1976

Quaternary Methylsulfonylammonium Salts And Other Topics In Organosulfur Chemistry

Manoir John Du

QUATERNARY METHYLSULFONYLAMMONIUM SALTS AND OTHER TOPICS IN ORGANOSULFUR CHEMISTRY

by

John Richard du Manoir

Department of Chemistry

Submitted in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy

Faculty of Graduate Studies
The University of Western Ontario
London, Ontario

November, 1975

ABSTRACT

This thesis describes the results from three projects in organosulfur chemistry.

The first topic concerns the sulfene multiexchange phenomenon which was previously observed when methanesulfonyl chloride was hydrolyzed in deuterium oxide in the presence of unhindered tertiary amine bases. The multiexchange was believed to occur via the methylsulfonylammonium ion, $CH_3SO_2\overset{+}{N}R_3$, and sulfene-amine zwitterion, $\bar{C}H_2SO_2\overset{+}{N}R_3$. In order to further investigate this phenomenon, four quaternary methylsulfonylammonium fluorosulfonate salts, $CH_3SO_2\overset{+}{N}R_3\ \bar{O}SO_2F$, were synthesized with R_3 varying in "size" from trimethyl to diethylmethyl.

When hydrolyzed in deuterium oxide with the corresponding amine (NR_3), the four salts underwent extensive multiexchange of the sulfonyl methyl group, paralleling the base "size" effects observed for methanesulfonyl chloride. Multiexchange also occurred when the salts reacted with p-toluidine-N,N-d_2. Product deuterium distributions suggested that both direct nucleophilic displacement on the salts and sulfene trapping were occurring simultaneously to give products. Calculated deuterium distributions based on a combined sulfene-trapping-displacement mechanism were in good agreement with experimentally observed values giving some support for the proposed mechanism.

The salts were also found to be excellent methanesulfonating reagents, surpassing the reactivity of methanesulfonyl chloride or methanesulfonic anhydride. The salts gave the expected sulfene-derived products when reacted with alcohols, p-toluidine, chloral and an enamine.

The second topic concerns α-hydrogen exchange in the sulfoxide 1,3-dihydrobenzo[c]thiophene 2-oxide. The stereochemistry of the exchange was examined with hydroxide in aqueous medium and methyllithium in aprotic medium. The rates of exchange were compared with those of benzyl methyl sulfoxide. The results were discussed in terms of the Rauk-Wolfe-Csizmadia calculations of α-sulfinyl carbanion stability.

The final topic involves the mechanism of thermal desulfonylation of 1,3-dihydrobenzo[c]thiophene 2,2-dioxide. Mild thermolysis of the cis-1,3-dideuterated sulfone gave trans-1,2-dideuterated benzocyclobutene, indicating concerted mechanisms for the two-step process. The results were in agreement with those predicted by the Woodward-Hoffmann rules for the conservation of orbital symmetry.

ACKNOWLEDGEMENTS

The author wishes to express his sincere gratitude to Prof. J.F. King for his encouragement, tireless enthusiasm and patient guidance during the laboratory work and the preparation of this thesis.

The author also wishes to thank those who provided expert technical assistance or helpful discussions, in particular, Prof. J.P. Guthrie, Mr. R. Lazier, Dr. M. Gordon, Dr. M.C. Woods and Prof. R.R. Fraser.

Especially, thanks to my wife, Valerie, whose encouragement has helped me through it all, and who has skillfully put this thesis into print.

TABLE OF CONTENTS

	Page
CERTIFICATE OF EXAMINATION	ii
ABSTRACT	iii
ACKNOWLEDGEMENTS	v
TABLE OF CONTENTS	vi
LIST OF TABLES	viii
LIST OF FIGURES	xi
INTRODUCTION	1
CHAPTER I - THE CHEMISTRY OF QUATERNARY METHYLSULFONYLAMMONIUM FLUOROSULFONATE SALTS	3
Introduction	3
Results and Discussion	12
Conclusions	68
CHAPTER II - α-HYDROGEN EXCHANGE IN 1,3-DIHYDROBENZO[C]THIOPHENE 2-OXIDE	70
Introduction	70
Results and Discussion	81
Conclusions	90
CHAPTER III - THE STERIC COURSE OF THE FORMATION OF BENZOCYCLOBUTENE BY THERMAL DESULFONYLATION OF 1,3-DIHYDROBENZO[C]THIOPHENE 2,2-DIOXIDE	92

Page

Introduction 92

Results and Discussion 96

Conclusions 165

EXPERIMENTAL 206

Introduction 206

I. The Chemistry of Quaternary Methylsulfonylammonium Fluorosulfonate Salts 108

II. α-Hydrogen Exchange in 1,3-Dihydrobenzo[c]thiophene 2-Oxide 147

III. The Steric Course of the Formation of Benzocyclobutene by Thermal Desulfonylation of 1,3-Dihydrobenzo[c]thiophene 2,2-Dioxide 160

REFERENCES 170

VITA 175

LIST OF TABLES

Table		Page
1	Multiexchange in the Reaction of Alkanesulfonyl Chlorides with Tertiary Amines and Water or Alcohols	5
2	Trialkyl(methylsulfonyl)ammonium Fluorosulfonate Salts	14
3	Tertiary Amine Formation from the Aqueous Hydrolysis of the Sulfonylammonium Fluorosulfonate Salts	16
4	Mesylation of 3β-Cholestanol: Comparison of Mesylating Reagents	18
5	Mesylation of Cyclohexanol: Comparison of the Salts as Mesylating Reagents	18
6	Reaction of Trimethyl(methylsulfonyl)ammonium Fluorosulfonate with l-Borneol in the Presence of Various Tertiary Amine Bases	21
7	Reaction of 1-Methyl-1-(methylsulfonyl)piperidinium Fluorosulfonate with l-Borneol in the Presence of Various Tertiary Amine Bases	24
8	Mesylation of Alcohols with Diethylmethyl(methylsulfonyl)ammonium Fluorosulfonate	25
9	Effect of Solvent on the Ratio of Mesylate to Mesylmesylate Formed in the Reaction of l-Borneol with Diethylmethyl(methylsulfonyl)ammonium Fluorosulfonate	26
10	Reaction of Diethylmethyl(methylsulfonyl)ammonium Fluorosulfonate with l-Borneol in the Presence of Various Tertiary Amine Bases	28

Table		Page
11	Reaction of Diethylmethyl(methylsulfonyl)ammonium Fluorosulfonate with p-Toluidine in the Presence of Tertiary Amine Bases	33
12	Multiexchange in the Base-Catalyzed Hydrolysis of the Trialkyl(methylsulfonyl)ammonium Fluorosulfonate Salt in Deuterium Oxide	39
13	Multiexchange in the Pyridine-Catalyzed Hydrolysis of the Trialkyl(methylsulfonyl)ammonium Fluorosulfonate Salts in Deuterium Oxide	41
14	Multiexchange in the Reaction of the Trialkyl(methylsulfonyl)ammonium Salts with p-Toluidine-N-d_2	42
15	Calculated Deuterium Distributions for Multiexchange in the Deuterium Oxide Hydrolysis of the Sulfonylammonium Salts	59
16	Calculated Deuterium Distributions for Multiexchange in the Deuterium Oxide Hydrolysis of the Sulfonylammonium Salts Based on Sulfene Trapping ($k_N = 0$)	60
17	Calculated Deuterium Distributions for Multiexchange in the Deuterium Oxide Hydrolysis of the Sulfonylammonium Salts Based on Direct Displacement ($k_T = 0$)	60
18	Calculated Deuterium Distributions for Multiexchange in the Deuterium Oxide Hydrolysis of Methanesulfonyl Chloride	62
19	Calculated Deuterium Distributions for the Reaction of the Sulfonylammonium Salts with p-Toluidine-N-d_2	64
20	Calculated Deuterium Distributions for the Reaction of the Sulfonylammonium Salts with p-Toluidine-N-d_2 Based on Sulfene Trapping ($k_N = 0$)	65

Table

Page

Calculated Deuterium Distributions for the Reaction of the Sulfonyl-ammonium Salts with p-Toluidine-N-d2 Based on Direct Displacement ($k_T = 0$) ...

α-Exchange of 1,2-Dihydrobenzo[c]thiophene 2-Oxide via the Lithio Salt ...

LIST OF FIGURES

Figure		Page
1	The Mechanism of Multiexchange in the Reaction of Methanesulfonyl Chloride with Tertiary Amines and Deuterium Oxide	7
2	Reaction Scheme for Formation of Methylsulfonylmethanesulfonate (Mesylmesylate) Esters	22
3	Reaction Pathways of the Trialkyl-(methylsulfonyl)ammonium Fluoro-sulfonate Salts	34
4	Mechanism of Multiexchange in the Reactions of the Trialkyl(methyl-sulfonyl)ammonium Fluorosulfonate Salts	50
5	Simplified Reaction Scheme for the Multiexchange Reactions of the Trialkyl-(methylsulfonyl)ammonium Fluoro-sulfonate Salts	55
6	Sample Calculation of Deuterium Distributions Derived from Simplified Multiexchange Reaction Scheme (Figure 5) for Deuterium Oxide Hydrolysis of the Trimethyl(methyl-sulfonyl)ammonium Salt	54
7	Total Energies of $HMSO^-$ and $DMSO^-$ as a Function of Rotation about the C-S Bond	72
8	Deuterium-decoupled ^{13}C-satellite Proton N.M.R. Spectra of 1,2-Dideuteriobenzo-cyclobutene Samples	97
9	Absorption Infra-red Spectrum of Equimolar cis/trans-1,2-Dideuteriobenzo-cyclobutene (7b)	100
10	Absorption Infra-red Spectrum of 1:3 cis/trans-1,2-Dideuteriobenzocyclobutene (7a)	101

Figure		Page
11	Absorption Infra-red Spectrum of trans-1,2-Dideuteriobenzocyclobutene (7c)	102
12	Kinetics Plot for Benzylic Hydrogen Exchange of Benzyl Methyl Sulfoxide	156

INTRODUCTION

The field of organosulfur chemistry covers a wide array of compounds in several sulfur oxidation states, and a full spectrum of chemical reactivity. As a reflection of this varied nature, this thesis is concerned with sulfur in several valencies, principally IV and VI. The compounds discussed include sulfoxides, sulfones and sulfonylammonium salts.

Described in the first chapter is the preparation of a new series of compounds, quaternary methylsulfonylammonium fluorosulfonate salts, $CH_3SO_2\overset{+}{N}R_3\ \bar{O}SO_2F$. These compounds have been found to be excellent reagents for the preparation of methanesulfonate esters and a number of practical examples of the potential of these salts as "mesylating" reagents have been given. Furthermore, the role of the methylsulfonylammonium ion in the mechanisms of sulfene reactions has been investigated, with particular emphasis on the formation of zwitterions and the multiexchange mechanisms of sulfene.

The second chapter deals with sulfoxide configuration and its effect upon the stereochemistry of α-sulfinyl hydrogen exchange in 1,3-dihydrobenzo[c]thiophene 2-oxide. Solvent and base effects have been examined and a comparison made with an open-chain analogue, benzyl methyl sulfoxide.

Chapter Three describes a study of the mechanism of thermal desulfonylation of the cyclic sulfone 1,3-dihydrobenzo[c]thiophene 2,2-dioxide. The sulfone was prepared in

cis-1,3-dideuterated form from the sulfoxide (preparation of which is described in the second chapter), and subjected to vapour phase thermolysis in a quartz tube. The deuterium distribution of the product showed the desulfonylation process to be stereospecific at lower temperatures.

Because of the variety of topics discussed in this thesis, this introduction is given only as a brief guide. Each chapter is introduced in greater detail and further commentary and background information has been reserved for each.

CHAPTER I

The Chemistry of Quaternary Methylsulfonylammonium Fluorosulfonate Salts

Introduction

Sulfene, $CH_2 = SO_2$, is a highly reactive intermediate species which is formed by the reaction of methanesulfonyl chloride with base. Low-temperature infra-red observations (1) suggest that sulfene is stable at liquid nitrogen temperatures, but it has never been isolated or observed at room temperature. Indeed, most of the evidence for the existence of sulfene is circumstantial. This evidence, which includes product analysis, reaction kinetics and various other experimental data, has been well reviewed (2) and will not be dwelled upon at length in this dissertation.

One of the strongest and least ambiguous pieces of supporting evidence for sulfenes was the observation of King and Durst (3) and Truce and coworkers (4) that the reaction of alkanesulfonyl chlorides with bases in the presence of deuterated traps such as deuterium oxide or methanol-d gave products having one and only one deuterium atom on the α-sulfonyl carbon.

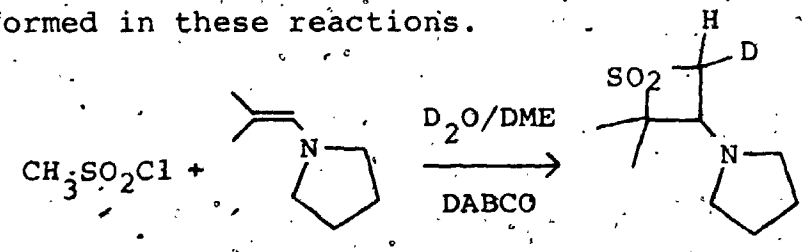
$$RCH_2SO_2Cl + D_2O + B \longrightarrow RCHDSO_2OH + BHCl$$

Notwithstanding this evidence, however, King and Luinstra (5,6) observed extensive multideuteration in the reaction of methanesulfonyl chloride with deuterium oxide and unhindered bases such as 1,2-diazobicyclo[2.2.2]octane

(DABCO), quinuclidine or trimethylamine in 1,2-dimethoxyethane (DME) solution. As the size of the base was increased, considerably less multiexchange was observed. Multiexchange was also observed with methanol-d as a trap.

It was subsequently shown by King and Harding (6,7) that phenylmethanesulfonyl chloride and p-nitrophenylmethanesulfonyl chloride also underwent multiexchange with D_2O as a trap, especially with DABCO as the base. It was also observed that the use of more hindered traps such as t-butyl alcohol-d resulted in an increase in multiexchange compared to the less hindered trap (D_2O). The results of these investigations are summarized in Table 1.

These unusual results appeared to contradict previous conclusions about the reactivity of sulfene. Nonetheless, when the reaction of methanesulfonyl chloride, deuterium oxide and DABCO was repeated in the presence of 1-(2-methylpropenyl)-pyrrolidine, the enamine-sulfene cycloadduct was isolated in 50% yield, indicating that sulfene was indeed being formed in these reactions.



Furthermore, it was found that the α-sulfonyl methylene group of the cycloadduct was partially deuterated (average composition $CH_{1.25}D_{0.75}$). Not only was sulfene being formed, then, but it was undergoing multiexchange before product formation.

TABLE 1

Multiexchange in the Reaction of Alkanesulfonyl Chlorides with Tertiary Amines and Water or Alcohols

Sulfonyl Chloride	Base	Trap	Product Composition* (%) d_0	d_1	d_2	d_3
$MeSO_2Cl$	Quinuclidine	D_2O	1.8	13.1	21.9	63.1
"	DABCO	"	1.3	16.1	22.8	59.8
"	Me_3N	"	1.8	25.6	24.7	48.0
"	Me_2EtN	"	4.8	71.4	17.6	6.2
"	$MeEt_2N$	"	4.8	92.0	2.5	0.8
"	Et_3N	"	9.6	89.8	0.5	0.0
"	Bu_3N	"	6	94	0	0†
"	DABCO	MeOD	~0	~15	~25	~60†
$EtSO_2Cl$	"	D_2O	5.5	81.4	13.1	--
$PhCH_2SO_2Cl$	Et_3N	"	2.5	95.6	1.9	--
"	DABCO	"	2.8	88.6	8.6	--
"	" (small excess)	"	4.5	93.0	2.5	--
"	"	Bu^tOD	6.3	58.1	35.6	--
$p\text{-}NO_2\text{-}PhCH_2SO_2Cl$	Et_3N	D_2O	5.7	88.4	5.9	--
"	DABCO	"	2.7	20.7	76.6	--

* Deuterium distribution of the sulfonyl methyl or methylene group of the sulfonic acid or ester product. The sulfonic acids were converted to the sulfonyl chlorides to facilitate mass spectrometric analysis.

† Estimated by n.m.r.

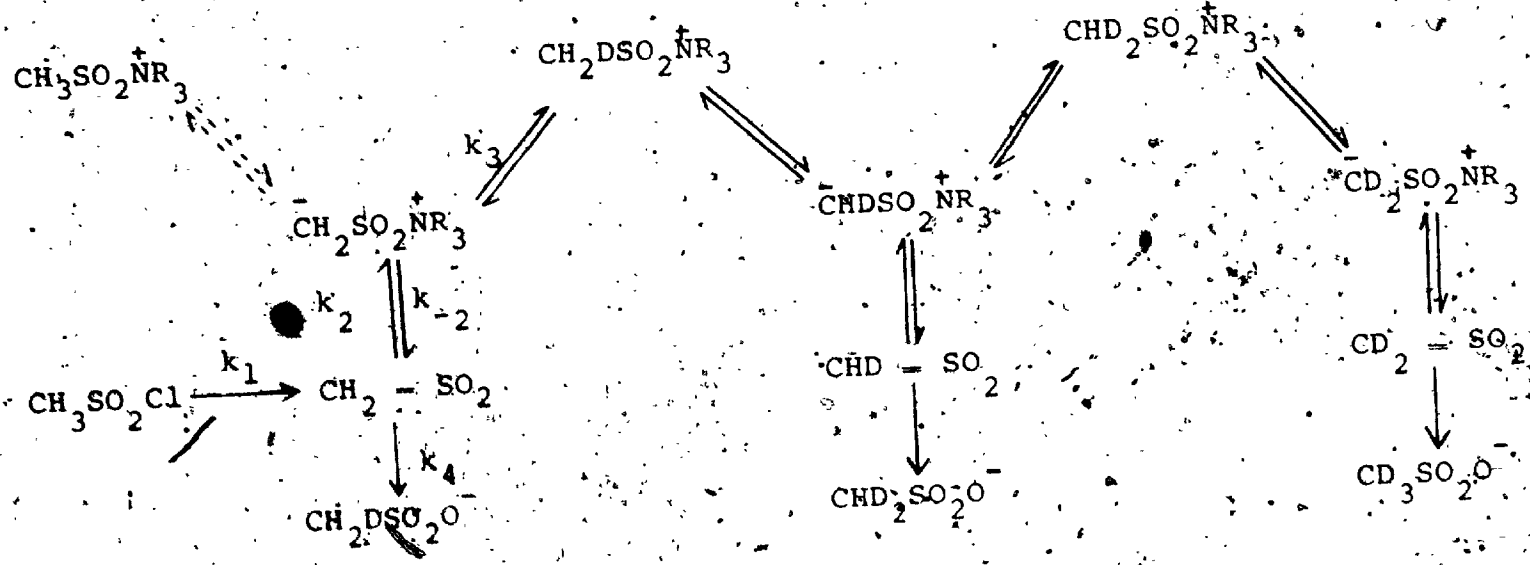
The data were in keeping with a proposed mechanism involving the intermediacy of a zwitterionic species $\bar{C}H_2SO_2\overset{+}{N}R_3$ formed by nucleophilic reaction of the tertiary base with sulfene (Figure 1). It can be seen from Figure 1 that the equilibrium ($K = k_2/k_{-2}$) between sulfene and the zwitterion would be greatly affected by the nature of the base. With bulkier R groups on nitrogen, the zwitterion would be less stable and equilibrium would lie towards sulfene. This would be evidenced by less multiexchange (via k_3) and more sulfene trapping (k_4).

Smaller R groups, on the other hand, would give more stable zwitterions and hence more multiexchange. Calculations based on this mechanism, using data from Table 1, indicated that the ratio k_2/k_4 decreased while k_{-2}/k_3 increased as the bulk of the base increased (6), corresponding to a decrease in multiexchange with larger bases. Other mechanisms, such as exchange via the conjugate base of sulfene ($\bar{C}H=SO_2$) or direct displacement of the base on the sulfonyl chloride to give the sulfonylammonium ion $CH_3SO_2\overset{+}{N}R_3$ were excluded.

This multiexchange mechanism was also compatible with the data for ethane-, phenylmethane- and p-nitrophenylmethanesulfonyl chlorides. The increased steric requirements of an ethyl or benzyl group resulted in a less stable zwitterion and, hence, less multiexchange in comparison to methanesulfonyl chloride. With p-nitrophenylmethanesulfonyl chloride, the effect of the stabilized

FIGURE 1

The Mechanism of Multiexchange in the Reaction of Methanesulfonyl Chloride with Tertiary Amines and Deuterium Oxide*



* Rate constants (k) are pseudo-first-order.

negative charge on the α-sulfonyl carbon was manifested by a large increase in the extent of multiexchange compared with phenylmethanesulfonyl chloride. This is an example of zwitterion stabilization by electronic interaction.

It was also demonstrated that the multiexchange could be enhanced by slowing down the sulfene-trapping rate. When t-butyl alcohol-d, a highly-hindered sulfene trap, was used, the extent of deuterium incorporation for phenylmethanesulfonyl chloride (DABCO) was remarkably enhanced relative to the same reaction with deuterium oxide as trap. The ratio k_2/k_4 was increased in this case due mainly to a decrease in k_4 (Figure 1).

The sulfene-amine zwitterion has also been shown to be a key intermediate in the formation of stilbenes from the reaction of phenylmethanesulfonyl chloride with tertiary amine bases in the absence of a sulfene trapping agent. As well, base-size effects in the formation of β-sultones from reaction of alkanesulfonyl chlorides with chloral suggest that zwitterions are involved (7).

The concept of a zwitterionic intermediate in sulfene reactions is not new. In 1962, Fusco and coworkers postulated that $ArCHSO_2\overset{+}{N}Et_3$ was involved in the formation of trans-stilbenes from $ArCH_2SO_2Cl$ and triethylamine (8) (this was only recently confirmed (7)). A number of stable sulfonyl zwitterionic species have been isolated, including $CH_3SO_2CHSO_2\overset{+}{N}Me_3$ (9), $CH_3SO_2CHSO_2\overset{+}{N}Et_3$ (9, 10), $(CH_3SO_2CH_2SO_2)$-$(CH_3SO_2)CSO_2\overset{+}{N}Et_3$ (11), $CF_3CFSO_2\overset{+}{N}C_5H_5$ (12), $R_3\overset{+}{N}SO_2\bar{N}SO_2NH_2$ (13),

$R_3\overset{+}{N}SO_2\overset{-}{N}COOEt$ (14), and $R_3\overset{+}{N}SO_2\overset{-}{O}$ (15). It can be seen that in each of these cases, the negative charge is well stabilized, giving the zwitterion sufficient stability to be isolated and characterized.

A less stable zwitterion, $RH\overset{+}{C}SO_2\overset{-}{O}$, has been postulated as an intermediate in the hydrolysis of alkyl hydrogen sulfate esters (16), although it has not been isolated. Strong precedent, then, exists for the sulfene-amine zwitterion. However, it is not unreasonable that it has not been isolated, since the negative charge on this molecule lacks the effective stabilization observed for the several examples listed above.

The latent stability of the methylsulfonylammonium salts, $CH_3SO_2\overset{+}{N}R_3A^-$, the conjugate acids of the zwitterions, has not been investigated. The salts are key intermediates in the multiexchange process and, by analogy to arylsulfonylammonium salts, would be expected to have appreciable stability--perhaps enough to be isolable. The first sulfonylammonium salts were prepared by Vorländer and Kauffmann in 1910 (17), who observed the formation of a 1:1 adduct between benzenesulfonyl chloride and trimethylamine.

$$PhSO_2Cl + NMe_3 \longrightarrow PhSO_2\overset{+}{N}Me_3Cl^-$$

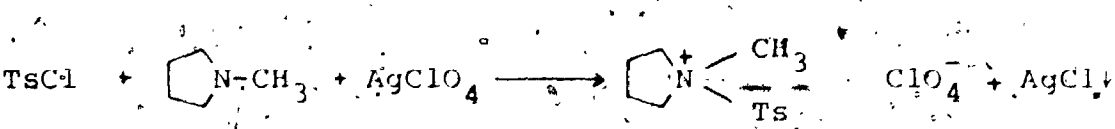
The adduct was a crystalline salt, stable to water (it was prepared in aqueous solution). This reaction has been shown to be responsible for false results in the classical Hinsberg test for amines (18). The corresponding pyridinium salts have also been reported (19). However, the adducts of more

hindered amines such as triethylamine could not be prepared (20).

More recently, arylsulfonylammonium hexachloroantimonates have been prepared by N-methylation of N,N-disubstituted arylsulfonamides with dimethoxycarbonium hexachloroantimonate (21).

$$ArSO_2NR_2 + (CH_3O)_2\overset{+}{C}H\ \overset{-}{SbCl_6} \longrightarrow ArSO_2\overset{+}{N}R_2CH_3\ \overset{-}{SbCl_6}$$

As well, a novel and selective tosylating reagent has been prepared by reaction of N-methylpyrrolidine and tosyl chloride in the presence of silver perchlorate (22).



This sulfonylammonium salt has been afforded an extra measure of stabilization by replacement of chloride ion by the less nucleophilic perchlorate counteranion. This prevents reverse reaction by attack of chloride ion on the sulfonyl group to regenerate tosyl chloride (a problem encountered with $\overset{-}{SbCl_6}$ as the counteranion).

The observation of a metastable trimethylamine-methanesulfonyl chloride "adduct" at low temperatures by Opitz and Fischer (23) and the demonstration of significant anion effects in the stability of arylsulfonylammonium salts by Oishi (22) suggested that salts with the structure $CH_3SO_2\overset{+}{N}R_3\overset{-}{A}$ would be stable if R was not too bulky and if $\overset{-}{A}$ was non-nucleophilic. Recently, Alder and Ahmed observed that N,N-dimethylmethanesulfonamide reacted with methyl fluorosulfonate to form a colourless, crystalline solid (24).

The n.m.r. of this material indicated that the sulfonamide had been N-methylated and that the structure of this product was that of the sulfonylammonium salt $CH_3SO_2\overset{+}{N}Me_3\ \overset{-}{O}SO_2F$. The requirements of non-bulky N-alkyl groups and a non-nucleophilic anion are apparently satisfied in this salt, with the anticipated results.

The observations of Alder and Ahmed have been confirmed. Four sulfonylammonium salts with the structure $CH_3SO_2\overset{+}{N}R_2Me\ \overset{-}{O}SO_2F$ have been synthesized and characterized. The reactivity of these salts as mesylating reagents and as model substrates for the study of the multiexchange phenomenon have been investigated, and these results are presented in the following sections.

Results and Discussion

A. Preparation and Characterization of the Methylsulfonylammonium Fluorosulfonate Salts

As observed by Alder and Ahmed (24), N,N-dimethylmethanesulfonamide and methyl fluorosulfonate ("Magic Methyl") reacted spontaneously at room temperature to produce long, colourless needles of trimethyl(methylsulfonyl)ammonium fluorosulfonate salt 1. The trimethylammonium salt was found to be insoluble in most organic solvents, but dissolved readily and without apparent decomposition in acetonitrile from which it could be recrystallized by addition of methylene chloride. The n.m.r. spectrum of the salt was recorded in fluorosulfonic acid solution and showed two singlets (δ 3.14 and 3.46 p.p.m.) in the ratio 3:1, as expected for the N-trimethylated salt.

Three other salts were prepared in a similar manner, but under more forcing conditions. The N-methylpiperidinium salt 2 was prepared from methanesulfonpiperidide by heating in methyl fluorosulfonate solution for 18 hours at 60°. Similarly, the diethylmethylammonium salt 4 was prepared by warming N,N-diethylmethanesulfonamide in methyl fluorosulfonate for 3 days at 50°. The ethyldimethylammonium salt 3 was prepared by double methylation of N-ethylmethanesulfonamide. The sulfonamide was dissolved in methyl fluorosulfonate and allowed to stand at room temperature for 16 days. In all cases, the reactions were worked up and the products isolated in a dry-box under a nitrogen atmosphere.

Attempts to prepare the adduct salts of more hindered methanesulfonamides (namely the N,N-diisopropyl-, N-N-dibutyl-, N,N-dibenzyl-, and N-phenyl-N-methylmethanesulfonamides) were unsuccessful. These attempts generally resulted in decomposition and are not reported in the experimental section.

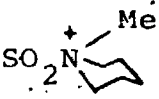
The structures of the four salts which were prepared were confirmed by n.m.r. spectrometry, satisfactory elemental analyses and hydrolytic decomposition to the corresponding tertiary amines. The data for the salts are summarized in Table 2.

The salts were hygroscopic crystalline solids. Since their melting points ranged over several degrees and were accompanied by decomposition, only approximate melting points could be reported. The salts were stored and handled in a nitrogen-atmosphere dry-box (over phosphorus pentoxide) to minimize any contact with moisture and resulting decomposition. Under these conditions, the trimethylammonium salt (1) could be kept for 2 or 3 months. However, the diethylmethylammonium salt (4) became an oily semi-solid after about 5 weeks in the dry box. When sealed in an ampoule under dry nitrogen, on the other hand, this salt underwent no visible decomposition, even after several months. The salts appeared to be less stable with increasing steric substitution on the nitrogen, but nonetheless, could be stored for several months under properly anhydrous conditions.

TABLE 2

Trialkyl(methylsulfonyl)ammonium

Fluorosulfonate Salts

Salt	Yield	Melting Point*
$CH_3SO_2\overset{+}{N}Me_3\ \bar{O}SO_2F$ (1)	88%	130° (dec)
$CH_3SO_2\overset{+}{N}(Me)$  $\bar{O}SO_2F$ (2)	81	120° (dec)
$CH_3SO_2\overset{+}{N}EtMe_2\ \bar{O}SO_2F$ (3)	28	100° (dec)
$CH_3SO_2\overset{+}{N}Et_2Me\ \bar{O}SO_2F$ (4)	64	115° (dec)

* Melting points were taken in sealed capillaries.

Treatment of the salts with aqueous alkali resulted in rapid hydrolysis with formation of the corresponding tertiary amines.

$$CH_3SO_2\overset{+}{N}R_3\ \overset{-}{A} + \overset{-}{O}H \longrightarrow CH_3SO_2OH + NR_3 + \overset{-}{A}$$

The amines were isolated as their picrate salts and these compared with authentic samples. In all cases, the mixture melting points with authentic picrates were undepressed, confirming that the sulfonamides had been N-methylated by methyl fluorosulfonate. The data are summarized in Table 3.

Trialkyl(methylsulfonyl)ammonium fluorosulfonate salts are, therefore, readily prepared by N-methylation of methanesulfonamides with methyl fluorosulfonate. The synthesis appears to be limited to relatively non-hindered sulfonamides. Although hygroscopic and readily hydrolyzed by water, the salts are very stable when stored under anhydrous conditions and must be handled accordingly to prevent decomposition.

TABLE 3

Tertiary Amine Formation from the Aqueous Hydrolysis of the Sulfonylammonium Fluorosulfonate Salts

Salt	Amine	Yield	Picrate Melting Point	Reported Melting Point
1	NMe_3	62%	215-217°	216° (25)
2	$MeN(CH_2)_5$	85%	145-147°	148° (26)
3	$NEtMe_2$	50%	202-203°	193-195° (26)
4	NEt_2Me	50%	183-184°	185° (26)

B. Reactions of the Trialkyl(methylsulfonyl)ammonium Fluorosulfonate Salts

The four sulfonylammonium salts were investigated as methanesulfonating (mesylating) reagents and potential sulfene precursors. The diethylmethylammonium salt (4) was found to be the most effective mesylating reagent and was investigated more thoroughly than the others. Nonetheless, all four salts were found to be highly effective reagents even under mild conditions and superior under limiting conditions to other mesylating reagents such as methanesulfonyl chloride (mesyl chloride) or methanesulfonic anhydride.

Mesylation of 3β-cholestanol was conducted with the trimethylammonium salt (1), methanesulfonic anhydride or mesyl chloride under identical conditions. The reagents were allowed to react with the alcohol for 30 seconds at 0° in the presence of excess pyridine. Under these conditions, the trimethylammonium salt gave almost complete conversion of the cholestanol to cholestanyl mesylate (>98% by n.m.r. and t.l.c.), while methanesulfonic anhydride gave only 60% and mesyl chloride less than 1% (Table 4).

Similarly, when cyclohexanol was mesylated with the salts or methanesulfonic anhydride at -78°, in all cases the salts were found to be more effective reagents, giving from 35% mesylate for 1 to 80% for 4. The anhydride gave only about 20% cyclohexyl mesylate. The results are summarized in Table 5.

