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sulphur-containing functional groups

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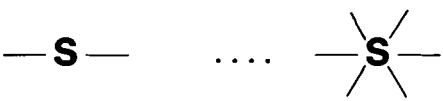

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The chemistry of
sulphur-containing functional groups

Edited by
SAUL PATAI
and
ZVI RAPPOPORT
The Hebrew University, Jerusalem

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Foreword

The series *The Chemistry of Functional Groups* contains seven volumes of a sub-series concerning sulphur containing functional groups, published between 1974 and 1991. These volumes were the following:

The chemistry of the thiol group (1974)
Supplement E. The chemistry of ethers, crown ethers, hydroxyl groups and their sulphur analogues (1980)
The chemistry of the sulphonium group (1981)
The chemistry of sulphones and sulphoxides (1988)
The chemistry of sulphinic acids, esters and their derivatives (1990)
The chemistry of sulphenic acids and their derivatives (1990)
The chemistry of sulphonic acids, esters and their derivatives (1991)

Many subjects dealt with in the chapters contained in the above volumes have developed considerably since their publication and we felt that they should be updated. In addition we were interested in publishing some chapters which did not materialize for the original volumes, as well as some chapters which were on completely new subjects. This was the motivation for offering the present supplementary volume to our readers.

Inevitably, not all the planned chapters materialized. Among these were chapters on the following subjects: 'Sulphur containing free radicals in photochemical processes', 'Sulphonates as nucleophiles', 'Sulphur containing ylides', and finally and most regrettably, 'Safety, toxicity and environmental effects'.

The authors' literature search in most cases extended up to the Spring of 1992.

We will be indebted to readers who will bring to our attention mistakes or omissions in this or in any other volume of *The Chemistry of Functional Groups* series.

Jerusalem
June 1993

SAUL PATAI
ZVI RAPPOPORT

The Chemistry of Functional Groups Preface to the series

The series 'The Chemistry of Functional Groups' was originally planned to cover in each volume all aspects of the chemistry of one of the important functional groups in organic chemistry. The emphasis is laid on the preparation, properties and reactions of the functional group treated and on the effects which it exerts both in the immediate vicinity of the group in question and in the whole molecule.

A voluntary restriction on the treatment of the various functional groups in these volumes is that material included in easily and generally available secondary or tertiary sources, such as Chemical Reviews, Quarterly Reviews, Organic Reactions, various 'Advances' and 'Progress' series and in textbooks (i.e. in books which are usually found in the chemical libraries of most universities and research institutes), should not, as a rule, be repeated in detail, unless it is necessary for the balanced treatment of the topic. Therefore each of the authors is asked not to give an encyclopaedic coverage of his subject, but to concentrate on the most important recent developments and mainly on material that has not been adequately covered by reviews or other secondary sources by the time of writing of the chapter, and to address himself to a reader who is assumed to be at a fairly advanced postgraduate level.

It is realized that no plan can be devised for a volume that would give a complete coverage of the field with no overlap between chapters, while at the same time preserving the readability of the text. The Editor set himself the goal of attaining reasonable coverage with moderate overlap, with a minimum of cross-references between the chapters. In this manner, sufficient freedom is given to the authors to produce readable quasi-monographic chapters.

The general plan of each volume includes the following main sections:

(a) An introductory chapter deals with the general and theoretical aspects of the group.

(b) Chapters discuss the characterization and characteristics of the functional groups, i.e. qualitative and quantitative methods of determination including chemical and physical methods, MS, UV, IR, NMR, ESR, and PES—as well as activating and directive effects exerted by the group, and its basicity, acidity and complex-forming ability.

(c) One or more chapters deal with the formation of the functional group in question, either from other groups already present in the molecule or by introducing the new group directly or indirectly. This is usually followed by a description of the synthetic uses of the group, including its reactions, transformations and rearrangements.

(d) Additional chapters deal with special topics such as electrochemistry, photochemistry, radiation chemistry, thermochemistry, syntheses and uses of isotopically labelled compounds, as well as with biochemistry, pharmacology and toxicology. Whenever applicable, unique chapters relevant only to single functional groups are also included (e.g. 'Polyethers'. 'Tetraaminoethylenes' or 'Siloxanes').

This plan entails that the breadth, depth and thought-provoking nature of each chapter will differ with the views and inclinations of the authors and the presentation will necessarily be somewhat uneven. Moreover, a serious problem is caused by authors who deliver their manuscript late or not at all. In order to overcome this problem at least to some extent, some volumes may be published without giving consideration to the originally planned logical order of the chapters.

Since the beginning of the Series in 1964, two main developments occurred. The first of these is the publication of supplementary volumes which contain material relating to several kindred functional groups (Supplements A, B, C, D, E and F). The second ramification is the publication of a series of 'Updates', which contain in each volume selected and related chapters, reprinted in the original form in which they were published, together with an extensive updating of the subjects, if possible, by the authors of the original chapters. A complete list of all above mentioned volumes published to date will be found on the page opposite the inner title page of this book.

Advice or criticism regarding the plan and execution of this series will be welcomed by the Editor.

The publication of this series would never have been started, let alone continued, without the support of many persons in Israel and overseas, including colleagues, friends and family. The efficient and patient co-operation of staff members of the publisher also rendered me invaluable aid. My sincere thanks are due to all of them, especially to Professor Zvi Rappoport who, for many years, shares the work and responsibility of the editing of this Series.

The Hebrew University
Jerusalem, Israel

SAUL PATAI

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List of abbreviations used

Ac	acetyl (MeCO)
acac	acetylacetone
Ad	adamantyl
Alk	alkyl
All	allyl
A·	anisyl
	aryl
Bz	benzoyl (C_6H_5CO)
Bu	butyl (also *t*-Bu or Bu^t)
CD	circular dichroism
CI	chemical ionization
CIDNP	chemically induced dynamic nuclear polarization
CNDO	complete neglect of differential overlap
Cp	η^5-cyclopentadienyl
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DME	1,2-dimethoxyethane
DMF	*N*,*N*-diamethylformamide
DMSO	dimethyl sulphoxide
ee	enantiomeric excess
EI	electron impact
ESCA	electron spectroscopy for chemical analysis
ESR	electron spin resonance
Et	ethyl
eV	electron volt
Fc	ferrocene
FD	field desorption
FI	field ionization
FT	Fourier transform
Fu	Furyl(OC_4H_5)
Hex	hexyl(C_6H_{13})
c-Hex	cyclohexyl(C_6H_{11})
HMPA	hexamethylphosphortriamide
HOMO	highest occupied molecular orbital

i-	iso
Ip	ionization potential
IR	infrared
ICR	ion cyclotron resonance
LCAO	linear combination of atomic orbitals
LDA	lithium diisopropylamide
LUMO	lowest unoccupied molecular orbital
M	metal
M	parent molecule
MCPBA	*m*-chloroperbenzoic acid
Me	methyl
MNDO	modified neglect of diatomic overlap
MS	mass spectrum
n	normal
Naph	naphthyl
NBS	*N*-bromosuccinimide
NMR	nuclear magnetic resonance
Pen	pentyl(C_5H_{11})
Pip	piperidyl($C_5H_{10}N$)
Ph	phenyl
ppm	parts per million
Pr	propyl (also *i*-Pr or Pr^i)
PTC	phase transfer catalysis
Pyr	pyridyl (C_5H_4N)
R	any radical
RT	room temperature
s-	secondary
SET	single electron transfer
SOMO	singly occupied molecular orbital
t-	tertiary
TCNE	tetracyanoethylene
THF	tetrahydrofuran
Thi	thienyl(SC_4H_3)
TMEDA	tetramethylethylene diamine
Tol	toly(MeC_6H_4)
Tos or Ts	tosyl(*p*-toluenesulphonyl)
Trityl	triphenylmethyl(Ph_3C)
Xyl	xylyl($Me_2C_6H_3$)

In addition, entries in the 'List of Radical Names' in *IUPAC Nomenclature of Organic Chemistry*, 1979 Edition. Pergamon Press, Oxford, 1979, p. 305–322, will also be used in their unabbreviated forms, both in the text and in formulae instead of explicitly drawn structures.

CHAPTER 1

General and theoretical

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I. INTRODUCTION

In a continuation of previous computational treatments of these systems[1,2], this chapter is concerned with a description of the generic sulfur compound structure types XSY (two coordinate), XS(O)Y (four coordinate) and XSO_2Y (six coordinate). The XS(O)Y notation indicates an S=O group and XSO_2Y means a  group. The S=O double bond representation is for coordination counting purposes and is not necessarily a literal electronic structure description, as has been discussed previously.[2] Novel aspects of the material presented here include a comparison between parent compounds, radicals and anions, discussion of aromatic species, an extensive study of dimers and water complexes and cation complexation. This latter work follows a similar survey of metal monocations interacting with amides and their derivatives, and the corresponding species[3]. There are also previous members of this review series that deal with the general XSO_nY ($n = 0,1$, or 2) type compounds[4,5]. Here, the emphasis is on a comparison of properties as a function of n, the number of oxygen atoms bound to the central sulphur atom. The XSY compounds were not considered previously within the context of this type[1-3] of presentation[5].

