium cyanoborohydride at -20°C gave mesityl sulfide in 62% yield (Equation 33). Displacement at the hindered sulfur atom did appear to be more facile when a smaller nucleophile was employed. This reaction was investigated as a possible


33

synthetic preparation of sulfides and the results of which are summarized in Table V. These results are comparable to those observed for similar reductive preparations of sulfides such as sulfoxide reduction using lithium alanate-$TiCl_4$[47] or Magic Methyl-sodium cyanoborohydride[48] (Scheme 35).

FSA was found to be a potent activating group for diaryl, dialkyl and aryl alkyl sulfoxides. Because it does react so readily with sulfoxides we became interested in its potential for use in DMSO oxidations of primary and secondary

Scheme 35

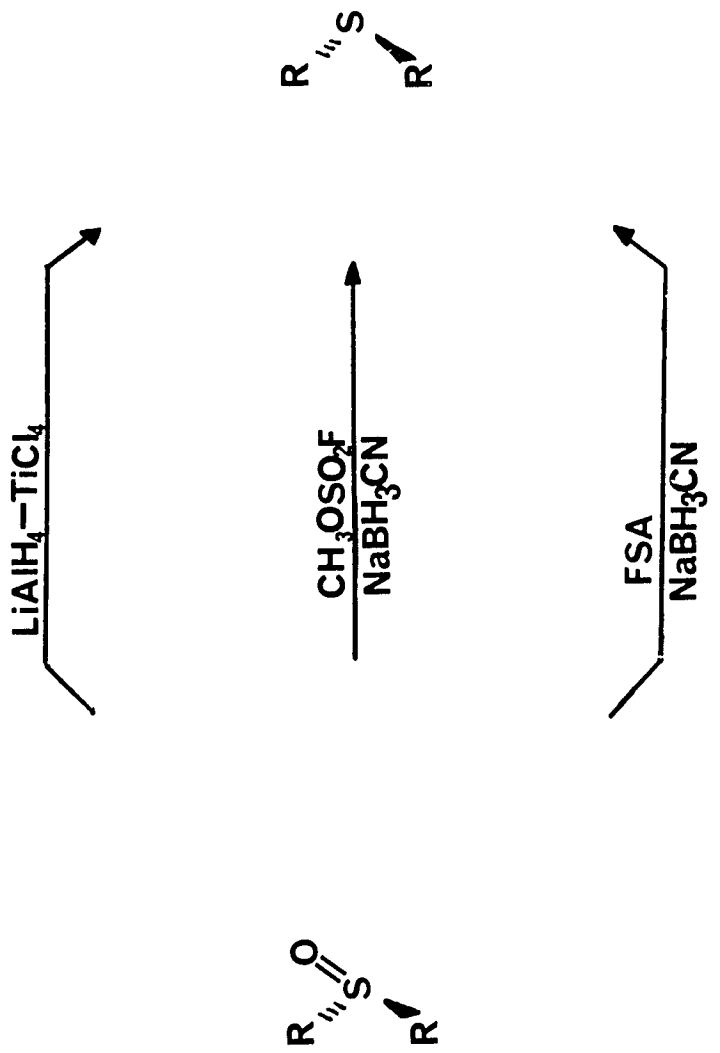


TABLE V

Reduction of Sulfoxides with FSA-Sodium Cyanoborohydride

| Compound | $R_1$ | $R_2$ | Yield (%) |
|---|---|---|---|
| Va | mesityl | mesityl | 62 |
| Vb | p-$NO_2$Ph | $CH_3$ | 75 |
| Vc | p-ClPh | p-ClPh | 77 |
| Vd | tolyl | tolyl | 81 |
| Ve[a] | tolyl | tolyl | 55 |
| Vf | m-$CF_3$Ph | $CH_3$ | 73 |
| Vg | $PhCH_2$ | $PhCH_2$ | 77 |

[a]run at -20°

alcohols (Equation 35).[49] A number of alcohols listed in Table VI were treated under DMSO-FSA oxidation conditions.

$$RCH_2OH \xrightarrow[(C_2H_5)_3N]{\text{DMSO/ FSA}} RCHO \qquad 35$$

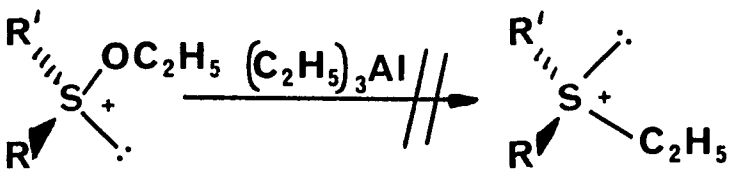
In all cases the products obtained gave positive tests for the presence of aldehydes (fuchsin test, nmr, ir) but tlc analysis showed the product to be contaminated with at least two other compounds (Parent alcohol plus an unidentified material). In general the oxidation did not give a clean conversion to the aldehyde and no attempts were made to optimize the conditions under which the conversion was carried out. Assistance in the execution of this study was provided by Mr. Charles Maclean.

It was now quite apparent that active anhydrides such as trifluoroacetic, trifluoromethanesulfonic, and fluorosulfonic anhydride would react readily with sulfoxides and were useful in the preparation of racemic sulfimides.[51] On the other hand, it was also apparent that these anhydrides were of no use in the preparation of optically active aulfimides, and in no case could sulfonium salts be prepared from sulfoxides by activation with these anhydrides.

TABLE VI

| Compound | Alcohol | C=O ($cm^{-1}$) |
|---|---|---|
| VIa | Piperonyl | 1690 |
| VIb | 3,4-Dimethoxybenzyl | 1695 |
| VIc | Cyclohexyl | 1723 |
| VId | Propargyl | 1682 |

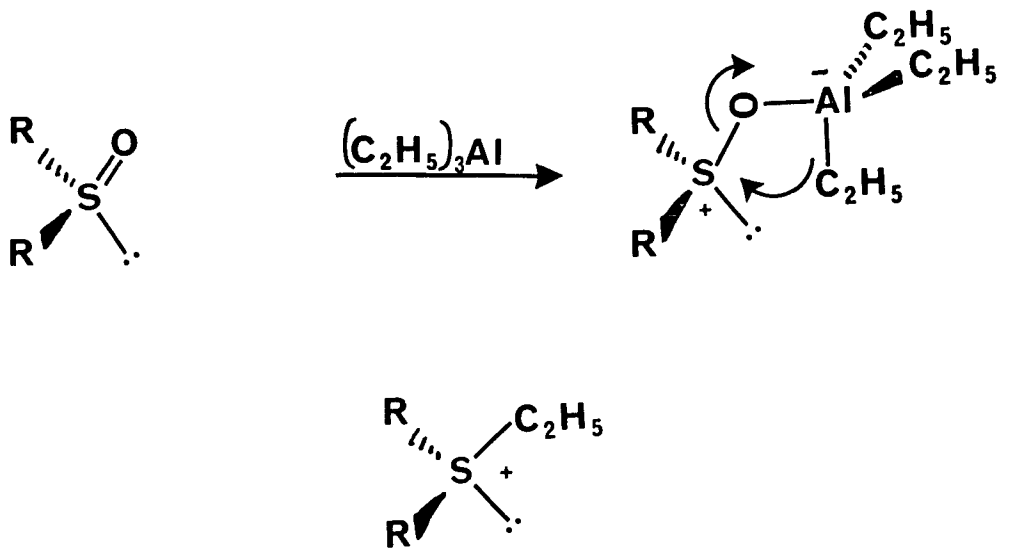
Because our original interest was in improving the preparative route to optically active sulfonium salts, it was decided to examine possible routes to these compounds that did not involve anhydride activation. As mentioned earlier, previous work[33] showed that the presence of halide ion in the organometallic reagent caused racemization and redutive side reactions. A halide-free organometallic was desired for the displacement step. Trialkylaluminum compounds were readily available and halide free. Unfortunately, when a number of arylalkylalkoxysulfonium salts were treated with solutions of triethylaluminum, no sulfonium salt was recovered (Equation 35).