TABLE 4

Mesylation of 3β-Cholestanol:

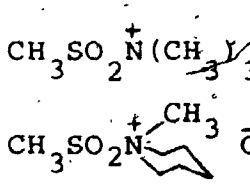
Comparison of Mesylating Reagents

Reagent	Crude Yield	Extent of Mesylation
$CH_3SO_2\overset{+}{N}(CH_3)_3\ \bar{O}SO_2F$	221 mg	> 98%
$CH_3SO_2OSO_2CH_3$	200 mg	60%
CH_3SO_2Cl	170 mg	< 1%

TABLE 5

Mesylation of Cyclohexanol:

Comparison of the Salts as Mesylating Reagents

Reagent	Crude Yield	Extent of Mesylation
$CH_3SO_2\overset{+}{N}(CH_3)_3\ \bar{O}SO_2F$	64 mg	35%
	132 mg	75%
$CH_3SO_2\overset{+}{N}(CH_3)_2CH_2CH_3\ \bar{O}SO_2F$	124 mg	70%
$CH_3SO_2\overset{+}{N}(CH_2CH_3)_2CH_3\ \bar{O}SO_2F$	144 mg	80%
$CH_3SO_2OSO_2CH_3$	93 mg	20%

Salts 1, 2 and 4 were also used to mesylate a variety of alcohols under mild reaction conditions. Typically, the salt was dissolved in acetonitrile solution and added to the alcohol in methylene chloride solution with a catalytic quantity of base such as pyridine or dimethylaminoacetonitrile (DMAAN). Only a catalytic amount of base (e.g. 0.1 equiv) was required in these reactions because the salts generate an equivalent amount of base as they react.

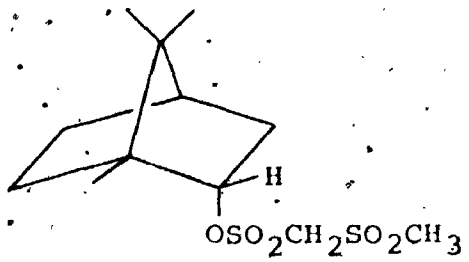
$$CH_3SO_2\overset{+}{N}R_3 + ROH \xrightarrow{B} CH_3SO_2OR + H\overset{+}{N}R_3$$

Thus, only sufficient base to initiate the reaction was required and even mild bases such as DMAAN were adequate. The reactions were performed at 0° or room temperature for 5 to 10 minutes and the products were isolated by a standard extraction procedure from aqueous acid. Where possible, the products were purified by recrystallization or distillation. However, the thermal instability of many liquid alkyl mesylates prevented their distillation. Nonetheless, the reactions gave very clean products and some were sufficiently pure to give satisfactory elemental analyses after a work-up procedure which included several water washes but no further purification.

Ethanol, benzyl alcohol, and 3β-cholestanol were mesylated with the trimethylammonium salt (1). Experiments with cholestanol as substrate indicated that when pyridine was used as the base, the yield of cholestanyl mesylate was

better than when DMAAN (80%) or 2,6-di-t-butylpyridine (<10%) were used. When no base was added, an isolated yield of only about 50% cholestanyl mesylate was obtained after 3.5 hours. The presence of a base was obviously necessary for a fast and efficient reaction.

With l-borneol as substrate, 1 was found to be a poor mesylating reagent. In a 1 minute reaction with pyridine as base, only a trace (<5% by n.m.r.) of bornyl mesylate was formed. However, after a 10 minute reaction, this yield was raised to 50%. Other bases, such as DMAAN, N-ethylmorpholine or triethylamine gave back the bulk of the l-borneol unreacted (see Table 6). Also observed in the n.m.r. of the crude products were trace amounts of l-bornyl methylsulfonyl-methanesulfonate ("mesylmesylate").



1

l-Bornyl Mesylmesylate

This product was presumed to be formed by trapping of "mesylsulfene" formed from the Opitz zwitterion $CH_3SO_2\bar{C}HSO_2\overset{+}{N}R_3$ (9, 11). The reaction scheme for formation of mesylmesylates is outlined in Figure 2. Only with DMAAN as base was no mesylmesylate observed.

The N-methylpiperidinium salt (2) was also found to be a good mesylating reagent. However, in the mesylation of 3β-cholestanol with this salt, the n.m.r. of the crude

TABLE 6

Reaction of Trimethyl(methylsulfonyl)ammonium Fluorosulfonate with l-Borneol in the Presence of Various Tertiary Amine Bases*

Base*	Relative Proportions of Products†		
	Recovered Borneol	Bornyl Mesylate	Bornyl Mesylmesylate
DMAAN (5 µl; 4.2)	95%	5%	--
Pyridine (4 µl; 5.23)	45	50	5
N-Ethylmorpholine (6.5 µl; 7.70)	90	5	5
Triethylamine (6 µl; 10.72)	78	17	5

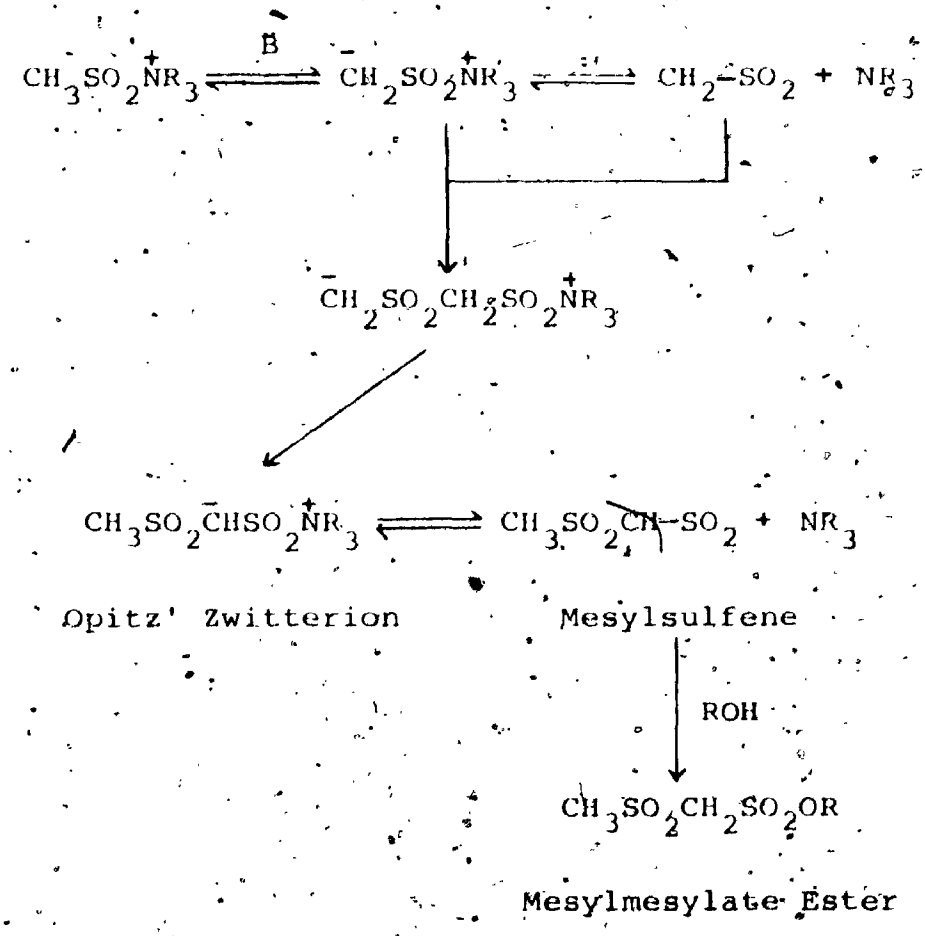
* Data in parentheses are respectively: amount of base used; pKa of conjugate acid of base (78).

† The n.m.r. spectra of l-bornyl mesylate and mesylmesylate (methylsulfonylmethanesulfonate) are described elsewhere (vide infra).

FIGURE 2

Reaction Scheme for Formation of

Methylsulfonylmethanesulfonate (Mesylmesylate) Esters



product showed peaks corresponding to cholestanyl mesylmesylate (by comparison with the spectrum of l-bornyl mesylmesylate). The yield of this by-product was about 5%.

With l-borneol as substrate and DMAAN as base, 2 gave a 69% yield of l-bornyl mesylate along with 19% of the mesylmesylate. With pyridine as base, the yield of mesylate and mesylmesylate were 66% and 8% respectively. N-Ethylmorpholine and triethylamine were found to be very poor catalysts, giving low yields of mesylate and mesylmesylate and 75 to 85% recovery of unreacted borneol. These results are summarized in Table 7.

Mesylation of alcohols with the diethylmethylammonium salt (4) was examined extensively and the results are listed in Table 8. All the reactions were run at 0° for 10 minutes with 0.1 equiv DMAAN as base. The extent of mesylation was determined from the isolated yields and n.m.r. and t.l.c. of the crude products. The purified products were characterized by n.m.r. and i.r. and wherever possible by elemental analyses or precise mass determinations.

Both l-borneol and 3α-cholestanol (epicholestanol) gave a small yield of the corresponding mesylmesylate ester. The extent of formation of l-bornyl mesylmesylate (relative to the mesylate) was found to be solvent-dependent with a more polar solvent mixture (acetonitrile and methylene chloride) giving higher yields of the mesylmesylate. These results are summarized in Table 9.

TABLE 7

Reaction of 1-Methyl-1-(methylsulfonyl)piperidinium Fluorosulfonate with l-Borneol in the Presence of Various Tertiary Amine Bases

Base*	Relative Proportions of Products		
	Recovered Borneol	Bornyl Mesylate	Bornyl Mesylmesylate
DMAAN (10 µl; 4.2)	12%	69%	19%
Pyridine (8 µl; 5.23)	26	66	8
N-Ethylmorpholine (13 µl; 7.70)	75	12	13
Triethylamine (15 µl; 10.72)	85	8	7

* Data in parentheses are respectively: amount of base used; pKa of conjugate acid of base (78).

TABLE 8

Mesylation of Alcohols with Diethylmethyl(methylsulfonyl)ammonium Fluorosulfonate

Alcohol	Equivalents of (4) Used	Extent of Mesylation**	Purified Yield††
Ethanol	2.0	98%	77%
Cyclohexanol	2.0	98	80
l-Menthol	1.2	100	99
1-Octanol	2.0	100	92
l-Borneol	1.5	89*	77
5α-Cholestan-3β-ol	1.2	100	79
5α-Cholestan-3α-ol	2.0	86†	73
Phenol	1.2	100	80
Allyl Alcohol	2.0	92	81
Benzyl Alcohol	2.0	100	95

* l-Bornyl mesylmesylate (11%) also formed.

† Epicholestanyl mesylmesylate (14%) also formed.

** Estimated from the isolated yield, n.m.r. and t.l.c. of the crude products.

†† Products were purified where possible by recrystallization or distillation; thermally-unstable liquid mesylates were purified by extensive washing during work-up and showed no detectable impurities by n.m.r.

TABLE 9

Effect of Solvent on the Ratio of Mesylate to Mesylmesylate Formed in the Reaction of l-Borneol with Diethylmethyl(methylsulfonyl)-ammonium Fluorosulfonate*

CH_2Cl_2:CH_3CN	Mesylate:Mesylmesylate**
5:1	9:1
1:1	3:1
1:5	2:1

* Base: DMAAN (0.1 equiv)

† Volume/Volume

** Mole/Mole

The formation of the Opitz zwitterion (Figure 2), and, hence mesylmesylate formation are apparently enhanced by increasing solvent polarity (stabilization of ionic species in acetonitrile solution is well known (27)). In a more polar solvent, the stability of the zwitterion $\bar{C}H_2SO_2\overset{+}{N}R_3$ would be enhanced. This would presumably result in an increased concentration of the zwitterion and more sulfene trapping by the zwitterion as a result of this increased concentration.

As observed with salts 1 and 2, the mesylation of l-borneol with the diethylmethylammonium salt was affected by the type of base used. DMAAN was superior as a catalyst to the other bases (Table 10), giving the mesylate (89%) and mesylmesylate (11%) and no unreacted borneol. 2,6-Di-t-butylpyridine gave 15% conversion to bornyl mesylate after 10 minutes reaction and 28% after 1 hour. The yield of mesylmesylate after 1 hour was 12%. Pyridine gave 30% mesylate and 5% mesylmesylate but stronger bases gave only minor amounts of the products with the bulk of the starting material being recovered unchanged.

In a reaction observed by n.m.r., t-butyl alcohol was mesylated by the diethylmethylammonium salt in the presence of pyridine (2 equiv) at -78°. The t-butyl mesylate was identified by bands at δ 1.57 and 3.01 p.p.m. in the ratio 3:1. The mesylate appeared to be stable at lower temperatures (≤-5°), with no apparent decomposition observed in

TABLE 10

Reaction of Diethylmethyl(methylsulfonyl)ammonium Fluorosulfonate with l-Borneol in the Presence of Various Tertiary Amine Bases

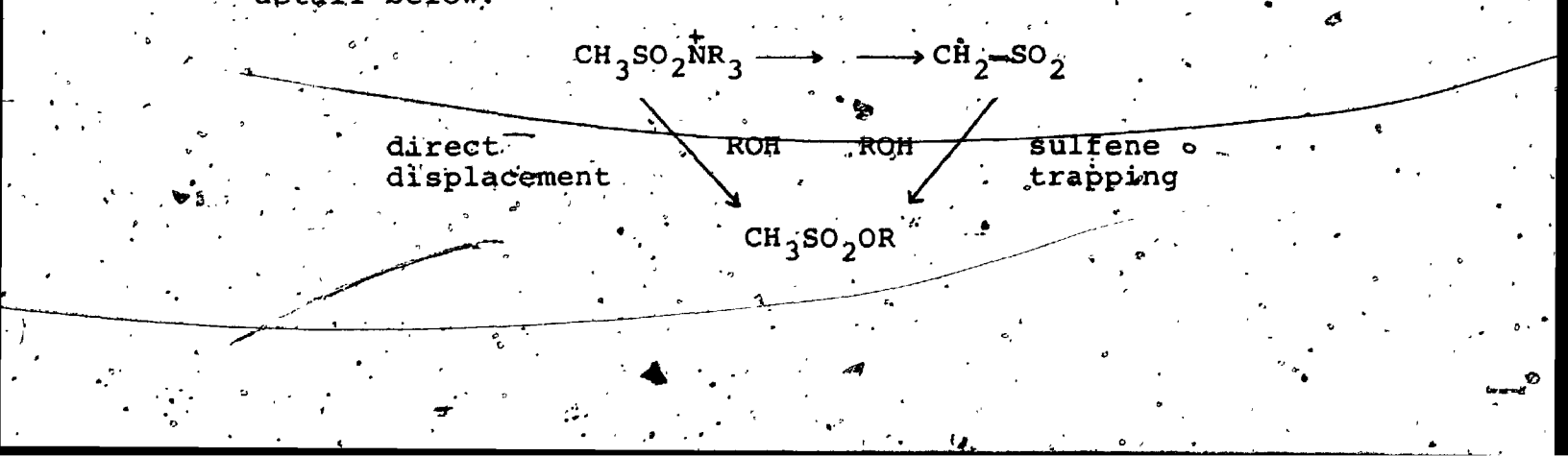
Base*	Relative Proportions of Products: Recovered Borneol	Bornyl Mesylate	Bornyl Mesylmesylate
2,6-di-t-Butylpyridine† (17 mg, 3.58 (81))	a) 82%	15%	3%
	b) 60	28	12
DMAAN (10 µl, 4.2 (78))	--	89	11
Pyridine (8 µl, 5.23 (78))	65	30	5
N-Ethylmorpholine (13 µl, 7.70 (78))	89	7	4
Triethylamine (14 µl, 10.72 (78))	>90	<5	<5

* Data in parentheses are respectively: amount of base used; pKa of conjugate acid of base; reference for pKa.

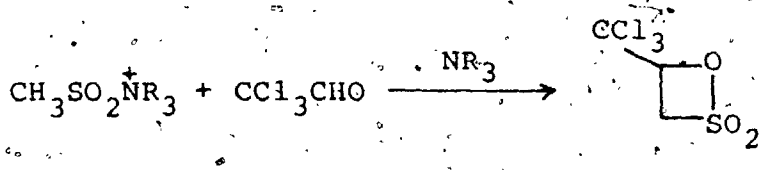
† Reaction with 2,6-di-t-butylpyridine was run for a) 10 min and b) 1 h.

the spectra recorded over a 2 hour period. However, on warming to room temperature, the peaks assigned to the mesylate rapidly disappeared and were replaced by bands at δ 3.44, 1.68 and 4.62 p.p.m. (ratio 3:6:2) corresponding to methanesulfonic acid and isobutene. Attempts to isolate the mesylate from a larger-scale preparation were fruitless.

The sulfonylammonium salts were thus found to be highly effective reagents for the preparation of mesylate esters. Evidence for sulfene formation from the salts came from the reaction of the diethylmethylammonium salt (4) with an enamine, 1-(2-methylpropenyl)pyrrolidine (5, 28). A very modest yield (12%) of the crystalline enamine-sulfene cycloadduct was obtained, even though the n.m.r. spectrum of the crude product indicated roughly a 50% yield (the isolation of the cycloadduct was made very difficult by the formation of resinous by-products from which the adduct had to be extracted using petroleum ether). Nonetheless, formation of this adduct indicates that sulfene is being generated from the salt. While this suggests that sulfene-trapping is the mechanism of formation of the mesylate esters, the alternative of a direct displacement mechanism cannot be excluded. This mechanistic dichotomy will be discussed in greater detail below.



The trimethylammonium salt (1) gave a 48% yield of the β-sultone when reacted with chloral and trimethylamine, but only a trace of the cycloadduct was observed when the diethylmethylammonium salt (4) was reacted with chloral and diethylmethylamine. Addition of 4 to chloral and base gave the same results as addition of base to chloral and 4.

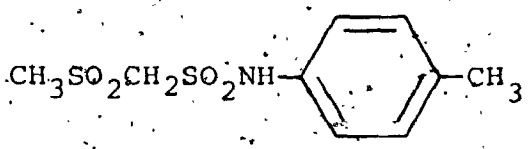


These observations correspond to the effects of increasing base size on cycloadduct yield reported by Harding for the reaction of ethanesulfonyl chloride with chloral and tertiary amines (7). However, it cannot be definitely concluded from these results (or those of Harding) whether the β-sultone is formed by reaction of the sulfene-amine zwitterion with chloral or by reaction of a chloral-amine zwitterion, $CCl_3\overset{\overset{O}{|}}{C}H-\overset{+}{N}R_3$, with sulfene. Further experiments in this area may shed more light on this problem.

The salts reacted quantitatively with p-toluidine to give the sulfonamide, methanesulfon-p-toluidide. However, when the trimethylammonium salt (1) was stirred in acetonitrile solution at room temperature for 1 hour followed by addition of excess p-toluidine, the sulfonamide was isolated in only 82% yield, indicating that 1 decomposes slowly in solution.

Reaction of 1 with trimethylamine for 30 seconds followed by addition of p-toluidine gave only methylsulfonyl-

methanesulfon-p-toluidide (mesylmethanesulfon-p-toluidide) in 70% yield.



Mesylmethanesulfon-p-toluidide

However, reaction of 1 with p-toluidine and trimethylamine together gave a mixture of the methanesulfonamide and mesylmethanesulfonamide in the mole ratio 2:1. When 1 was allowed to react with pyridine for 1 minute before addition of p-toluidine, the methanesulfonamide and mesylmethanesulfonamide were formed in the mole ratio 5.3:1.

Apparently, then, the sulfonylammonium salt is moderately stable in solution in the absence of base. However, in the presence of a strong base, the salt reacts to give the stable, dimerized Opitz zwitterion by the reaction pathway shown in Figure 2. Even in the presence of p-toluidine, a highly reactive sulfene trap (5), the reaction of the salt with trimethylamine to form the Opitz zwitterion could not be completely suppressed.

Likewise, the N-methylpiperidinium salt (2) gave a mixture of the methanesulfonamide (major) and mesylmethanesulfonamide in reaction with p-toluidine and pyridine. When the toluidine was added to the salt after pyridine, extensive decomposition occurred with only a small yield of the sulfonamides being isolated. Although the reason for this low yield is unclear, it is possible that the more

reactive salt 2 gave sulfene-oligomerized products which are known to be highly water-soluble (11) and would have been lost on work-up.

The results of reactions of the diethylmethylammonium salt (4) with p-toluidine in the presence of various bases are shown in Table 11. Weak bases, such as DMAAN or 2,6-di-t-butylpyridine, gave little or none of the mesylmethanesulfonamide, while strong bases, such as triethylamine, gave more of this product than methanesulfon-p-toluidide. As with the other salts, the presence of strong bases has catalyzed the formation of the Opitz zwitterion in these reactions.

While reaction of salt 4 with p-toluidine (pKa 5.09) alone gave only methanesulfon-p-toluidide, the same reaction in the presence of pyridine (pKa 5.23) resulted in the formation of the mesylmethanesulfonamide (30%) as well. Despite the fact that both p-toluidine and pyridine are of comparable basicity, the presence of pyridine in the reaction solution has had a distinct effect on the nature of the products, suggesting that pyridine has altered the mechanism of the reaction. These observations are in keeping with other reactions in which p-toluidine reacts as a nucleophile rather than a base. For example, p-toluidine reacts with camphor-10-sulfonyl chloride or methanesulfonyl chloride primarily by direct displacemnt rather than sulfene formation and trapping (as determined by deuterium-labelling experiments (29)). A direct displacemnt mechanism

TABLE 11

Reaction of Diethylmethyl(methylsulfonyl)ammonium Fluorosulfonate with p-Toluidine in the Presence of Tertiary Amine Bases

Base	Amount of Product	Yields Methanesulfonamide	Yields Mesylmethanesulfonamide	Mole Ratio
DMAAN	166 mg	90 %	--*	--
2,6-di-t-butylpyridine	166	87	<3%	30:1
Pyridine	157	63	30	2:1
Triethylamine	127	27	59	0.9:1
Diisopropylethylamine	133	28	57	0.9:1

* No mesylmethanesulfonamide was detectable by n.m.r.

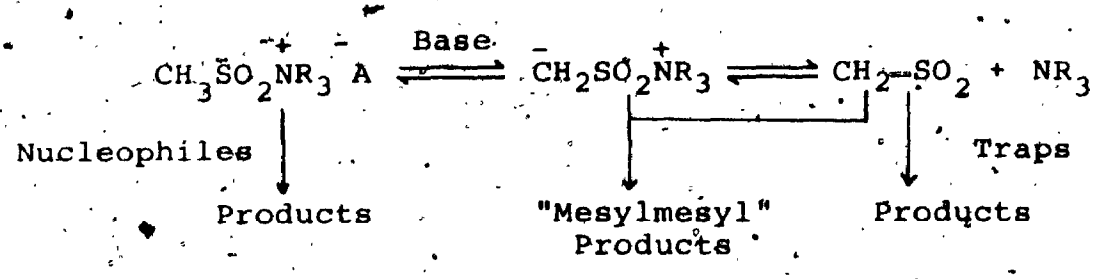
may indeed account for the lack of sulfene-derived product (namely the mesylmethanesulfonamide) in the absence of a suitable tertiary base (viz. pyridine). However, the extent of participation of this mechanism in these reactions cannot be determined from these data since sulfene-trapping by toluidine would also give rise to the same product, and, as mentioned previously, p-toluidine is a very effective sulfene trap. We may only surmise that pyridine and stronger tertiary bases catalyze sulfene formation and concomitant mesylsulfene formation (see Figure 2), better than p-toluidine alone.

From these results, it can be seen that methanesulfonylammonium salts are participants in a variety of sulfene reactions. They appear to be unsurpassed as mild and effective mesylating reagents, generating an array of mesylate esters, including the very unstable t-butyl mesylate.

Furthermore, the results are in good agreement with the reaction pathways shown in Figure 3.

FIGURE 3

Reaction Pathways of the Trialkyl(methylsulfonyl)-ammonium Fluorosulfonate Salts



As the R-groups on nitrogen increase in size, the salts become better mesylating reagents, reflecting a shift in the equilibrium away from the zwitterion towards sulfene. Presumably, the acidity of the α-sulfonyl protons on $CH_3SO_2\overset{+}{N}R_3$ is not significantly effected by the changes in the size of R in going from 1 to 4. For a given base (e.g., pyridine) the equilibrium between this ion and the zwitterion would be the same for all the salts. The differences in their reactivity, then arises from the zwitterion $\rightleftharpoons$ sulfene equilibrium, which will favour sulfene more and more as R becomes larger and the zwitterion is destabilized. Thus, the increasing reactivity of the salts from 1 to 4 as mesylating reagents confirms the decreasing stability of the zwitterion with increasing R-group size, as predicted by King, Harding and Luinstra (6). It can be seen that the decreasing zwitterion stability also explains why DMAAN was an adequate catalyst for mesylation of 1-borneol with 4, but a stronger base, pyridine, was required with 1.

From the formation of "mesylmesyl" products under various circumstances, it would appear that the zwitterion itself is a good sulfene-trapping agent. Mesylmesylate esters were observed with hindered alcohols such as 1-borneol or epicholestanol. The formation of 1-bornyl mesylmesylate did not appear to follow any trend either in the strength of the base used as catalyst or in the reactivity of the sulfonylammonium salt. However, experiments

with p-toluidine indicated that stronger bases indeed gave more of the mesylmethanesulfonamide, as discussed above.

This is the result expected from the reaction scheme (Figure 3). The formation of the zwitterion from the salt is enhanced by increases in both base strength and base concentration. Strong bases in greater concentration also favour recombination of sulfene with base ($CH_2{=}SO_2 + NR_3 \rightleftharpoons \bar{C}H_2SO_2\overset{+}{N}R_3$) to give the zwitterion. An increase in the concentration of the zwitterion relative to the sulfene trap will thus result in more sulfene-trapping by the zwitterion and more "mesylmesyl" products. This was especially obvious in the experiments with p-toluidine. The inconclusiveness of the results with l-borneol may have arisen from the poor reactivity of this alcohol as a sulfene trap. The fate of the Opitz zwitterion as a result was probably the formation of other sulfene-oligomerized products and/or hydrolysis on work-up to give water-soluble sulfonic acids (11).

The precise role of the direct displacement mechanism in the reactions of these salts is not fully understood. The formation of an enamine cycloadduct indicates that the salts do give sulfene. However, the anomalous formation of the mesylmethanesulfonamide when the salts react with p-toluidine and base suggest that a direct displacement reaction of the salts with p-toluidine occurs in the absence of additional base, when only methanesulfon-p-toluidide is formed. From the variation in the product

ratio as the base strength is altered, it is likely, in fact, that both mechanisms are operating, with more sulfene formation occurring with stronger bases. In the extreme, it is possible that p-toluidine reacts only by direct displacement and that the zwitterion is a far better sulfene trap than toluidine. Another possibility is that with strong bases such as triethylamine and diisopropylethylamine, the reaction pathway is entirely via sulfene and that the product ratio thus reflects the competition between toluidine and the zwitterion for sulfene (recall that these two bases gave identical product ratios when reacted with salt 4 and p-toluidine--Table II).

Unfortunately, there does not appear to be a good test for these hypotheses. The reactions are too fast to measure accurately by conventional techniques. As well, deuterium-labelling experiments would be useless because the salts undergo rapid and extensive multiexchange with p-toluidine-N,N-d_2, as we shall see in the following section. Carefully designed experiments are needed to settle this problem.

Having established by these results that the methylsulfonylammonium fluorosulfonate salts are not only sulfene sources, but that they surpass the mesylating reactivity of methanesulfonyl chloride or methanesulfonic anhydride, the salts were examined as potential intermediates in the multiexchange process observed by King, Luinstra and Harding. These results are discussed in the following section.

C. Multiexchange Reactions of the Trialkyl(methylsulfonyl)-ammonium Fluorosulfonate Salts

The methylsulfonylammonium salts, (1 - 4), were hydrolyzed with deuterium oxide and their corresponding tertiary amines in 1,2-dimethoxyethane (DME) solution under almost identical conditions to those described by Luinstra for methanesulfonyl chloride (5). The salts were added solid (because they were insoluble in DME) to a rapidly stirred solution of deuterium oxide (large excess) and the corresponding tertiary amine (e.g. trimethylamine with the trimethylammonium salt) in DME at room temperature. The salts dissolved almost instantly and within seconds the solutions became cloudy emulsions with the separation of a heavy layer (presumably a deuterium oxide solution of various salts). After stirring rapidly for 10 minutes, the mixtures were evaporated to dryness and the residual methanesulfonate salts were converted to methanesulfonyl chloride by a procedure described by Harding (7) to facilitate the analysis. The deuterium content and distribution of the products were determined by mass spectrometric (m.s.) analysis, examining the methylsulfonium ion peak, $CH_3SO_2^+$ (m/e 79). These results are given in Table 12.

In a similar manner, the multiexchange reaction of the diethylmethylammonium salt (4) was repeated but with diethylmethyldeuterioammonium chloride ($DNEt_2Me^+Cl^-$, 5 mmol) added. The amount of deuterium oxide used was reduced

TABLE 12

Multiexchange in the Base-Catalyzed Hydrolysis of the Trialkyl(methylsulfonyl)ammonium Fluorosulfonate Salts in Deuterium Oxide*

Salt	Base	Product Deuterium Distribution (%) CH_3	CH_2D	CHD_2	CD_3	Total (atom % excess D)
1	NMe_3	1.3	5.3	29.2	64.2	85.4
2	$MeN(CH_2)_5$	1.8	9.4	28.4	60.4	82.5
3	$NEtMe_2$	3.2	9.9	34.7	52.2	78.6
4	NEt_2Me	7.4	40.1	28.4	24.1	56.4
		11.8	24.2	29.5	34.5	62.2†

* Conditions: sulfonylammonium salt (4 mmol), base (10 mmol), deuterium oxide (2.0 ml, 111 mmol), DME (30 ml).

† Hydrolysis reaction with added $DNEt_2Me^+Cl^-$ (5 mmol), deuterium oxide (1.97 ml, 109 mmol).

proportionally to maintain the active deuterium pool at the same concentration as above. The product was analyzed as described above and the results are included in Table 12.

The pyridine-catalyzed hydrolysis of the salts (1, 2 and 4) in deuterium oxide solution was also studied. The salts (2 mmol) were added to a stirred solution of pyridine (5 mmol) in deuterium oxide (large excess). After stirring at room temperature for 15 minutes, the mixtures were evaporated to dryness and the residual methanesulfonates converted to the sulfonyl chlorides as described above. The products were analyzed for deuterium (m.s.) and the results are summarized in Table 13. In addition, the pyridine-catalyzed hydrolysis of the diethylmethylammonium salt (4) in deuterium oxide and DME solution was performed under identical conditions to those described above (cf. Table 12). These results are also given in Table 13.

Finally, the reaction of the salts with p-toluidine-N,-N-d_2 was investigated. The salts were dissolved in acetonitrile and added to a 5-fold excess of dideuterated toluidine in methylene chloride solution. After 5 minutes, the methanesulfon-p-toluidides were isolated, purified and analyzed for deuterium (m.s., n.m.r.). The extent of deuterium incorporation into the sulfonyl methyl groups of the products is summarized in Table 14. Also listed are the results of the reaction of the diethylmethylammonium salt (4) with a large excess (37-fold) of dideuterated toluidine.

TABLE 13

Multiexchange in the Pyridine-Catalyzed Hydrolysis of the Trialkyl(methylsulfonyl)ammonium Fluorosulfonate Salts in Deuterium Oxide*

Salt	Product Deuterium Distribution (%) CH_3	CH_2D	CHD_2	CD_3	Total (atom % excess D)
1	2.4	2.5	9.0	86.1	92.9
2	0.1	0.9	8.0	91.0	96.6
4	1.1	4.4	12.5	81.9	91.7
	14.2	48.4	27.1	10.3	44.5†

* Conditions: sulfonylammonium salt (2 mmol), pyridine (5 mmol), deuterium oxide (5 ml).

† Conditions: sulfonylammonium salt (4 mmol), pyridine (10 mmol), deuterium oxide (2.0 ml, 111 mmol), DME (30 ml).

TABLE 14

Multiexchange in the Reaction of the Trialkyl(methylsulfonyl)ammonium Salts with p-Toluidine-N-d_2*

Salt	Product Deuterium Distribution (%)† CH_3	CH_2D	CHD_2	CD_3	Total (atom % excess D)† by m.s.	by n.m.r.
1	8.1	23.5	36.4	31.9	64.0	61
2	13.0	24.6	33.9	28.6	59.4	60
3	21.2	30.4	29.3	19.1	48.8	49
4	34.0	41.6	17.2	7.3	32.6	32
	26.3	54.0	15.3	4.4	32.6	32††

* Conditions: sulfonylammonium salt (1 mmol), p-toluidine-N-d_2 (5 mmol), acetonitrile (5 ml), methylene chloride (5 ml).

† Deuterium distribution (%) or net deuterium content (atom % excess D) of the sulfonyl methyl group of methanesulfon-p-toluidide product.

†† Large excess (37-fold) of p-toluidine-N-d_2 used.

Comparison of the results in Table 12 with those for methanesulfonyl chloride (Table 1) reveals that for a given tertiary amine base, the sulfonylammonium salts underwent hydrolysis with considerably more extensive multiexchange than methanesulfonyl chloride. Nonetheless, the salts paralleled the behaviour of methanesulfonyl chloride in that bulkier amines (or salts with sterically larger R-groups on nitrogen) gave less multiexchange than less hindered amines (or salts).