Recent developments in the computational sciences, and especially in computational chemistry, have placed these methods, alongside experimental techniques, as useful tools

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Edited by S. Patai and Z. Rappoport

for chemists. Advances in theory and methodology, coupled with great technological strides in computer hardware and software, have often made computational experiments easier than laboratory experiments, with little or no loss of reliability and sometimes at even higher accuracy, and at a much lower cost. The computational chemists' armamentaria range from sophisticated *ab initio* tenchniques[6] through density functional[7], semi-empirical[8] and molecular mechanics[9] methods. Each tool has its range of accuracy, usefulness and applicability. The method of choice for a particular problem depends on the question being asked, the nature of the chemical system and the patience of the inquirer.

Ab initio electronic structure computations at the Hartree–Fock (HF) level are generally particularly adept at giving accurate equilibrium charge distributions[6]. Post-Hartree–Fock or correlation methods are needed, for example, when the single electronic configuration description of the molecular system is inadequate, or exaggerates the ionic (charges transfer) nature of the molecular charge distribution. Typical examples of such systems are molecules that have multiple bonds, crowded electron pairs or transition metal complexes (where the binding is not mainly electrostatic). HF and post-HF (correlation) methods suffer from the disadvantage that, because of their complexity and time demands, they can be used only on relatively small chemical structures. On the other hand, the progressive improvemnent in electronic structure and properties description is well-defined at the *ab initio* level. This positive characteristic is essentially unique to *ab initio*.

This review will therefore concentrate on an *ab initio* quantum chemical description of the XSY, XS(O)Y, XSO_2Y systems. It is assumed that the reader has sufficient familiarity with the theoretical methods from previous volumes of this series[1–3]. The particular computational techniques used will be described in each section, as appropriate. It is hoped that this compendium and discussions derived by computation 'experiments' will both serve and stimulate the sulphur community well.

II. SULPHENIC ACIDS AND XSY COMPOUNDS

There are several reviews of the general properties of the XSY system[5,10–14]. Here, we present the geometric and electronic structures of some 22 neutral sulphenic acids (Y=OH) and other XSY compounds, 13 radicals derived from the sulphenic acids by homolytic cleavage of a Z—H (Z = S or O) bond and then anions derived from the acids by heterolytic cleavage of the Z—H bond. As in the analogous studies on the sulphinic[1] and sulphonic[2] acid derivatives, the standard valence double-zeta plus (five) d-type polarization 6-31G* basis set[6] was used in a gradient optimization of the neutral parent and radical geometries. For the anions, the 6-31+G* basis set was used for the geometry optimization which includes diffuse functions better to describe the more radially exteneded charge distribution. This was followed by a single point MP2/6-31+G* calculation at the RHF calculated equilibrium geometry. The closed-shell species were treated at the spin- and space-restricted Hartree–Fock (RHF) level and the radicals were calculated using the spin-unrestricted HF (UHF) method. At each RHF/6-31G* optimized geometry of the neutral compounds the MP2 energies were obtained using both the 6-31G* and 6-31+G* basis sets as single point calculations. The GAUSSIAN 88[15] and GAUSSIAN 90[16] computer codes were used in these studies.

The results for the sulphenic acids and other XSY compounds are tabulated in Tables 1–3 and Figures 1–6 (neutrals), Tables 4–7 (radicals) and Tables 8–10 (anions). Comparisons of the geometric and electronic structural properties of the neutral parent XSY compounds with the XS(O)Y and XSO_2Y is postponed to Section 6, including a discussion of relative stabilities of isomers.

The simplest XSY compound is formally the sulphide H_2S (**1**) but the simplest sulphenic

TABLE 1. Energies and dipole moments of neutral XSY compounds[a]

Molecule	6-31G*			6-31+G*		
	Energy (a.u.)		RHF dipole moment[b]	Energy (a.u.)		RHF dipole moment[b]
	RHF	MP2[b]		RHF[b]	MP2[b]	
1 H_2S	−389.665762	−398.785392	1.409	−398.666588	−398.787178	1.439
2 HSF	−497.476522	−497.765634	1.905	−497.486269	−497.783656	1.991
3 HSOH	−473.487082	−473.784229	1.932	−473.492612	−473.795747	2.007
4 HSCl	−857.546725	−857.789994	1.678	−857.548672	−857.793902	1.679
5 $HSNH_2$	−453.672613	−453.954013	1.057	−453.677015	−453.963084	0.977
6 HSSH	−796.171215	−796.405263	1.558	−796.172541	−796.408554	1.592
7 $HSCH_3$	−437.698496	−437.948206	1.782	−437.699530	−437.951300	1.839
8 $HSOCH_3$	−512.514057	−512.937840	1.971	−512.519324	−512.950100	2.030
9 FSOH	−572.322345	−572.794238	2.125	−572.334640	−572.818696	2.163
10 HOSOH	−548.332607	−548.812164	0.461	−548.341007	−548.831155	0.395
11 ClSOH	−932.381531	−932.807526	2.066	−932.387515	−932.820498	2.005
12 NH_2SOH	−528.515809	−528.979532	2.525	−528.523681	−528.996929	2.522
13 CH_3OSOH	−587.359435	−587.966271	0.849	−587.368309	−587.986500	0.899
14 HSSOH[c]	−871.001978	−871.418926	2.740	−871.008246	−871.432553	2.797
15 CH_3SOH	−512.527680	−512.957102	2.200	−512.533291	−512.969633	2.324
16 CH_3SF	−536.520440	−536.941218	2.427	−536.529873	−536.959738	2.608
17 CH_3SCl	−896.586963	−896.962369	2.511	−896.589243	−896.968152	2.509
18 CH_3SNH_2	−492.710435	−493.124179	0.794	−492.712060	−493.131634	2.816
19 CH_3SSH	−835.207948	−835.574790	2.117	−835.209678	−835.580014	2.125
20 CH_3OSOCH_3	−626.386087	−627.120271	1.120	−626.394571	−627.141341	1.189
21 CH_3SCH_3	−476.733242	−477.115158	2.092	−476.734603	−477.119915	1.854
22 CH_3SOCH_3	−551.553832	−552.110577	2.095	−551.559060	−552.123761	2.176

[a]Geometry RHF/6-31G* optimized with no symmetry or equivalence constraints.
[b]In the RHF/6-31G* optimized geometry.
[c]Corrects result for structure 28 in Reference 1.

TABLE 2. Calculated bond lengths of neutral XSY compounds[a]

Molecule	Bond lengths (Å)								
	H—S	X	S—X	O—H	N—H	C—H[c]	C—O	C—S	O—S
1 H_2S	1.327	—	—	—	—	—	—	—	—
2 HSF	1.325	F	1.613	—	—	—	—	—	—
3 HSOH	1.328	—	—	0.949	—	—	—	—	1.655
4 HSCl	1.325	Cl	2.035	—	—	—	—	—	—
5 $HSNH_2$	1.325	N	1.711	—	0.999[b]	—	—	—	—
6 HSSH	1.327	S	2.064	—	—	—	—	—	—
7 $HSCH_3$	1.337		—	—	—	1.081	—	1.818	—
8 $HSOCH_3$	1.330	—	—	—	—	1.083	1.409	—	1.646
9 FSOH	—	F	1.607	0.952	—	—	—	—	1.612
10 HOSOH	—	—	—	0.951[b]	—	—	—	—	1.633
11 ClSOH	—	Cl	2.034	0.952	—	—	—	—	1.624
12 NH_2SOH	—	N	1.655	0.950	0.999[b]	—	—	—	1.657
13 CH_3OSOH	—	O	1.624	0.951	—	1.081	1.416	—	1.636[d]
14 HSSOH	1.329	S	2.040	0.950	—	—	—	—	1.647
15 CH_3SOH	—	C	—	0.950	—	1.082	—	1.798	1.658
16 CH_3SF	—	F	1.620	—	—	1.082	—	1.790	—
17 CH_3SCl	—	Cl	2.040	—	—	1.082	—	1.806	—
18 CH_3SNH_2	—	N	1.709	—	0.999[b]	1.082	—	1.803	—
19 CH_3SSH	1.328	S	2.060	—	—	1.082	—	1.815	—
20 CH_3OSOCH_3	—	—	—	—	—	1.082	1.415[b]	—	1.627[b]
21 CH_3SCH_3	—		—	—	—	1.082	—	1.809[b]	—
22 CH_3SOCH_3	—		—	—	—	1.083	1.408	1.799	1.651

[a] From RHF/6-31G* optimized geometries.
[b] Two equivalent bonds.
[c] Average value.
[d] O—S(OH); see Figure 3.

acid is HSOH (**3**), shown in Figure **1**, which has not been isolated. The numbers (in parenthesis here) refer to the listing of structures in the tables. The geometric structure of methansulphenic acid (**15**, Figure 4) has been determined experimentally[17] and the geometric parameters agree very well. The O–S distance is coincidentally perfect to three figures after the decimal at 1.658 Å. The calculated (Table 2) C–S distance (1.798 Å) is in more reasonable agreement with the experimental bond length of 1.806 Å. This is the agreement that we have also experienced with the $XS(O)Y^1$ and XSO_2Y^2 compounds, and gives us confidence in the calculated geometric structures. Barrett[18] has recently summarized the structural chemistry of the sulphenes.