35

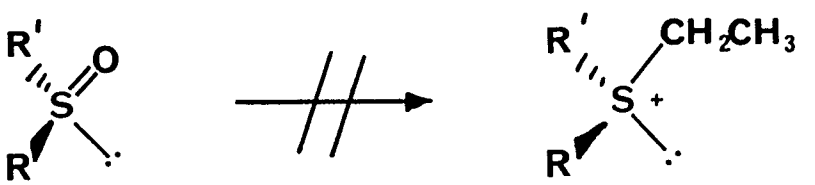
Alkylaluminum compounds are known to be good Lewis acids and since sulfoxides are bases, it was reasoned that perhaps complex formation between the two species would provide a driving force for alkyl transfer from aluminum to sulfur (Scheme 36). This could possibly provide a less drastic reaction pathway for the conversion of aryl alkyl sulfoxides to sulfonium salts. When a number of aryl alkyl sulfoxides were treated with triethylaluminum, however, only starting materials were recovered (Equation 36).

Scheme 36







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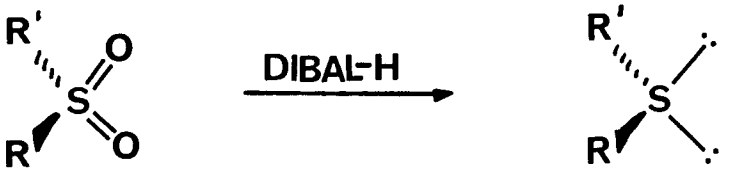
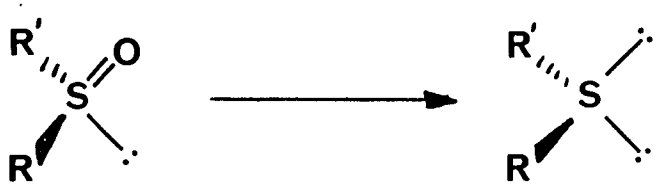
Recently, Gardiner and coworkers demonstrated that diisobutylaluminum hydride was effective in reducing sulfones to sulfides (Equation 37). Since we knew that sulfoxides




37

would not react with trialkylaluminum compounds, it was of interest to determine whether or not sulfoxides would react with dialkylaluminum hydrides. This would also address the question of sulfoxide intermediacy in the sulfone reduction reported by Gardiner et al. (Equation 38). When a number of

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diaryl, dialkyl, and aryl alkyl sulfoxides were treated with diisobutylaluminum hydride (DIBAL-H) the corresponding sulfides were recovered in good yield. Table VII contains a summary of these results. It appeared that sulfoxides would readily complex with diisobutylaluminum hydride and underwent subsequent reduction easily. In contrast, complexation with triethylaluminum followed by alkyl transfer seemed unfavorable. In both cases the first step (complexation with sulfoxide) would be identical (Scheme 37). However, it appears that

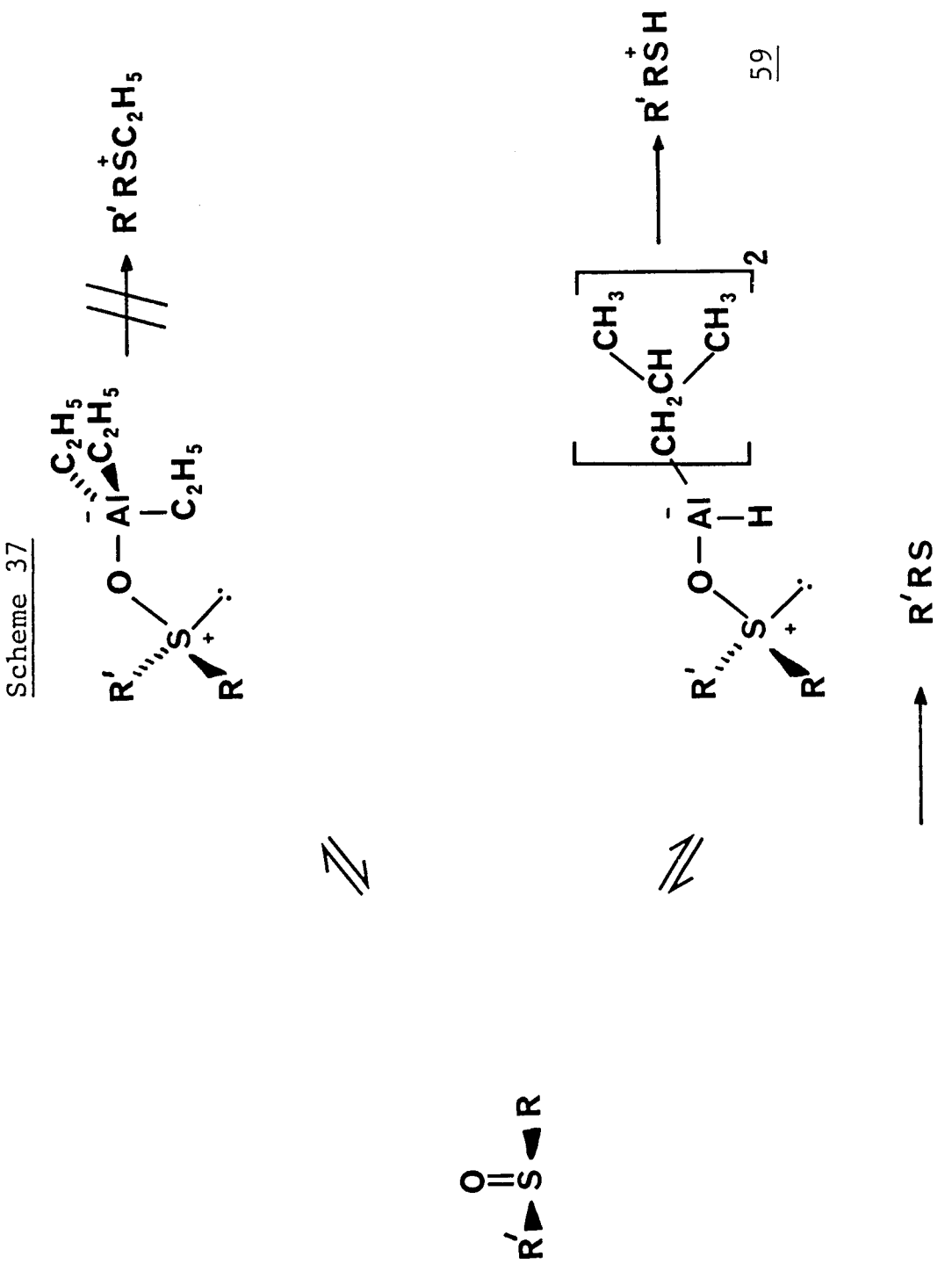
TABLE VI

Reduction of Sulfoxides with DIBAL-H

| R | $R^1$ | Yield | RR'SO/H |
|---|---|---|---|
| Ph | Ph | 83%[a,d] | 1:2 |
| p-Cl-Ph | p-Cl-Ph | 88%[a,c] | 1:2 |
| Mesityl | Mesityl | 82%[a,c] | 1:2 |
| Ph | p-Tolyl | 86%[b] | 1:1.5 |
| n-butyl | n-butyl | 81%[b] | 1:1.5 |
| $MCF_3$-Ph | $CH_3$ | 83%[b] | 1:1.3 |
| p-Tol | p-Tol | 87%[b] | 1:1.3 |
| p-Tol | $C_2H_5$ | 77%[b] | 1:1 |
| $CH_3$ | n-$C_3H_7$ | 75%[b] | 1:1 |