These results are compelling evidence for the intermediacy of sulfonylammonium salts and zwitterions in the multiexchange reactions of methanesulfonyl chloride and confirm the multiexchange mechanism postulated by King, Luinstra and Harding (Figure 1).

It is not unreasonable that the sulfonylammonium salts gave more extensive multiexchange than methanesulfonyl chloride. For one thing, methanesulfonyl chloride reacts with base initially to form sulfene which can either be trapped out directly or react with base to form the zwitterion. The salts, on the other hand, enter the multiexchange manifold directly by giving the zwitterion in the first step. Because they do not give sulfene directly, then, the salts can undergo more extensive exchange.

Another reason for their enhanced multiexchange capability is that the sulfonylammonium salts with the fluorosulfonate anion are more stable than those with the

chloride counteranion (22). The fluorosulfonate anion is less nucleophilic than chloride ion, resulting in less reaction of the anion with the sulfonylammonium ion. Reaction of chloride ion with the sulfonylammonium ion would generate the sulfonyl chloride and this would react to give sulfene, and so forth.

$$CH_3SO_2\overset{+}{N}R_3 + Cl^- \longrightarrow CH_3SO_2Cl + NR_3 \longrightarrow CH_2{=}SO_2 + \overset{+}{H}NR_3\bar{Cl}$$

It was expected that by addition of $D\overset{+}{N}Et_2Me\ \bar{Cl}$ to the hydrolysis reaction of the diethylmethylammonium salt (4), the extent of multiexchange would be enhanced. The mass-action effect of the deuterium chloride salt on the equilibrium between the sulfonylammonium ion and the zwitterion would result in less decomposition of the zwitterion to sulfene and thus an enhancement of the multi-exchange.

$$CH_3SO_2\overset{+}{N}R_3 + NR_3 \underset{D\overset{+}{N}R_3\bar{Cl}}{\rightleftharpoons} \bar{C}H_2SO_2\overset{+}{N}R_3 + \overset{+}{H}NR_3$$

In fact, a net increase of slightly less than 6 atom % excess deuterium was observed along with a redistribution of the deuterium. The amount of monodeuterated product decreased by 16% while the trideuterated product increased by 10%. The dideuterated product yield was almost unchanged, but the amount of non-deuterated material actually increased by over 4%.

The rather low net increase in deuterium content of the product along with the anomalous increase in non-deuterated material suggests that the addition of the deuterium chloride salt has had a complex effect on the multiexchange mechanism. The introduction of chloride ion to the system probably offset somewhat the enhancement of multiexchange by adversely affecting the stability of the zwitterion. As well, the increase in non-deuterated product yield suggests that a direct displacement reaction has occurred in the hydrolysis of the sulfonylammonium salt. An increase in non-deuterated product from a sulfene mechanism alone could only result from a considerable dilution of the deuterium pool, which was not the case here.

It is interesting to note that as the size of the N-alkyl groups on the salts increased from 1 to 4, the amount of non-deuterated product also increased. An analogous effect was also observed for methanesulfonyl chloride (Table 1). The increases are too large to be explained only by dilution of the active deuterium pool, particularly since the pool is diluted less and less as we go from salt 1 to salt 4 because the extent of multi-exchange decreases. We would predict, then, that the yield of non-deuterated product would increase very little, if at all, in that same order 1 to 4 if the products arise solely by a sulfene trapping mechanism.

This anomaly suggests that some of the product arises via a direct displacement hydrolysis of the sulfonylammonium salt (Figure 3). Furthermore, the amount of direct displacement appears to increase, relative to the amount of sulfene trapping, as the reactivity of the salt increases. In the absence of base, both methanesulfonyl chloride (29) and methanesulfonic anhydride (30) undergo hydrolysis by direct displacement. No deuterium is incorporated into the α-sulfonyl methyl group when mesyl chloride is hydrolyzed in deuterium oxide, precluding the intermediacy of sulfene in the reaction.

However, the observation of significant amounts of non-deuterated product in the base-catalyzed deuterium oxide hydrolysis of mesyl chloride in Table 1 (up to 9.6% for triethylamine) suggests that a direct displacement mechanism may participate to some extent in the presence of base as well. Dilution of the isotopic pool as the reaction proceeds cannot account for so large a yield of non-deuterated product, even assuming large isotope effects. There exists, then, the intriguing possibility that direct displacement is a competing mechanism with sulfene formation in the base-catalyzed hydrolysis of methanesulfonyl chloride. Moreover, the data in Table 12 suggests that direct displacement may be an important reaction pathway for the corresponding hydrolysis of methanesulfonylammonium salts as well.

The hydrolysis of the salts in deuterium oxide solution in the presence of pyridine resulted in very high levels of deuterium incorporation, approaching complete multiexchange. The products contained over 90 atom % excess deuterium (Table 13). This extent of multiexchange appeared to be a levelling-off effect as there was no apparent trend paralleling the increasing reactivity of the salts (1 - 4). When the hydrolysis of 4 was run in DME solution with pyridine, the deuterium-incorporation level fell considerably, indicating that the high levels observed without DME were largely due to the high concentration of deuterium oxide. Hydrolysis of the salts in deuterium oxide appears to be an excellent route to perdeuterated methylsulfonyl compounds.

Extensive multiexchange was observed in the reaction of the salts with p-toluidine-NN-d_2. The dideuterated toluidine was prepared by washing an organic solution of p-toluidine with several successive portions of deuterium oxide, and was assumed to be at least 95% dideuterated (no N-hydrogens were visible in the n.m.r. spectrum). Comparison of the results in Table 8 with those in Table 12 reveals that the reaction of the salts with toluidine-d_2 resulted in considerably less multiexchange than with deuterium oxide, although in both cases the same trend was observed, decreasing multiexchange with increasing N-alkyl group size. Particularly noticeable were the high levels of unexchanged product.

Amazingly, increasing the mole ratio of toluidine-$\underline{d}_2$ to salt $\underline{4}$ from 5:1 to 37:1 did not result in an increase in net deuterium incorporation (32.6 atom % excess deuterium in both cases). The major effect was a reduction in the amount of unexchanged product from 34% to 26% and an increase in monoexchanged product from 42% to 54%. The levels of dideuterated and trideuterated products decreased 2% and 3% respectively. Despite a 7-fold increase in the D/H ratio in the active isotope pool, the amount of non-deuterated product was still extensive. This confirms that the non-deuterated product does not arise solely from protium in the deuterium pool, and suggests that product formation proceeds to a large extent via direct displacement by p-toluidine on the salts.

The substantial increase in the level of monoexchanged product when the concentration of toluidine-$\underline{d}_2$ was increased, particularly in light of the decreases observed in $\underline{d}_0$-, $\underline{d}_2$- and $\underline{d}_3$-products, indicates that multiexchange has decreased and implies that the amount of sulfene trapping (and, hence, sulfene formation) has increased. A possible rationale for this is that with an increase in the base concentration (toluidine-$\underline{d}_2$), the equilibrium between the sulfonylammonium ion and the zwitterion has shifted towards the zwitterion and this has resulted in an extensive amount of sulfene formation.

$$CH_3SO_2\overset{+}{N}R_3 \xrightleftharpoons{\text{base}} \underset{-}{C}H_2SO_2\overset{+}{N}R_3 \rightleftharpoons CH_2{=}SO_2 + NR_3$$

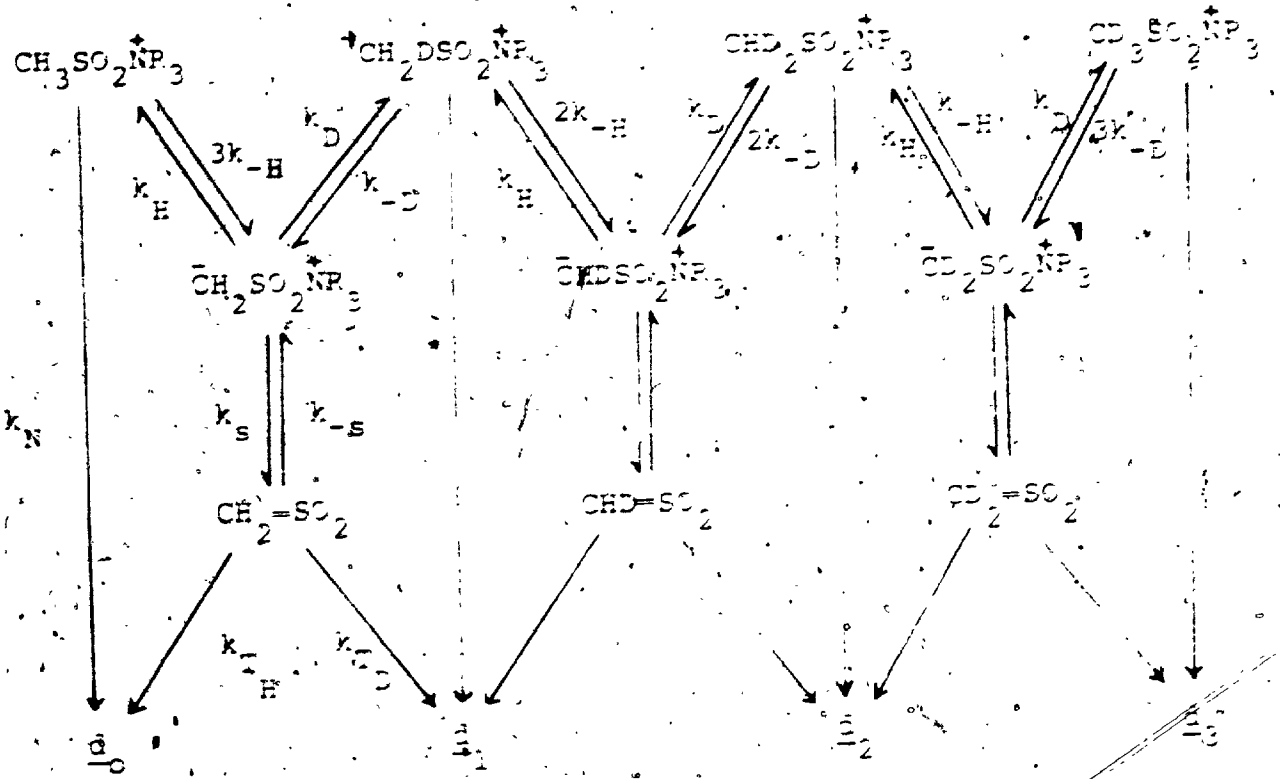
The decrease in zwitterion reprotonation to give exchanged sulfonylammonium ion would result in less di- and tri-deuterated product formation. Likewise, the lower concentration of sulfonylammonium ion would result in less direct displacement and less non-deuterated product, as observed. This explanation, while not intended to exclude other mechanisms, fits readily into the mechanistic scheme which has been postulated for reactions of the sulfonylammonium salts (Figure 3).

The combined reaction scheme involving both direct displacement and sulfene trapping is shown in Figure 4. If the pseudo-first-order rate constants (k_f) were known, it would be possible to calculate the proportions of the products ($\underline{d}_0$, $\underline{d}_1$, $\underline{d}_2$ and $\underline{d}_3$) to be expected from each sulfonylammonium salt using this scheme. Unfortunately, these rate constants are not known. However, if we are allowed a few assumptions, the scheme may be simplified somewhat, allowing us to calculate the deuterium distributions observed experimentally for both the D_2O/NR_3 hydrolysis reactions and the p-toluidine-$\underline{N},N$-$\underline{d}_2$ experiments. The assumptions are as follows:

1. Deuterium isotope effects for the exchange reactions are assumed to be small and may be ignored. Hence, $k_H = k_D = k_e$ (the rate of proton or deuteron uptake by the zwitterion) and $k_{-H} = k_{-D} = k_{-e}$ (the rate of proton or deuteron removal from the sulfonylammonium ion).

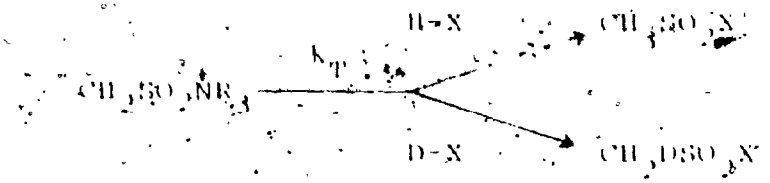
FIGURE 4

Mechanism of Multiexchange in the Reactions of the Trialkyl(methylsulfonyl)ammonium Fluorosulfonate Salts*



* Rate constants (k) are pseudo-first-order.

2. The equilibrium between the zwitterion and sultone, $CH_2SO_3NR_3 \underset{k=s}{\overset{k_s}{\rightleftharpoons}} CH_2{-}SO_2$, is assumed to be very fast allowing us to represent the sultone trapping step as a simple process from the zwitterion:



This does not imply that sultone is not present, but is merely intended to simplify the calculations.

3. The ratio of deuterium to hydrogen in the active isotope pool ($n = [D]:[H]$) is assumed to be constant for the duration of the reaction. Values of n were estimated from the following equations:

(a) for deuterium oxide exchanges:

$$n = \frac{222 \cdot \frac{\lambda}{100} \times 12}{2.2 + \frac{\lambda}{100} \times 12}$$

where 222 = millimoles of active deuterium

λ = percent exchange of sulfonyl methyl hydrogens (total of 12 mmol)

2.2 = estimated millimoles of active hydrogen from stray moisture, etc. (1% of active deuterium)

(b) for p-toluidine-d_2 exchanges:

$$n = \frac{10 - 0.5 - \frac{\lambda}{100} \times 3}{0.5 + \frac{\lambda}{100} \times 3}$$

where 10 millimoles of active deuterium

0.5 millimoles of active hydrogen (assuming p-toluidine is 95% dideuterated)

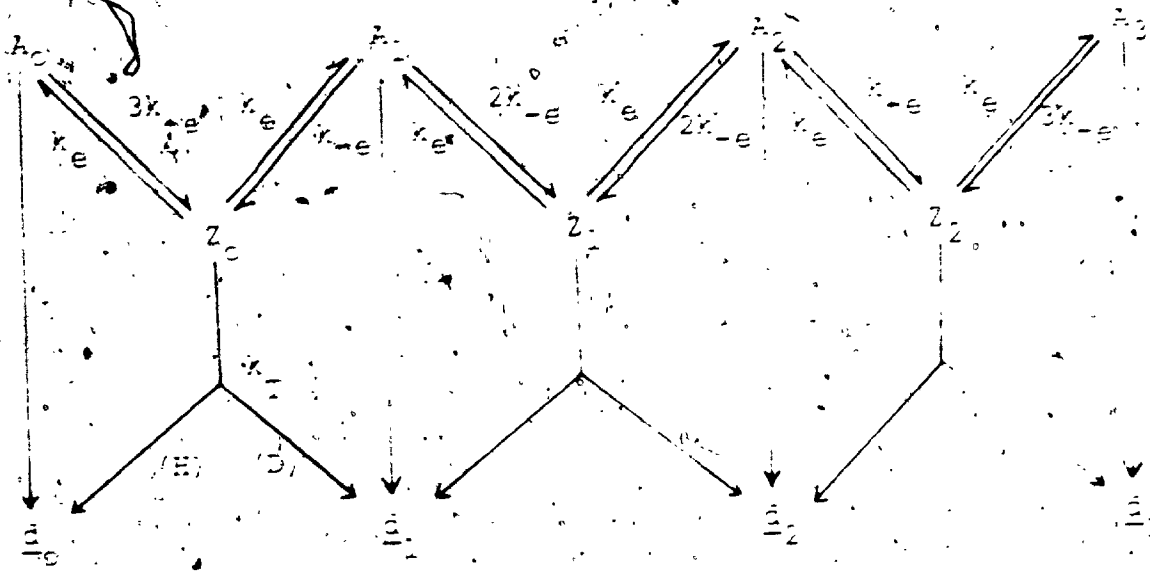
percent exchange of sulfonyl methyl hydrogens (total of 3 mmol).

4. A deuterium isotope effect of $k_H/k_D = 2$ is assumed for the sultene trapping step. Although little is known about the mechanism of sultene trapping or deuterium isotope effects for this process, recent experiments involving trapping of phenylsultene with isopropanol or sultene with p-toluidine (11) suggest that this value may be a reasonable estimate.

These assumptions are considered to be valid for a semi-quantitative evaluation of the mechanistic scheme shown in Figure 4. The simplified scheme based on these assumptions is shown in Figure 5. For the given value of n for each salt, the ratios k_e/k_T (rate of zwitterion protonation/rate of sultene trapping) and k_{-e}/k_N (rate of sulfonylammonium ion deprotonation/rate of direct displacement reaction) were varied to give as good an agreement as possible between the derived values of $\underline{d}_0$, $\underline{d}_1$, $\underline{d}_2$ and $\underline{d}_3$ (8) and those determined experimentally (Tables 6 and 8). As an example, the calculation for the D_2O/NR_3 hydrolysis of salt 1 (n = 17) is shown in Figure 6 for the optimized values $k_e/k_T = 22$ and $k_{-e}/k_N = 100$. The calculations were carried out as follows:

FIGURE 1

Simplified Reaction Scheme for the Multiexchange Reactions of the Trialkylmethylsulfonylammonium Fluorosulfonate Salts*



---

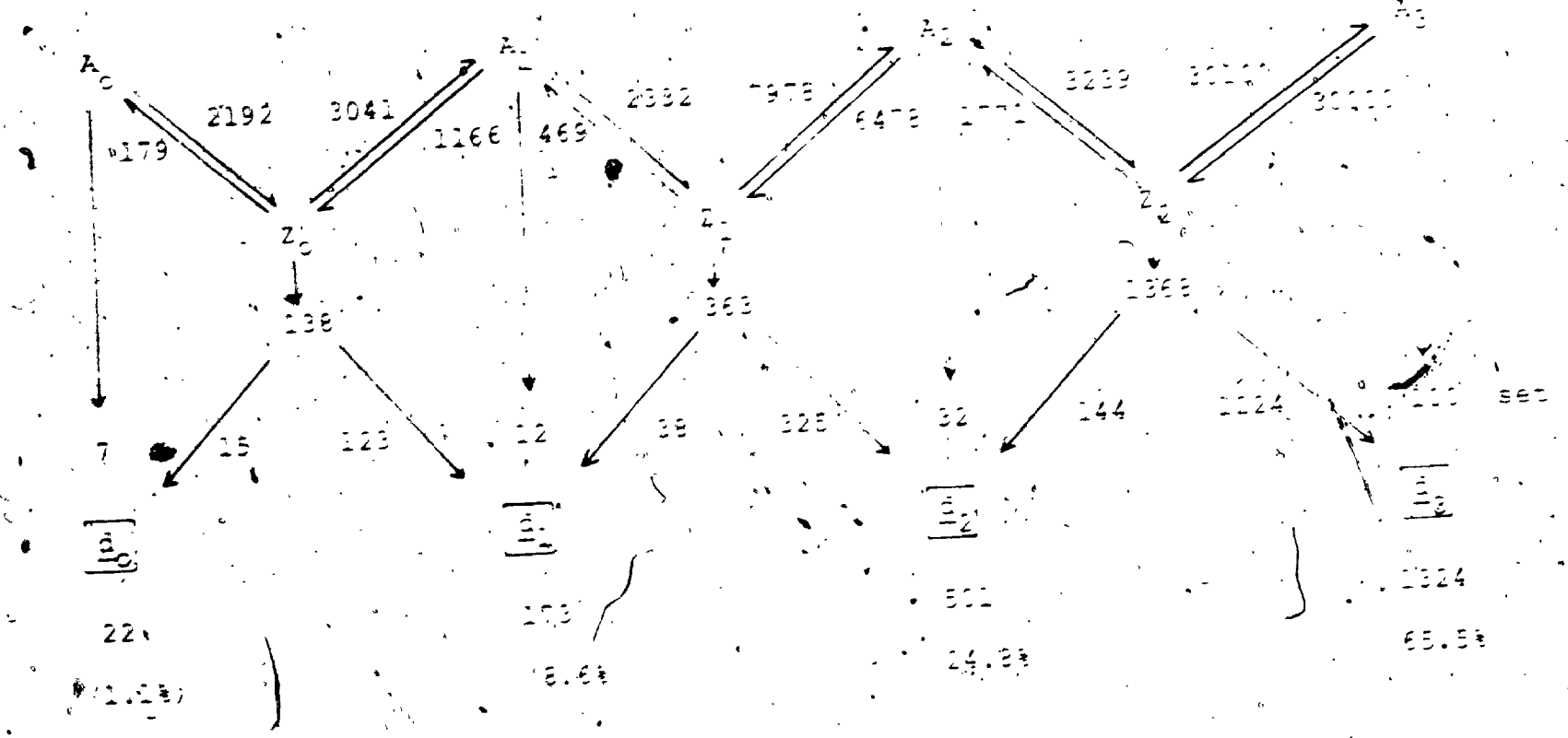
* A = sulfonylammonium ion, $CH_3SO_2\overset{+}{N}R_3$

Z = zwitterion, $\overset{-}{C}H_2SO_2\overset{+}{N}R_3$

$\underline{d}$ = product, CH_3SO_2OH or CH_3SO_2NH-Tol

FIGURE 9

Sample Calculation of Deuterium Distributions Derived from Simplified Multiexchange Reaction Scheme, Figure 5, for Deuterium Oxide Hydrolysis of the Trimethyl methylsulfonyl ammonium Salt*



* n = 17, k_e/k_1 = 22, k_{-e}/k_1 = 15

By setting the ratio k_{-e}/k_N, the number of molecules of A_3 going back to Z_2 (Figure 5) will be proportional to the number of A_3 molecules undergoing reaction to give $\underline{d}_3$. If the number of molecules of $\underline{d}_3$ being formed is 100 (arbitrarily), then the number of A_3 going back to Z_2 (that is, loss of a deuteron to give back the zwitterion) will be given by $3 \times (k_{-e}/k_N) \times 100 = 3 \times 100 \times 100 = 30{,}000$. The number 3 arises from the fact that A_3 has three deuterons, any one of which could be lost (that is, a statistical factor). If we assume that there is a steady-state concentration of A_3, then the amount of A_3 being formed from Z_2 must be equal to the amount of A_3 being consumed, or 30,000 + 100 = 30,100 molecules (Figure 6).

The number of molecules of Z_2 reacting to give sulfene-trapping products ($\underline{d}_2$ and $\underline{d}_3$) can be derived from the ratio $k_e/k_T = 22$. Thus, the number of molecules of product is $30{,}100/k_e/k_T = 30{,}100/22 = 1368$. Applying the deuterium isotope effect for sulfene trapping and $n = 17$ (the ratio of deuterium to hydrogen), these 1368 molecules can be proportioned to give 1224 molecules of $\underline{d}_3$ and 144 $\underline{d}_2$. Hence, the total number of molecules of $\underline{d}_3$ formed is 1324.

The number of Z_2 molecules which pick up a deuteron to give A_3 was determined to be 30,100. Hence, the number picking up a proton to give back A_2 is given by $30{,}100/n = 30{,}100/17 = 1771$. The number of A_2 molecules losing a

proton to give Z_2 will be equal to the total number of Z_2 being consumed, or 1771 + 1368 + 30,100 - 30,000 = 3239 (again assuming a steady-state condition for Z_2).

The number of A_2 molecules losing a deuteron to give back Z_1 will be twice the number of A_2 losing a proton to give Z_2 (since there are two deuterons but only one proton which can be lost from A_2, and assuming no isotope effect). Hence, $A_2 \rightarrow Z_1$ is given by $2 \times (A_2 \rightarrow Z_2) = 2 \times 3239 = 6478$. The number of A_2 reacting by displacement to give $\underline{d}_2$ can now be determined using the ratio for k_{-e}/k_N. Thus, $A_2 \rightarrow \underline{d}_2$ is $6478/2k_{-e}/k_N = 32$. (as before, the number 2 is a statistical factor arising from the fact that A_2 has two deuterons to be lost to generate Z_1).

Applying the steady-state approximation to A_2, the number of A_2 molecules being generated from Z_1 by picking up a deuteron will be equal to the number of A_2 molecules being consumed, or 6478 + 3239 + 32 - 1771 = 7978. The number of Z_1 being trapped (via sulfene) to give $\underline{d}_1$ and $\underline{d}_2$ can be calculated in an analogous manner to that used for Z_2. That is, $Z_1 \rightarrow (\underline{d}_1 + \underline{d}_2) = 7978/k_e/k_T = 7978/22 = 363$. Proportioning this between $\underline{d}_1$ and $\underline{d}_2$ gives $\underline{d}_1 = 38$ and $\underline{d}_2 = 325$. Hence, the total number of $\underline{d}_2$ molecules formed is 325 + 32 + 144 = 501.

The number of Z_1 molecules which picked up a deuteron to give A_2 was 7978, so the number of Z_1 picking up a proton to give back A_1 will be $7978/n = 7978/17 = 469$.

Furthermore, the number of A_1 losing a proton to give Z_1 will be equal to the number of Z_1 being consumed (the steady-state approximation again), or 469 + 363 + 7978 - 6478 = 2332.

The number of A_1 losing a deuteron to give back Z_o will be half the number losing a proton to give Z_1 (since there are two protons and only one deuteron which could be lost from A_1). Hence, $A_1 \rightarrow Z_o$ is given by 2332/2 = 1166. From this, the number of A_1 giving $\underline{d}_1$ by direct displacement can be calculated as $1166/k_{-e}/k_N = 1166/100 = 12$.

The number of A_1 being formed from Z_o will be the same as the number of A_1 being consumed (steady state), or 1166 + 12 + 2332 - 469 = 3041. The number of Z_o being trapped (via sulfene) to give $\underline{d}_o$ and $\underline{d}_1$ is given by $3041/k_e/k_T = 3041/22 = 138$ which can be proportioned to give $\underline{d}_o = 15$ and $\underline{d}_1 = 123$. The total number of $\underline{d}_1$ formed is thus 123 + 12 + 38 = 173.

The number of Z_o molecules which picked up a deuteron to give A_1 was 3041. Therefore, the number of Z_o picking up a proton to give A_o will be $3041/n = 3041/17 = 179$. As well, the number of A_o losing a proton to give Z_o will be equal to the number of Z_o being consumed (steady state), or 179 + 138 + 3041 - 1166 = 2192. Finally, the number of A_o reacting by direct displacement to give $\underline{d}_o$ will be $2192/3k_{-e}/k_N = 2192/300 = 7$. Thus, the total number of $\underline{d}_o$ molecules is 7 + 15 = 22.

The distribution of molecules is, therefore:

$\underline{d}_0$	22	(1.1%)
$\underline{d}_1$	173	(8.6%)
$\underline{d}_2$	501	(24.8%)
$\underline{d}_3$	1324	(65.5%)
Total	2020	(100 %)

The other calculations for the various salts were carried out in the same manner.

Comparison of Tables 12 and 15 shows moderate to good agreement between the experimental and calculated values for the deuterium distributions. In order to verify that the sulfene trapping or direct displacement reactions alone would not give as good a fit as the combined mechanisms, the calculations were also performed with either $k_N = 0$ (that is, sulfene trapping only) or $k_T = 0$ (direct displacement only). These results are given in Tables 16 and 17. Inspection of these calculated distributions confirms that neither sulfene trapping nor direct mechanisms alone can adequately generate the deuterium distributions observed experimentally using the simplified reaction scheme which has been proposed.

This simplified reaction scheme was also used to generate calculated deuterium distributions for the multi-exchange of mesyl chloride during deuterium oxide hydrolysis (Table 1). Some modifications were necessary since mesyl chloride reacts to give sulfene initially, some of which is trapped out before it can form the zwitterion. In order to

TABLE 15

Calculated Deuterium Distributions for Multiexchange in the Deuterium Oxide Hydrolysis of the Sulfonylammonium Salts

Salt	n	k_e/k_T	k_{-e}/k_N	Product Deuterium Distribution (%) d_o	d_1	d_2	d_3
1	17	22	100	1.1	8.6	24.8	65.5
2	18	15	60	1.6	11.5	26.4	60.5
3	18	12	14	3.6	15.5	28.6	52.4
4	24	2.5	7	7.5	39.3	32.5	20.7
	22	10	2.8	12.1	24.2	29.6	34.1*

* Multiexchange of the diethylmethylammonium salt (4) in the presence of $DNEt_2Me^+Cl^-$.

TABLE 16

Calculated Deuterium Distributions for Multiexchange in the Deuterium Oxide Hydrolysis of the Sulfonylammonium Salts Based on Sulfene Trapping ($k_N = 0$)

Salt	n	k_e/k_T	Product Deuterium Distribution (%) d_o	d_1	d_2	d_3
1	17	20	0.7	8.8	24.8	65.7
2	18	14	0.7	11.5	27.0	60.8
3	18	9	1.2	16.0	30.0	53.3
4	24	2	3.3	42.6	33.8	20.2
	22	4	2.3	28.3	33.5	36.0*

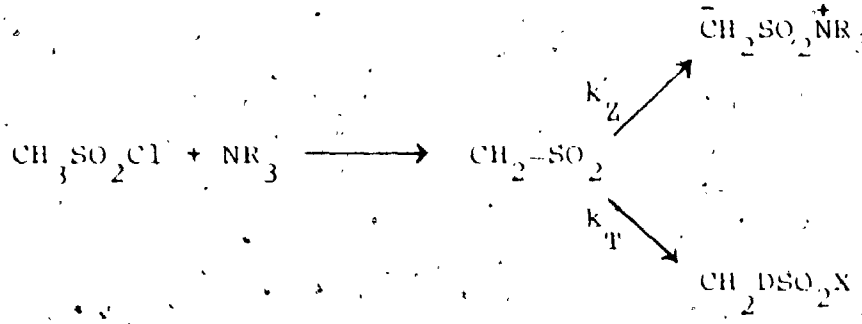
TABLE 17

Calculated Deuterium Distributions for Multiexchange in the Deuterium Oxide Hydrolysis of the Sulfonylammonium Salts Based on Direct Displacement ($k_T = 0$)

Salt	n	k_e/k_N	Product Deuterium Distribution (%) d_o	d_1	d_2	d_3
1	17	8	4.1	7.4	20.9	67.6
2	18	5	6.6	10.2	22.9	60.2
3	18	3	10.8	14.7	25.5	49.0
4	24	1	26.0	26.0	25.8	22.1
	22	1.5	19.2	21.4	26.9	32.5*

* Multiexchange of the diethylmethylammonium salt (4) in the presence of $DNEt_2Me^+Cl^-$

account for this, another parameter was defined, namely k_Z/k_T (rate of zwitterion formation/rate of sulfene trapping):



As well, since the initial concentration of protium in the active deuterium pool was very low when this initial sulfene trapping process was occurring, the initial ratio of active deuterium to active hydrogen, n_0, was set at 110 (corresponding to 1% hydrogen). The deuterium distribution for the fraction of the sulfene which was trapped by amine to give the zwitterion was then calculated according to the scheme (Figures 5 and 6) and the results are given in Table 18.

The agreement between the calculated distributions in Table 18 and the experimental results in Table 1 are excellent, suggesting that methanesulfonyl chloride also undergoes base-catalyzed hydrolysis according to the proposed reaction scheme for the sulfonylammonium salts. It is interesting to observe that the ratio k_Z/k_T falls progressively as the steric size of the base increases, as do the ratios k_e/k_T and k_{-e}/k_N. These are precisely the

TABLE 18

Calculated Deuterium Distributions for Multiexchange in the Deuterium Oxide Hydrolysis of Methanesulfonyl Chloride

Base	n*	k_Z/k_T	k_e/k_T	k_{-e}/k_N	Product Deuterium Distribution (%) d_0	d_1	d_2	d_3
NMe_3	20	6	12	35	1.8	26.0	23.3	48.8
$NEtMe_2$	31	1	2	5	4.9	71.5	15.6	8.1
NEt_2Me	36	0.17	1.5	1	4.8	91.9	2.6	0.7

* $n_0 = 110$ (see text).

trends predicted by the theory of zwitterion formation and stability proposed by King, Lainstra and Harding.

The calculated deuterium distributions for the products of the reaction of the salts with p-toluidine-N,N-d$_2$ are summarized in Table 19. As well, the results of the calculations based on sultene trapping or direct displacement only are listed in Tables 20 and 21 respectively. Comparison of the results with the experimental data (Table 14) again shows moderate to good agreement for the distributions calculated from the combined sultene trapping and direct displacement mechanisms. The calculations based on sultene trapping or direct displacements alone did not give a consistent correlation with the experimental data for all the salts.

In light of the simplifications and assumptions which have been made, the combined mechanisms of sultene trapping and direct displacement have provided a good semi-quantitative correlation between calculated and experimental results for the multiexchange phenomena observed for the sulfonylammonium salts. Neither sultene trapping nor direct displacement alone accounted for the deuterium distributions of the products observed experimentally.