Figures 1–6 show a sampling of the full geometric structures, including angles, for some sulphenic acids and other XSY compounds. Many of these compounds involve an attached oxygen as a part of at least one of the sulphide ligands. For methanesulphenic acid (Figure 4) the S—O—H angle is calculated to be 108.8° while the reported experimental value is 107.7° [17]. In fact, all the calculated S—O—H angles in the structures shown in the figures are in the 108.7°–109.8° range. The S—O—C angles are naturally larger, in the 116.0–116.6° range. The O—S—H, O—S—C and O—S—O angles are typically 98.6°, 100.2°–100.4° and 102.4° respectively. In CH_3SOH the measured O—S—C angle is 100.1° [17] and the C—S—O—H dihedral angle (not shown in Figure 4) is calculated to be 92.7°, compared to the experimental value of 93.9° [17]. The calculated 2.20*D* dipole moment in Table 1 for methanesulphenic acid is, as expected, larger than the 1.87*D* measured value due to the intrinsic exaggeration of ionic character at the Hartree–Fock

TABLE 3. Mulliken atomic charges and d-orbital occupancies on S in the neutral XSY compounds[a]

Molecule	Atomic charges								d-orbital occupancy on S
	S	H(—S)	X[f]	H(—O)	H(—N)	H(—C)[c]	C	O(—S)	
1 H_2S	−0.225	0.113	—	—	—	—	—	—	0.073
2 HSF	0.387	0.086	−0.473	—	—	—	—	—	0.109
3 HSOH	0.249	0.079	—	0.520	—	—	—	−0.811	0.111
4 HSCl	0.051	0.129	−0.180	—	—	—	—	—	0.085
5 $HSNH_2$	0.101	0.097	−0.959	—	0.380[b]	—	—	—	0.106
6 HSSH	−0.118[b]	0.118[b]	—	—	—	—	—	—	0.078
7 $HSCH_3$	−0.059	0.092	—	—	—	0.203	−0.644	—	0.074
8 $HSOCH_3$	0.252	0.078	—	—	—	0.174	−0.142[e]	−0.697	0.113
9 FSOH	0.771	—	−0.475	0.493	—	—	—	−0.789	0.160
10 HOSOH	0.654	—	—	0.484[b]	—	—	—	−0.811[b]	0.161
11 ClSOH	0.498	—	−0.211	0.495	—	—	—	−0.783	0.132
12 NH_2SOH	0.551	—	−0.959	0.529	0.385[c]	—	—	−0.830	0.154
13 CH_3OSOH	0.662	—	−0.818	0.483	—	0.178	−0.159[e]	−0.703[d]	0.163
14 HSSOH	−0.124	0.105	−0.336	0.482	—	—	—	−0.799	0.124
15 CH_3SOH	0.407	—	—	0.478	—	0.204	−0.662	−0.824	0.113
16 CH_3SF	0.535	—	−0.487	—	—	0.212	−0.684	—	0.111
17 CH_3Cl	0.209	—	−0.203	—	—	0.219	−0.655	—	0.086
18 CH_3SNH_2	0.260	—	−0.970	—	0.377[b]	0.194	−0.627	—	0.103
19 CH_3SSH	0.043	0.112	−0.132[f]	—	—	0.209	−0.650	—	0.081
20 CH_3OSOCH_3	0.676	—	—	—	—	0.177	−0.159[b,e]	−0.709[b]	0.164
21 CH_3SCH_3	0.121	—	—	—	—	0.196	−0.649[b]	—	0.077
22 CH_3SOCH_3	0.412	—	−0.664	—	—	0.201	−0.141[e]	−0.710	0.115

[a] From RHF/6-31G* geometries.
[b] Two equivalent values.
[c] Average value.
[d] (C)O(S).
[e] C(—O).
[f] Defined in Table 2.

TABLE 4. Energies and dipole moments of XSO· and XS(O)S· radicals[a]

Molecule	6-31G*			6-31 + G*		
	Energy (a.u.)		UHF dipole moment (*D*)[b]	Energy		UHF dipole momen (*D*)[b]
	UHF	MP2[b]		UHF[b]	MP2[b]	
23 HSO·	−472.890599	−473.162471	2.095	−472.895256	−473.173880	2.288
24 FSO·	−571.743048	−572.209489	2.115	−571.754319	−572.232584	2.215
25 HOSO·	−547.746172	−548.216496	2.021	−547.754935	−548.235859	2.127
26 ClSO·	−931.791783	−932.208559	1.827	−931.797749	−932.222398	1.903
27 NH_2SO·	−527.923966	−528.368959	2.058	−527.930979	−528.386265	2.136
28 HS(O)NH·	−527.852944	−528.289351	2.010	−527.861026	−528.305782	2.186
29 HSSO·	−870.405012	−870.798768	1.813	−870.410747	−870.812646	1.970
30 HS(O)S·	−870.354064	−870.759527	3.328	−870.363174	−870.775886	3.549
31 CH_3SO·	−511.933034	−512.343164	2.800	−511.938135	−512.356781	3.078
32 $HS(O)CH_2$·	−511.851541	−512.260225	4.245	−511.859926	−512.276357	4.528
33 CH_3OSO·	−586.774399	−587.372096	2.242	−586.783054	−587.392238	2.381
34 HOS(O)S· I	−945.211640	−945.798171	4.298	−945.227527	−945.824409	2.060
35 HOS(O)S· II	−945.220087	−945.805823	1.929	−945.230928	−945.828346	2.075

[a]Geometry UHF/6-31G* optimized with no symmetry or equivalence constraints.
[b]In the UHF/6-31G* optimized geometry.

TABLE 5. Calculated bond lengths of XSO· and XS(O)S· radicals[a]

Molecule	Bond lengths (Å)								HXSO angle
	H—S	S—O S=O	X	S—X	O—C	O—H	C—H	N—H	
23 HSO·	1.333	1.544	—	—	—	—	—	—	—
24 FSO·	—	1.449	F	1.593	—	—	—	—	—
25 HOSO·	—	1.468	O	1.626	—	0.954	—	—	58.7
26 ClSO·	—	1.472	Cl	2.041	—	—	—	—	—
27 NH_2SO·	—	1.510	N	1.671	—	—	—	1.001[b]	64.2
28 HS(O)NH·	1.339	1.466	N	1.677	—	—	—	1.013[b]	−23.7
29 HSSO·	1.328	1.529	S	2.062	—	—	—	—	85.3
30 HS(O)S·	1.341	1.463	S	2.062	—	—	—	—	—
31 CH_3SO·	—	1.525	C	1.810	—	—	1.082[c]	—	—
32 $HS(O)CH_2$·	1.344	1.479	C	1.754	—	—	1.075[c]	—	57.3
	—								−144.2
33 CH_3OSO·		1.468	—	—	1.421	—	1.081[c]	—	54.6
	—	1.613							
34 HOS(O)S· I[d]	—	1.622	S	2.089	—	0.954	—	—	—
35 HOS(O)S· II[e]		1.606	S	2.106	—	0.958	—	—	—

[a]From RHF/6-31G* optimized geometries.
[b]Two equal values.
[c]Average value.
[d]S=O = 1.440 Å.
[e]S=O = 1.499 Å.

TABLE 6. Mulliken atomic charges and d-orbital occupancy on S in XSO· and XS(O)S· radicals[a]

Molecule	atomic charge							d-orbital occupancy on S
	S	H(—S)	X[f]	O(—S) O(=S)	H(—O)	H(—N)	H(—C)	
23 HSO·	0.388	0.063	—	−0.452	—	—	—	0.150
24 FSO·	0.997	—	−0.466	−0.531	—	—	—	0.257
25 HOSO·	0.882	—	−0.817	−0.556	0.490	—	—	0.252
26 ClSO·	0.710	—	−0.229	−0.480	—	—	—	0.207
27 NH_2SO·	0.704	—	−0.981	−0.507	—	0.392	—	0.214
28 HS(O)NH·	0.957	0.050	−0.640	−0.755	—	0.388	—	0.327
29 HSSO·	0.462	0.125	−0.150	−0.437	—	—	—	0.166
30 HS(O)S·	0.701	0.067	−0.045	−0.723	—	—	—	0.300
31 CH_3SO·	0.574	—	−0.720	−0.507	—	0.221[c]	—	0.164
32 $HS(O)CH_2$·	0.867	0.027	−0.579	−0.774	—	—	0.229[c]	0.294
33 CH_3OSO[b]·	0.896	—	−0.575	−0.713	—	—	0.189[c]	0.257
34 HOS(O)S· I[d]	1.059	—	−0.058	−0.806	0.493	—	—	0.356
35 HOS(O)S· II[e]	1.102	—	−0.059	−0.807	0.496	—	—	0.352

[a] From RHF/6-31G* optimized geometries.
[b] C(—O) = −0.176.
[c] Average value.
[d] O(=S) = −0.687.
[e] O(=S) = −0.732.
[f] Defined in Table 5.