[a]isolated yield
[b]yield via glpc analysis
[c]isolated and recrystallized
[d]purified by distillation

Scheme 37



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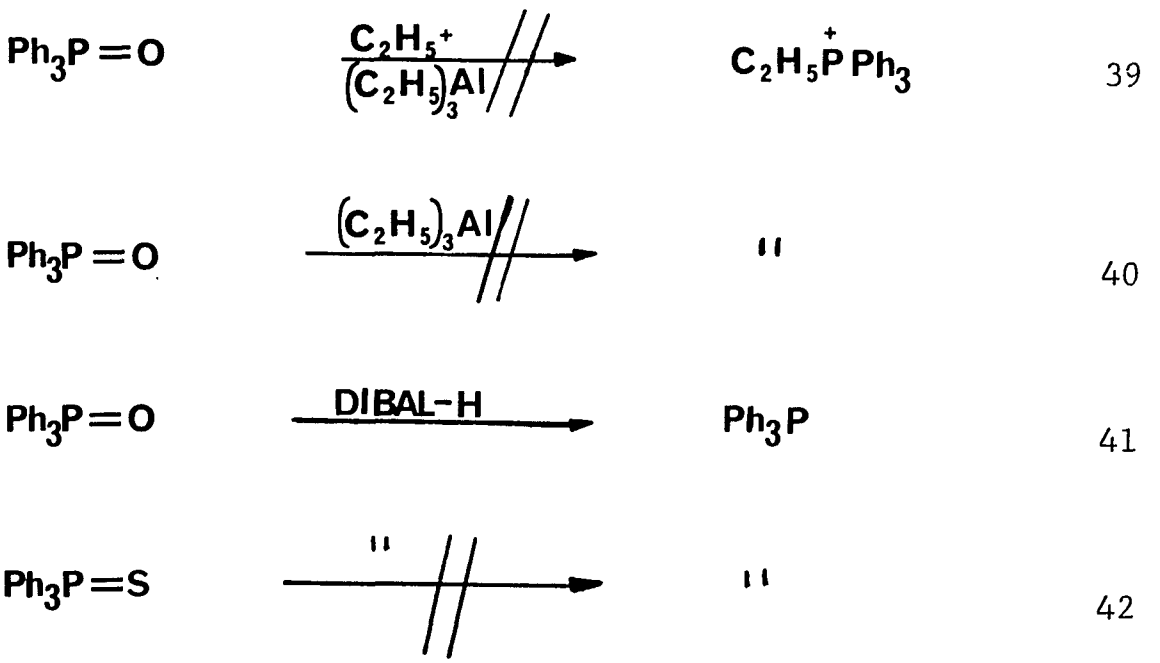
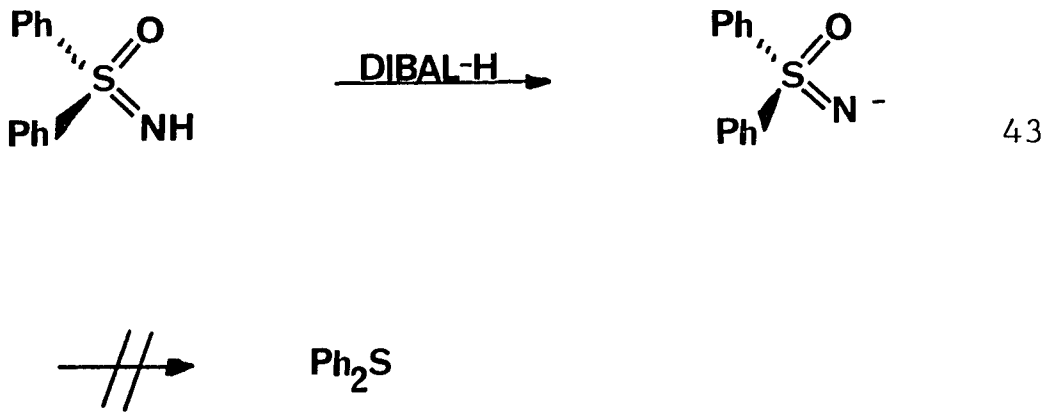
hydride transfer occurs more readily than alkyl transfer. Rapid deprotonation of the hydridosulfonium intermediate (59) would give the sulfide.

Analogous results were obtained when triphenylphosphine oxide was used as a substrate. Alkylation of triphenylphosphine oxide with ethyl fluorosulfonate followed by treatment with triethylaluminum resulted in recovery of the phosphine oxide (Equation 39). Likewise, when the phosphine oxide was directly treated with triethylaluminum, no phosphonium salt was recovered (Equation 40). When triphenylphosphine oxide was treated with diisobutylaluminum hydride, triphenylphosphine was recovered in good yield (83%) (Equation 41). Interestingly, all attempts to reduce triphenylphosphine sulfide with diisobutylaluminum hydride failed (Equation 42).



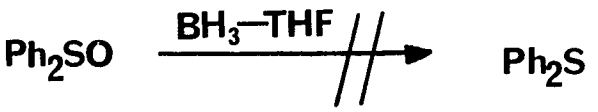



43




Reductions of other tricoordinate sulfur substrates were undertaken. When anisyl N-tosyl sulfimide was treated with diisobutylaluminum hydride tlc analysis of the reaction mixture showed the presence of sulfide, which, however, was not the major component. Treatment of diphenyl sulfoximine with excess diisobutylaluminum hydride followed by normal work-up gave only starting material (Equation 43). This result is somewhat curious since diphenyl sulfoximine is isoelectronic with diphenyl sulfone, an easily reduced substrate. However, the basic nature of diisobutylaluminum hydride could favor proton abstraction in the sulfoximine and thereby lower its potential for reduction drastically (Equation 43).

Other attempted reductions of sulfoxides with Lewis acid hydride sources such as $BH_3$-THF were less successful.




Treatment of phenyl sulfoxide with excess $BH_3$-THF resulted in incomplete reduction (50% by glpc) and no variation in conditions could improve this result.

# EXPERIMENTAL

Instrumentation: Nmr spectra were obtained on a Jeolco HM-100 spectrometer and are recorded in ppm downfield from tetramethylsilane. Infrared spectra were obtained on a Perkin-Elmer Model 337 grating infrared spectrophotometer. A table of relevant nmr parameters for sulfides, sulfoxides, and sulfilimines, as well as ir spectra is included in Appendix A. Optical rotations were obtained on a Carl Zeiss $0.005^{o}$ photoelectric precision polarimeter and on a Cary 60 recording spectro-polarimeter. Melting points, obtained on a Hoover capillary melting point apparatus, are uncorrected. Glpc analysis of reaction mixtures was performed on an Aerograph Model 90-P Gas Chromatograph with decalin as an internal standard.