Rapid formation of a two-phase system during the multi-exchange reactions of the salts in D$_2$O-DME was also observed with methanesulfonyl chloride (5). This phenomenon is apparently a salting-out effect by which water molecules

TABLE 19

Calculated Deuterium Distributions for the Reaction of the Sulfonylammonium Salts with p-Toluidine-N-S_2 *

Salt	n	k_c/k_π	k_{-c}/k_N	Product Deuterium Distribution (%) d_4	d_3	d_2	d_1
1	3.2	100	5	11.5	22.1	37.5	29.3
2	3.3	50	4	12.6	24.1	35.4	27.1
3	4.5	13	2	21.6	29.6	30.3	18.5
4	5.7	2	1.1	33.6	41.7	19.4	5.3
	15.4	0.8	1.1	29.3	53.1	15.2	2.5

* Large excess of p-toluidine-N-S_2 used.

TABLE 20

Calculated Deuterium Distributions for the Reaction of the Sulfonylammonium Salts with p-Toluidine-N-d_2 Based on Sulfonic Trapping ($k_N = 0$)*

Salt	n	k_o	k_p	Product Deuterium Distribution (%) d_0	d_1	d_2	d_3
1	1.2	15		5.6	24.8	41.9	28.7
2	1.1	10		6.9	25.8	40.8	26.6
3	4.0	5		9.1	30.7	36.9	23.3
4	5.7	1		15.9	52.9	24.6	6.6
	15.4	1		6.9	56.9	27.6	8.6

TABLE 21

Calculated Deuterium Distributions for the Reaction of the Sulfonylammonium Salts with p-Toluidine-N-d_2 Based on Direct Displacement ($k_{sp} = 0$)

Salt	n	k_{-a}	k_N	Product Deuterium Distribution (%) d_0	d_1	d_2	d_3
1	1.2	5.5		9.4	20.3	38.1	32.3
2	1.1	3.3		11.7	21.3	35.6	27.4
3	4.0	1.6		22.5	27.2	30.4	19.9
4	5.7	1.0		29.4	29.1	26.2	15.4
	15.4	0.1		54.5	29.4	12.7	3.4*

* Large excess of p-toluidine-N-d_2 used.

cluster around and solvate the salts (and zwitterions). As a result, the aggregated water molecules and entrained salts are forced out of DME solution, forming a heavier aqueous layer. It would appear, then, that the salts (and zwitterions) with their solvating shells, have a much higher local concentration of active deuterium compared to the solution as a whole. Furthermore, when the solution separates into two phases, the salts are then surrounded by almost pure water with very little DME present. The effect of this on the extent of exchange of the salts is difficult to assess, although it would be expected that an increase in deuterium concentration would enhance the multiexchange process. Another effect which cannot be assessed is a possible difference in solubility between D_2O and H_2O in DME which could affect the local concentration of active hydrogen and deuterium around the salts. However, since the exchange behavior of the salts in D_2O/DME closely parallels that of methanesulfonyl chloride, it is most likely that the same effects (if any) are operating in both cases so that a comparison of the salts with methanesulfonyl chloride is indeed valid.

It must be emphasized that these calculations were not intended to exclude all other multiexchange mechanisms, but rather to demonstrate that the proposed mechanism is consistent with the experimental results. Application of the mechanistic scheme to methanesulfonyl chloride resulted

an excellent correlation between calculated and experimental data providing further evidence for the intermediacy of the sulfonylammonium ion and zwitterion in the multiexchange reactions of methanesulfonyl chloride.

conclusions

Four methylsulfonylammonium fluorosulfonate salts have been synthesized and characterized. Thus, the synthesis of sulfonylammonium salts has been extended from the aromatic species to alkyl derivatives by taking advantage of small N-alkyl groups and a non-nucleophilic anion.

The salts have been found to be highly reactive and effective mesylating reagents, apparently superior under mild conditions to the more common mesylating reagents. Because they react in the presence of only catalytic amounts of mild bases, the salts will no doubt be found very useful for the mesylation of base-sensitive compounds or for the formation of reactive mesylates.

The salts have also been found to undergo extensive multiexchange in reaction with active deuterium sources such as deuterium oxide or deuterated p-toluidine, paralleling results observed for methanesulfonyl chloride under identical conditions. These results provide strong evidence for the intermediacy of the sulfonylammonium ion and zwitterion in the multiexchange reactions observed for alkanesulfonyl chlorides. Because they undergo almost complete multiexchange in the presence of a large excess of deuterium oxide, the salts provide a good synthetic route to trideuterated methanesulfonyl derivatives.

The mechanism of reaction of the salts is not fully understood. They appear to react both as sulfene sources

and zwitterion sources and are capable of undergoing nucleophilic displacement. Semi-quantitative calculations based on the proposed reaction mechanism suggest that formation of multiexchanged products with both deuterium oxide and deuterated p-toluidine proceeds by both the sulfene mechanism and the direct displacement route simultaneously.

This introduction into the chemistry of methylsulfonylammonium salts has proven both interesting and revealing. However, as with any new organic species, there remains much to be determined about these compounds, about their potential as synthetic reagents and about their reaction mechanisms. Hopefully, this dissertation will serve as a basis for further experimentation and discussion.

CHAPTER II

α-Hydrogen Exchange in 1,3-Dihydrobenzo[c]thiophene 2-Oxide

Introduction

Sulfoxides possess a tetrahedral geometry with a high barrier to inversion (35-42 kcal/mol (32)) and are therefore, potentially optically active if asymmetrically substituted (33). Thus, the hydrogens of an α-sulfinyl methylene group, RCH_2SOR', are diastereotopic* and, hence, may vary in reactivity. For example, α-sulfinyl methylene hydrogens vary significantly in kinetic acidity (34-38, 40-53).

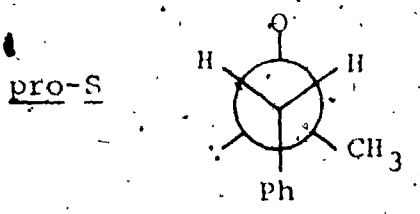
The first experimental evidence for this was observed by Cram and Pine (34) in 1963. Both the rate and stereochemistry of exchange of the α-sulfinyl hydrogen of 2-octyl phenyl sulfoxide were affected by the stereochemistry at sulfur. The exchange was carried out with t-butoxide in t-butyl alcohol and the asymmetric induction effects were more pronounced in dimethyl sulfoxide solution. It was thought at this time that asymmetric solvation was responsible for the inductive effects.

Shortly thereafter, Wolfe and coworkers (35) reported that the methylene protons of benzyl methyl sulfoxide exchanged at different rates in $NaOD/D_2O$. At 15°, the rate

---

* Two hydrogens (or other groups) are diastereotopic if substitution of one of them gives rise to a diastereomeric molecule.

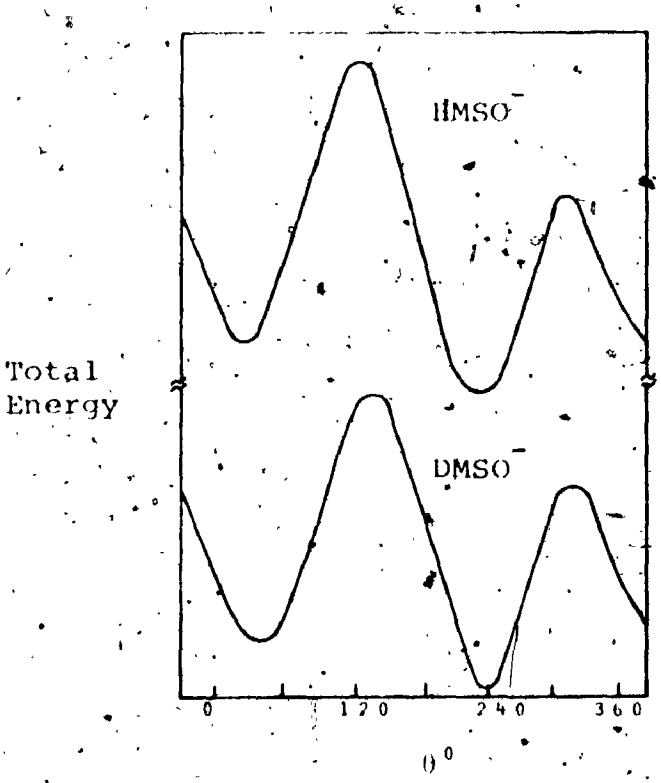
ratio for these diastereotopic protons was almost 14:1. From exchange studies with S-benzyl methyl sulfoxide, Baldwin showed that the pro-R hydrogens were exchanging more rapidly than pro-S (36). This assignment was opposite to that which had been determined by Wolfe and Rauk (37), but was confirmed by independent synthesis of the chiral exchanged products:

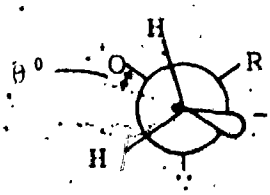


S-Benzyl Methyl Sulfoxide

In an attempt to formulate a predictive theoretical description of α-sulfinyl carbanion stability, Rauk, Wolfe and Csizmadia (38) presented extensive, non-empirical LCAO-MO-SCF calculations of the gas-phase stability of the hypothetical hydrogen methylsulfinyl carbanion, $HSOCH_2^-$, and the dimethylsulfinyl carbanion, $CH_3SOCH_2^-$. These calculations specifically omitted solvation and other external effects and indicated that α-sulfinyl carbanions were intrinsically asymmetric, pyramidal and most stable in a conformation in which the electron pair lies along the bisector of the oxygen : sulfur : lone pair angle (Figure 7). This conformation maximizes the number of gauche interactions between the adjacent lone pairs and polar bonds (the so-called "gauche effect" (39)).

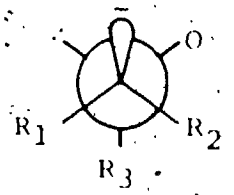
FIGURE 7





Total Energies of $HMSO^-$ and $DMSO^-$ as a Function of Rotation about the C-S Bond*

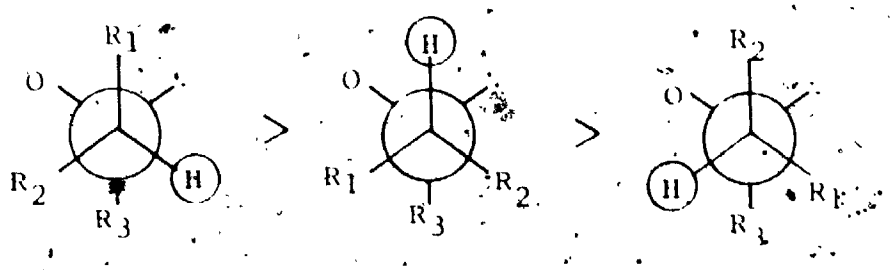
* From reference 38.



Gauche Conformation

It was also postulated by these authors that the stereochemistry of proton abstraction from an α-sulfinyl carbon would be dependant upon the stability of the resulting α-sulfinyl carbanion, assuming a carbanion-like transition state for abstraction. In other words, a proton would be abstracted so as to give directly the most stable carbanion configuration. Moreover, if there were two protons which could be abstracted, the one which would lead to the most stable carbanion configuration would be abstracted preferentially. Thus, the kinetic acidities of α-sulfinyl protons were correlated with α-sulfinyl carbanion stabilities.

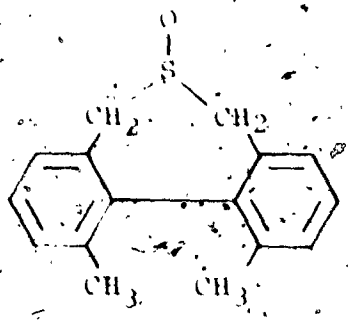
A number of studies were initiated by various workers to provide experimental evidence relevant to the Rauk-Wolfe-Csizmadia calculations. The results in protic media appeared to be at odds with the calculations. Studies by Hutchinson, Andersen and Katritzky (40) on the α-sulfinyl exchange rates of cis- and trans-4-phenyltetrahydrothiopyran 1-oxide indicated the following order of preference of proton abstraction:



The media used for these studies were water (hydroxide), methanol (methoxide), t-butyl alcohol (t-butoxide) and DMSO-methanol (methoxide). There was no stereoselectivity of exchange in t-butyl alcohol or DMSO and this was attributed to fast carbanion inversion in the absence of stabilization by solvation. This order of acidity was also deduced by Marquet and coworkers (41).

Exchange studies by Fraser (42) on a rigid, cyclic sulfoxide and by Nishio (43) on an acyclic sulfoxide appeared to be in agreement with the Rauk-Wolfe-Csizmadia calculations. However, in both cases, reinvestigations by the same researchers resulted in reversals of the conclusions (44,45). The stereochemistries of exchange were opposite to those predicted on the basis of the calculated carbanion stabilities. For the cyclic sulfoxide studied by Fraser, rate differences as high as 1250:1 were found for α-sulfinyl hydrogens differing only in their conformation with respect to the sulfinyl group. The medium used was t-butyl alcohol/t-butoxide. The sulfoxide, shown below, has four diastereotopic α-sulfinyl protons with rate ratios 1:1100:310:1250. Both the slowest and the second-fastest exchanging protons lie

close to the energy minimum predicted by the calculations. However, the fastest exchanging proton lies "gauche" to the S=O bond and trans to the lone pair. This carbanion conformation is also opposite to that shown by Hutchinson, et al. (40), to be the most rapidly exchanging (see above).



A significant study into the effect of solvation upon sulfinyl hydrogen exchange was made by Durst, Fraser and coworkers (46). Their experiments with benzyl methyl sulfoxide indicated that in protic, polar media such as D_2O or CH_3OD, the pro-R hydrogen (S at sulfur, see above) exchanges more rapidly than the pro-S hydrogen, while in protic apolar media (for example, t-BuOD), the pro-S hydrogen exchanges faster. Similar results were obtained when benzyl methyl sulfoxide was treated with alkyllithium followed by quenching with D_2O. In the polar solvent (DMSO), the stereochemistry of exchange was opposite to that observed in non-polar solvents (benzene, tetrahydrofuran (THF)). The necessary conclusion of this work was that solvation was an important factor in the determination of proton abstraction. Similar results were observed by

Nishihata and Nishio (45) regarding the reactivity of benzyl t-butyl sulfoxide towards n-butyllithium in THF.

Subsequent investigations by Durst, Viau and McClory (46-48) have provided further evidence for stereoselectivity of α-lithiation of benzyl methyl and benzyl t-butyl sulfoxides in THF solution. The stereoselectivity observed for the t-butyl sulfoxide was greater than for benzyl methyl sulfoxide, which was attributed to the greater steric requirements of the t-butyl group and resulting decreased conformational mobility of this sulfoxide. It was also shown that the lithio salts reacted with deuterium oxide or electrophiles such as ketones with retention but reacted with methyl iodide with inversion of configuration. The reason for this anomaly is not clear. It was concluded that the reaction of these sulfoxides with alkyllithium in THF corresponded to the Rauk-Wolfe-Csizmadia calculations possibly because non-polar solvents such as THF better approximate gas-phase conditions than do polar solvents.

Sulfoxide lithiation studies by Nishihata and Nishio (49) gave similar results to those of Durst, above. However, they concluded that the stereospecificity of proton abstraction was of little consequence because the carbanion undergoes rapid equilibration by inversion to give the most stable configuration before quenching. Similarly, exchange studies of methyl 1-phenylethyl sulfoxide in aqueous medium have led D'Amore and Brauman (50) to the conclusion that

α-sulfinyl carbanions are either rapidly inverting pyramidal species or essentially planar. Their experiments on lithiation and quenching of benzyl methyl sulfoxide indicate that this process occurs with inversion, which is contrary to previous conclusions. They indicate as well that the pro R hydrogen is preferentially removed by alkyl lithium, in agreement with Nishio (49), but contrary to Durst (48).

From a study of the stereochemistry of exchange of a third, bicyclic sulfoxide, Fraser and coworkers (50) concluded that in protic medium, the α-sulfinyl carbanion decreases in stability as it approaches an eclipsing situation with the lone pair on sulfur. The proton cis to the C-S bond was abstracted at least 250 times faster than the proton cis to the sulfur lone pair. The exchange reactions proceeded with retention of configuration, a necessary requirement for a stereoselective exchange process in which there is a significant rate difference between exchanging protons. The rates of proton abstraction observed in this study showed no correlation with Hückel-Coulson calculations, and this was attributed to steric solvation effects. It was argued, however, that the rates of proton abstraction did provide a valid method of determining relative carbanion stabilities based on the retention of configuration observed during the exchange reaction. However, since nothing is known about the rate

of the conformation of the carbanion (or lithio salt) between the proton abstraction and quenching steps. This argument does not appear to be justified by experimental evidence.

Bolli and coworkers (42) have repeated the work of Fraser et al., with 2-thiabicyclo[2.2.1]heptane 2-oxides and have produced kinetic data for the α sulfinyl exchange reactions qualitatively in agreement with those of Fraser and coworkers. For the exo sulfoxide, H_x was exchanged 3

2-thiabicyclo[2.2.1]heptane 2-oxide

times faster than H_n (Fraser's value is 1.5) (41). For the endo sulfoxide, H_n was exchanged 8 times faster than H_x (Fraser's value is 2.5) respectively (41). Bolli has concluded that H_x is abstracted preferentially from the exo sulfoxide and that the resulting carbanion is reprotonated with retention. However, with endo sulfoxide, abstraction of H_x (stereochemically favored) gives rise to a carbanion which undergoes inversion followed by endo reprotonation. On the other hand, abstraction and reprotonation of H_n (stereochemically favored) proceeds with retention. When treated

with n-butyllithium (THF) followed by D_2O quenching, the endo sulfoxide decomposed while the exo sulfoxide was deuteriated in the exo position. In both media, the results were in contradiction of those predicted by the Rauk-Wolfe-Csizmadia calculations.

Pollet and coworkers[69] have also studied the exchange behaviour of 2H naphtho[1,8-b,c]thiophene 2-oxide (shown below). The exchange rates for H_1 and H_3 in CH_3OD-CH_3ONa

2H Naphtho[1,8-b,c]thiophene 2-Oxide

were in the ratio 1:9.1. Pollet argues in favour of an exchange mechanism with net inversion, even though, as shown by exchange studies of the 2-sulfinyl methyl analogue of this sulfoxide (H_1 or H_3 - CH_3), the proton adjacent to the lone pair is kinetically more acidic than the proton adjacent to the sulfinyl oxygen. This is opposite to the results observed with 2-thiabicyclo[2.2.1]heptane 2-oxide (above).

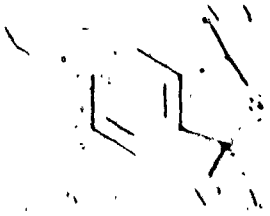
Recently, Durst and Nolin[70] have demonstrated that the stereochemistry of 2-sulfinyl proton exchange in benzyl methyl and benzyl ethyl sulfoxides via the lithio salts is

affected by the source of the methyllithium used (that is, prepared for methyl bromide vs. methyl iodide), by the presence of lithium halide salts in the reaction solution, and even the nature of the base (methyllithium vs. n-butyllithium). They caution that because of the great sensitivity of these reactions to often unexpected and seemingly unimportant differences in reaction conditions (such as methyllithium purchased from two different sources), great care should be taken when comparing results obtained from different laboratories.

It can be seen from these examples that the study of a sulfinyl carbanion stereochemistry and stability has led neither to firm conclusions nor to predictive theory. In an effort to contribute to the development of a truly predictive theoretical description of a sulfinyl carbanion formation, stability and reactivity, the exchange behavior of 5,5-dihydrobenzo[c]thiophene 2-oxide, a cyclic sulfoxide with significant stereochemical features, has been examined. The results of those investigations are presented in the following section.

Results and Discussion

The sulfoxide 4,5-dihydrothieno[c]thiophene-2-oxide, (5) was synthesized from the corresponding sulfide (54) by periodate oxidation. In the n.m.r. spectrum of 5a (CDCl$_3$), the diastereotopic methylene protons absorbed as an AB quartet, ν_A 4.13 and ν_B 4.38 p.p.m. (J_{AB} 16 Hz). The four aromatic protons (7.3 - 7.6 p.p.m.) provided an internal standard for quantitative study of the exchange behaviour of this sulfoxide.



a	X	X'	Y	Y'	H
b	X	Y	H,	X'	D
c	X	Y	D,	X'	H
d	X (or X')	D,	Y	Y'	X'' (or X) = H
e	X (or X')	H,	X	Y'	X'' (or X) = D
f	X = X'	Y	Y'	D	

On treatment of 5a with NaOD in D_2O, the AB quartet was rapidly replaced by a 1:1:1 triplet at ν 4.12 p.p.m. (J_{HD} 2.2 Hz), increasing to almost half the area of the original quartet. This triplet then gradually disappeared. Apparently, the lower field protons exchanged rapidly followed by much slower exchange of the epimeric hydrogens. N.m.r. shift reagents were used to determine the configuration of the two sets of epimeric hydrogens (55).

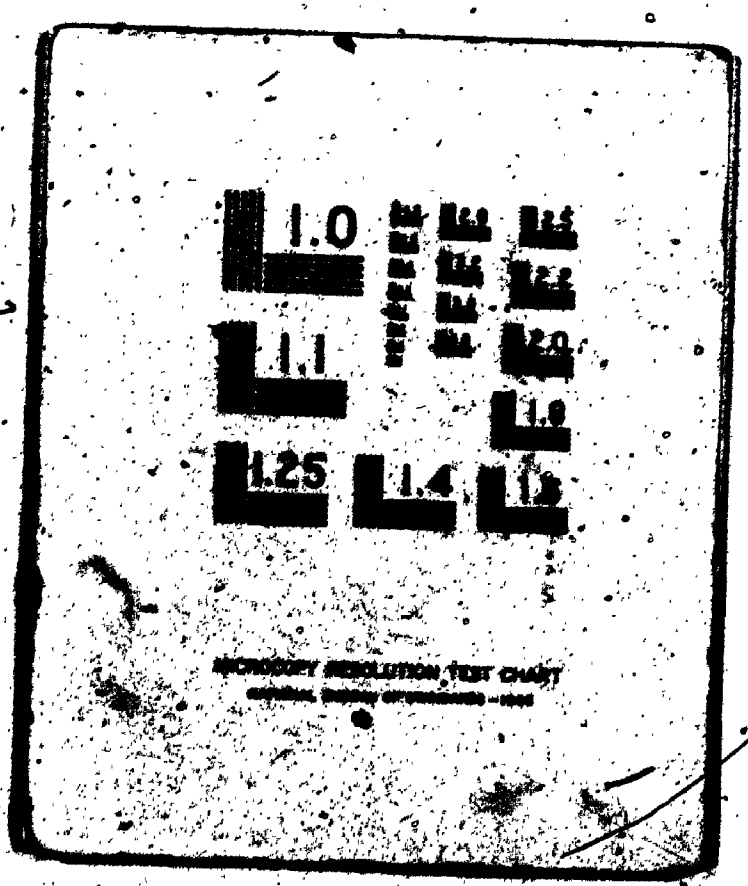
Addition of tris(dpm) shift reagent (0.1 equivalents) to the solution of 5a resulted in a very strong downfield shift of the higher field signal to δ_A 0.90 ppm and a weaker shift of the lower field signal to δ_B 0.71 ppm. Similarly, on addition of shift reagent to the partially exchanged sulfoxide, the 1:1:1 triplet was shifted downfield to δ 0.85 ppm. Thus, the lower field protons, which exchanged more rapidly in NaOD/D_2O, were trans to the oxygen and cis to the lone pair on sulfur, while the slower exchanging protons were cis to the oxygen and trans to the lone pair. Hence, the structure of the partially exchanged sulfoxide (dideuterated) is 5b.

The exchange rates for the two equivalent sets of hydrogens were measured by quantitative n.m.r. studies. The pseudo-first order rate constants for the exchange in 0.1 N NaOD in D_2O at 5° were k_{trans} = 2.2 x 10^{-5} s^{-1} and k_{cis} = 1.1 x 10^{-5} s^{-1}; k_{trans}/k_{cis} = 2. Exchange of the benzylic hydrogens of benzyl methyl sulfoxide was studied under the same conditions and the pseudo first-order rate constants were determined to be k_1 = 1.1 x 10^{-6} s^{-1} and k_2 = 1.4 x 10^{-6} s^{-1}, k_1/k_2 = 2.2. The rate for the faster exchanging proton of benzyl methyl sulfoxide was slightly slower than for the slower exchanging protons of 5a.

Treatment of 5a with methyllithium in THF at 0° followed by rapid quenching of the resulting lithio salt with 0.1 N D_2O resulted in the uptake of one deuterium atom

2 2

OF/DE



cis to the oxygen to give 5d. Although it was obvious that the exchange of 5a in NaOD/D_2O was proceeding with retention (since there would be no rate difference between the cis and trans hydrogens for deuterium uptake with inversion apart from very small differences due to secondary deuterium isotope effects), this quenching experiment gives no information about the stereochemistry of proton abstraction.

In order to clarify this, sulfoxides 5b, 5c and 5f were prepared. Exchange of 5a in 0.1 N NaOD in D_2O at 0° for 1 hour gave 5b, while exchange of 5a in 0.1 N NaOD in D_2O at 50° for 1 hour gave 5f. Treatment of 5f with 0.1 N NaOH (aqueous) at 0° for 3 hours gave 5c. These sulfoxides were then treated with methyllithium in THF and quenched with either DCl or HCl. The products were isolated, purified and examined by n.m.r., mass spectrometry and deuterium analysis to determine the extent and stereochemistry of isotopic exchange. The results, shown in Table 22, indicate clearly that both proton abstraction and lithio salt quenching proceed with same stereochemistry, namely cis to the oxygen. Thus, the lithio salt of 5b on quenching with DCl gave 5e while on quenching with HCl gave back 5b. Similarly, quenching of the 5c lithio salt with HCl gave back 5d, while quenching with DCl gave back 5c.

Inspection of Table 22 reveals evidence of multi-exchange in the lithiation and quenching reactions. For

TABLE 22

α-Exchange of 1,3-Dihydrobenzo[c]thiophene 2-Oxide via the Lithio Salt

Starting material			Product		Change in deuterium content (atom % D)			
Structure	Isotopic composition (%)	Quenching acid*	Structure	Isotopic composition (%)	From mass spectrum	From D analysis	From n.m.r.	Stereochemistry of exchange (from n.m.r.)
5a	d_0 100	DCl	5d	d_0 14.7 d_1 71.7 d_2 12.8 d_3 0.2 d_4 0.5	12.5 increase	12.3 increase	13.7 increase	cis (88%) trans (12%)
5b	d_0 0 d_1 6.0 d_2 79.0 d_3 12.6 d_4 2.4	DCl	5e	d_0 0 d_1 3.1 d_2 11.3 d_3 62.2 d_4 23.3	11.7 increase	10.6 increase	11.9 increase	cis†
5c	d_0 0 d_1 10.6 d_2 71.6 d_3 12.6 d_4 5.1	HCl	5d	d_0 11.9 d_1 63.6 d_2 20.8 d_3 2.8 d_4 0.8	12.0 decrease	11.3 decrease	10.7 decrease	cis†
5f	d_0 0 d_1 0 d_2 0 d_3 5.3 d_4 94.6	HCl	5e	d_0 0 d_1 0 d_2 17.9 d_3 77.0 d_4 5.1	12.7 decrease	13.4 decrease	13.9 decrease	cis (93%) trans (7%)

* The lithio derivatives of 5a and 5b were also quenched with HCl, and those of 5c and 5f with DCl. The product was in each case indistinguishable from starting material except with 5c (and DCl), which showed a slight increase (2.5% by n.m.r., 1.5% by deuterium analysis) in the amount of deuterium; the apparently exceptional behaviour of 5c probably arises from the presence of a significant proportion of cis hydrogens in the starting material (note particularly the relatively high proportion of d_1 sulfoxide).

† The n.m.r. spectra show the cis exchange to be much the more important, but do not appear to warrant a more quantitative interpretation.

example, in the formation of 5d from 5a, dideuterated product was also formed (12.8%) along with traces of tri- and tetradeuterated products. Treatment of 5a with 2 equivalents of methyllithium (instead of the 1.1 used in the experiments summarized in Table 22) followed by DCl quenching gave a product in which about 1.5 hydrogens per molecule were exchanged. Experiments in which the quenching acid was added at different rates or different stirring rates gave essentially the same result, which would indicate that multiexchanged products probably arose by reaction of a single sulfoxide molecule with more than one molecule of methyllithium rather than by base-catalyzed exchange in the aqueous medium during quenching.

The reaction of 5f with the lithio salt of 5a for 10 minutes prior to HCl quenching resulted in a product whose n.m.r. spectrum showed peaks due to CH_2 and CHD of roughly equal intensity, indicating intermolecular hydrogen scrambling. This scrambling was almost completely suppressed when the contact time between 5a lithio salt and 5f before quenching was reduced to a few seconds (corresponding to the conditions used to generate the data in Table 22). Rapid quenching was also found to result in higher yields of a cleaner product, which was more readily purified and recrystallized. When the lithio salt of 5a was quenched after 10 minutes (DCl), the product composition was essentially the same as that from rapid quenching.

As noted above, sulfoxide 5 exchanged more rapidly than benzyl methyl sulfoxide in aqueous medium. It was also determined that 5 is more reactive towards methyllithium than benzyl methyl sulfoxide. Thus, when 5a (1 mmol) and benzyl methyl sulfoxide (2 mmol) were treated with methyllithium (2 mmol) followed by DCl quenching, the n.m.r. spectrum of the product indicated that 5 was extensively exchanged, whereas the benzyl methyl sulfoxide was almost unchanged. The ratio of deuterium incorporation for 5a vs. benzyl methyl sulfoxide was estimated to be 11 to 1.

Although the geometry of 5 is not precisely known, a fully planar molecule would give the dihedral angles for the hydrogens cis and trans to the oxygen of 0° and 120° respectively. While these eclipsing interactions may lead to some distortion from full planarity, the resulting dihedral angles would not be expected to vary beyond ± 30° and, hence, the Klyne-Prelog descriptors syn-periplanar and anti-clinal (56) for cis and trans respectively are applicable here. However, for simplicity, the terms cis and trans are used herein to describe the relationships of the appropriate hydrogens to the sulfinyl oxygen.

In terms of the Rauk-Wolfe-Csizmadia calculations (Figure 7), the configuration of the cis carbanion of 5 corresponds to $\theta \approx 180^{\circ}$ while the trans carbanion configuration has $\theta \approx 300^{\circ}$. In other words, the trans (anti-clinal) anion lies close to the calculated lower energy maximum. From Figure 7, we would predict that the

trans-anion would be formed preferentially to the cis-anion for 5. In fact, this is the case observed for 5 in aqueous medium. However, in THF with methyllithium, the opposite stereochemistry is observed.

Changes in the stereochemistry of α-sulfinyl proton abstraction with changes in solvent have also been observed by Hutchinson (40) and Durst and Fraser (46). However, observations by Viau and Durst (48) with benzyl t-butyl sulfoxide suggest that stereochemistry of exchange in THF corresponds more closely to the calculations than in polar solvents. They concluded that THF more closely approximates gas-phase conditions than do polar solvents. This contradicts our observations with 5.

The stereochemistry of exchange of 5 in aqueous medium corresponds to the results obtained by Folli (52) for 2H-naphtho[1,8-b,c]thiophene 2-oxide in methanol solution. These two compounds have very similar structures and this is apparently reflected in their parallel exchange behaviour in polar, protic media. However, the stereochemical results observed for these systems is opposite to those observed for 2-thiabicyclo[2.2.1]heptane 2-oxide in methanol-methoxide solution (where the α-protons cis to the sulfinyl oxygen were preferentially exchanged) (51,52). It is obvious from these results that the stereochemistry of α-sulfinyl hydrogen exchange is very sensitive to the structure of the substrate, making the prospects for a

predictive theory more remote without more precise knowledge of molecular geometries and their effect on the exchange mechanism.

In theory, an acyclic sulfoxide should be able to orient itself into the most stable conformation such that proton abstraction by base would lead to the most stable conformation of the resulting α-sulfinyl carbanion. However, it was found that benzyl methyl sulfoxide in both the aqueous and non-polar media was slower to react than the more rigid, cyclic sulfoxide 5, even though 5 is not able to orient itself in the most stable conformation for α-sulfinyl carbanions predicted by the calculations.

It is apparent by these experiments and those performed by other workers that solvation and other effects of the medium cannot be excluded when discussing the stability of α-sulfinyl carbanions. A change in the stereochemistry of exchange observed for 5 by a change in solvent and base indicate that conformation alone cannot determine the kinetic acidity of α-sulfinyl hydrogens and that theoretical calculations of α-sulfinyl carbanion stability based on conformational effects alone are not in themselves sufficient to enable prediction of the ease of formation of these carbanions. The factors which appear to affect carbanion stability include solvent polarity, protic vs. aprotic solvents, sulfoxide structure, base, cation, and even the source of the base (53), in addition to conformational

effects. Because they omit solvation and other external factors, the Rauk-Wolfe-Csizmadia calculations cannot provide a truly predictive theory of the stereochemistry of α-sulfinyl carbanion formation in solution.