TABLE 7. Spin populations[a] on atoms[b] in XSO· and XS(O)S· radicals

Molecule	S		O
	pz	py	pz
23 HSO·	0.185		0.755
24 FSO·	0.534		0.368
25 HOSO·	0.493		0.485
26 ClSO·	0.428		0.553
27 NH_2SO·	0.267		0.649
28 HS(O)NH·	*d*		*d*
29 HSSO·	0.199		0.735
30 HS(O)S·	0.912		
31 CH_3SO·	0.251		0.670
32 $HS(O)CH_2$·[c]	*e*		*e*
33 CH_3OSO·	0.446		0.392
34 HOS(O)S· I	0.940		
35 HOS(O)S· II	0.336	0.627	

[a]Only values larger than 0.09 are listed.
[b]From the UHF/6-31G* optimized geometries
[c]The spin populations on the hydrogen atoms bonded to the radical carbon are both −0.085.
[d]Nitrogen: px = 0.323; py = 0.107; pz = 0.518.
[e]Carbon: s = 0.100; pz = 0.899.

TABLE 8. Energies and dipole moments of XSO^- and $XS(O)S^-$ anion species[a]

Molecule	Energy (a.u.)*		RHF Dipole moment (*D*)[b,c]
	RHF	MP2[b]	
36 HSO^-	−472.901730	−473.218919	2.902
37 FSO^-	−571.776850	−572.281808	2.286
38 $HOSO^-$	−574.763466	−548.272594	3.858
39 $ClSO^-$	−931.841093	−932.290959	2.120
40 NH_2SO^-	−527.934859	−528.424877	3.144
41 $HSSO^-$	−870.438464	−870.879511	3.699
42 $HOSS^-$	−870.468187	−870.897234	3.022
43 CH_3SO^-	−511.939149	−512.392296	4.732
44 CH_3OSO^-	−586.789934	−587.427684	4.356
45 $HOS(O)S^-$	−945.319859	−945.947703	2.460

[a]Geometry RHF/6-31+G* optimized with no symmetry or equivalence constraints.
[b]In the RHF/6-31+G* optimized geometry.
[c]Origin dependent.

level of theory. Post-Hartree–Fock calculations typically reduce the HF value of dipole moments. Finally, the XSSY dihedral angle for the S—S systems is typical for these systems: 89.2° for HSSOH (**14**), 89.8° for HSSH (**6**) and 87.4° for CH_3SSH (**19**). It should be noted that the entries here (Tables 1–4) for HSSOH (**14**) correct the results reported in Reference 1.

TABLE 9. Calculated bond lengths for XSO^- and $XS(O)S^-$ anions[a]

Molecule	Bond lengths (Å)						
	H—S	S—O	X	S—X	O—H	N—H	O—C
36 HSO^-	1.351	1.586	—	—	—	—	—
37 FSO^-	—	1.518	F	1.717	—	—	—
38 $HOSO^-$	—	1.540	O	1.718	0.949	—	—
39 $ClSO^-$	—	1.499	Cl	2.347	—	—	—
40 NH_2SO^-	—	1.563	N	1.738	—	1.004[b]	—
41 $HSSO^-$	1.333	1.540	S	2.144	—	—	—
42 $HOSS^-$	—	1.696	S	2.054	0.950	—	—
43 CH_3SO^-	—	1.581	C	1.812	1.088[c]	—	—
44 CH_3OSO^-	—	1.539	O	1.712	—	—	1.389
45 $HOS(O)S^-$[d]	—	1.658	S	2.025	0.955	—	—

[a]From RHF/6-31+G* optimized geometries.
[b]Two equivalent values.
[c]Average value.
[d]S=O = 1.477 Å.

TABLE 10. Mulliken atomic charges and d-orbital occupancies on S in the XSO^- and $XS(O)S^-$ anions[a]

Molecule	atomic charge							d-Orbital occupancy on S
	S	H(—S)	X[f]	O(—S)	H(—N)	H(—O)	H(—C)	
36 HSO^-	−0.069	−0.035	—	−0.897	—	—	—	0.150
37 FSO^-	0.293	—	−0.467	−0.826	—	—	—	0.191
38 $HOSO^-$	0.220	—	−0.815	−0.880	—	0.476	—	0.193
39 $ClSO^-$	0.204	—	−0.525	−0.679	—	—	—	1.162
40 NH_2SO^-	0.159	—	−1.035	−0.900	0.388[b]	—	—	0.184
41 $HSSO^-$	0.031	0.050	−0.284	−0.797	—	—	—	0.170
42 $HOSS^-$	0.015	—	−0.750	−0.756	—	0.491	—	0.111
43 CH_3SO^-	0.002	—	−0.598	−0.913	—	—	0.170[c]	0.156
44 CH_3OSO^-[d]	0.195	—	−0.518	−0.877	—	—	0.118[c]	0.195
45 $HOS(O)S^-$[e]	0.673	—	−0.647	−0.778	—	0.506	—	0.330

[a]From RHF/6-31+G* optimized geometries.
[b]Two equivalent values.
[c]Average value.
[d]C(—O) = −0.259.
[e]O(=S) = −0.754.
[f]Defined in Table 9.

The properties of the XSY type compounds displayed in Tables 1–3 for the purely aliphatic or inorganic substituents (with no oxygen double bonded to sulphur) show their covalent character. The dipole moments are low (Table 1), and both the charge on S and its d orbital population are relatively low (Table 3), even with two electronegative atoms or groups attached to the divalent sulphur atom. As has been observed previously[2],