Materials: Dimethyl sulfoxide (DMSO) was stirred overnight or longer over sodium hydroxide pellets, distilled at reduced pressure, and stored over 4A molecular sieves. Methylene chloride was distilled from phosphorus pentoxide and stored over oven-dried potassium carbonate. Ethyl ether was dried over sodium wire. Tetrahydrofuran (THF) was dried by refluxing over lithium aluminum hydride and distilled.

A number of compounds used in the course of this research were obtained commercially and are listed with their distributors: trifluoroacetic anhydride (TFAA), trifluoromethanesulfonic anhydride (TFMSA), methyl fluorosulfonate

(Magic Methyl), Aldrich Chemical Co., Inc.; titanium (IV) chloride, ethylmagnesium bromide (1 M in THF), benzylmagnesium bromide (1 M in THF), antimony (V) chloride, and diisobutylaluminum hydride (DIBAL-H) (1 M in hexane), Ventron, Inc.; fluorosulfonic acid, J. T. Baker Chemical Co.

Methyl p-Tolyl Sulfide. p-Thiocresol (18.6 g, 0.15 mol) was dissolved in 200 ml of 3.5 M aqueous sodium hydroxide in a 500-ml, round-bottomed flask equipped with a magnetic stirrer, an addition funnel and a Friedrichs condenser. Methyl sulfate (21.4 g, 0.17 mol) was added dropwise over a period of one hour and stirring was continued overnight at room temperature. The organic and aqueous layers were separated and the aqueous phase was extracted several times with ether. The combined organic layers were dried over sodium sulfate and concentrated on a rotary evaporator. Distillation at reduced pressure gave 16.5 g (80%) of the desired product: bp 73-77° (5 mm) lit.[52] bp 62-63° (0.25 mm) . Ir spectrum no. 22756; ν max 3080, 2030, 2920, 1500, 1445, 1020, 960 and 800 $cm^{-1}$. Nmr spectrum no. 5985.

Ethyl p-Tolyl Sulfide. p-Thiocresol (37.2 g, 0.30 mol) was dissolved in 250 ml of 6.0 M sodium hydroxide in a 1000-ml, three-necked, round bottomed flask equipped with a magnetic stirrer, an addition funnel, and a Friedrichs condenser. Ethyl bromide (32.4 g, 0.30 mol) and tetrabutylammonium hydroxide (25% in methanol, 5 ml) were added dropwise over a period of one hour and stirring was continued

for two more hours. The aqueous and organic layers were separated and the aqueous layer was washed with several portions of ether. All organic layers were combined and dried over sodium sulfate. Concentration on a rotary evaporator and distillation at reduced pressure gave 39.15 g (85%) of the desired product. bp 132-134° (10 mm) lit.[53] bp 82-85° (4 mm) . Ir spectrum no. 22757. Nmr spectrum no. 5988.

n-Propyl p-Tolyl Sulfide. p-Thiocresol (37.2 g, 0.30 mol) was dissolved in 250 ml of 6.0 M aqueous sodium hydroxide in a 1000-ml, three-necked, round-bottomed flask equipped with a magnetic stirrer, an addition funnel, and a reflux condenser. n-Propyl chloride (23.50 g, 0.30 mol) was added dropwise over a one-hour period and stirring was continued for two hours more. The aqueous and organic layers were spearated, and the aqueous layer was washed with several portions of methylene chloride. The combined organic fractions were dried over sodium sulfate and concentrated on a rotary evaporator. Distillation at reduced pressure gave 41.75 g (83%) of the desired product: bp 79-81° (2mm) lit.[53] bp 120° (15 mm). Ir sprectrum no. 22758. Nmr spectrum no. 5990.

(±) Methyl p-Tolyl Sulfoxide. Methyl p-tolyl sulfide (27.60 g 0.20 mol) was dissolved in 150 ml of glacial acetic acid in a 500-ml Erlenmeyer flask equipped with a magnetic stirrer. The flask was immersed in ice and hydrogen peroxide (30%, 28.50 g) was introduced slowly over a two-

hour period. Stirring was continued for an additional two-hour period. The solution was neutralized with aqueous sodium carbonate and extracted with methylene chloride. The combined organic layers were dried over sodium sulfate and concentrated on a rotary evaporator. Distillation at reduced pressure gave 22.11 g (72%) of the desired product: bp 119-123° (2.3 mm) lit.[54] bp 150-152° (8 mm) . Ir spectrum no. 22773 (neat). Nmr spectrum no. 5991.

Sodium p-Toluenesulfinate.[55] p-Toluenesulfonyl chloride (190.7 g, 1.0 mol) was pulverized with a mortar and pestle and was added to distilled water (1.8 liters). This slurry was added to a 4 liter beaker equipped with a steam inlet tube and a mechanical stirrer. Steam was introduced until the water temperature reaches 70°. Zinc dust (260 g, 2.0 gram-atoms) was added slowly over a period of one-half hour. Stirring was continued until all the zinc had been added. Steam was introduced until the water temperature reached 90°. Aqueous sodium hydroxide (12 N, 200 ml) was then added followed by sodium carbonate (100 g, 0.9 mol). Care was taken to avoid frothing while this addition took place. The mixture was filtered by suction through diatomaceous earth and the filtrate was concentrated in a large evaporating dish after which it was cooled to 0°. Crystals of sodium p-toluenesulfinate dihydrate were recovered by filtration and recrystallized from water giving 165.0 g (77%). Ir spectrum no. 22759 (KBr pellet). Nmr spectrum no. 5992 ($D_2O$).

p-Toluenesulfinyl Chloride[56] Sodium p-toluenesulfinate dihydrate (112.1 g, 0.5 mol) was added to a 1000-ml round-bottomed flask equipped with a Claisen adapter, a mechanical stirrer, and an addition funnel. Doubly distilled thionyl chloride (297 g, 2.5 mol) was added dropwide over a one-hour period. Stirring was continued for two hours at room temperature. Excess thionyl chloride was removed by aspiration and any traces of thionyl chloride were removed by addition of a portion of dry ether followed by concentration on a rotary evaporator. The crude reaction mixture was dissolved in dry ether and filtered in a nitrogen atmosphere. The inorganic salts were washed with dry ether twice. The combined ether solution was concentrated to give 65.8 g (73%) of a light yellow oil. Ir spectrum no. 22763 (neat). Nmr spectrum no. 5993 ($CDCl_3$).

(-)-Menthyl p-Toluenesulfinate. p-Toluenesulfinyl chloride (174.4 g, 1.0 mol) was dissolved in dry ether (75 ml) in a 500-ml, three-necked, round-bottomed flask equipped with a Friedrichs condenser and drying tube, an addition funnel, and mechanical stirrer. A solution of (-)-menthol (156.27 g, 1.00 mol) and dry pyridine (79.0 g, 1.0 mol) in ether was added dropwise at $-20^{\circ}$ over a one-hour period. Stirring was continued for one hour more and the reaction mixture was allowed to warm to room temperature. Aqueous hydrochloric acid (5%, 50 ml) was added to quench the reaction mixture. The organic layer was separated and the aqueous layer was washed with several portions of ether. The combined organic phase

was washed with several portions of dilute hydrochloric acid (5%), aqueous sodium carbonate, and distilled water. After drying over sodium sulfate, the organic layer was concentrated and cooled to -70°. Tetraethylammonium chloride (0.1 g) was added to the oil and hydrogen gas was bubbled into the oil until crystals were obtained. The crystals were isolated and the process was repeated until no more crystals could be obtained. (-)-Menthyl p-toluenesulfinate was recrystallized from acetone-water (3.5:1) three times to give 61.87 g (49%) of purified product: mp 100-102° lit.[57] mp 106-107° $[\alpha]_D^{25}$ -198.7° (c 1.30, acetone) lit.[58] $[\alpha]_D^{25}$ 199.19° (c 2, acetone) . Ir spectrum no. 22763, soln. Nmr spectrum no. 5594.