Conclusions

Examination of α-sulfinyl hydrogen exchange in 1,3-dihydrobenzo[c]thiophene 2-oxide (5) has shown that the hydrogens trans to the sulfinyl oxygen exchange 67 times faster than the cis hydrogens in NaOD/D$_2$O solution at 5°. Furthermore, the cis hydrogens exchange faster than the faster-exchanging benzylic hydrogen of benzyl methyl sulfoxide.

Treatment of 5 with methyllithium followed by rapid quenching with DCl gave predominantly the cis-monodeuterated product. It was also shown that proton removal in the lithiation step involves the loss of the cis hydrogen. Thus, the exchange reactions of 5 in both polar and non-polar media proceed with overall retention of configuration. In direct competition of reactivity towards methyllithium, 5 was lithiated 11 times faster than benzyl methyl sulfoxide.

The Rauk-Wolfe-Csizmadia noempirical calculations of α-sulfinyl carbanion stability specifically omit solvation and other external factors and as such the change in the stereochemistry of exchange observed for 5 in going from a polar, protic solvent to a non-polar solvent is not predicted by these calculations. Furthermore, the faster reaction rates for 5 in both solvents compared to benzyl methyl sulfoxide is contrary to expectation based on the calculations. The acyclic sulfoxide should be able to

adopt the most stable conformation for the α-sulfinyl carbanion being generated whereas the more rigid, cyclic sulfoxide is essentially fixed in an apparently less stable conformation.

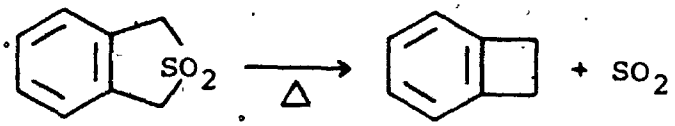
It is concluded, therefore, that calculations such as those of Rauk, Wolfe and Csizmadia which ignore solvation and other external effects cannot adequately predict the stereochemistry of formation of α-sulfinyl carbanions in solution.

CHAPTER III

The Steric Course of the Formation of Benzocyclobutene by Thermal Desulfonylation of 1,3-Dihydrobenzo[c]-thiophene 2,2-Dioxide

Introduction

Thermal desulfonylation of 1,3-dihydrobenzo[c]thiophene 2,2-dioxide (6) as a synthetic route to benzocyclobutene (7) was first reported by Cava and Deana (57). By analogy with

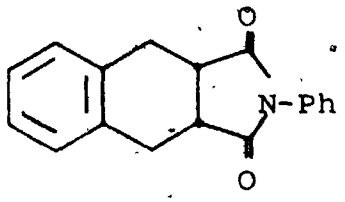


6 7

the thermal desulfonylation of 2,5-dihydrothiophene 1,1-dioxide (58), o-quinodimethane (8) was believed to be an intermediate in this reaction, although the formation of condensed dimers of 8 and o-xylene suggested that a biradical species may also have been present along with 8.

8

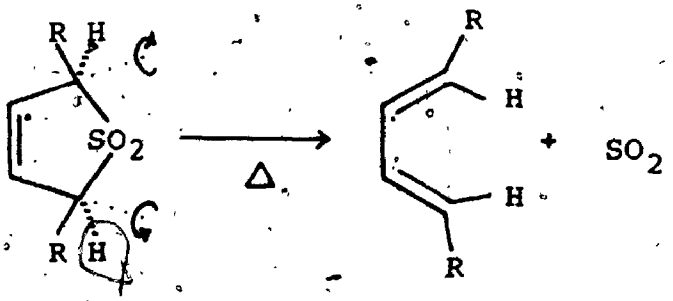
Evidence for the formation of 8 came from trapping experiments in which the desulfonylation of 6 was conducted in the melt with N-phenylmaleimide. The cycloadduct (9) was formed in 78% yield.



9

However, it was later shown by Alder and Fremery (59) and Jensen, Coleman and Berlin (60) that cycloaddition products of o-quinodimethane could also be formed from benzocyclobutene. Thus, cycloadduct formation is inconclusive evidence for the intermediacy of o-quinodimethane in the conversion of 6 to 7. It was also shown in this latter paper that the desulfonylation of 6 was reversible.

Experiments on the thermal desulfonylation of substituted 2,5-dihydrothiophene 1,1-dioxide have shown that the extrusion of sulfur dioxide proceeds in a disrotatory fashion (61, 62).

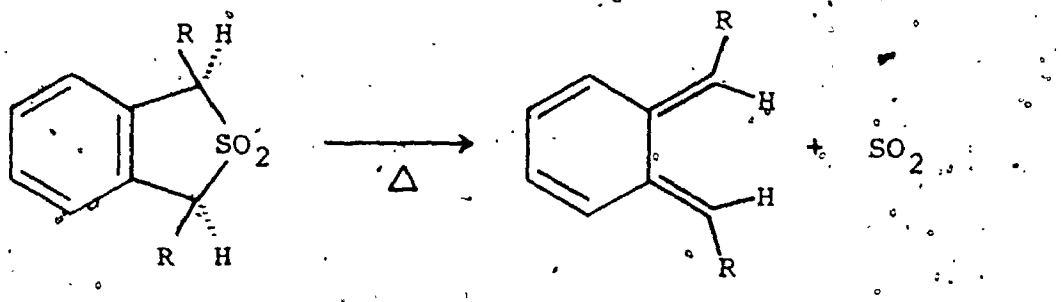


This stereochemical result is predicted by the Woodward-Hoffmann rules (63) for a linear cheletropic reaction*, and

---

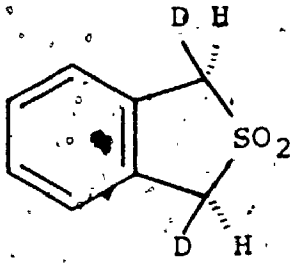
* A cheletropic reaction is defined (63) as a process in which two σ bonds which terminate at a single atom are made, or broken, in a concerted fashion. The term linear refers to the orbital symmetry of the transformation.

is a consequence of orbital symmetry considerations for the thermally-allowed, ground-state process. For the dihydrobenzothiophene sulfones such as 6, by analogy, the formation of o-quinodimethanes is also predicted to be a disrotatory process.



Unfortunately o-quinodimethanes are very unstable species; 8 has been observed at -196° (64) while the diphenyl and tetraphenyl derivatives of 8 have been observed at -189° and below -110° respectively (65,66). These molecules undergo rapid cyclization to benzocyclobutenes, relieving steric interactions and restoring aromaticity, or, in the case of the diphenyl o-quinodimethane, rearrange to give 9-phenyl-9,10-dihydroanthracene (67).

Because the sulfone 6a was readily available by oxidation of the cis-dideuterated sulfoxide 5b (prepared via the stereoselective exchange reaction described in the previous chapter), the vapour-phase thermolysis of 6a was studied to determine whether or not thermal desulfonylation of 6 is a concerted process, and, hence, to provide evidence for the intermediacy of o-quinodimethane in this reaction.

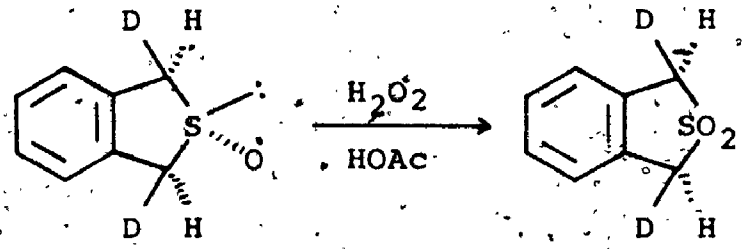


6a

Because of the deuterium substitution, this sulfone is free from steric effects which would be present if larger alkyl or aryl groups were used, and furthermore, it cannot undergo rearrangements such as that observed in the desulfonylation of the 1,3-diphenyl sulfone (67). The results of the thermolysis experiments with 6a are discussed in the following section.

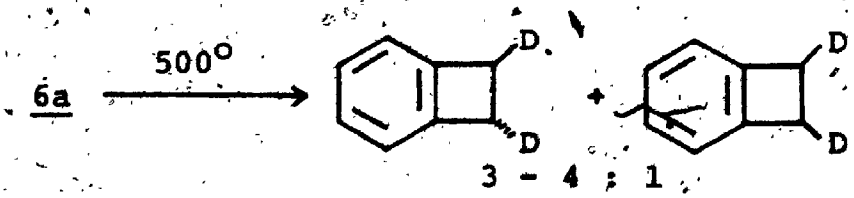
Results and Discussion

Thermolysis of 1,3-dihydrobenzo[c]thiophene 2,2-dioxide (6) (57) by sublimation through a quartz tube heated at 500° at 1 μm Hg pressure gave a 93% yield of benzocyclobutene (7). The cis-dideuterated sulfone 6a was prepared from the sulfoxide* by oxidation with hydrogen peroxide in acetic acid. Thermolysis of 6a at 500° gave a quantitative yield of 1,2-dideuteriobenzocyclobutene (7a).



5b 6a

The stereochemistry of the two deuterium atoms of was determined by examination of the deuterium-decoupled ^{13}C-satellite n.m.r. signal of the benzylic protons, which appeared as two superimposed doublets, J = 2.8 and 5.5 Hz, due to the trans- and cis-isomers respectively (68, 69), relative areas 3 or 4 to 1 (Figure 8(b)). Thus, thermolysis of 6a at 500° gave mainly the trans-isomer of 7a (75-80%).



7a

---

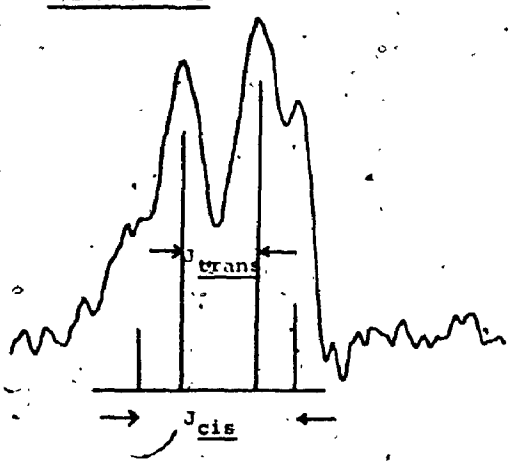
* For preparation of this sulfoxide, see previous chapter.

FIGURE 8

J_{trans} = 2.8 Hz

J_{cis} = 5.6 Hz

trans/cis = 3 or 4:1

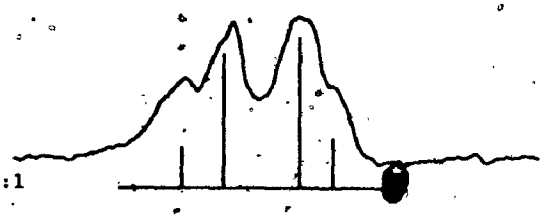


(a) From flash thermolysis of cis-1,3-dideuteriobenzo[c]thiophene 2,2-dioxide at 500° (low-field side-band).

J_{trans} = 2.8 Hz

J_{cis} = 5.5 Hz

trans/cis = 3 or 4:1

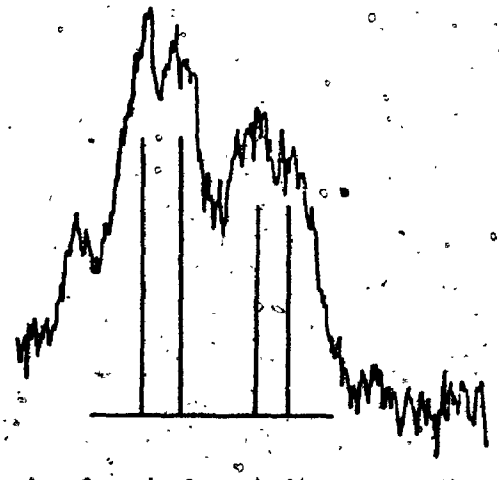


(b) From quartz-tube thermolysis of cis-1,3-dideuteriobenzo[c]thiophene 2,2-dioxide at 500° (low-field side-band).

J_{trans} = 2.8 Hz

J_{cis} = 5.5 Hz

trans/cis = 1:1



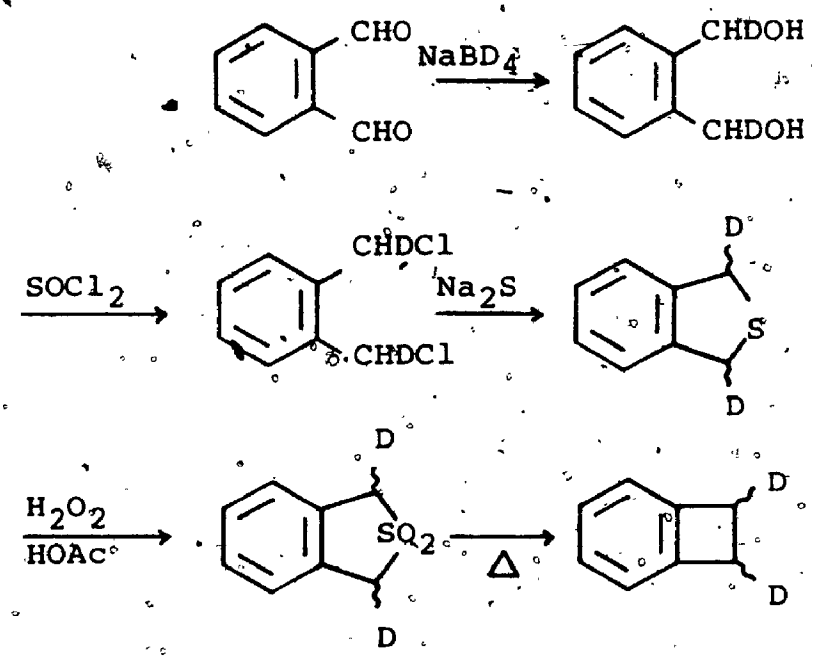
(c) From quartz-tube thermolysis of equimolar cis/trans-1,3-dideuteriobenzo[c]-thiophene 2,2-dioxide at 500° (high-field side-band).

Deuterium-decoupled ^{13}C-satellite proton n.m.r. spectra of 1,2-dideuteriobenzocyclobutene samples*

---

* Sweep width 100 Hz. Sensitivity of signals enhanced by the CAT technique.

For comparison, a 1:1 (equimolar) mixture of cis- and trans-dideuteriobenzocyclobutene was prepared according to the following synthetic scheme:



6b 7b

Phthalaldehyde was reduced with sodium borodeuteride to the diol, which, on treatment with thionyl chloride gave the α,α'-dideuterio-α,α'-dichloro-o-xylene. Reaction of this dichloride with sodium sulfide gave the 1,3-dideuteriobenzo[c]thiophene which was oxidized to the sulfone 6b. The overall yield of the sulfone was 17%.

Thermolysis of 6b at 500° gave 7b, assumed by this method of preparation to be an equimolar mixture of the cis- and trans-isomers. The ^{13}C-satellite proton n.m.r. spectrum of the benzylic hydrogens of 7b (Figure 8(c)) showed, as expected, a 1:1 ratio of intensities of the cis and trans signals.

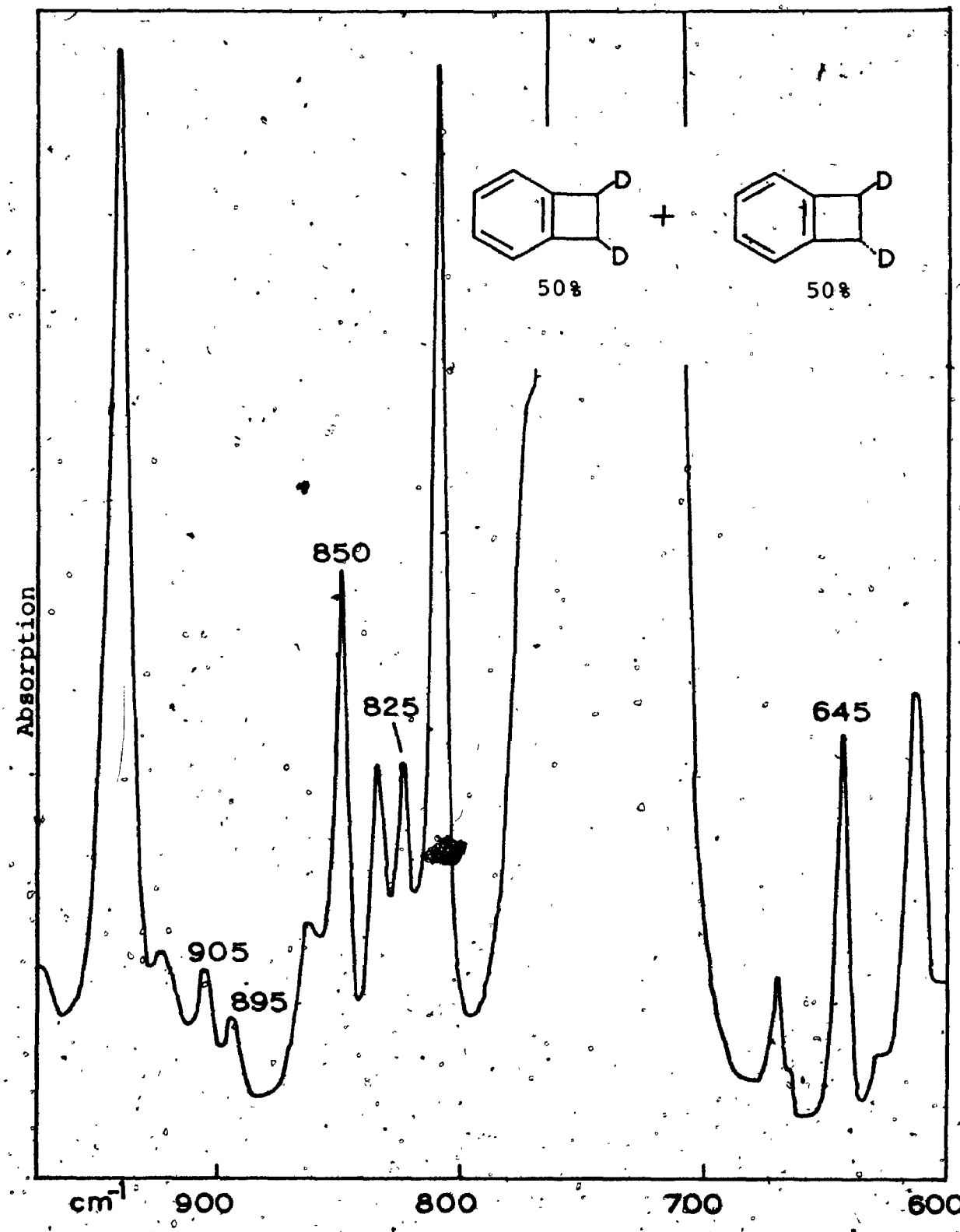
The infra-red spectra of both the equimolar cis/trans mixture (7b) and the mainly trans sample of 7a were recorded using 0.1 mm neat samples. Comparison of the spectra (Figures 9 and 10) allowed the assignment of characteristic bands to each isomer: cis, 645 and 895 cm^{-1}; trans, 825, 850 and 905 cm^{-1}. The composition of 7a was found to be 75% trans-isomer and 25% cis from the intensities of the bands in comparison to those of 7b, in agreement with the values determined by n.m.r. Conformance with Beer's law* was assumed for these quantitative determinations.

A sample of 6a was thermolyzed at 500° and the product (7a, trans:cis 75:25 by i.r.) was subject again to thermolysis, once at 500° and twice at 600°. Examination of the i.r. spectrum after each run showed a trans:cis ratio of 65:35 for the run at 500° and 50:50 for the two 600° thermolyses. Since the thermolyses appeared to be less stereospecific as the temperature was increased, the thermolysis of 6a was repeated at 430-440°. This gave a 20% yield of benzocyclobutene-d_2 (7c) which was shown by i.r. to be almost pure trans-isomer (Figure 11). Less than 4% of the cis-isomer could be detected. The recovered starting material (78%) was desulfonylated at 600° and this

---

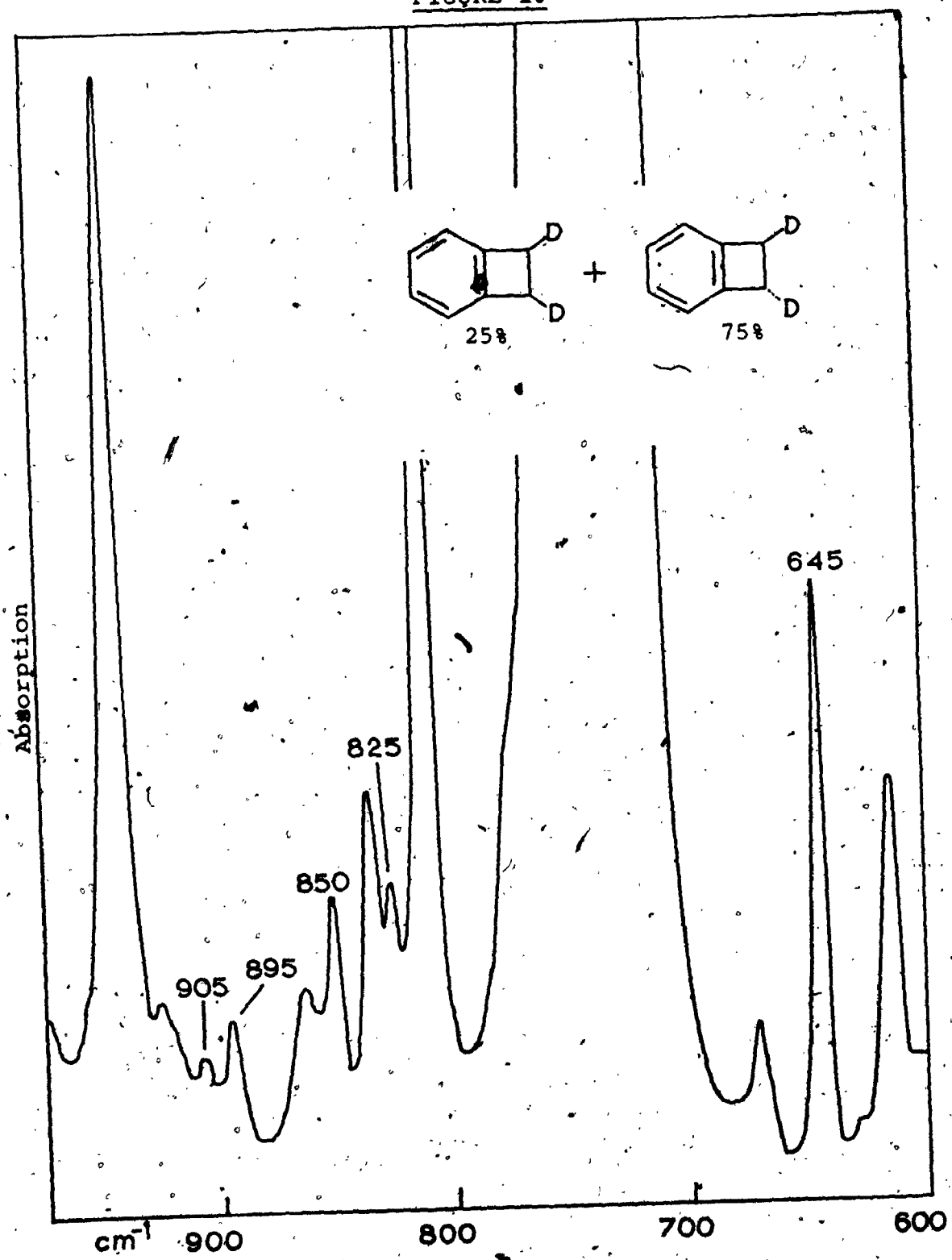
* Beer's law (or the Lambert-Beer law) states (70):
Optical Density = ε c l
where ε is the molar extiction coefficient, c is the concentration (moles/litre) and l is the length of the sample (cm). Thus, the optical density of a compound is directly proportional to its concentration.

FIGURE 9



Absorption Infra-red Spectrum of Equimolar cis/trans-1,2-Dideuteriobenzocyclobutene (7b)

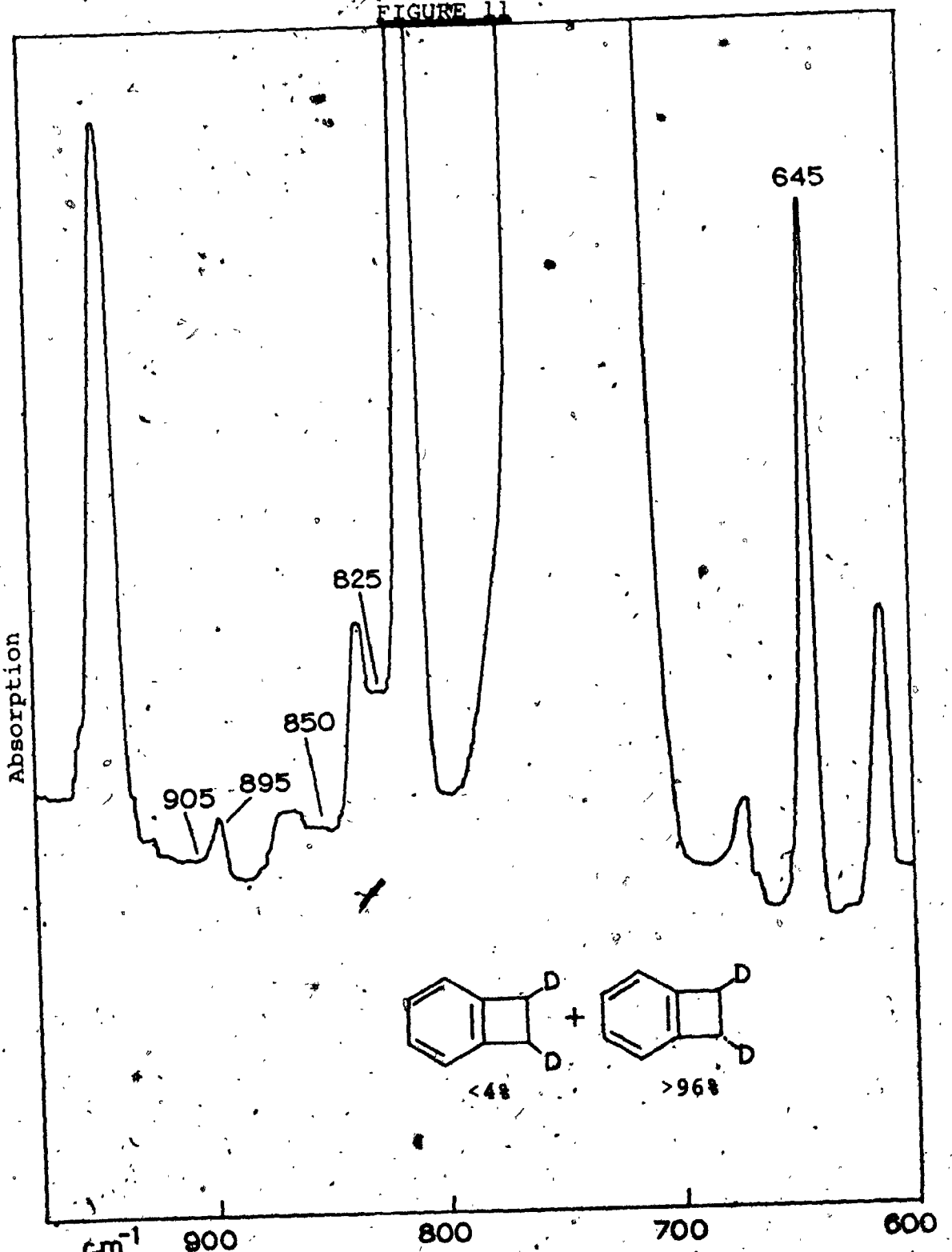
FIGURE 10



Absorption Infra-red Spectrum of 1:3 cis/trans

1,2-Dideuteriobenzocyclobutene (7a)

FIGURE 11



Absorption Infra-red Spectrum of trans-1,2-Dideuteriobenzocyclobutene (7c)

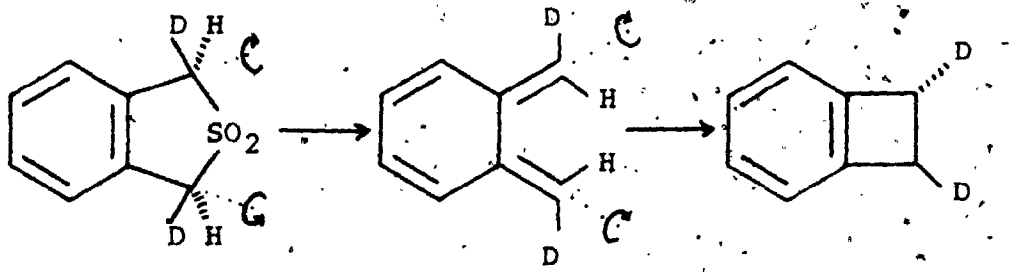
product run again at 600° to give benzocyclobutene-d_2 whose i.r. spectrum was identical to that of the equimolar trans/cis mixture produced by multiple thermolysis of 6a at 600° or thermolysis of 6b at 500°.

Finally, flash thermolysis (71) of 6a at 500° and 14 μm Hg pressure through a ceramic oven gave 7a in 90% yield. The composition of the product was shown by i.r. to be 75% trans- and 25% cis-isomer, which was confirmed by n.m.r. (Figure 8(a)). These results are identical to those obtained by quartz-tube thermolysis of 6a and suggest that significant surface effects upon the desulfonylation of 6 are absent.

From these results it can be seen that thermal desulfonylation of 1,3-dihydrobenzo[c]thiophene 2,2-dioxide in the gas phase to give benzocyclobutene is a stereospecific reaction. Thus, thermolysis of the cis-dideuterated sulfone 6a gave mainly trans-dideuterated benzocyclobutene (7a).

At a temperature of 430-440°, only 20% desulfonylation of the sulfone occurred. However, at this temperature, the yield of the trans-isomer was over 96% compared with the cis, or a stereospecificity of over 92%. On the other hand, at 500°, the desulfonylation was quantitative, but the yield of trans product was only 75%, or 50% stereospecificity. Double thermolysis of 6a or 7a (trans:cis 65:35) at 600° both gave an equimolar trans/cis mixture (7b), indicating complete loss of stereospecificity at this temperature.

In terms of the Woodward-Hoffmann rules, the low temperature thermolysis of 6 is a concerted process. The linear extrusion of sulfur dioxide from the sulfone is predicted to proceed in a disrotatory fashion to give o-quinodimethane. Ring closure of this species to give benzocyclobutene is also a concerted process, and occurs in a conrotatory manner in the ground state. Thus,



The observations with 6a are in complete agreement with the predicted stereochemistry of these transformations. The loss of stereospecificity at higher temperatures may conceivably be attributed to a non-concerted process such as diradical formation or perhaps to a competing symmetry-forbidden, concerted process (72). However, the precise mechanism which is operating at higher temperatures is not understood.

Nonetheless, the thermal desulfonylation of 6 to form benzocyclobutene is a concerted process under mild conditions. The stereospecificity observed for this transformation is thus further evidence for the intermediacy of o-quinodimethane in the overall reaction.

Conclusions

Thermal desulfonylation of cis-1,3-dideuterio-1,3-dihydrobenzo[c]thiophene 2,2-dioxide in the vapour phase at 500° resulted in formation of mainly trans-1,2-dideuterio-benzocyclobutene along with some cis-isomer. The yield of the trans-isomer relative to that of the cis-isomer was enhanced at lower temperatures (430-440°), although the desulfonylation was inefficient at these temperatures (20%). At 600°, the desulfonylation process was non-stereospecific, giving an equimolar mixture of the cis and trans products. Trans-benzocyclobutene-d_2 was also converted to an equimolar cis/trans mixture under these conditions.

These results require stereoelectronic control in both steps of the reaction and can only be rationalized in present-day concepts by the Woodward-Hoffmann rules for the conservation of orbital symmetry. Thus, the overall stereospecificity of this desulfonylation-cyclization process is entirely consistent with a disrotatory extrusion of sulfur dioxide to form o-quinodimethane followed by a conrotatory ring-closure reaction to give benzocyclobutene.

EXPERIMENTAL

Introduction

Infra-red (i.r) spectra were recorded on Beckmann IR-7, IR-20A, and Acculab-4 instruments and were calibrated with a polystyrene reference film. Nuclear magnetic resonance (n.m.r.) spectra were recorded on Varian HA-100, A-60, and T-60 spectrometers with tetramethylsilane (TMS) as an internal reference standard. Spectra recorded in aqueous media were calibrated with an external TMS reference sample. Mass spectra and precise mass determinations were obtained on a Varian M-66 instrument. The correction tables of Hamming and Foster (73) were used when estimating isotopic compositions from mass spectra.