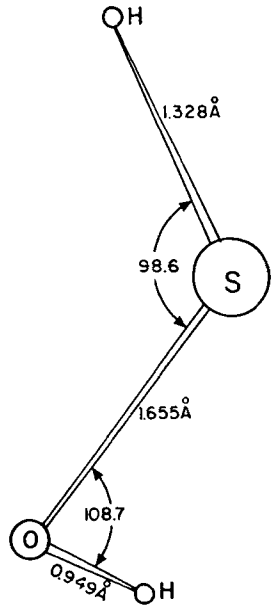


FIGURE 1. HSOH, structure **3** in Table 3

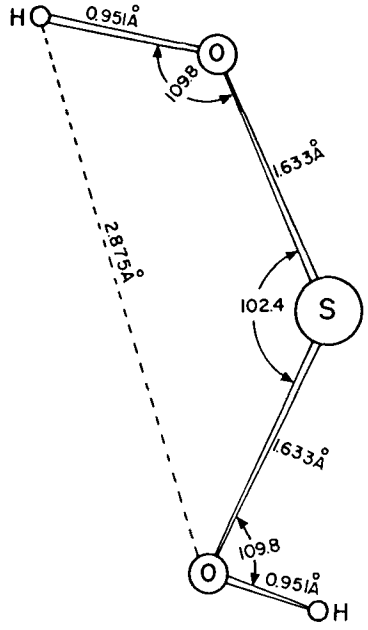


FIGURE 2. HOSOH, structure **10** in Table 3

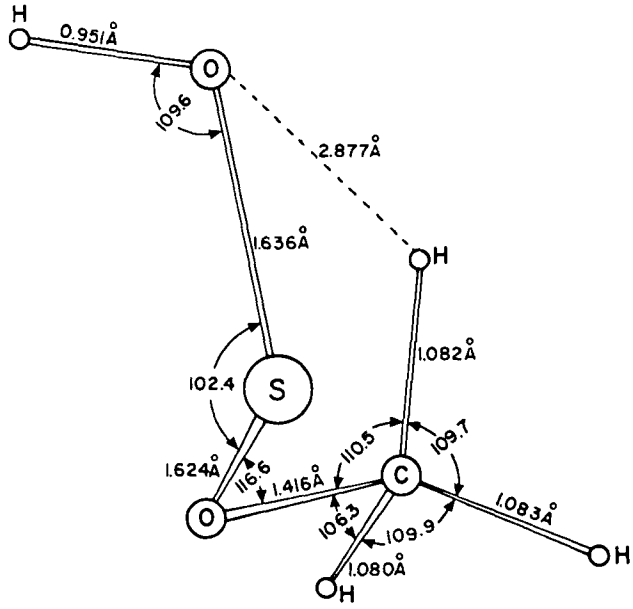


FIGURE 3. CH_3OSOH, structure **13** in Table 3

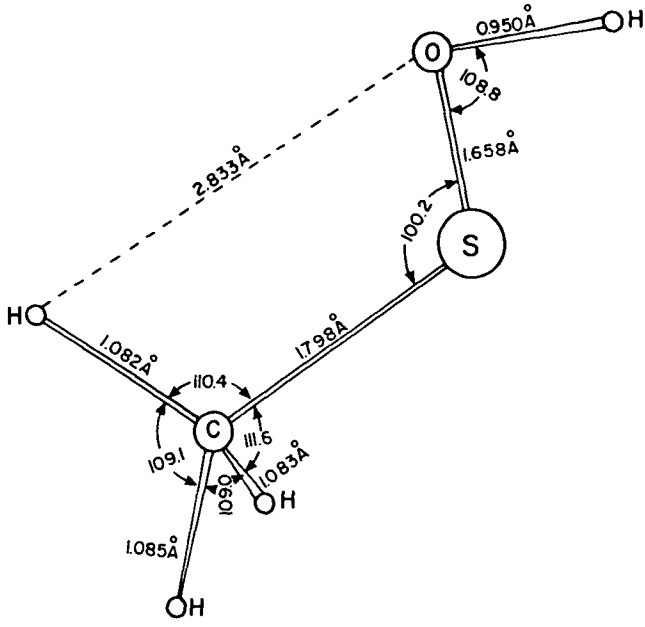


FIGURE 4. CH_3SOH, structure **15** in Table 3

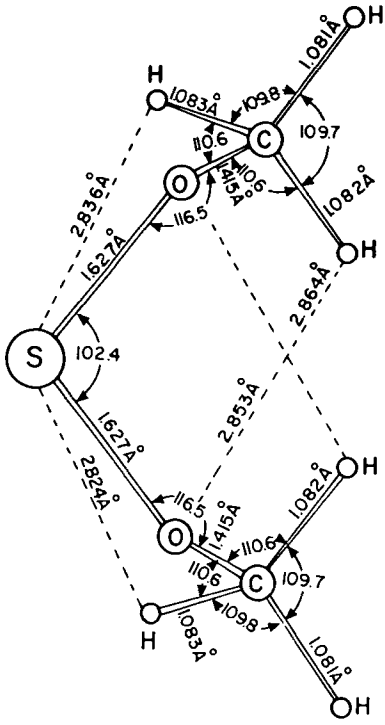


FIGURE 5. CH_3OSOCH_3, structure **20** in Table 3

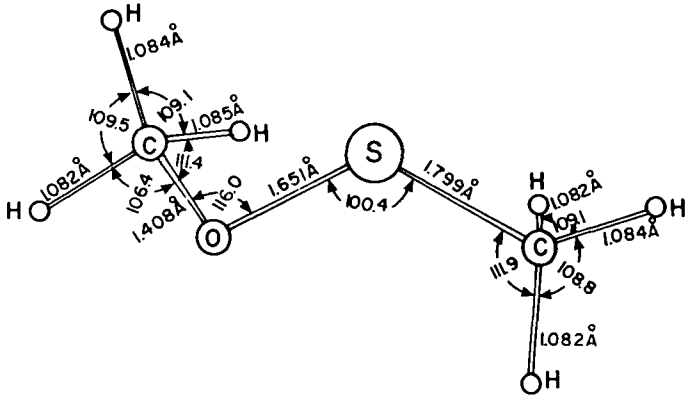


FIGURE 6. CH_3SOCH_3, structure **22** in Table 3

the atomic charge on a central sulphur atom and its d orbital occupancy move in the same direction with ligand substitution. As expected, the more electronegative the substituent the larger its value. Apparently, the stabilization of the central sulphur d orbitals with increased atomic charge draws electron density from the valence p shell into the d orbital even as the former is also being depleted by electronegative ligand(s). These apparently contradictory processes complicate the interpretation of property trends. A number of aliphatic sulphides have also been studied by Ohsaku[19], in particular with regard to conformation.

An interesting phenomenon is the effect of methyl substitution (for hydrogen or other inorganic ligands) on the wave function properties of the sulphides. Thus, the general trends in dipole moment change indicate that the methyl group acts in its usual fashion as an electron-releasing agent. This analysis is, of course, complicated by the local dipole magnitudes and directions of each individual bond which, summed together, give the overall molecular dipole moment. However, the Mulliken atomic charges on sulphur, q(S), increase when methyl is substituted for hydrogen, indicating an electron-withdrawing role for the methyl group. The d orbital population on sulphur, d(S), stays sensibly constant with methyl substitution. However, the overall charge on the methyl group that is attached to the central sulphide atom in these situations is usually more negative than the hydrogen atom it replaces. We have no facile explanation for these effects except to point out their existence as a warning of some of the apparent oddities occasionally encountered in tracking atomic charges, especially those involving hydrogen atoms.

The properties of sulphenyl and sulphenyl-related radicals are tabulated in Tables 4–7, which also include some unrelated sulphenyl radicals not included in the previous review[2] and placed here for convenience and completeness. Radicals 24–27 are repeated in these Tables from previously[1] in order to present their orbital spin populations in Table 7. In many of these cases the sulphenyl radical (XSO·) derived from the acid form competes with the sulphinyl from [XS(O)·] in stability, depending on the location of the radical electron. These are just extreme, asymptotic representations derived from the parent XSOH and XS(O)H isomers, respectively. The radical electron could actually be divided between the sulphur and oxygen atoms in the electronic ground state. The free radical chemistry of sulphenyl radicals and their derivatives has recently been reviewed by Chatgilialoglu[20].

As has been pointed out previously[2], spin properties are notoriously difficult to calculate accurately. In Table 7 we give the calculated atomic spin populations, which are not observables. These, however, can be related to experimental electron spin resonance hyperfine interactions through an analysis of the experimental data using a rigid linear combination of atomic orbitals (LCAO) molecular orbital (MO) model. The *ab initio* extended basis set used here and the rigid LCAO-MO representation are very different. Agreement between the calculated and 'observed' atomic orbital populations cannot therefore be expected to be better than qualitative.

With this reservation, we can now analyze the results in Table 7 together with the calculated sulphur–oxygen bond lengths in Table 5. Comparing the oxygen radical structure (XSO·) having the S—O single bond and unpaired spin on the oxygen atom, with the sulphur radical structure [XS(O)·] having the S=O double bond and the unpaired spin on the sulphur atom, we expect a correlation between the location of the unpaired spin population and the S—O bond length. This, in fact, is observed in the calculated results. In those radicals where the spin population is concentrated mainly on the oxygen atom (structures **23**, **27**, **29** and **31**) the S—O bond is 0.06 Å longer, on the average, than those radicals that have substantial spin population on the sulphur atom. A similar correlation, noted previously[2], exists between the change in X—S bond length in going from the neutral parent to the radical, and the unpaired spin population.

Thus, for the mainly XS(O)· spin distribution the X—S bond length usually decreases upon homolytic dissociation of the acidic hydrogen atom. This has been explained[2] in terms of the classic two MO, three electron interaction which is stabilizing. The two structures found for HOS(O)S· [34 (I) and 35 (II)] actually represent two different radical species, π (I) and σ (II) radicals, which are adiabatically very close in energy (Table 4). The H—X—S—O or H—X—S=O dihedral angles for these radicals shown in Table 5 are almost all close to 60°.

Another correlation can be gleaned from comparing Tables 3 and 6, noting the change in q(S) and d(S) in going from the neutral parent to the acid radical. In all cases, both q(S) and d(S) increase, often substantially, irrespective of the primary radical structure [S(O)·*vs* SO·], and even for $HS(O)CH_3$ (**8**) → $HS(O)CH_2$· (**32**) where all the unpaired spin population is on the carbon atom. Since the departing hydrogen atom in the neutral parent that was attached to oxygen typically carries a positive charge of about 0.5 (Table 3) the full electron that the departing hydrogen atom carries with it, leaving the radical behind, means that the complementary amount of electron density comes from the other atoms. There must, however, be another mechanism at work to explain the large increases in both q(S) and d(S) for $HSOCH_3$ and $HSONH_2$ in going to the methyl and amine radicals, respectively. In these cases, the atomic charges on the departing hydrogen atoms in the precursor species are not that large.

Experimental values have been determined for the geometric and electronic properties of both the HSO (**23**) and FSO (**24**) radicals[21–23]. The calculated S—O (1.449 Å) and S—F bond distances (1.593 Å) in Table 5 compare very well with the measured 1.452 Å and 1.602 Å, respectively, for FSO. The dipole moments (2.116*D* in Table 4 and the experimental value of 1.662*D*) are not so close. As pointed out above, post-Hartree–Fock methods should reduce the calculated dipole moment values. On the other hand, for HSO the (calculated, experimental) S—H (1.333 Å, 1.389 Å) and S—O (1.544 Å, 1.494 Å) bond lengths agree less well, while the dipole moments (2.095*D*, 2.20*D*) are much closer. The calculated geometric parameters for the radicals (and anions) are generally expected to be less accurate than for the neutral parents.

The calculated data on the anions of the form X—S—O^- are known in Tables 8–10. Since the geometric results for the parent neutrals were obtained in the 6-31G* basis while the anions were geometry optimized in the 6-31 + G* basis sets, comparisons of geometry and charge density distribution changes should be treated with caution. However, there are some general trends that agree with those noted in the sulphinyl study[1] and are consistent with expectations. Thus, comaparing Table 9 with 2 shows that the X—S bond distance increases and the S—O bond length generally decreases in going from the parent neutral to the (deprotonated) anion. The former change can be understood as resulting from an increased electron density in a saturated bond which can only increase general electron repulsion. In contrast, the X—S—O^- system is partially unsaturated and the increased electron density can be transferred towards sulphur and enter the S—O region to give that bond partial double-bond character [$XS(O)^-$]. Thus, S—O decreased in length upon deprotonation at the oxygen atom.