Preparation of Optically Active Alkyl Aryl Sulfoxides. The following is a description of the preparation of R-(+)-ethyl p-tolyl sulfoxide and will serve to illustrate the general procedure followed in the preparation of alkyl aryl sulfoxides.

(-)-Menthyl p-toluenesulfinate (35.04 g, 0.11 mol, $[\alpha]_D^{25}$ -198.7° was dissolved in dry ether (250 ml) in a dry, 1000-ml, three-necked, round-bottomed flask, equipped with a mechanical stirrer, an addition funnel and a Friedrichs condenser with drying tube. The mixture was cooled to -20° and ethylmagnesium bromide (1 M in THF, 200 ml) was added dropwise over a two-hour period. Stirring was continued and the reaction mixture was allowed to warm to room temperature. The mixture was allowed to stand at room temperature for two

hours, followed by hydrolysis with 5% sulfuric acid. The organic layer was separated and the aqueous layer was washed with several portions of ether. The combined ether layers were dried over sodium sulfate and concentrated to give a crude oil. Distillation at reduced pressure gave 3.32 g (18%) of the desired product: bp 106-111° (0.9-1.1 mm) lit.[5] bp 94° (0.4 mm) $[\alpha]_D^{25}$ 184.50° (c 1.8, acetone) lit.[58] $[\alpha]_D^{25}$ 187.5 (acetone) (98.4% optical purity). Ir spectrum no. 22765, neat. Nmr spectrum no. 5995 ($CDCl_3$).

General Procedure for Sulfoxide Activation with Trifluoromethanesulfonic Anhydride (TFMSA) in Sulfimide Preparation. The following is a general outline of the procedure employed when sulfoxides are allowed to react with TFMSA. The sulfoxide (10 mmol) was dissolved in dry methylene chloride in a 50-ml round-bottomed, three-necked flask flushed with nitrogen and equipped with a magnetic stirrer, a thermometer, and an addition funnel and cooled to -78°. TFMSA (11 mmol) in methylene chloride was added dropwise to the stirred solution, the temperature not being allowed to rise above -50°. After the solution had been stirred one hour, p-toluenesulfonamide (15 mmol) was added, followed by 5 ml of 10% aqueous sodium hydroxide. The organic layer was separated and the aqueous layer was extracted with several portions of methylene chloride. All organic layers were combined, washed with aqueous sodium carbonate, distilled water, and dried over sodium sulfate. Concentration on a rotary evaporator gave the desired N-(p-toluenesulfonyl) sulfimide.

Attempted Preparation of S,S-Bis-(2,4,6-Trimethylphenyl)-N-(p-Toluenesulfonyl) Sulfimide. Bis-(2,4,6-Trimethylphenyl) sulfoxide (1.45 g, 5.0 mmol) was dissolved in methylene chloride in a 50-ml round-bottomed, three-necked flask equipped with a magnetic stirrer, a thermometer, and an addition funnel. The apparatus was flushed with nitrogen and was cooled to -70°. TFMSA (1.41 g, 5.0 mmol) in methylene chloride (5 ml) was added dropwise over a ten-minute period and stirring was continued for thirty minutes. p-Toluenesulfonamide (0.85 g, 5.0 mmol) was added in one portion followed by 10% aqueous sodium hydroxide (5 ml) and the reaction was allowed to warm up to room temperature. The organic layer was separated and the aqueous layer was extracted with several portions of methylene chloride. All organic layers were combined, washed with sodium carbonate, distilled water, and then were dired over sodium sulfate. Concentration on a rotary evaporator gave 1.31 g (71%) of bis-(2,4,6-trimethylphenyl) sulfoxide mp 150-151° lit.[59] mp 153.5-154° . Nmr spectrum no. 5994. Ir spectrum no. 22767 (KBr pellet).

NOTE: This procedure was also attempted using TFAA and FSA with the same results; in all cases the starting sulfoxide was recovered.

S-Ethyl-S-p-Tolyl-N-(p-Toluenesulfonyl) Sulfimide. R-(+)-Ethyl p-tolyl sulfoxide (1.68 g, 10 mmol) (83% enantiomeric excess) was dissolved in methylene chloride in a 50-ml round-bottomed, three-necked flask equipped with a magnetic stirrer, a thermometer, and an addition funnel. The apparatus

was flushed with nitrogen and cooled to -70°. TFMSA (3.10 g, 11 mmol) in methylene chloride was added dropwise over a period of ca. ten minutes and stirring was continued for thirty minutes more. p-Toluenesulfonamide (1.88g, 11 mmol) was added in one portion followed by 10% aqueous sodium hydroxide (5 ml). The reaction was allowed to warm to room temperature and the organic layer was separated. The aqueous layer was washed with several portions of methylene chloride and all organic layers were combined, washed with aqueous sodium carbonate, distilled water and dried over sodium sulfate. Concentration on a rotary evaporator gave an oil which was added to a column containing 450 g of silica gel (ICN Pharmaceuticals) and eluted with acetonitrile. Concentration gave 2.5 g (79%) of the desired sulfimide which was recovered as a thick oil. $[\alpha]_D^{25}$ 0.00° (c 0.38, acetone). Nmr spectrum no. 5998. Ir spectrum no. 22768.

Attempted Inversion of R-(+)-Ethyl p-Tolyl Sulfoxide Using TFMSA. R-(+)-Ethyl p-tolyl sulfoxide (0.84 g, 5.0 mmol) (83% enantiomeric excess) was dissolved in methylene chloride (10 ml) in a 50-ml round-bottomed, three-necked flask equipped with a magnetic stirrer and an addition funnel. The apparatus was flushed with nitrogen and cooled to ca. -70°. TFMSA (1.50 g, 5.3 mmol) was added dropwise over a ten-minute period and stirring was continued for thirty minutes. Aqueous sodium hydroxide (10%, 20 ml) was added to the stirred solution in one portion via syringe and stirring was continued while the reaction warmed to room temperature. The organic layer

was separated and the aqueous layer was extracted with chloroform, ethyl acetate, and methylene chloride. All organic layers were combined, dried over sodium sulfate and filtered through silica gel. Concentration on a rotary evaporator gave 0.71 g (85%) of an oil whose spectral (Nmr, Ir) and chromatographic (tlc, glpc) properties were identical to authentic ethyl p-tolyl sulfoxide. $[\alpha]_D^{25} = 0.00^o$ (c 0.413, acetone). Nmr spectrum no. 5996 ($CDCl_3$). Ir spectrum no. 22766, neat.