The dry-box used for storage and handling of the methylsulfonylammonium fluorosulfonate salts was a K.S.E. (model 2C380, with controlled-atmosphere interchange compartment). An atmosphere of dry nitrogen (certified grade) was maintained in the dry-box and an open dish of phosphorus pentoxide was used in the box to ensure anhydrous conditions. Kinetic experiments at 5°C were run in a Gebruder-Haake KT62 cooling bath which maintained this temperature within ±0.1°C. Melting points were obtained on a Kofler hot-stage and are uncorrected.

Deuterium oxide used for exchange experiments was obtained from Merck, Sharpe and Dohme Canada Limited, Kirkland, Quebec, minimum isotopic purity 99.7 atom % excess

D. Magnesium sulfate (anhydrous) was used as the drying agent for organic solutions. Elemental microanalyses were performed by A.B. Gygli, Toronto, Ontario, and deuterium analyses were performed by J. Nemeth, Urbana, Illinois, U.S.A.

I. The Chemistry of Quaternary Methylsulfonylammonium Fluorosulfonate Salts

Preparation of Trimethyl(methylsulfonyl)ammonium Fluorosulfonate (1)

N,N-Dimethylmethanesulfonamide (5 g) was dissolved in methyl fluorosulfonate ("Magic Methyl", Aldrich, 10 ml) in a stoppered flask. After a brief induction period (within 30 min), an exothermic reaction occurred accompanied by formation of a crystalline precipitate. When crystallization appeared complete (1 h), the product was collected and washed with dry methylene chloride in a dry-box under nitrogen. The crude trimethylammonium salt (8.5 g, 88%) was recrystallized from acetonitrile-methylene chloride solution to give 8.2 g (85%) colourless crystals, m.p. ~ 130° (dec.). The n.m.r. spectrum (FSO_3H) showed: δ 3.14 (9 H, singlet) and 3.48 (3 H, singlet). Anal. calcd. for $C_4H_{12}FNO_5S_2$: C 20.24; H 5.10; N 5.90; S 27.04. Found: C 20.47; H 5.35; N 5.95; S 27.20.

Preparation of 1-Methyl-1-(methylsulfonyl)piperidinium Fluorosulfonate (2)

Methanesulfonpiperidide (5 g) was dissolved in methyl fluorosulfonate (10 ml) and the solution sealed in a Carius tube. The tube was heated to 60° for 18 h and the product, which crystallized on cooling the tube, was collected and washed with dry methylene chloride in a dry-box under

nitrogen. Recrystallization from acetonitrile-methylene chloride solution gave colourless plates, 6.9 g (81%) m.p. ~ 120° (dec.). The n.m.r. spectrum (CD_3CN) of the N-methylpiperidinium salt showed: δ 1.95 (6 H, multiplet), 3.57 (4 H, multiplet), 3.30 (3 H, singlet) and 3.77 (3 H, singlet). Anal. calcd. for $C_7H_{16}FNO_5S_2$: C 30.32; H 5.82; N 5.05; S 23.08. Found: C 30.41; H 5.90; N 4.98; S 23.02.

Preparation of Ethyldimethyl(methylsulfonyl)ammonium Fluorosulfonate (3)

N-Ethylmethanesulfonamide (5 g) was dissolved in methyl fluorosulfonate (10 ml) in a well-stoppered flask and the solution left at room temperature for 16 days. The solution was diluted with dry methylene chloride and cooled in a dry ice-acetone bath. The resulting crystalline precipitate was collected and washed with dry methylene chloride in a dry-box under nitrogen. Recrystallization from acetonitrile-methylene chloride solution afforded 2.81 g (28%) of the ethyldimethylammonium salt, m.p. ~ 100° (dec.). The n.m.r. spectrum showed (CD_3CN): δ 1.43 (3 H, triplet, J = 7 Hz), 3.18 (6 H, singlet), 3.65 (2 H, quartet, J = 7 Hz) and 3.75 (3 H, singlet). Anal. calcd. for $C_5H_{14}FNO_5S_2$: C 23.91; H 5.62; N 5.58; S 25.48. Found: C 23.78; H 5.74; N 5.52; S 25.25.

Preparation of Diethylmethyl(methylsulfonyl)ammonium Fluorosulfonate (4)

N,N-Diethylmethanesulfonamide (10 g) was dissolved in methyl fluorosulfonate (20 ml) in a two-necked, round-bottom flask equipped with an inlet tube for dry nitrogen and a condenser fitted with a drying tube containing indicating silica gel. The contents of the flask were heated at 50° for 3 days under dry nitrogen, then diluted with dry methylene chloride (50 ml) and cooled in a dry ice-acetone bath. When crystallization appeared complete, the diethylmethylammonium salt was collected and washed in dry methylene chloride in a dry-box under nitrogen, yield 11.15 g (64%), m.p. ~ 115° (dec.), The product was used for reactions without further purification. After about 5 wk in the dry-box, the salt became an oily semisolid. However, a sample sealed in an ampoule under nitrogen was kept for several mo without noticeable decomposition. The n.m.r. spectrum showed (CD_3CN): δ 1.40 (6 H, triplet, J = 7 Hz), 3.11 (3 H, singlet), 3.60 (4 H, quartet, J = 7 Hz) and 3.70 (3 H, singlet). An analytical sample was recrystallized from acetonitrile-methylene chloride solution at -78°. Anal. Calcd. for $C_6H_{16}FNO_5S_2$: C 27.17; H 6.08; N 5.28; S 24.13. Found: C 27.20; H 6.02; N 5.29; S 24.24.

Hydrolysis of Trimethyl(methylsulfonyl)ammonium Fluorosulfonate

Into a 25 ml, three-necked, round-bottom flask fitted with a nitrogen inlet, serum cap and outlet tube was placed a sample of the trimethylammonium salt (1, 140 mg). Water (2 ml) was injected through the serum cap to dissolve the salt, followed by the addition of solid sodium hydroxide (0.2 g). Nitrogen was passed over the surface of the basic solution and the outlet tube of the flask was directed into an ethereal solution of picric acid (0.5 g). After about 20 min, the resulting yellow precipitate was collected and washed with ether, yield 106 mg (62%) trimethylammonium picrate. After recrystallization from hot water, m.p. 215-217° (reported 216°, (25)). The mixed m.p. with authentic picrate gave no depression.

Hydrolysis of 1-Methyl-1-(methylsulfonyl)piperidinium Fluorosulfonate

The N-methylpiperidinium salt (2, 0.28 g, 1 mmol) was dissolved in 5% aqueous sodium hydroxide solution (5 ml) and stirred for 5 min. The solution was extracted twice with ether and the extracts dried. To the dried ethereal solution was added a solution of picric acid (0.5 g) in ether. When crystallization of N-methylpiperidinium picrate was complete, it was collected and washed with ether. The yield was 280 mg (85%). Recrystallization from hot water gave yellow

needles, m.p. 145-147° (reported 148°, (26)). Mixed m.p. with authentic N-methylpiperidinium picrate gave no depression.

Hydrolysis of Ethyldimethyl(methylsulfonyl)ammonium Fluorosulfonate

The ethyldimethylammonium salt (3, 0.25 g, 1 mmol) was dissolved in 20% aqueous sodium hydroxide (10 ml) cooled in an ice-bath. After a few minutes, the solution was extracted twice with ether and the extracts dried. The ethereal amine solution was reacted with picric acid, as described for the N-methylpiperidinium salt, to give 0.15 g (50%) ethyldimethylammonium picrate. Recrystallization from hot water gave yellow needles, m.p. 202-203° (reported 193-5°, (26)). Mixed m.p. with authentic picrate gave no depression.

Hydrolysis of Diethylmethyl(methylsulfonyl)ammonium Fluorosulfonate

The diethylmethylammonium salt (4, 0.27 g, 1 mmol) was hydrolyzed in 20% sodium hydroxide solution and the diethylmethylamine converted to the picrate, as described for the ethyldimethylammonium salt. The yield of picrate was 0.16 g (50%). Recrystallization from hot water gave yellow needles, m.p. 183-184° (reported 185° (26)). Mixed m.p. with authentic picrate gave no depression.

Reactions of Trimethyl(methylsulfonyl)ammonium Fluorosulfonate

1. Mesylation of Ethanol

The trimethylammonium salt (1, 0.40 g) was added to absolute ethanol (3 ml, dried over molecular sieves) and one drop of pyridine was added. After stirring at room temperature for 1 h, the precipitate was filtered off and washed with a small volume of absolute ethanol. The filtrate and washings were dissolved in water and extracted three times with methylene chloride. The extracts were washed briefly with 0.5 N hydrochloric acid and water, then dried and the solvent carefully evaporated off to give a clear, colourless, volatile liquid (0.14 g, 65%). The spectra of the ethyl mesylate were identical with those of an authentic sample (vide infra). The i.r. spectrum (film): 1350 (s), 1175 (s), 1010 (ms), 975 (ms), 920 (s) and 815 cm^{-1} (m). The n.m.r. spectrum showed ($CDCl_3$): δ 1.40 (3 H, triplet, J = 7 Hz), 2.97 (3 H, singlet) and 4.26 (2 H, quartet, J = 7 Hz).

2. Mesylation of Benzyl Alcohol

Freshly distilled benzyl alcohol (108 mg, 1 mmol) and pyridine (40 µl) were dissolved in dry acetonitrile and cooled in an ice-bath (under a drying tube). The trimethylammonium salt (1, 0.5 g, 2.1 mmol) was added and the solution stirred for 5 min at 0°. The reaction solution was diluted with methylene chloride and washed with 0.5 N hydrochloric acid and water (twice). The methylene chloride

solution was dried and the solvent evaporated to give a quantitative yield (190 mg) of clear, pale yellow benzyl mesylate. The spectra indicated very pure product, identical with the spectra of an authentic sample (74). The i.r. spectrum showed (film): 1495 (w), 1455 (mw), 1345 (s), 1165 (s), 960 (ms), 925 (ms) and 905 (ms) cm^{-1}. The n.m.r. spectrum showed ($CDCl_3$): δ 2.83 (3 H, singlet), 5.16 (2 H, singlet) and 7.30 (5 H, singlet). Precise mass calcd. for $C_8H_{10}O_3S$: 186.0350. Found: 186.0358.

3. Mesylation of 5α-Cholestan-3β-ol

To an ice-cooled solution of 3β-cholestanol (195 mg, 0.5 mmol) and one drop pyridine in dry methylene chloride (10 ml, under a drying tube) was added a solution of the trimethylammonium salt (1, 0.47 g, 2 mmol) in dry acetonitrile (15 ml). The reaction solution was stirred for 10 min, then diluted with methylene chloride and washed with 0.5 N hydrochloric acid and water. The solution was dried and the solvent evaporated to yield a colourless solid (0.21 g, 90%). The cholestanyl mesylate was recrystallized from ether-methanol solution to give colourless needles, m.p. 115-117° (reported 116.5-118.5° (75)). The i.r. spectrum ($CHCl_3$): 1465 (w), 1350 (s), 1330 (ms), 1170 (s) and 920 cm^{-1} (s). The n.m.r. spectrum showed ($CDCl_3$): δ 0.4-2.2 (43 (± 2) H, multiplets), 2.93 (3 H, singlet) and 4.3-4.9 (1 H, broad mound).

This experiment was repeated using one drop of dimethylaminoacetonitrile (DMAAN) instead of pyridine as base. The reaction was allowed to run for 5 min at room temperature, then worked up as described for the previous experiment. The crude yield was 0.25 g of colourless solid which was shown by t.l.c. to contain no unreacted starting material. Recrystallization from ether-methanol solution gave 0.17 g (74%) cholestanyl mesylate as colourless needles, m.p. 114-5°.

When only 10 µl of DMAAN was used, the crude product (234 mg) was shown by n.m.r. and t.l.c. to contain only 80% cholestanyl mesylate along with unreacted cholestanol and some minor impurities (unidentified).

Using 2,6-di-t-butylpyridine as base was found to give only small amounts of the mesylate with the bulk of the cholestanol (>90%) being recovered unchanged.

When the cholestanol was allowed to react with the salt without base for 3.5 h, the crude product was shown by n.m.r. and t.l.c. to contain the mesylate (~ 50% yield), unreacted cholestanol and minor impurities.

4. Reaction of the Trimethylammonium Salt with Chloral

To a solution of freshly distilled chloral (1 ml, 10 mmol) in dry acetonitrile (25 ml) was added a solution of the salt (1, 0.24 g, 1 mmol) in acetonitrile (25 ml). The solution was cooled in an ice-salt bath to about -10° (under a drying tube) and a small amount of trimethylamine (2-4

drops) added. After 10 min at -10°, the reaction was quenched with 0.5 N hydrochloric acid and extracted twice with methylene chloride. The extracts were washed twice with water, dried and the solvent evaporated to give a crystalline solid (0.37 g). Recrystallization from benzene-pentane solution gave 0.11 g (48%) colourless, crystalline β-trichloromethyl-β-sultone, m.p. 105-107° (reported 106.5-107.5° (76)). The spectra were identical to those of an authentic sample. The i.r. spectrum (CH_2Cl_2): 1385 (s), 1220 (s) and 810 cm^{-1} (s). The n.m.r: spectrum showed ($CDCl_3$): δ 4.7-5.2 (multiplets).

5. Mesylation of p-Toluidine

(a) Without added base

Freshly recrystallized p-toluidine (0.21 g, 2 mmol) was dissolved in dry acetonitrile (10 ml) and the trimethyl-ammonium salt (1, 0.10 g, 0.42 mmol) added with stirring. After 5 min, the reaction solution was diluted with methylene chloride and washed with 0.5 N hydrochloric acid and twice with water. The methylene chloride solution was dried and the solvent evaporated to give a crystalline solid, yield 78 mg (100%). The crude sulfonamide melted at 102-103° (reported 103-104° (77)) and no impurities were evident from the spectra. The i.r. spectrum ($CHCl_3$): 3390 (mw), 3280 (mw), 1510 (m), 1390 (m), 1330 (s), 1300 (m), 1155 (s) and 975 cm^{-1} (ms). The n.m.r. spectrum showed

($CDCl_3$): δ 2.28 (3 H, singlet), 2.93 (3 H, singlet), 7.08 (4 H, singlet) and 7.2 (1 H, broad mound).

The trimethylammonium salt (0.10 g) was dissolved in dry acetonitrile and stirred at room temperature for 1 h. Then, excess p-toluidine was added and allowed to react for 5 min. The reaction was worked up as described for the previous experiment to give 63 mg (82%) of the methanesulfon-p-toluidide. Recrystallization from ether-pentane solution gave colourless plates (48 mg, 62%), m.p. 103-4°, whose spectra were identical to those obtained in the previous experiment.

(b) Reaction of the salt with base before addition of p-toluidine

When a solution of the trimethylammonium salt (1, 0.10 g) in dry acetonitrile was allowed to react with one drop of trimethylamine for 30 sec before addition of excess p-toluidine, 39 mg pale yellow needles were obtained, identified as methylsulfonylmethanesulfon-p-toluidide ("mesylmethanesulfon-p-toluidide") (yield 70%). Recrystallization from chloroform-carbon tetrachloride solution gave fine needles, m.p. 165-166°. The i.r. spectrum (CH_2Cl_2): 3330 (mw), 1510 (m), 1395 (m), 1325 (s), 1205 (s) and 1140 cm^{-1} (s). The n.m.r. spectrum showed ($CDCl_3$): δ 2.33 (3 H, singlet), 3.26 (3 H, singlet), 4.30 (2 H, singlet), 7.15 (4 H, singlet) and 7.0 (1 H, broad mound). Anal. calcd.

for $C_9H_{13}NO_4S_2$: C 41.06; H 4.98; N 5.32; S 24.31. Found: C 40.85; H 4.84; N 5.42; S 24.13.

When the trimethylammonium salt (1, 0.10 g) in dry acetonitrile solution was allowed to react with one drop of pyridine for 1 min before addition of excess p-toluidine, the crude product (57 mg) was shown by n.m.r. to be a mixture of the methanesulfonamide and mesylmethanesulfonamide in the mole ratio of 5.3 to 1.

(c) With added base

The trimethylammonium salt (1, 0.24 g, 1 mmol) in dry acetonitrile solution (10 ml) was added to a solution of p-toluidine (0.21 g, 2 mmol) and trimethylamine (0.5 ml) in acetonitrile (10 ml). After stirring for 1 min, the reaction was quenched with 0.5 N hydrochloric acid and extracted twice with methylene chloride. The extracts were washed with water (twice), dried and the solvent evaporated to give a colourless liquid (126 mg). The n.m.r. of this crude product showed both the methanesulfonamide and mesylmethanesulfonamide in the mole ratio of 2 to 1, as well as other minor products.

6. Mesylation of 1-Borneol

To a solution of 1-borneol (154 mg, 1 mmol) and pyridine (one drop) in dry acetonitrile (20 ml) was added the trimethylammonium salt (1, 0.5 g). After stirring for 1 min, the reaction was quenched with 0.5 N hydrochloric

acid and extracted with methylene chloride. The extracts were washed twice with water, dried and the solvent evaporated to yield 157 mg crystalline solid. The n.m.r. of the crude product indicated unreacted starting material plus a trace of bornyl mesylate (<5%).*

In a series of experiments, l-borneol (77 mg, 0.5 mmol) was reacted with the trimethylammonium salt (0.24 g, 1 mmol) in the presence of various tertiary amine bases (.05 mmol, catalytic quantity). The salt was dissolved in 5 ml dry acetonitrile and added with stirring to the l-borneol and base in 5 ml dry methylene chloride, cooled in an ice-bath (drying tube). The ice-bath was then removed and the reaction solution allowed to warm up to room temperature for 10 min. The solution was poured into 0.1 N hydrochloric acid and extracted with methylene chloride. The extracts were washed twice with water, dried and the solvent evaporated. The crude products (crystalline solids) were examined by n.m.r. ($CDCl_3$) to determine the extent of mesylation. The yield of recovered starting material and products accounted for over 90% of the material balance in all cases. The results are summarized in Table 6.

---

* The n.m.r. spectrum of l-bornyl mesylate is described elsewhere (*vide infra*).

Reactions of N-Methylmethanesulfonpiperidinium Fluorosulfonate

1. Mesylation of 5α-Cholestan-3β-ol

To a solution of cholestanol (195 mg, 0.5 mmol) and pyridine (one drop) in dry methylene chloride (10 ml) was added a solution of the N-methylpiperidinium salt (2, 0.28 g, 1 mmol) in dry acetonitrile (5 ml). After stirring for 10 min, the reaction solution was diluted with methylene chloride and washed with 0.5 N hydrochloric acid and water (twice), dried and the solvent evaporated to give a colourless solid, 243 mg. The n.m.r. spectrum ($CDCl_3$) of the crude product showed, in addition to the peaks due to cholestanyl mesylate, two broad singlets at δ 3.2 and 4.6 in the ratio 3:2. By analogy to the spectrum of bornyl mesylmesylate, there were apparently due to cholestanyl mesylmesylate (methylsulfonylmethanesulfonate). This by-product (yield ~ 5%) was not isolated or further characterized. Recrystallization from methanol gave 145 mg (65%) colourless, crystalline 3β-cholestanyl mesylate, m.p. 113-116°. The spectra were identical to those described above.

2. Mesylation of p-Toluidine

The N-methylpiperidinium salt (2, 0.28 g, 1 mmol) was dissolved in dry acetonitrile (5 ml) and added to a stirred solution of recrystallized p-toluidine (0.21 g, 2 mmol) in dry methylene chloride (10 ml). After 5 min, the reaction

solution was diluted with methylene chloride and washed with 0.5 N hydrochloric acid and water, dried and the solvent evaporated. The yield of the crude sulfonamide was quantitative. Recrystallization from ether-pentane solution gave the methanesulfon-p-toluidide as colourless plates, 120 mg (65%), m.p. 102-102.5°. The spectra were identical to those described (vide supra).

The reaction was repeated with pyridine (80 µl, 1 mmol) added. The crude product (165 mg) was shown by n.m.r. ($CDCl_3$) to contain methanesulfon-p-toluidide (80%) and mesylmethanesulfon-p-toluidide (13%).

When the N-methylpiperidinium salt (1 mmol) was allowed to react with pyridine (1 mmol) for 30 sec before addition of excess p-toluidine, the yield of crude product (a viscous yellow oil) was only 33 mg. The n.m.r. of this material ($CDCl_3$) indicated the methanesulfonamide and mesylmethanesulfonamide (ratio 5:1) as well as several unidentified impurities.

3. Mesylation of l-Borneol

In a series of experiments, l-borneol was reacted with the N-methylpiperidinium salt (2) using various tertiary amine bases. A solution of recrystallized l-borneol (154 mg, 1 mmol) and base (0.1 mmol) in dry methylene chloride (5 ml) was prepared and cooled in an ice-bath (under a drying tube). To this was added with stirring a solution of the salt (0.55 g, 2 mmol) in dry acetonitrile (3 ml).

The ice-bath was removed and the reaction solution allowed to warm to room temperature for 10 min. The solution was poured into 0.1 N hydrochloric acid and extracted with methylene chloride. The extracts were washed twice with water, dried and the solvent evaporated to give a crystalline solid (the yield of recovered starting material and products was over 90% in all cases). The crude product was then examined by n.m.r. ($CDCl_3$) to determine the extent of conversion to the mesylate or mesylmesylate (the spectra of these compounds has been described, vide infra). Table 7 summarizes the results.

Reactions of Diethylmethyl(methylsulfonyl)ammonium Fluorosulfonate

1. Mesylation of 5α-Cholestan-3β-ol

To an ice-cooled, stirred solution of 3β-cholestanol (389 mg, 1 mmol) and dimethylaminoacetonitrile (DMAAN, 10 µl, distilled) in dry methylene chloride (10 ml) was added a solution of the diethylmethylammonium salt (4, 0.32 g, 1.2 mmol) in dry acetonitrile (1 ml). The reaction solution was stirred for 10 min at 0° (under a drying tube), then poured into 0.1 N hydrochloric acid and extracted with methylene chloride. The extracts were washed twice with water, dried and solvent evaporated to give 471 mg (quantitative yield) of colourless, crystalline cholestanyl mesylate.

Recrystallization from methylene chloride-methanol solution gave 367 mg (79%) fine needles, m.p. 118-120°, whose spectra were identical to those described (vide supra).

2. Mesylation of 5α-Cholestan-3α-ol

Epicholestanol (389 mg, 1 mmol, containing about 10% 3β-cholestanol) and DMAAN (10 µl) were dissolved in dry methylene chloride (15 ml) and cooled in an ice-bath (under a drying tube). To this was added with stirring a solution of the diethylmethylammonium salt (4, 0.53 g, 2 mmol) in dry acetonitrile (1 ml). The ice-bath was removed and the reaction solution was allowed to warm to room temperature for 10 min, then poured into 0.1 N hydrochloric acid and extracted with methylene chloride.

The extracts were washed twice with water, dried and the solvent evaporated to give 481 mg slightly yellow solid. The n.m.r. of the crude product ($CDCl_3$) showed the mesylate (86%) and mesylmesylate (14%)*. The crude product was titurated with hot petroleum ether (60°-80°) to dissolve the epicholestanyl mesylate. The petroleum ether was then evaporated off and the residue was treated with activated charcoal in methylene chloride. The colourless product was recrystallized from methylene chloride-methanol solution to yield 339 mg (73%) fine needles, m.p. 112-115°. The i.r.

---

* The mesylmesylate was identified by characteristic peaks at δ 3.2 and 4.6 (ratio 3:2). See above.

spectrum (CH_2Cl_2): 1355 (s) and 1180 cm^{-1} (s). The n.m.r. spectrum showed ($CDCl_3$): δ 0.4-2.3 (43 H, multiplets), 2.96 (3 H, singlet) and 4.8-5.0 (1 H, broad mound). The t.l.c. indicated that the 3α-cholestanyl mesylate contained about 10% of the β-mesylate.

3. Mesylation of Ethanol

Absolute ethanol (58 µl, 1 mmol, dried over molecular sieves) and DMAAN (10 µl) were reacted with the diethylmethylammonium salt (4, 0.53 g, 2 mmol) as described for 3β-cholestanol. On work up, the dried extract solution was evaporated to a few ml on a rotary evaporator, then the last of the solvent evaporated off with a steam of nitrogen at room temperature to give 142 mg of clear, volatile liquid. The crude ethyl mesylate was distilled under reduced pressure (1-2 mm Hg) without heating (room temperature) into a cold trap, yield 95 mg (77%). The spectra were identical to those described (vide supra). Anal. calcd. for $C_3H_8O_3S$: C 29.04; H 6.50; S 25.79. Found: C 29.28; H 6.69; S 25.86.

4. Mesylation of Cyclohexanol

Distilled cyclohexanol (104 µl, 1 mmol, dried over molecular sieves) and DMAAN (10 µl) were reacted with the diethylmethylammonium salt (4, 0.53 g, 2 mmol) as described for 3β-cholestanol. The crude yield of cyclohexyl mesylate was 181 mg of clear, colourless liquid. The product was flash distilled under vacuum (<5 µm, Hg) to give 140 mg (80%)

pure mesylate. The i.r. spectrum (film): 1350 (s), 1175 (s) and 940 cm^{-1} (s). The n.m.r. spectrum showed ($CDCl_3$): δ 1.2-2.2 (10 H, unresolved), 3.00 (3 H, singlet) and 4.4-5.0 (1 H, broad mound). Anal. calcd. for $C_7H_{14}O_3S$: C 47.19; H 7.92; S 17.96. Found: C 47.05; H 7.91; S 17.91.

5. Mesylation of l-Menthol

Freshly sublimed l-menthol (156 mg, 1 mmol) and DMAAN (10 µl) were reacted with the diethylmethylammonium salt (4, 0.32 g, 1.2 mmol) as described for 3β-cholestanol. The methylene chloride solution of extracts was washed thoroughly with several successive portions of water, then dried and the solvent evaporated. The clear liquid product was placed under vacuum for 18 h to assure complete removal of solvent. The yield of l-menthyl mesylate was 231 mg (99%), which was shown to be pure by t.l.c. and spectra. The i.r. spectrum (film): 1350 (s), 1175 (s) and 920 cm^{-1} (s). The n.m.r. spectrum showed ($CDCl_3$): δ 0.7-2.4 (18 H, multiplets), 2.97 (3 H, singlet) and 4.3-4.8 (1 H, broad multiplet). Anal. calcd. for $C_{11}H_{22}O_3S$: C 56.39; H 9.47; S 13.66. Found: C 56.58; H 9.41; S 13.59.

6. Mesylation of 1-Octanol

Freshly distilled 1-octanol (0.13 g, 1 mmol, dried over molecular sieves) and DMAAN (10 µl) were reacted with the diethylmethylammonium salt (4, 0.53 g, 2 mmol) as described for 3β-cholestanol. The crude yield was 202 mg clear,

colourless liquid. The crude product was flash distilled under vacuum (1 μm Hg) to give 191 mg (92%) pure 1-octyl mesylate. The i.r. spectrum (film): 1360 (s), 1180 (s) and 950 cm^{-1} (ms). The n.m.r. spectrum consisted of ($CDCl_3$): δ 0.8-2.0 (15 H, unresolved), 2.96 (3 H, singlet) and 4.2 (2 H, triplet, J = 7 Hz). Anal. calcd. for $C_9H_{20}O_3S$: C 51.91; H 9.68; S 15.37. Found: C 51.94; H 9.72; S 15.59.

7. Mesylation of Allyl Alcohol

Allyl alcohol (67 μl, 1 mmol, distilled and dried over molecular sieves) and DMAAN (10 μl) were reacted with the diethylmethylammonium salt (4, 0.53 g, 2 mmol) as described for 3β-cholestanol. The crude yield was 137 mg clear liquid. The crude allyl mesylate was flash distilled under vacuum (0.2 mm Hg) to yield 110 mg (81%) colourless liquid. The product underwent decomposition within a few hours at room temperature, becoming yellow in colour. The i.r. spectrum (film): 1425 (m), 1350 (s), 1180 (s), 945 (s) and 840 cm^{-1} (ms). The n.m.r. spectrum showed ($CDCl_3$): δ 8.0 (3 H, singlet), 4.68 (2 H, multiplet) and 5.2-6.3 (3 H, multiplets).

8. Mesylation of Phenol

Phenol (94 mg, 1 mmol, distilled) and DMAAN (10 μl) were reacted with the diethylmethylammonium salt (4, 0.32 g, 1.2 mmol) as described for 3β-cholestanol. The crude phenyl mesylate (184 mg) was recrystallized from benzene-pentane solution to give 137 mg (80%) colourless crystals, m.p. 59-61°

(reported 59° (79)). The i.r. spectrum (CH_2Cl_2): 1490 (m), 1375 (s), 1200 (m), 1175 (m), 1150 (s), 970 (m) and 865 cm^{-1} (s). The n.m.r. spectrum showed ($CDCl_3$): δ 3.07 (3 H, singlet) and 7.23 (5 H, multiplet). Precise mass calcd. for $C_7H_8O_3S$: 172.0192. Found: 172.0171.

9. Mesylation of Benzyl Alcohol

Benzyl alcohol (104 µl, 1 mmol, distilled) and DMAAN (10 µl) were reacted with the diethylmethylammonium salt (4, 0.53 g, 2 mmol) as described for 3β-cholestanol. The yield of benzyl mesylate was 176 mg (95%) clear, colourless liquid. The spectra were identical to those described (vide supra) and indicated pure mesylate. Attempts to distill the product resulted in spontaneous decomposition to a coloured, solid mass.

10. Mesylation of l-Borneol

Recrystallized l-borneol (154 mg, 1 mmol) and DMAAN (10 µl) were reacted with the diethylmethylammonium salt (4, 0.40 g, 1.5 mmol) as described for 3β-cholestanol. The crude yield of l-bornyl mesylate was 245 mg of crystalline solid which was shown by n.m.r. to be a mixture of the bornyl mesylate (89%) and the mesylmesylate (11%). Recrystallization from petroleum ether (30°-60°) gave 179 mg (77%) colourless crystals, m.p. 93-94° (reported 95° (80)). The i.r. spectrum (CH_2Cl_2): 1355 (s), 1180 (s), 960 (ms) and 890 cm^{-1} (ms). The n.m.r. spectrum ($CDCl_3$) consisted

of δ 0.7-2.2 (16 H, multiplets, 3.09 (3 H, singlet) and 4.86 (1 H, doublet of multiplets). The product decomposed after several hours at room temperature to a yellow-brown solid,

When this reaction was repeated in 1:1 methylene chloride: acetonitrile solution (3 ml of each), the crude product (276 mg crystalline solid) was shown by n.m.r. to be a mixture of mesylate and mesylmesylate in the ratio 3:1. When the solvent ratio was changed to 1 ml methylene chloride and 5 ml acetonitrile, the product ratio fell to 2:1.

In a series of experiments, l-borneol was mesylated with the diethylmethylammonium salt using various tertiary amine bases. A solution of l-borneol (154 mg, 1 mmol) and base (0.1 mmol) in 3-5 ml dry methylene chloride was cooled in an ice-bath (under a drying tube) and a solution of the salt (0.53 g, 2 mmol) in 3 ml dry acetonitrile added. After stirring for 10 min at 0°, the reaction solution was poured into 0.1 N hydrochloric acid and extracted with methylene chloride. The extracts were washed twice with water, dried and the solvent evaporated. The crude products were then examined by n.m.r. to determine the extent of reaction (the yields of recovered starting material and products were over 90% for all cases). The results are summarized in Table 10.

11. l-Bornyl Mesylmesylate

Recrystallized l-borneol (154 mg, 1 mmol) and DMAAN (10 µl) were dissolved in dry methylene chloride (1 ml) and a solution of the diethylmethylammonium salt (4, 1.10 g, 3.8 mmol) in dry acetonitrile (5 ml) added with stirring. After 10 min, the reaction solution was poured into 0.1 N hydrochloric acid and extracted with methylene chloride. The extracts were washed twice with water, dried and solvent evaporated to give 138 mg crystalline solid. The crude product was recrystallized twice from petroleum ether (30°-60°) to give 72 mg (23%) l-bornyl mesylmesylate, m.p. 65-70° (dec.). The i.r. spectrum (CH_2Cl_2): 1355 (ms), 1330 (s), 1230 (m), 1185 (ms), 1145 (s), 955 (m), 940 (m), 915 (ms), 895 (s) and 850 cm^{-1} (m). The n.m.r. spectrum ($CDCl_3$) consisted of δ 0.9-2.6 (16 H, multiplets), 3.20 (3 H, broad singlet), 4.53 (2 H, broad singlet) and 4.97 (1 H, doublet of multiplets). The product decomposed rapidly and was not characterized further.