Comparing Table 10 to Table 3 shows that q(S) decreases in going to the anion, as expected from the above analyses, while d(S) increases. The increased charged density on the central sulphur atom apparently prefers to go into the d orbital rather than the valence p sub-shell. This should make the anion reactive at both the sulphur and oxygen sites[24].

III. SULPHENIC ACIDS AND XS(O)Y COMPOUNDS

The geometric and electronic structure of the sulphinic acids and their derivatives from a computational chemical point of view has recently been reviewed[1]. This category

includes both the XS(O)OH structures and the sulphoxide XS(O)Y compounds, where the X substituent can also contain an oxygen atom singly bonded to the central sulphur atom. The same calculational procedure described for the sulphenic acids and XSY compounds in Section 2 was used also here for the sulphinyl and sulphoxide systems. The results are tabulated in Tables 11–14 and shown selectively in Figures 7–11. A small number of sulphinic acid derivatives are repeated in the Tables here from the previous study[1] for convenience and completeness. In particular, in two cases, this will allow a discussion of rotamer geometries and energies which were not addressed previously[1]. It should be noted that the entries here for HS(O)F (**23**) in Tables 11–13 correct the results reported in Reference 2.

The properties of the sulphinyl compounds and sulphoxides in Tables 11–13 show generally larger dipole moments, larger atomic charges on the central sulphur atom and increased *d*(S), relative to the XSY systems. The clear-cut difference in bond length between S=O and S—O of about 0.15–0.17 Å, where they both appear in the same compound within the class of XS(O)Y, is found uniformly. The effect of X substitution in X—S(O)OH is generally to decrease both the S=O and S—O bond lengths, increase both *q*(S) and *d*(S) and reduce (to less negative values) the atomic charges on both (the singly and doubly bonded) types of oxygen atoms, with increased electronegativity of X. All these effects are moderate and the bond lengths, atom charges and population parameters stay within a relatively narrow range. Actually, the trends with regards to *q*(O) are not completely unambiguous. In any event, the reduced SO bond lengths with increased electronegativity of X is an accord with other such observations. An interpretation in terms of MO interaction effects was given previously[2]. The same general trend with regard to S=O shortening is found for the HS(O)Y series as a function of increased electronegativity of Y, but with even greater scatter. As the molecules increase in size and flexibility, intramolecular interactions become increasingly important and can dominate or confound straightforward electronegativity and MO interaction effects.

Table 14 compares the relative MP2/6-31G* and MP2/6-31+G* stabilities and dihedral angles of the two or three rotamer structure of a given sulphinic acid or derivative XS(O)Y that have been found computationally. The various conformations can be characterized by the three dihedral angles described in footnotes b–d of this table which in projection along the S—O bond define the proximity relationship of the Y group (usually OH) hydrogen atom to O(=S) and X in terms of three possibilities. Angle (type) *a* (footnote b) measures the O=S—O—H angle where H lies between O(=S) and X. Angle (type) *b* (footnote c) is the X—S—O—H dihedral angle where the O(=S) atom (in projection) is remote from both H and X. Dihedral angle (type) *c* (footnote d) again measures O=S—O—H but with X remote from both H and O(=S). For example, both fluorosulphinic (**1** and **2** in Tables 11–14) and chlorosulphinic acids (**6** and **7**) have two rotamer forms each, where the more stable geometry is type *a* and the acidic hydrogen atom is also able to interact and form long hydrogen bonds with both the electronegative atoms O(=S) and F or Cl. The higher-energy form is of type *b* where interaction with H(O) is only possible with the F or Cl atoms, in preference to a single interaction with O(=S). Methanesulphinic acid (**15** and **14**, Fig. 7), for example, with a bulky X group that also cannot stabilize the acidic hydrogen atom, has type *c* stability where the interaction is only between H(O) and O(=S). The ionic character of the S=O bond[2] makes this interaction very favourable. $HS(O)CH_3$ (**16**, **17**) has a bulky, but interacting group (X=OCH_3 with SH instead of OH) and a preferred type a stability as the H(S) atom interacts with both oxygen atoms. $CH_3S(O)OCH_3$ (**18**, **19**, Figures 8, 9) has two bulky (X and Y) groups and the lower-energy rotamer has type *c* stability.

The situation becomes more complicated when both X and Y have an acidic hydrogen atom (X = OH, SH, NH_2). For steric reasons, the most stable HOS(O)OH (**48–50**) rotamer is simultaneously both type *a* and type *c*, depending on which S—O(H) axis is used for

TABLE 11. Energies and dipole moments of XS(O)Y compounds[a]

Molecule	6-31G*			6-31+G*		
	energy (a.u.)		RHF dipole moment[b]	energy (a.u.)		RHF dipole moment[b]
	RHF	MP2[b]		RHF[b]	MP2[b]	
46 FS(O)OH I	−647.177264	−647.841038	4.094	−674.190427	−647.868930	4.115
47 FS(O)OH II	−647.184194	−647.846890	1.545	−647.196559	−647.873694	1.590
48 HOS(O)OH I	−623.180582	−623.848156	3.292	−623.191952	−623.873126	3.361
49 HOS(O)OH II	−623.184245	−623.850876	1.726	−623.195137	−623.874994	1.700
50 HOS(O)OH III	−623.169427	−623.837603	5.902	−623.181543	−623.863592	5.982
51 ClS(O)OH I	−1007.210289	−1007.832182	4.102	−1007.226994	−1007.858871	1.703
52 ClS(O)OH II	−1007.217780	−1007.838422	1.778	−1007.220378	−1007.853501	4.104
53 $NH_2S(O)OH$ I	−603.349290	−603.998536	1.969	−603.360257	−604.023186	2.051
54 $NH_2S(O)OH$ II	−603.351074	−604.000493	3.360	−603.362143	−604.024832	3.396
55 $NH_2S(O)OH$ III	−603.349873	−604.000223	3.464	−603.361675	−604.025498	3.561
56 HSS(O)OH I	−945.815286	−946.426468	2.736	−945.826781	−946.450110	2.726
57 HSS(O)OH II	−945.822174	−946.430640	2.844	−945.832408	−946.452783	3.039
58 HSS(O)OH III	−945.821340	−946.430367	1.589	−945.831509	−946.452435	1.760
59 $CH_3S(O)OH$ I	−587.356863	−587.974140	3.134	−587.366317	−587.994979	3.356
60 $CH_3S(O)OH$ II	−587.354792	−587.972664	2.302	−587.364940	−587.994552	2.511
61 $HS(O)OCH_3$ I	−587.332839	−587.945143	3.076	−587.342414	−587.966198	3.242
62 $HS(O)OCH_3$ II	−587.329858	−587.943489	3.170	−587.339774	−587.964812	3.317
63 $CH_3S(O)OCH_3$ I	−626.382687	−627.127776	3.270	−626.391534	−627.149083	3.472
64 $CH_3S(O)OCH_3$ II	−626.383121	−627.128869	3.053	−626.392853	−627.151257	3.245
65 HS(O)OH	−548.303809	−548.788598	2.645	−548.313765	−548.808984	2.818
66 $HS(O)NH_2$ I	−528.478845	−528.948124	3.024	−528.488264	−528.967119	3.208
67 $HS(O)NH_2$ II	−528.469995	−528.937517	5.047	−528.480497	−528.958063	5.206
68 HS(O)F	−572.300118	−572.781386	3.122	−572.312108	−572.805305	3.280
69 HS(O)Cl	−932.343052	−932.781104	3.148	−932.350718	−932.795646	3.270
70 HS(O)SH I	−870.952178	−871.377726	3.086	−870.961155	−871.396038	3.477
71 HS(O)SH II	−870.951906	−871.379428	3.270	−870.961084	−871.394196	3.315
72 $HS(O)CH_3$	−512.480700	−512.916085	4.417	−512.488894	−512.931989	4.744
73 HS(O)H	−473.435726	−473.739931	4.083	−473.443995	−473.754631	4.383
74 $CH_3S(O)CH_3$	−551.534621	−552.102604	4.497	−551.542592	−552.119925	4.839

[a]Geometry RHF/6-31G* optimized with no symmetry or equivalence constraints.
[b]In the RHF/6-31G* optimized geometry.