General Procedure for Sulfimide Preparation Using Fluorosulfonic Anhydride (FSA). The following is a general outline of the procedure employed when sulfoxides are allowed to react with FSA. The sulfoxide (10 mmol) was dissolved in dry methylene chloride in a 50-ml round-bottomed, three-necked flask, flushed with nitrogen and equipped with a magnetic stirrer, a thermometer, and an addition funnel, and cooled to $-78^o$. FSA (11 mmol) in methylene chloride was added dropwise to the stirring solution, the temperature not being allowed to rise above $-50^o$. After one hour p-toluenesulfonamide (15 mmol) was added followed by 5 ml of 10% aqueous sodium hydroxide. The organic layer was separated and the aqueous layer was washed with several portions of methylene chloride. The organic layers were combined, washed with distilled water, dried over sodium sulfate and concentrated on a rotary evaporator. The sulfimide was usually isolated as a thick oil or solid and recrystallized from methylene chloride-ether.

S,S Dimethyl-N-(p-Toluenesulfonyl) Sulfimide. Dimethyl sulfoxide (0.78 g, 10.0 mmol) was dissolved in methylene chloride in a 50-ml round-bottomed, three-necked flask flushed with nitrogen and equipped with a magnetic stirrer, a thermometer, and an addition funnel. The solution was cooled to -70° and FSA (2.0 g, 11.0 mmol) was added dropwise over a ten-minute period. Care was taken so that the temperature of the solution did not exceed -50°. The stirring was continued for one-half hour at the end of which p-toluenesulfonamide (1.88 g, 11.0 mmol) was added in one portion followed by 10% aqueous sodium hydroxide (5 ml). The reaction was allowed to warm to room temperature and the organic layer was separated. The aqueous layer was washed with several portions of methylene chloride and all organic layers were combined, washed with aqueous sodium carbonate, distilled water and dried over sodium sulfate. Concentration on a rotary evaporator gave 1.91 g (82.6%) of S,S-dimethyl-N-(p-toluenesulfonyl) sulfimide: recrystallized from methylene chloride-ether (1:1); mp 156-158° lit.[60] mp 159-160° . Nmr spectrum no. 4522. Ir spectrum no. 22775 (KBr pellet).

General Procedure for Sulfimide Preparation Using Trifluoroacetic Anhydride. The following is a general outline of the procedure employed when allowing sulfoxides to react with TFAA. The sulfoxide (10 mmol) was dissolved in dry methylene chloride in a 50-ml round-bottomed, three-necked flask flushed with nitrogen and equipped with a magnetic stirrer, thermometer, and an addition funnel. The solution

was allowed to stir and cooled to -78°. Trifluoroacetic anhydride (11 mmol) in methylene chloride was added dropwise and the temperature was not allowed to rise above -50°. The solution was stirred for one hour and then p-toluenesulfonamide (0.15 mmol) was added followed by 5 ml of 10% aqueous sodium hydroxide. The organic layer was separated and the aqueous layer was washed with several portions of methylene chloride. All organic layers were combined, washed with distilled water, dried over sodium sulfate and concentrated on a rotary evaporator. The sulfimide was usually recovered as an oil or a solid and recrystallized from methylene chloride-ether (1:1, v:v).

S,S-Dibenzyl-N-(p-Toluenesulfonyl) Sulfimide. Dibenzylsulfoxide (2.32 g, 10.0 mmol) was dissolved in methylene chloride in a 50-ml round-bottomed, three-necked flask equipped with a magnetic stirrer, a thermometer and an addition funnel. The flask was flushed with nitrogen and cooled to -70°. TFAA (2.20 g, 10 mmol) in methylene chloride was added dropwise over a period of ten minutes. The stirring was continued for one-half hour at the end of which p-toluenesulfonamide (1.88 g, 11.0 mmol) was added in one portion followed by 10% aqueous sodium hydroxide (5 ml). The reaction was allowed to warm to room temperature and the organic layer was separated. The aqueous layer was washed with several portions of methylene chloride and all organic layers were combined, washed with sodium carbonate, distilled water and then dried over sodium sulfate. Concentration on a rotary

evaporator gave the desired product: 3.11 g (81%) recrystallized from methylene chloride-ether (1:1), mp 188-189° lit.[60] mp 190-191° . Nmr spectrum no. 4508. Ir spectrum no. 22776.

Attempted Preparation of S,S-Bis-(p-Chlorophenyl)-N-(p-Toluenesulfonyl) Sulfimide. Bis-(p-chlorophenyl) sulfoxide (2.71 g, 10 mmol) was dissolved in methylene chloride in a 50-ml round-bottomed, three-necked flask equipped with a magnetic stirrer, a thermometer, and an addition funnel. The apparatus was flushed with nitrogen and cooled to -70°. TFAA (2.3 g, 11.0 mmol) in methylene chloride was added dropwise over a ten-minute period and stirring was continued for thirty minutes. p-Toluenesulfonamide (1.88 g, 11.0 mmol) was added in one portion followed by addition of 10% aqueous sodium hydroxide (5 ml) and the reaction was allowed to warm to room temperature. The organic layer was separated and the aqueous layer was washed with several portions of methylene chloride. All organic layers were combined, washed with aqueous sodium carbonate, distilled water, and then were dried over sodium sulfate. Concentration on a rotary evaporator and recrystallization from methylene chloride-ether (1:1) gave a solid (2.51 g, 92.6%), mp 141-142° whose spectral (Nmr, Ir) and chromatographic (tlc) properties were identical to authentic bis-(p-chlorophenyl) sulfoxide lit.[61] mp 142-144°. Ir spectrum no. 22769 (KBr pellet). Nmr spectrum no. 5999.

NOTE: The exact same procedure was employed in the attempted preparation of the above-named sulfimide using TFMSA. The same results were observed in this case; only

unreacted sulfoxide was recovered.

N-(p-Toluenesulfonyl) Methyl p-Tolyl Sulfimide. R-(+)-Methyl p-tolyl sulfoxide (1.54 g, 10.0 mmol) was dissolved in methylene chloride (10 ml) in a 50-ml round-bottomed, three-necked flask equipped with a magnetic stirrer, a thermometer and an addition funnel. The apparatus was flushed with nitrogen and cooled to -70°. TFAA (2.3 g, 11.0 mmol) in methylene chloride (5 ml) was added dropwise over a ten-minute period. Stirring was continued for one-half hour after which p-toluenesulfonamide (1.88 g, 11.0 mmol) was added in one portion followed by 10% aqueous sodium hydroxide (5 ml). The reaction was allowed to warm to room temperature and the organic layer was separated. The aqueous layer was washed with several portions of methylene chloride and all organic layers were combined, washed with aqueous sodium carbonate, distilled water, and then were dried over sodium sulfate. Concentration on a rotary evaporator gave the sulfimide which was recrystallized three times from methylene chloride-ether (1:1). Yield 1.53 g (56%): mp 125-126° lit.[62] mp 125-126° $[\alpha]_D^{25}$ 0.0° (c 0.46, acetone). Nmr spectrum no. 3327. Ir spectrum no. 22777.

General Procedure for Sulfoxide Reductions Using Silyl Chlorides. The following is a general outline of the procedure employed when a sulfoxide was reduced with dimethyldichlorosilane or methyltrichlorosilane. The sulfoxide (10 mmol) was dissolved in methylene chloride in a 50-ml round-bottomed, three-necked flask flushed with nitrogen and

equipped with a magnetic stirrer, thermometer, and addition funnel and was cooled to -78°. The silyl chloride (20 mmol) was added dropwise over a short period and the reaction mixture was allowed to warm to room temperature. Aqueous sodium hydroxide (5 ml, 10%) was added to the solution and the organic layer was separated. The aqueous layer was washed several times with methylene chloride and the combined organic layers were washed with distilled water, dried over sodium sulfate and concentrated on a rotary evaporator. Most sulfides are isolated as clear oils.