12. Mesylation of t-Butyl Alcohol

In an n.m.r. tube, t-butyl alcohol (24 µl, 0.25 mmol, distilled from lime and stored over molecular sieves) was dissolved in 0.2 ml CD_2Cl_2 and pyridine (40 µl, 0.5 mmol) added. This solution was cooled in dry-ice and the diethylmethylammonium salt (4, 0.13 g, 0.5 mmol) in 0.2 ml CD_3CN added. The n.m.r. spectrum of the resulting solution was

recorded at a probe temperature of -5°, then at room temperature. At -5°, the peaks due to t-butyl alcohol (δ 1.32 (9H) and 3.9 (1 H)) had disappeared and were replaced by a singlet at δ 1.57 (9H) and a singlet at 3.01 (3 H), apparently ascribable to t-butyl mesylate. After 2 h at -5°, no appreciable change had occurred in the spectrum, but on warming to room temperature, within 20 min the peaks due to t-butyl mesylate disappeared and were replaced by a singlet at δ 3.44 (3 H, CH_3SO_3H), and a triplet 1.68 (6 H, $J \simeq 1.5$ Hz), corresponding to isobutene (reported chemical shifts δ 1.70 and 4.66 respectively (82)).

In an attempt to isolate the t-butyl mesylate, t-butyl alcohol (0.20 ml, 2 mmol) was mesylated with the salt (4, 1.06 g, 4 mmol) and pyridine (0.32 ml, 4 mmol) at -78°. The salt, in dry acetonitrile (5 ml) was added to a solution of t-butyl alcohol and pyridine in methylene chloride (25 ml) cooled in a dry-ice-acetone bath (under a drying tube). After 5 min, the resulting bright-yellow solution was poured into 100 ml 0.1 N nitric acid slurried with crushed ice. Ice-cold methylene chloride was added and the whole was shaken in a separatory funnel. The methylene chloride layer was washed with an ice-water slurry, then filtered through a cotton plug and evaporated down on a rotary evaporator with an ice-bath under the flask. The remaining yellow liquid was examined by n.m.r. ($CDCl_3$) at -40°, but was found to be only acetonitrile containing a small amount of

methylene chloride. The t-butyl mesylate had apparently decomposed during work-up.

13. Reaction of the Diethylmethylammonium Salt with Chloral

Chloral (1 ml, freshly distilled from H_2SO_4) was dissolved in dry acetonitrile (10 ml) and a small amount of diethylmethylamine added (~4 drops). This solution was cooled to about -10° (ice-salt bath) and a solution of the diethylmethylammonium salt (4, 0.27 g, 1 mmol) in dry acetonitrile (10 ml) added. After 10 min, the reaction solution was poured into 0.1 N hydrochloric acid and extracted twice with methylene chloride. The extracts were washed with water (twice), dried and the solvent evaporated to give 77 mg pink liquid which had a strong odour of chloral. Crystallization from ether-pentane afforded 10 mg (4%) oily crystals which were shown to be contaminated β-trichloromethyl-β-sultone from the i.r. spectrum (vide supra).

This reaction was repeated, but the diethylmethylamine was added to the cooled solution of chloral and the diethylmethylammonium salt in acetonitrile. Work-up of the reaction, as above, gave a pale yellow liquid (~150 mg). Attempted crystallization of this material from ether-pentane gave about 12 mg (5%) oily crystals whose i.r. spectrum was virtually identical to that of the product obtained above.

14. Reaction of the Diethylmethylammonium Salt with an Enamine

The diethylmethylammonium salt (4, 0.27 g, 1 mmol) in a few ml dry acetonitrile was added to freshly distilled 1-(2-methylpropenyl)pyrrolidine (0.25 g, 2 mmol) with stirring. After 30 min, the reaction solution was diluted with methylene chloride and extracted with 0.5 N hydrochloric acid. The extracts were washed twice with methylene chloride, then solid sodium carbonate added until basic. An oily layer separated and was taken up in methylene chloride (two portions). The methylene chloride solution was dried and evaporated to give 116 mg (57%) viscous, yellow oil. The i.r. and n.m.r. spectra of this material indicated that the enamine-sulfene cycloadduct was the major product (see below) but was contaminated with unidentified minor impurities. The crude product was triturated with three 10 ml portions of petroleum ether (30°-60°). The triturates were concentrated to about 5 ml and allowed to crystallize at -20° (freezer). The crystals were recrystallized from petroleum ether, yield 25 mg (12%), m.p. 64-66° (reported 64.5-66° (5)). The i.r. spectrum (CH_2Cl_2): 1457 (m), 1314 (vs), 1204 (s), 1108 (s) and 909 cm^{-1} (m). The n.m.r. spectrum ($CDCl_3$) consisted of: δ 1.52 (3 H, singlet), 1.58 (3 H, singlet), 1.80 (4 H, multiplet), 2.46 (4 H, multiplet), 2.80 (1 H, multiplet) and 3.92 (2 H, multiplet). The spectra were identical to those of an authentic sample prepared by E.A. Luinstra (5).

15. Mesylation of p-Toluidine

The diethylmethylammonium salt (4, 0.10 g, 0.38 mmol) was dissolved in dry acetonitrile (1-2 ml) and added to a solution of excess p-toluidine (0.2 g, recrystallized) in dry methylene chloride (5 ml). After 5 min, the reaction solution was diluted with methylene chloride and washed with 0.5 N hydrochloric acid and twice with water. The methylene chloride solution was dried and the solvent evaporated to give 67 mg (96%) methanesulfon-p-toluidide, m.p. 100-2°. The spectra were identical to those described (vide supra).

Toluidine was mesylated with the diethylmethylammonium salt in the presence of various tertiary amine bases. The salt (1 mmol) was dissolved in a few ml dry acetonitrile and added to a solution of p-toluidine (1 mmol) and the base (1 mmol) in dry methylene chloride (5 ml). After 5 min, the reaction solution was diluted with methylene chloride and washed with 0.5 N hydrochloric acid and twice with water. The solution was dried and solvent evaporated and the crude product examined by n.m.r. ($CDCl_3$) to determine its composition. In all cases, the methanesulfonamide and mesylmethanesulfonamide were the only detectable products. Table 11 summarizes the results.

Mesylation of 3β-Cholestanol: Comparison of Mesylating Reagents

To determine their relative effectiveness as mesylating reagents, 3β-cholestanol was mesylated with the trimethyl-

ammonium salt, methanesulfonic anhydride and methanesulfonyl chloride under limiting conditions. Cholestanol (195 mg, 0.5 mmol) and pyridine (0.16 ml, 2 mmol) were dissolved in dry methylene chloride (10 ml) and cooled in an ice-bath (under a drying tube). The mesylating reagent (2 mmol) was dissolved in dry acetonitrile (15 ml) and added to the chilled cholestanol-pyridine solution with stirring. After 30 sec, the reaction was stopped with a few ml of 3 N hydrochloric acid and the solution extracted with methylene chloride. The extracts were washed briefly with 5% NaOH and twice with water, then dried and the solvent evaporated. The crude product was examined by t.l.c. and n.m.r. ($CDCl_3$) to determine the extent of mesylation. The results are summarized in Table 4.

Mesylation of Cyclohexanol: Comparison of the Salts and Methanesulfonic Anhydride as Mesylating Reagents

The four salts (1 - 4) and methanesulfonic anhydride were used to mesylate cyclohexanol at low temperatures to compare their relative effectiveness as mesylating reagents. A solution of cyclohexanol (1 mmol, distilled and dried over molecular sieves) and pyridine (2 mmol) in dry methylene chloride (10 ml) was placed in a two-neck, round-bottom flask fitted with a drying tube and a serum cap. The flask and contents were cooled in a dry-ice-acetone bath and the reagent (salt or anhydride, 1.2 mmol) in dry acetonitrile solution (5 ml) was introduced through

the serum cap by means of a hypodermic syringe. After 10 min, the cold reaction solution was poured into 0.1 N hydrochloric acid and extracted with methylene chloride. The extracts were washed twice with water, dried and the solvent evaporated. The crude product* was then examined by n.m.r. to determine the extent of formation of cyclohexyl mesylate. The results are summarized in Table 5.

Base-Catalyzed Multiexchange Experiments

1. Reaction of the Trimethylammonium Salt with Trimethylamine and Deuterium Oxide.

The multiexchange reaction procedure was based on Luinstra's method with methanesulfonyl chloride (5). The trimethylammonium salt (1, 0.95 g, 4 mmol) was added to a rapidly stirred solution trimethylamine (1-1.5 ml, >10 mmol, distilled from CaH_2) and deuterium oxide (2.0 ml, 111 mmol) in 1,2-dimethoxyethane (DME, 30 ml, distilled from CaH_2 and stored over molecular sieves) at room temperature. The reaction solution immediately became cloudy and a heavy, oily layer separated out. After 10 min, the mixture was evaporated to dryness on a rotary evaporator, then stored overnight in a vacuum desiccator over phosphorus pentoxide.

---

* The products were generally clean, having a small amount of methanesulfonic anhydride as the only detectable impurity (presumably from mesylation of water). The unreacted cyclohexanol was washed out during work-up.

The colourless solid salts which remained (1.27 g, 100%) was converted to the sulfonyl chloride by addition of methylene chloride (50 ml) and excess phosphorus pentachloride. This mixture was stirred for 3 h at room temperature, then filtered to remove unreacted PCl_5 and the filtrate cautiously washed with water. The methylene chloride layer was washed with several successive portions of water until the washings were almost neutral on pH paper (pH ≈ 6). The solution was then dried and evaporated down to a pale yellow liquid (0.20 g, 43%). The crude methanesulfonyl chloride was flash-distilled in a short-path apparatus at atmospheric pressure. The clear, almost colourless distillate was analyzed by m.s. to determine the deuterium content and distribution. Comparison of the relative intensities of the peaks at m/e 79, 80, 81 and 82 ($CH_3SO_2^+$) indicated the following composition for the methyl group (85.4 atom % excess D):

CH_3	1.3%
CH_2D	5.3
CHD_2	29.2
CD_3	64.2

2. Reaction of the N-Methylpiperidinium Salt with N-Methylpiperidine and Deuterium Oxide

This experiment was performed as described for the trimethylammonium salt using the N-methylpiperidinium salt (2, 1.11 g, 4 mmol), N-methylpiperidine (1.21 ml, 10 mmol,

distilled from CaH_2), deuterium oxide (2.0 ml, 111 mmol) and DME (30 ml). The yield of dried salts was 1.54 g (97%) and the yield of the sulfonyl chloride was 0.14 g (30%). The m.s. indicated the following deuterium distribution from the peaks at m/e 79, 80, 81 and 82 ($CH_3SO_2^+$, 82.5 atom % excess D):

CH_3	1.8%
CH_2D	9.4
CHD_2	28.4
CD_3	60.4

3. Reaction of the Ethyldimethylammonium Salt with Ethyldimethylamine and Deuterium Oxide

This experiment was performed as described for the trimethylammonium salt using the ethyldimethylammonium salt (3, 1.00 g, 4 mmol), ethyldimethylamine (1.0 ml, 10 mmol, distilled from CaH_2), deuterium oxide (2.0 ml, 111 mmol) and DME (30 ml). The yield of dried salts was 1.32 g (92%) semi-solid material. Conversion to methanesulfonyl chloride yielded 0.24 g (52%). The m.s. indicated the following deuterium distribution from the peaks at m/e 79, 80, 81 and 82 ($CH_3SO_2^+$, 78.6 atom % excess D):

CH_3	3.2%
CH_2D	9.9
CHD_2	34.7
CD_3	52.2

4. Reaction of the Diethylmethylammonium Salt with Diethylmethylamine and Deuterium Oxide

This experiment was performed as described for the trimethylammonium salt using the diethylmethylammonium salt (4, 1.06 g, 4 mmol), diethylmethylamine (1.22 ml, 10 mmol, distilled from CaH_2), deuterium oxide (2.0 ml, 111 mmol) and DME (30 ml). The yield of dried salts was 1.41 g (95%) viscous liquid. Conversion to methanesulfonyl chloride yielded 0.18 g (39%). The m.s. indicated the following deuterium distribution from the peaks at m/e 79, 80, 81 and 82 ($CH_3SO_2^+$, 56.4 atom % excess D):

CH_3	7.4%
CH_2D	40.1
CHD_2	28.4
CD_3	24.1

5. Reaction of the Diethylmethylammonium Salt with Diethylmethylamine and Deuterium Oxide in the Presence of Diethylmethyldeuterioammonium Chloride

Diethylmethyldeuterioammonium chloride ($D\overset{+}{N}Et_2Me\ \bar{Cl}$) was prepared by reacting DCl gas (generated by cautious addition of D_2O to PCl_5) with diethylmethylamine in methylene chloride solution. The resulting white precipitate was collected and washed with methylene chloride in a dry-box under nitrogen. The salt was dried over phosphorus pentoxide (vacuum desiccator). The i.r. spectrum (CH_3CN) showed broad bands due to N-D (1750 -2700 cm^{-1}), but no N-H bands.

The n.m.r. spectrum (CD_3CN) showed: δ 1.30 (6 H, triplet, J = 7 Hz), 2.65 (3 H, triplet, J = 2 Hz) and 3.1 (4 H, quartet of multiplets, J = 7 Hz). No N-H peak was visible. The product was assumed to be over 95% monodeuterated.

The multiexchange experiment was performed as described for the trimethylammonium salt. The diethylmethylammonium salt (4, 1.06 g, 4 mmol) was added to a rapidly stirred emulsion of $DN^+(CH_2CH_3)_2CH_3\ Cl^-$ (2.5 g, 20 mmol*) diethylmethylamine (1.22 ml, 10 mmol), deuterium oxide (1.8 ml, 101 mmol*) and DME (30 ml) at room temperature. Evaporation of the reaction solution gave 3.63 g (97%) semi-solid salt mixture. Conversion to methanesulfonyl chloride yielded 0.24 g (52%). The m.s. indicated the following deuterium distribution from the peaks at m/e 79, 80, 81 and 82 ($CH_3SO_2^+$, 62.2 atom % excess D):

CH_3	11.8%
CH_2D	24.2
CHD_2	29.5
CD_3	34.5

* The amount of D_2O was reduced to compensate for the addition of 20 mmol active deuterium from $DNEt_2Me\ Cl^-$. The total amount of active deuterium was thus maintained at 222 mmol.

Pyridine-Catalyzed Multiexchange Experiments

1. Reaction of the Trimethylammonium Salt with Pyridine and Deuterium Oxide

The trimethylammonium salt (1, 0.47 g, 2 mmol) was added to a stirred solution of pyridine (0.4 ml, 5 mmol) and deuterium oxide (5 ml). After stirring at room temperature for 15 min, the reaction solution was evaporated to dryness on a rotary evaporator, then overnight in a vacuum desiccator over phosphorus pentoxide. The dried salt mixture (0.68 g, 96%) was dissolved in methylene chloride (30 ml) and excess phosphorus pentachloride added. This mixture was stirred for 3 h, then the excess PCl_5 was filtered off and the filtrate washed cautiously with water. The filtrate was washed with several successive portions of water until the washings were almost neutral to pH paper (pH ≈ 6). The solution was dried and the solvent evaporated to yield 0.16 g (70%) methanesulfonyl chloride. The crude product was flash-distilled and the distillate examined by m.s. to determine the deuterium content and distribution. Comparison of the relative intensities of the peaks at m/e 79, 80, 81 and 82 ($CH_3SO_2^+$) indicated the following composition for the methyl group (92.9 atom % excess D):

CH_3	2.4%
CH_2D	2.5
CHD_2	9.0
CD_3	86.1

2. Reaction of the N-Methylpiperidinium Salt with Pyridine and Deuterium Oxide

This experiment was performed as described for the trimethylammonium salt using the N-methylpiperidinium salt (2, 0.55 g, 2 mmol), pyridine (0.4 ml, 5 mmol) and deuterium oxide (5 ml). The yield of methanesulfonyl chloride was 55 mg (24%). The m.s. indicated the following deuterium distribution from the peaks at m/e 79, 80, 81 and 82 ($CH_3SO_2^+$, 96.6 atom % excess D):

CH_3	0 %
CH_2D	0.9
CHD_2	8.0
CD_3	91.0

3. Reaction of the Diethylmethylammonium Salt with Pyridine and Deuterium Oxide

This experiment was performed as described for the trimethylammonium salt using the diethylmethylammonium salt (4, 0.53 g, 2 mmol), pyridine (0.4 ml, 5 mmol) and deuterium oxide (5 ml). The yield of methanesulfonyl chloride was 89 mg (39%). The m.s. indicated the following deuterium distribution from the peaks at m/e 79, 80, 81 and 82 ($CH_3SO_2^+$, 91.7 atom % excess D):

CH_3	1.1%
CH_2D	4.4
CHD_2	12.5
CD_3	81.9

4. Reaction of the Diethylmethylammonium Salt with Pyridine and Deuterium Oxide in 1,2-Dimethoxyethane Solution

The diethylmethylammonium salt (4, 1.06 g, 4 mmol) was added to a rapidly stirred solution of pyridine (0.8 ml, 10 mmpl), deuterium oxide (2.0 ml, 111 mmol) and DME (30 ml, distilled from CaH_2) at room temperature. The reaction solution immediately became cloudy and a heavy, oily layer separated out. After 10 min, the mixture was evaporated to dryness on a rotary evaporator, then overnight in a vacuum desiccator over phosphorus pentoxide. The resulting salt mixture (1.51 g) was converted to the sulfonyl chloride as described above, yield 0.32 g (70%). The crude methanesulfonyl chloride was flash distilled and the deuterium content and distribution of the distillate determined by m.s. Comparison of the relative peak intensities at m/e 79, 80, 81 and 82 ($CH_3SO_2^+$) indicated the following composition for the methyl group (44.5 atom % excess D):

CH_3	14.2%
CH_2D	48.4
CHD_2	27.1
CD_3	10.3

Multiexchange Experiments with p-Toluidine-N,N-d_2

1. Preparation of p-Toluidine-N,N-d_2

N,N-Dideuterated p-toluidine was prepared by shaking an ethereal solution of recrystallized p-toluidine (5 g) in a

separatory funnel with 10 successive portions of deuterium oxide (5 ml each) in a glove-bag filled with dry air. The wet ethereal solution of p-toluidine-$\underline{d}_2$ was evaporated to dryness (rotary evaporator), then dried overnight in a vacuum desiccator over phosphorus pentoxide. The n.m.r. spectrum of the exchanged material showed no detectable signal due to N-H and the product was assumed to be over 95% N-dideuterated. The p-toluidine-$\underline{d}_2$ was stored over P_2O_5 and used without further purification.

2. Reaction of the Trimethylammonium Salt with p-Toluidine-N,N-$\underline{d}_2$

The trimethylammonium salt (1, 0.24 g, 1 mmol) in dry acetonitrile solution (5 ml) was added with stirring to excess p-toluidine-$\underline{d}_2$ (0.55 g, 5 mmol) in dry methylene chloride (5 ml). After 5 min, the reaction solution was poured into 0.5 N hydrochloric acid and extracted with methylene chloride. The extracts were washed twice with water, dried and the solvent evaporated to yield 185 mg (100%) methanesulfon-p-toluidide. Recrystallization from ether-pentane solution afforded 140 mg (76%), m.p. 102-104°. The n.m.r. spectrum showed 61 atom % excess D on the sulfonyl methyl group ($CDCl_3$). The deuterium distribution was determined by m.s. by comparing the relative peak intensities at m/e 185, 186, 187 and 188 (molecular ion). The sulfonyl methyl group was found to have the following composition (64.0 atom % excess D):

CH_3	8.1%
CH_2D	23.5
CHD_2	36.4
CD_3	31.9

3. Reaction of the N-Methylpiperidinium Salt with p-Toluidine-N,N-d_2

This experiment was performed as described for the trimethylammonium salt, but using the N-methylpiperidinium salt (2, 0.28 g, 1 mmol). The yield of methanesulfon-p-toluidide was 178 mg (96%). Recrystallization from ether-pentane solution gave 152 mg (82%), m.p. 102-104°. The n.m.r. spectrum indicated 60 atom % excess D on the sulfonyl methyl group ($CDCl_3$). Comparison of the m.s. peaks at m/e 185, 186, 187 and 188 (molecular ion) gave the following composition for the sulfonyl methyl group (59.4 atom % excess D):

CH_3	13.0%
CH_2D	24.6
CHD_2	33.9
CD_3	28.6

4. Reaction of the Ethyldimethylammonium Salt with p-Toluidine-N,N-d_2

This experiment was performed as described for the trimethylammonium salt, but using the ethyldimethylammonium salt (3, 0.25 g, 1 mmol). The crude yield of methanesulfon-

p-toluidide was 164 mg (89%). Recrystallization from ether-pentane solution gave 130 mg (70%), m.p. 102-103°. The n.m.r. spectrum indicated 49 atom % excess D on the sulfonyl methyl group ($CDCl_3$). Comparison of the m.s. peaks at m/e 185, 186, 187 and 188 (molecular ion) gave the following composition for the sulfonyl methyl group (48.8 atom % excess D):

CH_3	21.2%
CH_2D	30.4
CHD_2	29.3
CD_3	19.1

5. Reaction of the Diethylmethylammonium Salt with p-Toluidine-N,N-d_2

This experiment was performed as described for the trimethylammonium salt, but using the diethylmethylammonium salt (4, 0.27 g, 1 mmol). The crude yield of methanesulfon-p-toluidide was 170 mg (92%). Recrystallization from ether-pentane solution gave 120 mg (65%), m.p. 102-104°. The n.m.r. spectrum indicated 32 atom % excess D on the sulfonyl methyl group ($CDCl_3$). Comparison of the m.s. peaks at m/e 185, 186, 187 and 188 (molecular ion) gave the following composition for the sulfonyl methyl group (32.6 atom % excess D):

CH_3	34.0%
CH_2D	41.6

CHD_2	17.2%
CD_3	7.3

The diethylmethylammonium salt (0.09 g, 0.3 mmol) in 5 ml dry acetonitrile was reacted with a large excess of p-toluidine-d_2 (2.20 g, 12.3 mmol, 37-fold excess) in 10 ml dry methylene chloride. The reaction solution was worked up as described for the trimethylammonium salt reaction to give 63 mg (100%) methanesulfon-p-toluidide. Recrystallization from ether-pentane solution gave 31 mg (50%), m.p. 102.5-103.5°. The n.m.r. spectrum showed 32 atom % excess D on the sulfonyl methyl group ($CDCl_3$). Comparison of the m.s. peaks at m/e 185, 186, 187 and 188 (molecular ion) gave the following composition for the sulfonyl methyl group (32.6 atom % excess D):

CD_3	26.3%
CH_2D	54.0
CHD_2	15.3
CH_3	4.4

II. α-Hydrogen Exchange in 1,3-Dihydrobenzo[c]thiophene 2-Oxide

Preparation of 1,3-Dihydrobenzo[c]thiophene 2-Oxide (5a)

To a rapidly stirred solution of sodium metaperiodate (25.7 g, 0.12 mol) in water (230 ml) was added dropwise molten 1,3-dihydrobenzo[c]thiophene (14.8 g, 0.11 mol (54)). The mixture was stirred at room temperature for 1 h, then cooled to 0° for 3 h. The white precipitate (sodium iodate) was removed by filtration and washed with cold water. The filtrate and washings were extracted three times with methylene chloride. The extracts were dried and the solvent evaporated to give yellow crystals (16.4 g). The crude sulfoxide was dissolved in ether and filtered through neutral alumina to remove the coloured impurities. The ether was evaporated and the crystalline residue recrystallized from benzene-pentane solution to give 15.6 g (94%) colourless plates, m.p. 89-91°. The i.r. spectrum ($CHCl_3$): 1485 (w), 1210 (w), 1125 (w) and 1040 cm^{-1} (s). The n.m.r. spectrum consisted of ($CDCl_3$): AB quartet, δ_A 4.13 and δ_B 4.28 (4 H, J = 16 Hz) and 7.35 (4 H, singlet). With $Eu(dpm)_3$ shift reagent (0.3 equiv): AB quartet, δ_A 6.92 and δ_B 5.73. Anal. calcd. for C_8H_8OS: C 63.13; H 5.30; S 21.06. Found: C 63.35; H 5.49; S 21.18.

Preparation of trans-1,2-cis-1,3-dideuterio-1,3-dihydrobenzo[c]thiophene 2-Oxide (5b)

To a stirred, ice-cooled solution of NaOD in D_2O (10 ml, 0.1 N) was added 1,3-dihydrobenzo[c]thiophene 2-oxide (0.76 g, 5 mmol). This solution was stirred at 0° for 60 min, then quenched with 0.1 N hydrochloric acid (12 ml) and extracted twice with methylene chloride. The extracts were dried and the solvent evaporated to give a quantitative yield of crystalline sulfoxide. Recrystallization from benzene-pentane solution gave colourless plates, m.p. 89-90°. The n.m.r. spectrum showed ($CDCl_3$): δ 4.12 (2 H, triplet, $J_{H,D}$ = 2.2 Hz) and 7.35 (4 H, singlet). With Eu(dpm)$_3$ shift-reagent (0.3 equiv): δ 6.87 (2 H, triplet, $J_{H,D}$ = 2.2 Hz). Comparison of the m.s. peaks at m/e 152, 153, 154, 155 and 156 (molecular ion) gave the following deuterium distribution: d_0 0; d_1 6.0; d_2 79.0; d_3 12.6; d_4 2.4% (26.4 atom % excess D). Anal. calcd. for $C_8H_6D_2OS$: 25.00 atom % excess D. Found: 25.50 atom % excess D.

Preparation of 1,1,3,3-Tetradeuterio-1,3-dihydrobenzo[c]-thiophene 2-Oxide (5f)

A solution of 1,3-dihydrobenzo[c]thiophene 2-oxide (1 g) in 0.1 N NaOD (25 ml) was warmed at 50° for 1 h. The reaction was quenched with 0.5 N hydrochloric acid (10 ml) and extracted with methylene chloride. The extracts were dried and solvent evaporated to give the crystalline sulfoxide (1.0 g, 98%). Recrystallization from benzene-pentane

solution gave colourless plates, m.p. 90-91°. The n.m.r. spectrum indicated quantitative exchange of the benzylic protons. Comparison of the m.s. peaks at m/e 152, 153, 154, 155 and 156 gave the following deuterium distribution: d_0-d_2 0; d_3 5.3; d_4 94.6% (49.3 atom % excess D). Anal. calcd. for $C_8H_4D_4OS$: 50.00 atom % excess D. Found 47.85 atom % excess D.

Preparation of cis-1,2-cis-1,3-Dideuterio-1,3-dihydrobenzo-[c]thiophene 2-Oxide (5c)

The tetradeuterated sulfoxide (400 mg) was dissolved in aqueous sodium hydroxide (10 ml, 0.1 N) at 0° and allowed to react for 3 h. The reaction solution was quenched with 0.5 N hydrochloric acid (4 ml) and extracted with methylene chloride. The extracts were dried and the solvent evaporated to give crystalline sulfoxide (391 mg, 99%). Recrystallization from benzene-pentane solution gave colourless plates, 340 mg (86%), m.p. 89-90.5°. The n.m.r. spectrum showed ($CDCl_3$): δ 4.25 (2 H, triplet, $J_{H,D}$ = 2.2 Hz) and 7.31 (4 H, singlet). With $Eu(dpm)_3$ shift reagent (0.3 equiv): δ 5.81 (2 H, triplet, $J_{H,D}$ = 2.2 Hz). Comparison of the m.s. peaks at m/e 152, 153, 154, 155 and 156 gave the following deuterium distribution: d_0 0; d_1 10.6; d_2 71.6; d_3 12.6; d_4 5.1% (26.5 atom % excess D). Anal. calcd. for $C_8H_6D_2OS$: 25.00 atom % excess D. Found 24.90 atom % excess D.

Measurement of Deuterium Exchange Rates in Aqueous Medium

1. 1,3-Dihydrobenzo[c]thiophene 2-Oxide

The rate of exchange of the hydrogens trans to the oxygen was much faster than the exchange rate of the cis hydrogens, so that the exchange of either set could be studied separately. In both cases, a solution (25.0 ml) of the sulfoxide (10.00 mmol, 0.40 N) in 0.1 N NaOD-D_2O was prepared at 5.0° and 2 ml aliquots were withdrawn at appropriate intervals (2 min for the trans hydrogens or 60 min for the cis hydrogens). The samples were quenched in 0.5 N hydrochloric acid (1 ml) and the partially exchanged sulfoxide recovered by extraction with methylene chloride. The crude samples were recrystallized from benzene-pentane solution and the n.m.r. spectrum of each was then recorded on a Varian T-60 n.m.r. spectrometer equipped with a signal-lock device. The samples were run in $CDCl_3$ (TMS) solution with an equal weight of $Eu(fod)_3$ shift reagent and the percent exchange of either the trans or cis hydrogens was determined by comparing the integral for these hydrogens with that of the aromatic hydrogens. A plot of log (100-% exchange) against time was then made for both the trans and cis hydrogens and the slope (obtained by method of least squares) multiplied by 2.303, thereby giving directly the pseudo-first-order rate constant for each trans or cis hydrogen.

A. Kinetics of the trans-hydrogen exchange of 1,3-dihydrobenzo[c]thiophene 2-oxide in 0.1 N NaOD

Time (min)	Exchange (%)	(100-% Exch)	Log (100-% Exch)
0	0	100	2.00
2.2	40.8	59.2	1.77
4.0	51.1	48.9	1.69
6.0	67.3	32.7	1.51
8.0	77.0	23.0	1.36
10.0	80.3	19.7	1.29
12.0	84.9	15.1	1.18
14.0	86.2	13.8	1.14
16.0	89.6	10.4	1.02
18.0	92.4	7.6	0.88
20.0	93.8	6.2	0.79
22.0	95.8	4.2	0.62
24.0	96.6	3.4	0.53

$k_{trans} = 2.2 \times 10^{-3}\ sec^{-1}$

B. Kinetics of the cis-hydrogen exchange of 1,3-dihydrobenzo[c]thiophene 2-oxide in 0.1 N NaOD

Time (min)	Exchange (%)	(100-% Exch)	Log (100-% Exch)
0	0	100	2.00
61	12.3	87.7	1.94
120	21.0	79.0	1.90
180	30.3	69.7	1.84
240	39.8	60.2	1.78
300	44.7	55.3	1.74
360	51.5	48.5	1.69
420	58.2	41.8	1.62
480	61.2	38.8	1.59
540	64.4	35.6	1.55
600	69.8	30.2	1.48

$k_{cis} = 3.3 \times 10^{-5} sec^{-1}$

2. Benzyl Methyl Sulfoxide

The exchange-rate difference between the diastereotopic benzylic hydrogens of benzyl methyl sulfoxide was not sufficiently large to allow determination of the individual rates, so a special graphic method was used. A solution (20.0 ml) of benzyl methyl sulfoxide (8.00 mmol, 0.40 N) in 0.10 N NaOD-D_2O at 5.0° was prepared. Aliquots (2 ml) were withdrawn and quenched in 0.5 N hydrochloric acid (1 ml) at suitable intervals (2 h for the fast exchange or 12 h for the slow exchange). The sulfoxide was isolated by extraction into methylene chloride and purified by recrystallization from petroleum ether (30°-60°). The n.m.r. spectrum of each sample was recorded on a Varian T-60 spectrometer with signal-lock device and the total amount of exchange of the benzylic protons determined by integration. The rates of exchange of the two hydrogens were calculated (using the method of least squares) from a plot of log (100-% exchange) against time (Figure 12). The slower pseudo-first-order exchange rate constant was determined directly from the linear part of the graph and the best slope extrapolated back to t = 0. The logarithms of the differences in (100-% exchange), derived from the differences between this line and the data for the faster exchanging proton, were plotted as a function of time to give a linear slope from which the faster rate constant (pseudo-first-order) was calculated.

A. Kinetics of the slower hydrogen exchange of benzyl methyl sulfoxide in 0.1 N NaOD

Time (h)	Exchange (%)*	(100-% Exch)	Log (100-% Exch)
0	0	100	2.00
12	41.9	58.1	1.76
24	50.0	50.0	1.70
36	54.6	45.4	1.66
48	58.4	41.6	1.62
60	59.6	40.4	1.61
72	62.8	37.2	1.57
84	63.3	36.7	1.56
96	65.1	34.9	1.54
108	69.6	30.4	1.48
168	77.3	22.7	1.36

$k_2 = 1.4 \times 10^{-6} sec^{-1}$

---

* Percent exchange of both benzylic hydrogens.