TABLE 12. Calculated bond length of XS(O)Y compounds[a]

Molecule	Bond lengths (Å)								
	S=O	S—O	O—H	X	S—X	C—H	N—H	S—H	C—O
46 FS(O)OH I	1.417	1.598	0.954	F	1.593	—	—	—	—
47 FS(O)OH II	1.426	1.589	0.958	F	1.590	—	—	—	—
48 HOS(O)OH I	1.434	1.617	0.958	—	—	—	—	—	—
		1.607	0.954						
49 HOS(O)OH II	1.446	1.606[c]	0.957[c]	—	—	—	—	—	—
50 HOS(O)OH III	1.428	1.613[c]	0.952[c]	—	—	—	—	—	—
51 ClS(O)OH I	1.422	1.601	0.955	Cl	2.092	—	—	—	—
52 ClS(O)OH II	1.431	1.592	0.959	Cl	2.084	—	—	—	—
53 $NH_2S(O)OH$ I	1.456	1.615	0.956	N	1.667	—	1.004[b]	—	—
54 $NH_2S(O)OH$ II	1.452	1.627	0.957	N	1.656	—	1.003[b]	—	—
55 $NH_2S(O)OH$ III	1.449	1.606	0.958	N	1.682	—	1.002[c]	—	—
56 HSS(O)OH I	1.443	1.628	0.954	S	2.090	—	—	1.327	—
57 HSS(O)OH II	1.447	1.609	0.958	S	2.105	—	—	1.328	—
58 HSS(O)OH III	1.450	1.608	0.957	S	2.111	—	—	1.327	—
59 $CH_3S(O)OH$ I	1.462	1.625	0.957	C	1.789	1.083[b]	—	—	—
60 $CH_3S(O)OH$ II	1.461	1.640	0.954	C	1.784	1.082[b]	—	—	—
61 $HS(O)OCH_3$ I	1.456	1.609	—	—	—	1.081[b]	—	1.347	1.422

62 $HS(O)OCH_3$ II	1.455	1.624	—	—	—	1.081[b]	—	1.334	1.418
63 $CH_3S(O)OCH_3$ I	1.462	1.621	—	C	1.793	1.082[b] 1.080[b,d]	—	—	1.421
64 $CH_3S(O)OCH_3$ II	1.459	1.629	—	C	1.783	1.082[b]	—	—	1.417
65 HS(O)OH	1.457	1.620	0.956	—	—	—	—	1.342	—
66 $HS(O)NH_2$ I	1.468	—	—	N	1.679	—	1.003[b]	1.336	—
67 $HS(O)NH_2$ II	1.465	—	—	N	1.662	—	0.998[b]	1.342	—
68 HS(O)F	1.439	—	—	F	1.597	—	—	1.338	—
69 HS(O)Cl	1.448	—	—	Cl	2.077	—	—	1.337	—
70 HS(O)SH I	1.468	—	—	S	2.094	—	—	1.339[e] 1.327[f]	—
71 HS(O)SH II	1.463	—	—	S	2.101	—	—	1.340[e] 1.326[f]	—
72 $HS(O)CH_3$	1.483	—	—	C	1.818	1.082[b]	—	1.340	—
73 HS(O)H	1.479	—	—	—	—	—	—	1.343[c]	—
74 $CH_3S(O)CH_3$	1.485	—	—	C	1.796[c]	1.083[b]	—	—	—

[a] From the RHF/6-31G* optimized geometry.
[b] Average value.
[c] Two equivalent values.
[d] H—(C—O).
[e] H—(S=O).
[f] H—(S—S).

TABLE 13. Mulliken atomic charges and d-orbital occupancy on S in XS(O)Y compounds[a]

Molecule	Atomic charges								d-Orbital occupancy on S
	S	H(—S)	X[f]	H(—O)	H(—N)	H(—C)	O(=S)	O(—S)	
46 FS(O)OH I	1.419	—	−0.475	0.497	—	—	−0.646	−0.794	0.416
47 FS(O)OH II	1.459	—	−0.471	0.498	—	—	−0.689	−0.796[b]	0.411
48 HOS(O)OH I	1.380	—	—	0.488[b]	—	—	−0.713	−0.821[b]	0.410
49 HOS(O)OH II	1.429	—	—	0.483[b]	—	—	−0.765	−0.815[b]	0.404
50 HOS(O)OH III	1.317	—	—	0.486[b]	—	—	−0.679	−0.805[b]	0.416
51 ClS(O)OH I	1.216	—	−0.295	0.502	—	—	−0.632	−0.791	0.373
52 ClS(O)OH II	1.236	—	−0.274	0.505	—	—	−0.675	−0.792	0.371
53 $NH_2S(O)OH$ I	1.319	—	−0.984	0.485	0.390[c]	—	−0.776	−0.824	0.383
54 $NH_2S(O)OH$ II	1.345	—	−0.990	0.478	0.391[c]	—	−0.773	−0.844	0.383
55 $NH_2S(O)OH$ III	1.327	—	−1.025	0.483	0.393[c]	—	−0.760	−0.815	0.378
56 HSS(O)OH I	1.077	0.115	−0.161	0.498	—	—	−0.697	−0.833	0.356
57 HSS(O)OH II	1.121	0.109	−0.182	0.495	—	—	−0.732	−0.812	0.352
58 HSS(O)OH III	1.119	0.149	−0.215	0.492	—	—	−0.741	−0.804	0.347
59 $CH_3S(O)OH$ I	1.231	—	−0.737	0.481	—	0.215	−0.780	−0.839	0.340
60 $CH_3S(O)OH$ II	1.214	—	−0.735	0.489	—	0.231[c]	−0.773	−0.856	0.337
61 $HS(O)OCH_3$ I	1.092	0.008	−0.191[d]	—	—	0.190[e]	−0.762	−0.726	0.348

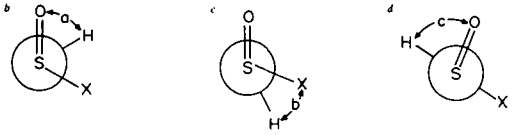
62 $HS(O)OCH_3$ II	1.061	0.023	−0.187[d]	—	—	0.190[c]	−0.739	−0.731	0.349
63 $CH_3S(O)OCH_3$ I	1.258	—	−0.748 −0.193[d]	—	—	0.203[c]	−0.790	−0.744	0.343
64 $CH_3S(O)OCH_3$ II	1.204	—	−0.732 −0.183[d]	—	—	0.204[c]	−0.766	−0.746	0.345
65 HS(O)OH	1.083	0.013	—	0.488	—	—	−0.754	−0.829	0.345
66 $HS(O)NH_2$ I	0.951	0.033	−1.001	—	0.392[b]	—	−0.769	—	0.330
67 $HS(O)NH_2$ II	0.977	0.008	−1.021	—	0.393[b]	—	−0.760	—	0.336
68 HS(O)F	1.155	0.017	−0.482	—	—	—	−0.690	—	0.347
69 HS(O)Cl	0.867	0.070	−0.261	—	—	—	−0.676	—	0.314
70 HS(O)SH I	0.730	0.058 0.136[e]	−0.184	—	—	—	−0.740	—	0.288
71 HS(O)SH II	0.726	0.056 0.130[e]	−0.187	—	—	—	−0.785	—	0.288
72 $HS(O)CH_3$	0.855	0.018	−0.756	—	—	0.225[c]	−0.789	—	0.275
73 HS(O)H	0.700	0.033	—	—	—	—	−0.767	—	0.278
74 $CH_3S(O)CH_3$	0.997	—	−0.728[b]	—	—	0.212[c]	−0.810	—	0.282

[a] From RHF/6-31G* optimized geometries.
[b] Two equivalent values.
[c] Average value.
[d] C(—O).
[e] H(—X).
[f] Defined in Table 12.

TABLE 14. Relative stabilities[a] of XS(O)Y rotamers

Molecule	Dihedral angles HOS=O and HOSX (in degrees) angle a^b	angle b^c	angle c^d	Dipole moment (D)	$\Delta E^{e,f}$ MP2/ 6-31G*	MP2/ 6-31+G*
47 FS(O)OH II	28.3	—	—	1.545	—	—
46 FS(O)OH I	—	68.2	—	4.094	3.7	3.0
52 ClS(O)OH II	31.9	—	—	1.778	—	—
51 ClS(O)OH I	—	69.3	—	4.102	3.9	3.9
59 $CH_3S(O)OH$ I	—	—	26.6	3.134	—	—
60 $CH_3S(O)OH$ II	31.6	—	—	2.302	0.9	0.3
49 HOS(O)OH II	20.1	—	19.9	1.726	—	—
48 HOS(O)OH I	—	73.2	32.0	3.292	1.7	1.2
50 HOS(O)OH III	153.1	—	152.7	5.902	6.6	6.0[f]
57 HSS(O)OH II	—	(67.6)[g]	36.2	2.844	—	—
58 HSS(O)OH III	(8.4)[g]	—	36.8	1.589	0.2	0.2
56 HSS(O)OH I	84.9	—	(57.9)[g]	2.736	2.4[f]	1.5
54 $NH_2S(O)OH$ II[j]	—	—	17.3	3.360	—	—
55 $NH_2S(O)OH$ III[k]	—	—	49.8	3.464	0.2	0.4
53 $NH_2S(O)OH$ I[i]	—	—	9.5	1.969	1.1	1.0
61 $HS(O)OCH_3$ I[h]	42.6	—	—	3.076	—	—
62 $HS(O)OCH_3$ II[h]	—	—	73.9	3.170	1.0	0.9
64 $CH_3S(O)OCH_3$ II[h]	—	—	69.6	3.053	—	—
63 $CH_3S(O)OCH_3$ I[h]	31.6	—	—	3.271	0.7	1.3
70 HS(O)SH I	45.2	—	—	3.086	—	—
71 HS(O)SH II	—	—	90.3	3.270	1.1	1.2

[a] In kcal mol^{-1} from MP2 difference of RHF/6-31G* optimized geometries from Table 11.