Ethyl p-Tolyl Sulfide. Ethyl p-tolyl sulfoxide (1.68 g, 0.01 mol) was dissolved in methylene chloride in a 50-ml round bottomed, three-necked flask, flushed with nitrogen and equipped with magnetic stirrer and addition funnel and cooled to -70°. Dichlorodimethylsilane (2.58 g, 0.02 mol) was added dropwise over a period of ten minutes. The reaction mixture was allowed to warm to room temperature and aqueous sodium hydroxide (5 ml, 10%) was added to the reaction mixture. The organic layer was separated and the aqueous layer was washed with several portions of methylene chloride. All organic layers were combined, washed with distilled water, dried over sodium sulfate and concentrated on a rotary evaporator. The crude oil was dissolved in dry methylene chloride and filtered through silica gel. Concentration yielded an oil (1.26 g, 83%) whose spectral (Ir, Nmr) and chromatographic properties (tlc, glpc) were identical with authentic

ethyl p-tolyl sulfide. Ir spectrum no. 22775, neat. Nmr spectrum no. 5604 ($CDCl_3$).

General Procedure for Sulfoxide Reduction Using FSA and Sodium Cyanoborohydride.[63] The following is a general outline of the procedure employed in the reduction of a sulfoxide with FSA and sodium cyanoborohydride. The sulfoxide (10 mmol) was dissolved in dry methylene chloride in a 50-ml round-bottomed, three-necked flask, flushed with nitrogen, equipped with a magnetic stirrer, a thermometer and an addition funnel, and cooled with stirring to -78°. FSA (11 mmol) in dry methylene chloride was added dropwise over a one-half hour period and stirring was continued for one hour. Sodium cyanoborohydride (1.1 g, 17.0 mmol) in cellosolve (ethylene glycol monoethyl ether) was added dropwise over a one-half hour period. The reaction was allowed to warm to room temperature, and stirring was continued for one hour. The crude reaction mixture was added to distilled water; the organic layer was separated, and the aqueous layer was washed with several portions of methylene chloride. All organic layers were combined, washed with distilled water, dried over sodium sulfate and concentrated on a rotary evaporator. The crude oil recovered was dissolved in dry methylene chloride, filtered through florisil and concentrated to yield products whose spectral and chromatographic properties were compared to authentic samples.

m-Trifluoromethylphenyl Methyl Sulfide. m-Trifluoromethylphenyl methyl sulfoxide (1.03 g, 5 mmol) was dissolved

in dry methylene chloride in a 50-ml round-bottomed, three-necked flask, equipped with a magnetic stirrer, a thermometer, an addition funnel, and flushed with nitrogen. The solution was cooled to -70° and fluorosulfonic anhydride (0.95 g, 5.2 mmol) in dry methylene chloride was added over a period of ca. ten minutes. Stirring was continued for one hour and then sodium cyanoborohydride (10.0 g, 15.0 mmol) in ethylene glycol monoethyl ether was added dropwise over a period of ten minutes. The reaction was allowed to warm to room temperature and stirring continued for ca. one-half hour. The crude reaction mixture was added to distilled water, the organic layer was separated, and the aqueous layer was washed with several portions of methylene chloride. All organic layers were combined, washed with distilled water, and dried over sodium sulfate. Filtration through florisil and concentration on a rotary evaporator gave 0.69 g (73%) of the sulfide whose spectral (Nmr and Ir) and chromatographic (tlc and glpc) properties were identical with authentic m-trifluoromethylphenyl methyl suflide. Ir spectrum no. 22697. Nmr spectrum no. 5600 ($CDCl_3$).

Methyl p-Nitrophenyl Sulfide. Methyl p-nitrophenyl sulfoxide (1.85 g, 0.01 mol) was dissolved in dry methylene chloride in a 50-ml round-bottomed, three-necked flask, flushed with nitrogen and equipped with a magnetic stirrer, a thermometer, and an addition funnel and cooled to -78°. Fluorosulfonic anhydride (2.0 g, 11.0 mmol) in dry methylene chloride was added dropwise over a period of about ten minutes.

A rise in temperature was observed but at no time was the temperature allowed to exceed -50°. Stirring was continued for one hour and at the end of this period sodium cyanoborohydride (1.0 g, 15.0 mmol) in ethylene glycol monoethyl ether was added dropwise over a ten-minute period. The reaction was then allowed to warm to room temperature and stirring was continued for ca. thirty minutes. The crude reaction mixture was then added to distilled water; the organic layer was separated and the aqueous layer was washed with several portions of methylene chloride. All organic layers were combined, dried over sodium sulfate and filtered through florisil. Concentration on a rotary evaporator gave an oil which slowly crystallized: 1.26 g (75%) mp 68-70° lit.[64] mp 71-72° . Ir spectrum no. 22696, neat. Nmr spectrum no. 5601 ($CDCl_3$).

General Procedure for Sulfoxide Reduction with Diisobutylaluminum Hydride (DIBAL-H). The sulfoxide (10 mmol) was dissolved in a minimum amount of dry ether in a 100-ml round bottomed, three-necked flask equipped with a magnetic stirrer, an addition funnel and a condenser. The system was flushed with nitrogen and kept under a nitrogen atmosphere as DIBAL-H (1 M in hexane, 15 ml) was added dropwise over a ten-minute period. The reaction mixture was heated to reflux and stirring was continued for twelve hours. The reaction mixture was cooled, added to moist ether, and hydrolysed with water and then dilute sulfuric acid. The organic layer was separated and the aqueous layer was washed with several

portions of ether. All organic layers were combined and dried over sodium sulfate and concentrated on a rotary evaporator to give an oil which was purified by column chromatography on a silica gel column or by distillation.

Mesityl Sulfide. Mesityl sulfoxide (2.86 g, 10.0 mmol) was dissolved in dry ether (10 ml) in a 100-ml, round-bottomed, three-necked flask equipped with magnetic stirrer, a condenser and an addition funnel. The system was flushed with nitrogen and kept under a nitrogen atmosphere as DIBAL-H (1 M in hexane, 20 ml) was added dropwise over a twenty-minute period. The reaction mixture was then heated to reflux and allowed to stir for eight hours. The reaction mixture was then cooled, added to moist ether, and hydrolysed with water and then dilute sulfuric acid. The organic layer was separated and the aqueous layer was washed with several portions of ether. All organic layers were combined, dried over magnesium sulfate and concentrated on a rotary evaporator. The desired product was contaminated with a trace of starting material (tlc) and was recrystallized from absolute ethanol to give 2.23 g (82%) of mesityl sulfide; mp 88.5-89.5° (lit.[65] mp 91-92°). Ir spectrum no. 22739. Nmr spectrum no. 5602.