B. Kinetics of the faster hydrogen exchange of benzyl methyl sulfoxide in 0.1 N NaOD

Time (h)	Exchange (%)*	(100-% Exch)	Log (100-% Exch)	Δ(100-% Exch)†	Log Δ(100-% Exch)
0	0	100	2.00	45.2	1.66
2	11.8	88.2	1.95	33.8	1.53
4	20.8	79.2	1.90	26.3	1.42
6	23.8	76.2	1.88	23.9	1.38
8	29.1	70.9	1.85	19.0	1.28
10	34.6	65.4	1.82	14.0	1.15
12	37.9	62.1	1.79	11.3	1.05
14	43.5	56.5	1.75	6.3	0.80
16	44.3	55.7	1.75	6.0	0.78
18	48.4	51.6	1.71	2.4	0.38
20	48.4	51.6	1.71	2.9	0.46

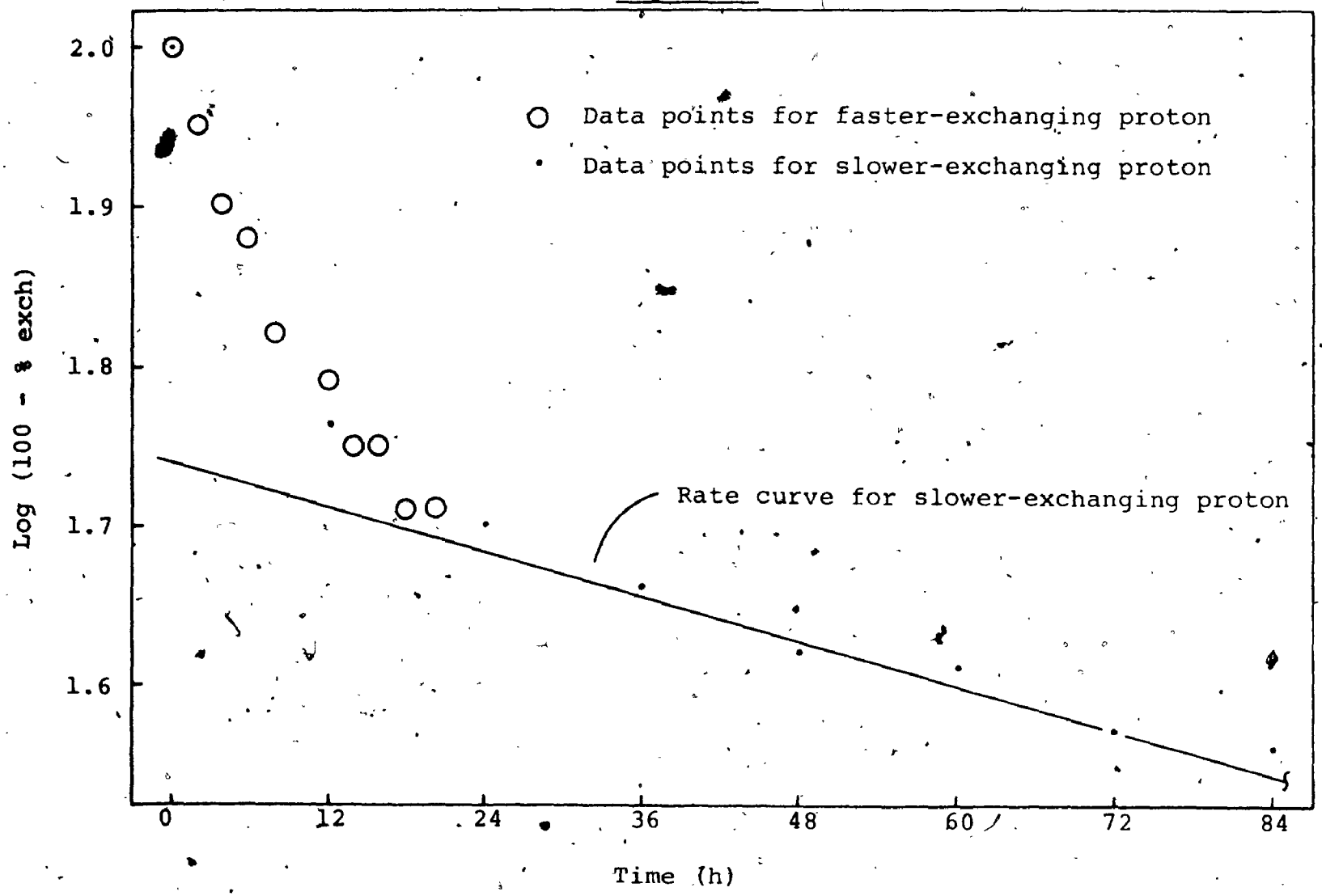
$$k_1 = 3.12 \times 10^{-5} \text{ sec}^{-1}$$

---

* Percent exchange of both benzylic hydrogens.

† Derived from Figure 12.

Figure 12



Kinetics Plot for Benzylic Hydrogen Exchange of Benzyl Methyl Sulfoxide

α-Exchange of 1,3-Dihydrobenzo[c]thiophene 2-Oxide via the Lithio Salt

Typically, the sulfoxide* (1 mmol) was dissolved in 30 ml tetrahydrofuran (freshly distilled from calcium hydride) under nitrogen and the solution cooled to 0°. Methyllithium (1.1 mmol, in ether) was then added to the rapidly stirred solution through a serum cap, using a hypodermic syringe. The resulting yellow solution was rapidly quenched (within 10 sec) with DCl-D_2O (1 ml, ~4 N) or aqueous HCl (5 ml, 0.5 N). This mixture was quickly worked up by diluting with water and extracting twice with methylene chloride. The extracts were dried and the solvent evaporated. The residue was transferred immediately to a thick-layer silica gel plate and developed with ethyl acetate. The first band above the baseline was isolated, treated with decolourizing carbon, and crystallized from benzene-pentane solution. Recrystallization gave colourless plates with sharp melting points (yields 50% or better). The products were examined by n.m.r., m.s. and deuterium analysis to determine the change in deuterium content and the stereochemistry of the exchange. The results are summarized in Table 22.

---

* The sulfoxides used were: (a) non-deuterated (5a); (b) trans-1,2-cis-1,3-dideuterated (5b); (c) cis-1,2-cis-1,3-dideuterated (5c); (d) 1,3-tetradeuterated (5f).

When 1,3-dihydrobenzo[c]thiophene 2-oxide was treated with methyllithium (as described above) for 10 min before addition of DCl, the purified product (~30% yield) was shown by n.m.r. ($CDCl_3$) to contain 12 atom % excess D. Comparison of the m.s. peaks at m/e 152, 153, 154, 155 and 156 (molecular ion) showed the following deuterium distribution: d_o 19.2; d_1 68.0; d_2 11.9; d_3 0.5; d_4 0.4% (11.9 atom % excess D).

Treatment of the non-deuterated sulfoxide (1 mmol) with 2 mmol of methyllithium under the conditions described above followed by rapid quenching with DCl gave a low yield of purified product (24 mg, 15%). The n.m.r. spectrum ($CDCl_3$) indicated 19 atom % excess D (or about 1.5 deuterium atoms per molecule). Comparison of the m.s. peaks at m/e 152-156 (molecular ion) indicated the following deuterium distribution: d_o 4.0; d_1 60.2; d_2 31.5; d_3 3.9; d_4 0.4% (17.1 atom % excess D).

The non-deuterated sulfoxide (76 mg, 0.5 mmol) in dry tetrahydrofuran (40 ml) was treated with methyllithium (0.5 mmol) at 0° as described above and allowed to stand at 0° for 10 min. Then the tetradeuterated sulfoxide (78 mg., 0.5 mmol) in dry THF (5 ml) was added and the solution left for 10 min more. The reaction was quenched with 0.5 N hydrochloric acid and worked up in the usual manner to give an oily product (127 mg, 83%). The product was purified by t.l.c. (developed with methylene chloride). The n.m.r. spectrum ($CDCl_3$) showed considerable exchange of the

benzylic hydrogens as manifested by a decrease in the size of the AB quartet pattern of these hydrogens and the appearance of a CHD triplet, estimated to be equal in area to the CH_2 quartet. When this experiment was repeated, but with rapid quenching (within a few sec) after addition of the tetradeuterated sulfoxide, the n.m.r. spectrum ($CDCl_3$) of the product (137 mg, 87%) indicated only a trace of exchange (CHD products, <5%).

Competition of 1,3-Dihydrobenzo[c]thiophene 2-Oxide and Benzyl Methyl Sulfoxide for Methyllithium

The cyclic sulfoxide (5a, 152 mg, 1 mmol) and benzyl methyl sulfoxide (308 mg, 2 mmol) were dissolved in dry tetrahydrofuran (40 ml, freshly distilled from calcium hydride) under nitrogen*. This solution was cooled in a dry-ice-acetone bath and methyllithium (1 mmol, in ether) was added through a serum cap (hypodermic syringe). The resulting yellow solution was quenched within 10 sec with DCl-D_2O (1 ml, ~4 N) and worked up by diluting with water and extracting twice with methylene chloride. The extracts were dried, treated with decolourizing carbon, and the solvent evaporated to give a yellow oil (417 mg, 90%). The n.m.r. spectrum ($CDCl_3$) of the crude product showed no detectable impurities. From the integration, the ratio of deuterium incorporation for the cyclic sulfoxide vs benzyl methyl sulfoxide was about 11 to 1.

---

* The ratio of sulfoxides gives a 1:1 ratio of benzylic hydrogens α to the sulfinyl groups.

III. Steric Course of Formation of Benzocyclobutene by Thermal Desulfonylation of 1,3-Dihydrobenzo[c]thiophene 2,2-Dioxide

Preparation of cis-1,3-Dideuterio-1,3-dihydrobenzo[c]-thiophene 2,2-Dioxide (6a)

To a stirred, ice-cooled solution of 30% aqueous hydrogen peroxide (5 ml) in glacial acetic acid (5 ml) was added drop-wise a solution of cis-1,3-dideuterio-1,3-dihydrobenzo[c]thiophene 2-oxide* (5b, 1.3 g, 8.5 mmol, 25.50 atom % excess D) in glacial acetic acid (2 ml). The reaction solution was stirred at room temperature for two days, then diluted with water. The resulting crystalline precipitate was collected and washed with water to yield 1.55 g of the sulfone. Recrystallization from methylene chloride-pentane solution gave cis-dideuterated sulfone as colourless needles, 1.13 g (80%), m.p. 150-151° (reported 150-151°, (57)). The i.r. spectrum ($CHCl_3$): 1320 (s), 1185 (s), 1115 (m) and 1100 cm^{-1} (m). The n.m.r. spectrum showed ($CDCl_3$): δ 4.30 (2 H, triplet, $J_{H,D}$ = 2.3 Hz) and 7.31 (4 H, multiplet). The n.m.r. integration gave 26.6 atom % excess D. From comparison of the m.s. peaks at m/e 168, 169, 170, 171 and 172 (molecular ion), the product was found to have the following deuterium distribution: d_0 0; d_1 6.0; d_2 81.7; d_3 11.1; d_4 1.2% (25.9 atom % excess D).

---

* For the preparation of this sulfoxide, see P. 148.

Preparation of α,α'-Dideuterio-o-xylene-α,α'-diol

A solution of phthalaldehyde (3.1 g, 23 mmol, Aldrich) in ethanol-d (10 ml) was added slowly to a stirred, ice-cooled solution of sodium borodeuteride (1.0 g, 24 mmol, Merck, Sharp and Dohme) in ethanol-d (10 ml). After stirring at room temperature for 2 h, the reaction mixture was diluted with water, neutralized cautiously with 6 N hydrochloric acid and extracted with methylene chloride. The extracts were dried and the solvent evaporated to give an oil (2.97 g, 86%). Crystallization from ether-pentane solution gave pure phthalyl alcohol-α,α'-d_2 1.22 g (35%), m.p. 60.5-61.5° (reported 65-67.5°, (83)). The i.r. spectrum ($CHCl_3$): 3610 (w), 3100-3600 (broad), 2350 (vw), 2150 (vw), 1195 (m), 1020 (m) and 725 cm^{-1} (m). The n.m.r. spectrum showed ($CDCl_3$): δ 4.25 (2 H, broad mound), 4.49 (2 H, broad singlet) and 7.25 (4 H, multiplet). The n.m.r. integration gave 20.0 atom % excess D.

Preparation of α,α'-Dideuterio-α,α'-dichloro-o-xylene

Phthalyl alcohol-α,α'-d_2 (α,α'-dideuterio-o-xylene-α,α'-diol, 1.0 g, 7 mmol) was dissolved in thionyl chloride (5 ml). When the ensuing exothermic reaction had subsided (a few sec), the solution was transferred to a Carius tube and the tube sealed. The reaction solution was heated to 125° for 18 h, then cooled and the tube opened. The excess thionyl chloride was distilled off and the residue dissolved in methylene chloride. The solution was washed with water

and saturated aqueous sodium chloride and dried. Evaporation of the solvent gave a readily-crystallized, yellow oil, 1.15 g (91%). The dichloride was purified by sublimation (90-110°, 6 mm Hg) to give colourless crystals, 1.06 g (84%), m.p. 51-53° (reported 52-54° (84)). The i.r. spectrum ($CHCl_3$): 2220 (w), 1775 (m), 1450 (w), 1315 (w) and 905 cm^{-1} (ms). The n.m.r. spectrum showed ($CDCl_3$): δ 4.66 (2 H, triplet, $J_{H,D}$ = 1.8 Hz) and 7.29 (4 H, multiplet). Integration gave 26.0 atom % excess D.

Preparation of 1,3-Dideuterio-1,3-dihydrobenzo[c]thiophene

To a refluxing solution of sodium sulfide nonahydrate (2.1 g, BDH) in 67% aqueous ethanol (30 ml) was added dropwise a solution of α,α'-dideuterio-α,α'-dichloro-o-xylene (1.0 g, 5.7 mmol) in ethanol (5 ml). After refluxing for 2 h, the yellow-green solution was diluted with an equal volume of water and extracted with methylene chloride (three times). The extracts were dried and the solvent evaporated to give a yellow oil (0.84 g). The dideuterated sulfide was not purified further but oxidized directly to the sulfone (below).

Preparation of 1,3-Dideuterio-1,3-dihydrobenzo[c]thiophene 2,2-Dioxide (6b) (Equimolar cis/trans)

To a stirred, ice-cooled solution of 30% aqueous hydrogen peroxide (5 ml) in glacial acetic acid (5 ml) was added a solution of crude 1,3-dideuterio-1,3-dihydrobenzo-

[c]thiophene (0.74 g, 5.4 mmol), in a few ml glacial acetic acid. After stirring at room temperature for 40 h, the solution was diluted with an equal volume of water and the resulting crystalline precipitate collected and washed with cold water. Recrystallization from methylene chloride-pentane solution gave 0.75 g (58% over two steps) colourless needles of the equimolar cis/trans-1,3-dideuterated sulfone, m.p. 143-144° (reported 150-151° (57)). The i.r. spectrum (CH_2Cl_2): 1320 (s), 1190 (s), 1115 (m) and 1110 cm^{-1} (m). The n.m.r. spectrum consisted of ($CDCl_3$): δ 4.31 (2 H, triplet, $J_{H,D}$ = 2.3 Hz) and 7.32 (4 H, multiplet). The n.m.r. integration gave 24.5 atom % excess D.

Thermolysis of 1,3-Dihydrobenzo[c]thiophene 2,2-Dioxide

A sample of 1,3-dihydrobenzo[c]thiophene 2,2-dioxide (6, 336 mg, 2 mmol (57)) was placed in a quartz-tube thermolysis apparatus* and the quartz tube heated to 500°. The sulfone was sublimed slowly through the hot tube at a pressure of 1 μm Hg (measured between the product cold-trap and pump cold-trap) and the products were collected at the end of the tube in a liquid-nitrogen-cooled trap. The product was a pale yellow liquid with a strong odour of sulfur dioxide. Evaporation of the sulfur dioxide gave 196 mg (93%) crude benzocyclobutene. The product was

* For a description of this apparatus, see references 7, 85.

distilled in a short-path apparatus (reported b.p. 149-150° (57%) to give a colourless aromatic liquid. The i.r. spectrum (film): 1460 (m), 1200 (w), 775 (ms) and 710 cm^{-1} (ms). The n.m.r. spectrum consisted of ($CDCl_3$): δ 3.16 (4 H, singlet) and 7.1 (4 H, multiplet).

Thermolysis of cis-1,3-Dideuterio-1,3-dihydrobenzo[c]-thiophene 2,2-Dioxide

The cis-dideuterated sulfone (6a, 1.0 g) was thermolysed at 500° in the quartz-tube apparatus as described for the non-deuterated sulfone. The crude yield of benzocyclobutene-d_2 was 630 mg (100%) and distillation gave pure 1,2-dideuteriobenzocyclobutene. The i.r. spectrum (film): 2080 (w), 1450 (m), 895 (mw) and 725 cm^{-1} (ms). The i.r. spectrum was also recorded in the absorption mode (0.1 mm neat sample, KBr cell, air reference). Bands at 645 and 895 cm^{-1} were assigned to the cis-1,2-dideuterated benzocyclobutene, while bands at 825, 850 and 905 cm^{-1} were assigned to the trans-isomer*. Comparison of these bands

* These assignments were made after examination of several spectra of 1,2-dideuteriobenzocyclobutene of varying cis- and trans-isomer compositions. The height of each band was measured (after appropriate baseline adjustments to correct for large adjacent peaks) to determine the relative amounts of cis- and trans-isomer. A sample of known composition (trans:cis = 1:1, from thermolysis of equimolar cis/trans-1,3-dideuterio-1,3-dihydrobenzo[c]-thiophene 2,2-dioxide at 500° or multiple thermolysis of cis-1,3-dideuterio-1,3-dihydrobenzo[c]thiophene 2,2-dioxide at 600°) was used as a reference. Sample spectra are shown in Figures 9-11.

gave a trans:cis ratio of 3:1 for this sample. The n.m.r. spectrum showed ($CDCl_3$): δ 3.12 (2 H, broad singlet) and 7.07 (4 H, multiplet) and integrated to 25.7 atom % excess D. The deuterium-decoupled ^{13}C-satellite proton n.m.r. spectrum of the benzylic protons showed two superimposed doublets (J_{cis} = 5.5 Hz and J_{trans} = 2.8 Hz) in the ratio trans:cis of 3 or 4:1. Comparison of the m.s. peaks at m/e 104, 105, 106, 107 and 108 (molecular ion) gave the following deuterium distribution: d_o 0; d_1 2.9; d_2 81.4; d_3 15.2; d_4 0.6% (26.3 atom % excess D). Anal. calcd. for $C_8H_6D_2$: 25.00 atom % excess D. Found 25.55 atom % excess D.

Thermolysis of 1,3-Dideuterio-1,3-dihydrobenzo[c]thiophene 2,2-Dioxide (Equimolar cis/trans)

The equimolar cis/trans-dideuterated sulfone (6b, 726 mg) was thermolysed at 500° in the quartz-tube apparatus as described for the non-deuterated sulfone. The crude yield of benzocyclobutene-d_2 was 430 mg (95%). The product was distilled and its spectra recorded, including the absorption-mode i.r. spectrum (neat sample, 0.1 mm KBr cell, air reference). This spectrum of equimolar cis- and trans-1,2-dideuteriobenzocyclobutene was used as a reference to calibrate other i.r. spectra of various cis and trans compositions (see footnote, P. 164). The deuterium-decoupled ^{13}C-satellite proton n.m.r. spectrum of the benzylic protons indicated a 1:1 mixture of cis- and trans-1,2-dideuteriobenzocyclobutene. Comparison of the m.s.

peaks of m/e 104, 105, 106, 107 and 108 (molecular ion) gave the following deuterium distribution: d_0 0.6; d_1 3.2; d_2 92.5; d_3 3.3; d_4 0.3% (24.9 atom % excess D).

Multiple Thermolysis of cis-1,3-Dideuterio-1,3-dihydrobenzo[c]thiophene 2,2-Dioxide

A sample of the cis-dideuterated sulfone (6a, 2.22 g) was thermolysed at 500° in the quartz-tube apparatus as described for the non-deuterated sulfone. The crude product was distilled and the absorption-mode i.r. spectrum recorded on a neat sample (0.1 mm KBr cell, neat sample, air reference). Recovered starting material (0.06 g) indicated 96% desulfonylation.

The benzocyclobutene-d_2 from the first run was thermolysed again at 500° and the absorption-mode i.r. spectrum of the product recorded. The product was thermolysed twice again at 600°, each time recording the absorption-mode i.r. spectrum of the product. The final product was assumed to be equimolar cis/trans-1,2-dideuteriobenzocyclobutene. From comparison of the i.r. bands at 645 and 895 cm^{-1} (cis-dideuterated product) and 825, 850 and 905 cm^{-1} (trans-dideuterated product), the four products were found to have the following compositions*:

---

*See footnote P. 164.

Run (Temp)	trans	cis
1 (500°)	75%	25%
2 (500°)	65	35
3 (600°)	50	50
4 (600°)	50	50

The spectrum of the sample from run 4 was identical to that of equimolar cis/trans-1,2-dideuteriobenzocyclobutene (above).

Mild Thermolysis of cis-1,3-Dideuterio-1,3-dihydrobenzo[c]-thiophene 2,2-Dioxide

A sample of the cis-dideuterated sulfone (6a, 730 mg) was thermolysed at 430-440° in the quartz-tube apparatus as described for the non-deuterated sulfone. A yield of 90 mg (20%) benzocyclobutene-d_2 was obtained and 570 mg (78%) of the starting material recovered. The benzocyclobutene-d_2 was distilled and the absorption-mode i.r. spectrum recorded (0.1 mm neat sample, KBr cell, air reference).

The recovered starting material was thermolysed at 600° and the crude product thermolysed again at 600° to give 330 mg (93%) benzocyclobutene, assumed to be equimolar cis/trans-1,2-dideuterated. The distilled product was examined by absorption-mode i.r. spectroscopy and the spectrum compared with that of the product obtained from thermolysis at 430-440° (the spectrum of the equimolar cis/trans product was found to be identical with that of an authentic

sample prepared by thermolysis (500°) of 1,3-dideuteriobenzo[c]thiophene 2,2-dioxide (6b) (equimolar cis/trans). Comparison of the bands at 645 and 895 cm^{-1} (cis) and 825, 850 and 905 cm^{-1} (trans) indicated that the product obtained from mild thermolysis of the sulfone was almost pure trans-1,2-dideuteriobenzocyclobutene*. Only a trace of the cis-isomer (<4%) was visible in the i.r. spectrum.

Flash Thermolysis of cis-1,3-Dideuterio-1,3-dihydrobenzo[c]-thiophene 2,2-Dioxide

A sample of the cis-dideuterated sulfone (6a, 100 mg) was subjected to flash thermolysis (71, 86) at 500° and 10-14 μm Hg pressure (ceramic oven). The sample was sublimed into the oven and the products were trapped out on a liquid-nitrogen-cooled cold finger. The crude yield of benzocyclobutene-d_2 was 70 mg and 12 mg (12%) starting material were recovered. The product was distilled and its spectra recorded. The absorption-mode i.r. spectrum (0.1 mm neat sample, KBr cell, air reference) showed an identical cis/trans-1,2-dideuterated composition as observed for the product of quartz-tube thermolysis (trans:cis ≈ 3:1, see above). The deuterium-decoupled ^{13}C-satellite proton n.m.r. spectrum of the benzylic protons showed the trans:cis ratio of 3 or 4:1. Comparison of the m.s. peaks at m/e 104, 105,

---

* See footnote, P. 164.

106, 107 and 108 (molecular ion) gave the following deuterium distribution: d_o 0.6; d_1 4.4; d_2 81.5; d_3 12.5; d_4 1.1% (26.1 atom % excess D).

REFERENCES

1. J.F. King, P. de Mayo and D.L. Verdun, Can. J. Chem. 47, 4509 (1969). J.F. King, R.A. Marty, P. de Mayo and D.L. Verdun, J. Amer. Chem. Soc. 93, 6304 (1971).

2. G. Opitz, Ang. Chem., Int. Ed. Eng., 6, 107 (1967). J.F. King, Accts. Chem. Res. 8, 10 (1975).

3. J.F. King and T. Durst, J. Amer. Chem. Soc. 86, 287 (1964). Ibid. 87, 5684 (1965).

4. W.E. Truce, R.W. Campbell and J.R. Norell, J. Amer. Chem. Soc. 86, 288 (1964). W.E. Truce and R.W. Campbell, ibid. 88, 3599 (1966).

5. E.A. Luinstra, Ph.D. Thesis, University of Western Ontario (1971).

6. J.F. King, E.A. Luinstra and D.R.K. Harding, J. Chem. Soc. Chem. Commun., 1313 (1972).

7. D.R.K. Harding, Ph.D. Thesis, University of Western Ontario (1973).

8. R. Fusco, S. Rossi and S. Maiorana, Chim.Ind. (Milan) 44, 873 (1962). (Chem. Abstr. 60, 13240 (1964)).

9. G. Opitz and D. Bücher, Tetrahedron Lett., 5263 (1966).

10. G. Opitz, M. Kleeman, D. Bücher and K. Kieth, Ang. Chem., Int. Ed. Eng., 5, 594 (1966).

11. J.S. Grossert and M.M. Bharadwaj, J. Chem. Soc. Chem. Commun., 144 (1974).

12. I.L. Knunyants and G.A. Sokolskii, Ang. Chem. Int. Ed. Eng., 11, 583 (1972). L.J. Ragulin, P.O. Rapalo, G.A. Sokolskii and I.L. Knunyants, Izvest. Akad. Nauk, SSSR, Ser. Khim. 20, 1045 (1971). (Chem. Abstr. 75, 87784d (1971)).

13. R. Appel and R. Helwerth, Ang. Chem., Int. Ed. Eng., 6, 952 (1967).

14. G.M. Atkins and E.M. Burgess, J. Amer. Chem. Soc. 90, 4744 (1968).

15. E.E. Gilbert, Chem. Rev. 62, 549 (1962).

16. R.D. Batts, J. Chem. Soc. B, 547 (1966). Ibid., 551.

17. D. Vorländer and M. Kauffmann, Ber. 43, 2735 (1910).

18. C.R. Gambill, T.D. Roberts and H. Schechter, J. Chem. Ed. 49, 287 (1972).

19. H. Majda and K. Okon, Biul. Wojskowej Akad. Tech. 10, 101 (1961). (Chem. Abstr. 57, 11162 (1962)).

20. L. Horner and H. Nickel, Ann. 597, 20 (1955).

21. T. Oishi, K. Kamata and Y. Ban, Chem. Commun., 777 (1970).

22. T. Oishi, K. Kamata, S. Kosuda and Y. Ban, J. Chem. Soc. Chem. Commun., 1148 (1972).

23. G. Opitz and K. Fischer, Z. Naturforsh. 18b, 775 (1963).

24. R.W. Alder and M.G. Ahmed, University of Bristol, private communication.

25. Tables for Identification of Organic Compounds. Chemical Rubber Publishing Company, Cleveland, Ohio, U.S.A., 1960.

26. Dictionary of Organic Compounds. I. Heilbron and H.M. Bunbury, Eds., Eyre and Spottiswoode, London, 1953.

27. E.M. Kosower, J. Amer. Chem. Soc. 80, 3253 (1958).

28. G. Stork and I.J. Borowitz, J. Amer. Chem. Soc. 84, 313 (1962). G. Opitz and H. Adolph, Ang. Chem., Int. Ed. Eng., 1, 113 (1962). W.E. Truce, et al., J. Amer. Chem. Soc. 84, 3030 (1962).

29. J.F. King and S.K. Sim, unpublished results.

30. R.M. Laird and M.J. Spence, J. Chem. Soc. B, 1434 (1971).

31. J.F. King and Y.I. Yang, unpublished results.

32. D.R. Rayner, A.J. Gordon and K. Mislow, J. Amer. Chem. Soc. 90, 4854 (1968)

33. H. Phillips, J. Chem. Soc. 127, 2552 (1925).

34. D.J. Cram and S.H. Pine, J. Amer. Chem. Soc. 85, 1096 (1963).

35. A. Rauk, E. Buncel, R.Y. Moir and S. Wolfe, J. Amer. Chem. Soc. 87, 5498 (1965).

36. J.E. Baldwin, R.E. Hackler and R.M. Scott, Chem. Commun., 1415 (1969).

37. S. Wolfe and A. Rauk, Chem. Commun., 778 (1966).

38. A. Rauk, S. Wolfe and I.G. Csizmadia, Can. J. Chem. 47, 113 (1969).

39. S. Wolfe, Accounts Chem. Res. 5, 102 (1972).

40. B.J. Hutchinson, K.K. Andersen and A.R. Katritzky, J. Amer. Chem. Soc. 91, 3839 (1969).

41. R. Lett, S. Bory, B. Moreau and A. Marquet, Tetrahedron Lett., 3255 (1971).

42. R.R. Fraser and F.J. Schuber, Chem. Commun., 397 (1969).

43. M. Nishio, Chem. Commun., 562 (1968).

44. R.R. Fraser and F.J. Schuber, Can. J. Chem. 48, 633 (1970).

45. N. Nishihata and M. Nishio, Tetrahedron Lett., 4839 (1972).

46. T. Durst, R.R. Fraser, M.R. McClory, R.B. Swingle, R. Viau and Y.Y. Wigfield, Can. J. Chem. 48, 2148 (1970).

47. T. Durst, R. Viau and M.R. McClory, J. Amer. Chem. Soc. 93, 3077 (1971).

48. R. Viau and T. Durst, J. Amer. Chem. Soc. 95, 1346 (1973).

49. N. Nishihata and M. Nishio, J. Chem. Soc. Perkin II, 1730 (1972).

50. M.B. D'Amore and J.I. Brauman, J. Chem. Soc. Chem. Commun., 398 (1973).

51. R.R. Fraser, F.J. Schuber and Y.Y. Wigfield, J. Amer. Chem. Soc. 94, 8795 (1972).

52. U. Folli, D. Iarossi, I. Moretti, F. Taddei and G. Torre, J. Chem. Soc. Perkin II, 1655 (1974). U. Folli, D. Iarossi and F. Taddei, ibid., 1658.

53. T. Durst and M. Molin, Tetrahedron Lett., 63 (1975).

54. J.F. King, A. Hawson, B.L. Huston, L.J. Danks and J. Komery, Can. J. Chem. 49, 943 (1971).

55. R.R. Fraser and Y.Y. Wigfield, Chem. Commun., 1471 (1970).

56. W. Klyne and V. Prelog, Experientia 16, 521 (1960).

57. M.P. Cava and A.A. Deana, J. Amer. Chem. Soc. 81, 4266 (1959).

58. O. Grummitt, A.E. Ardis and J. Fick, J. Amer. Chem. Soc. 72, 5167 (1950).

59. K. Alder and M. Fremery, Tetrahedron 14, 190 (1961).

60. F.R. Jensen, W.E. Coleman and A.J. Berlin, Tetrahedron Lett., 15 (1962).

61. W.L. Mock, J. Amer. Chem. Soc. 88, 2857 (1966).

62. S.D. MacGregor and D.M. Lemal, J. Amer. Chem. Soc. 88, 2858 (1966).

63. R.B. Woodward and R. Hoffmann, The Conservation of Orbital Symmetry. Academic Press, New York, N.Y., 1971.

64. C.R. Flynn and J. Michl, J. Amer. Chem. Soc. 95, 5802 (1973).

65. G. Quinkert, M. Finke, J. Palmowski and W.W. Wiersdorff, Mol. Photochem. 1, 433 (1969).

66. G. Quinkert, Photochem. Photobiol. 7, 783 (1968).

67. M.P. Cava, M.J. Mitchell and A.A. Deana, J. Org. Chem. 25, 1481 (1960).

68. G. Fraenkel, Y. Asahi, M.J. Mitchell and M.P. Cava, Tetrahedron 20, 1179 (1964).

69. H. Hart, J.A. Hartlage, R.W. Fish and R.R. Rafos, J. Org. Chem. 31, 2244 (1966).

70. J.M. Wilson, et al., Experiments in Physical Chemistry. Pergamon Press, New York, 1962.

71. P. de Mayo, Endeavour 31, 135 (1972), and references cited therein.

72. J.E. Baldwin, A.H. Andrist and R.K. Pinschmidt, Jr., Accounts Chem. Res. 5, 402 (1972). J.A. Berson, ibid., 406.

73. M.C. Hamming and N.G. Foster, Interpretation of Mass Spectra of Organic Compounds. Academic Press, New York, 1972.

74. Wm. D. Emmons and A.F. Ferris, J. Amer. Chem. Soc. 75, 2257 (1953).

75. J.L. Pinkus, G. Pinkus and T. Cohen, J. Org. Chem. 27, 4356 (1962).

76. A. Novak and E. Whalley, Trans Faraday Soc. 55, 1490 (1959).

77. I.B. Douglass and B.S. Farah, J. Org. Chem. 24, 973 (1959).

78. J.F. King in A. Weissberger, Ed., Elucidation of Structures by Physical and Chemical Methods, Part One. Interscience, New York, 1963.

79. W.E. Truce and L.W. Christensen, J. Org. Chem. 33, 2261 (1968).

80. J.M. Salietti Vinué and J.J. Bonet-Sugrañes, Afinidad 24, 20 (1967).

81. H.C. Brown and B. Kanner, J. Amer. Chem. Soc. 75, 3865 (1953).

82. L.M. Jackman, Applications of Nuclear Magnetic Resonance in Organic Chemistry. Pergamon Press, New York, 1959.

83. W.E. Rosen, V.P. Toohey and A.C. Shabica, J. Amer. Chem. Soc. 80, 935 (1958).

84. A.L. Mndzhoyan and G.L. Payayan, Chem. Abstr. 60, 7976f (1964).

85. J.F. King, P. de Mayo, C.L. McIntosh, K. Piers and D.J.H. Smith, Can. J. Chem. 48, 3704 (1970).

86. D.L. Verdun, Ph.D. Thesis, University of Western Ontario (1971).