Bis-(p-Chlorophenyl) Sulfide. p-Chlorophenyl sulfoxide (2.71 g, 10.0 mmol) was dissolved in dry ether (10 ml) in a 50-ml, round-bottomed, three-necked flask equipped with a magnetic stirrer, a condenser, and an addition funnel. The system was flushed with nitrogen and kept under a nitrogen atmosphere while DIBAL-H (1 M in hexane, 15 ml) was added

dropwise over a twenty-minute period. The reaction mixture was then heated to reflux and stirring was continued for eight hours. The reaction mixture was cooled, added to moist ether, and hydrolysed with water and then dilute sulfuric acid. The organic layer was separated and the aqueous layer was washed with several portions of ether. All organic layers were combined, dried over sodium sulfate, and concentrated on a rotary evaporator to give 2.25 g (88%) of the desired product contaminated with a small amount of the starting sulfoxide (tlc). Recrystallization from hexane gave the sulfide, mp 89.5-92.5° (lit.[66] mp 92-94°). Ir spectrum no. 22738.

Triphenylphosphine. Triphenylphosphine oxide (5.58 g, 20.0 mmol) was dissolved in dry ether (50 ml) in a three-necked, round-bottomed flask equipped with an addition funnel, condenser, and a magnetic stirrer. Diisobutylaluminum hydride (1 M in hexane 40 ml) was added dropwise over a twenty-minute period and when addition was complete the reaction was heated to reflux. Stirring was continued for twelve hours after which the reaction mixture was cooled, added to moist ether and hydrolysed with water and then dilute sulfuric acid. The organic layer was separated and the aqueous layer was washed with several portions of ether. All organic layers were combined, dried over magnesium sulfate and concentrated on a rotary evaporator. Concentration gave an oil which quickly crystallized to give triphenylphosphine 4.47 g (85%) recrystallized from ether mp 78-79,5° (lit.[67]

mp 80.5°). Mixed melting point with authentic sample 78-79°. Ir spectrum no. 22735.

Attempted Reduction of Phenyl Sulfoxide with Borane-THF Complex.[68] Phenyl sulfoxide (2.02 g, 10.0 mmol) was dissolved in THF (10 ml) in a 50-ml, three-necked, round-bottomed flask equipped with a magnetic stirrer, a condenser, and an addition funnel. Borane-THF complex (1 M in THF, 10 ml) was added dropwise at room temperature over a ten-minute period. The reaction mixture was then warmed to reflux and allowed to stir for four hours. The reaction mixture was then cooled, added to moist ether, and hydrolysed with water and then dilute sulfuric acid. The organic layer was separated and the aqueous layer was washed with several portions of ether. All organic layers were combined, dried over sodium sulfate and concentrated on a rotary evaporator. An oil was obtained and glpc revealed it to be a mixture of sulfide and sulfoxide (about 1:1).

Phenyl Sulfide by Reduction with DIBAL-H. Phenyl sulfoxide (10.1 g, 50 mmol) was dissolved in dry ether in a 250-ml, three-necked, round-bottomed flask equipped with a mechanical stirrer, a condenser, and an addition funnel. The system was flushed with dry nitrogen and kept under a nitrogen atmosphere. DIBAL-H (1 M in hexane, 80 ml) was added dropwise over a one-hour period. The reaction mixture was then heated to reflux and stirred overnight. The reaction mixture was cooled and hydrolysed sequentially with moist ether, water, and dilute sulfuric acid. The organic layer was

separated and the aqueous layer was washed with several portions of ether. All organic layers were combined and dried over sodium sulfate. Concentration on a rotary evaporator gave a clear liquid, which was distilled at reduced pressure bp 123-125° (3.8 mm) lit.[69] bp 117-118° (2 mm) to give 7.71 g (83%) of a clear colorless liquid. Ir spectrum no. 22734, neat.

Silver p-Toluenesulfonate.[70] p-Toluenesulfonic acid monohydrate (95.11 g, 0.50 mol) was dissolved in 150 ml of dry acetonitrile and added to a 1 liter Erlenmeyer flask equipped for magnetic stirring. Silver oxide (57.94 g, 0.25 mol) in acetonitrile was added in one portion and the mixture stirred with protection from light for two hours. Then the solution was filtered, dried over sodium sulfate and concentrated on a rotary evaporator to give 132.50 g (95%) of the desired product: positive test for silver. Ir spectrum no. 22778 (KBr pellet).

p-Toluenesulfonic Anhydride. Silver tosylate (69.77 g, 0.25 mol) was dissolved in dry acetonitrile in a 1 liter round-bottomed flask equipped with a magnetic stirrer and cooled to 0°. Tosyl chloride (47.66 g, 0.25 mol) in dry acetonitrile was added in one portion. The mixture was protected from light and the atmosphere was warmed to room temperature. After three hours, the precipitated silver chloride was removed by filtration. The filtrate was concentrated on a rotary evaporator and the crude solid was recrystallized from anhydrous ether to give 75.10 g (92%) of toluenesulfonic

anhydride: mp 125.5-128.5° (lit.[71] mp 129-132°). Ir spectrum no. 22773.

Fluorosulfonic Anhydride. Cyanuric chloride (61.5 g, 0.33 mol) was added to a 500-ml round-bottomed flask equipped with a magnetic stirrer, a thermometer, and a 50 cm Vigreaux column connected to a condenser and a receiver. All ground joints had been lubricated with Kel-F-90 grease and a trap, immersed in ice water, was connected to the receiver. Fluorosulfonic acid (400 g, 4 mol) was carefully added to the cyanuric chloride with occasional stirring. The reaction mixture's temperature was slowly raised to 155-160° by means of a heating mantle. The crude product was collected over a period of about eighteen hours. The combined crude product was cooled to 0°, washed with 100 ml of cold 98% sulfuric acid and distilled to give 158 g (92.3%) of the desired product: bp 49-51° (lit.[72] bp 50-52°).

# APPENDIX A

Ir Parameters for Some N-(Tosyl) Sulfimides

| Sulfimide | $\nu$ S-N ($cm^{-1}$) | $\nu$ $SO_2$ ($cm^{-1}$) |
|---|---|---|
| Dimethyl | 943 | 1129, 1165, 1088 |
| Diphenyl | 950 | 1280, 1135, 1082 |
| Dibenzyl | 983 | 1275, 1134, 1086 |
| Methyl Tolyl | 950 | 1270, 1133, 1088 |
| Tetramethylene | 965 | 1264, 1132, 1079 |
| Ethyl Tolyl | 971 | 1274, 1134, 1082 |
| Toluenesulfonamide | 906 | 1330, 1155, 1096 |

Nmr Parameters for Some N-(Tosyl) Sulfimides

| Sulfimide | |
|---|---|
| Dimethyl | δ 7.35 (a, 4H), δ 2.60 (s, 6H), δ 2.37 (s, 3H). |
| Diphenyl | δ 7.58 (m, 14H), δ 2.20 (s, 3H). |
| Tetramethylene | δ 7.40 (m, 4H), δ 3.00 (t, 4), δ 2.35 (s, 3H), δ 2.00 (m, 4). |
| Methyl p-Tolyl | δ 7.45 (m, 8H), δ 2.90 (s, 3H), δ 2.40 (d, 6H). |
| n-Propyl p-Tolyl | δ 7.40 (m, 8H), δ 2.80 (m, 2H), δ 2.30 (d, 6H), δ 1.50 (m, 2H), δ 1.00 (t, 3H). |
| n-Propyl Phenyl | δ 7.38 (m, 9H), δ 2.90 (m, 2H), δ 2.30 (s, 3H), δ 1.60 (m, 2H), δ 0.90 (t, 3H). |

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