[e] ΔE between the given rotamer and the former. The first rotamer is the most stable.
[f] ΔE between given rotamer and the first rotamer.
[g] The dihedral angle HSS=O.
[h] X is defined as H or $C(H_3)$ in the dihedral angle HOSX.
[i] $NH_2S(O)OH$ I HNS=O:36.0, −87.4.
[j] $NH_2S(O)OH$ II HNS=O:38.7, 169.0.
[k] $NH_2S(O)OH$ III HNS=O: − 32.5, − 158.3.

projection. For both HSS(O)OH (**56–58**) and $NH_2S(O)OH$ (**53–55**), with the more bulky X groups, type *c* structures are preferred, which also allow auxiliary hydrogen bond interactions for the thio and amine hydrogen atoms with the semi-polar oxygen atom. The steric effect of bulky lone-pair interactions in determining rotamer stability is probably manifest in the HS(O)SH (**70** and **71**) case with type *a* character. The higher-energy form has the O(=S) atom equidistant from the two thio hydrogen atoms.

Figures 7–11 show some representative geometric parameters calculated for the sulphinic acids and XS(O)Y compounds. The S—O—H angle (Fig. 7) is 109°, as for the sulphenic acids. The C—S—O angle is always less than 100°, C—S=O and O—S=O fall between 105–110°, with the former usually the smaller of the two, and the S—O—C angle is in the 115–120° range. Different rotamers can have noticeable differences in

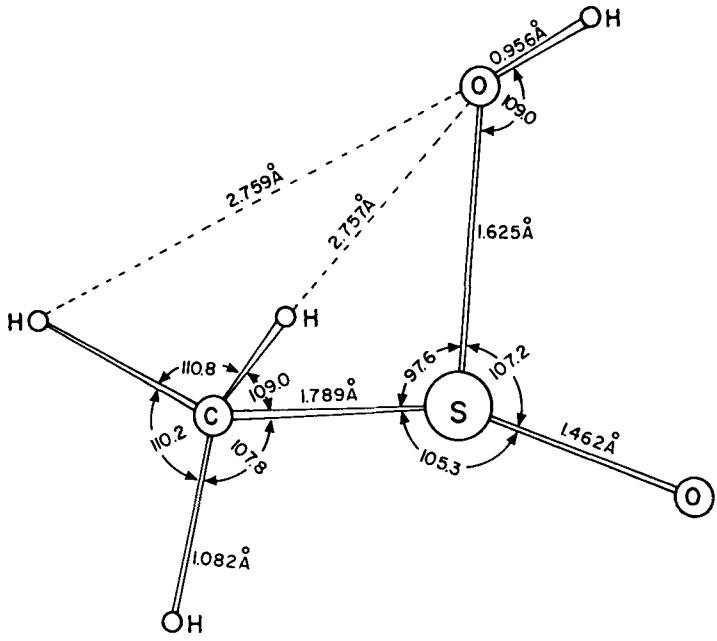


FIGURE 7. $CH_3S(O)OH$ I, structure **59** in Table 14

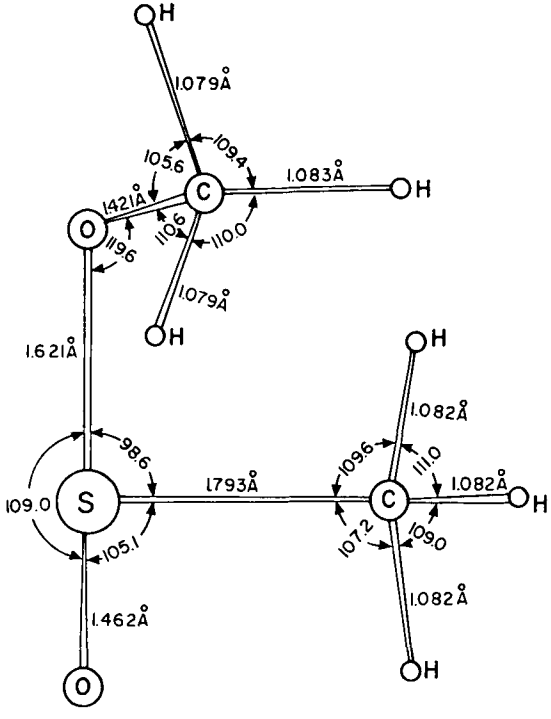


FIGURE 8. $CH_3S(O)OCH_3$ I, structure **63** in Table 14

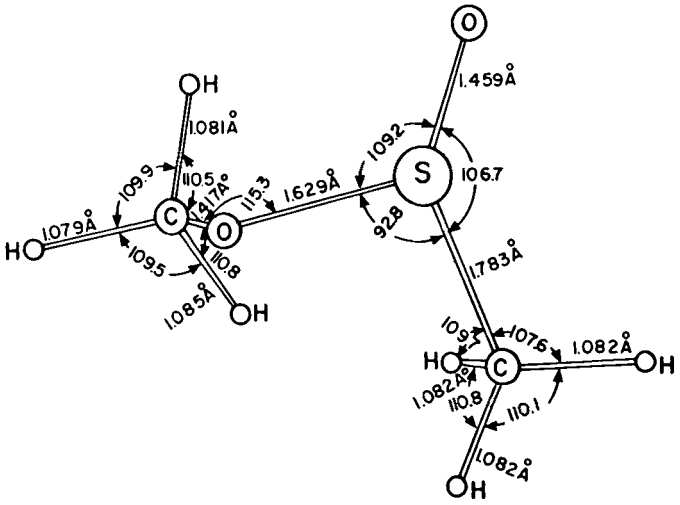


FIGURE 9. $CH_3S(O)OCH_3$ II, structure **64** in Tables 11–14

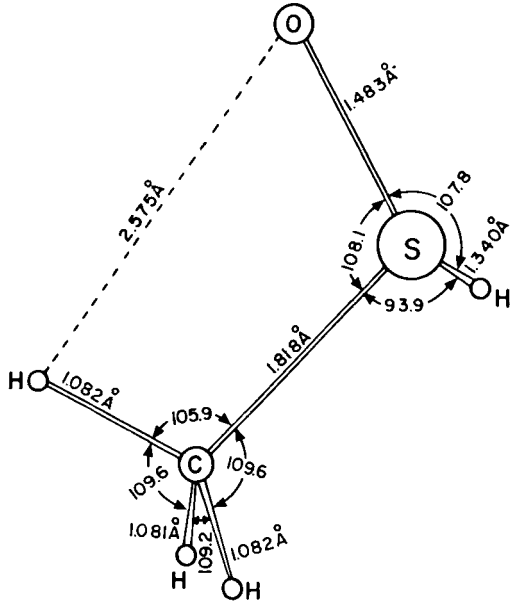


FIGURE 10. $HS(O)CH_3$, structure **72** in Tables 11–14

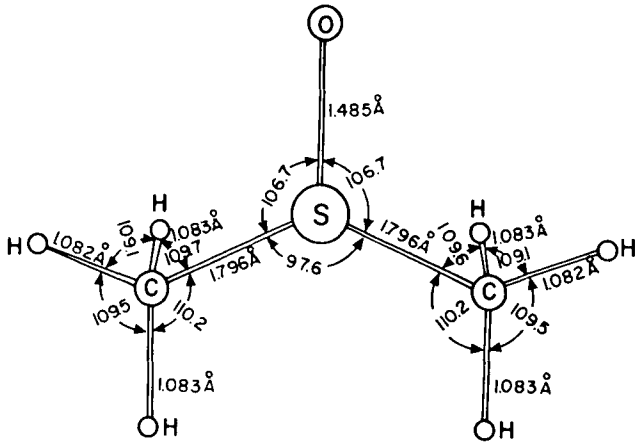


FIGURE 11. $CH_3S(O)CH_3$, structure **74** in Tables 11–14

their bond angles as with the C—S—O and S—O—C angles in $CH_3S(O)OCH_3$ (**63**, Figure 8 and **64**, Figure 9). It should be noted that in Reference 1 only the lower-energy rotamer conformation of $HS(O)NH_2$ (**66** and **67**) was reported. These systems will be discussed in more detail in Section 8. In general, more rotamers of a given compound were found here than in the previous reports.[1,2]

Some XS(O)· radicals are included in Tables 4–7. Two in particular that deserve attention are the two HOS(O)S· radicals (**34** and **35**). As can be seen Table 7, in both cases the unpaired spin is localized on the terminal sulphur atom. Conformer II, the more stable, has rotamer structure (type) *a* in Table 14, footnote *b*, with X = S. This allows a 2.537 Å distance hydrogen bond between (O—)H and O(=S). Conformer I has the type *b* orientation (viewed along the S—O axis) with the angle *b* close to 120°. This rotamer cannot have the intramolecular hydrogen bond and is therefore less stable than II.

Another comparison involves the generation of the XSO_2· type radicals. In Reference 2 these radicals were discussed from the point of view of being derived from the sulphones (XSO_2H) by homolytically breaking the S—H bond. However, they can also be obtained directly from the corresponding sulphinic acids XS(O)OH by dissociating the hydrogen atom to form two radicals. A comparison of the two processes, using the lowest MP2/6-31+G* energies tabulated in Table 11 and References 1 and 2 for each comformer with X = F, Cl, OH, NH_2, SH, H and CH_3, shows that the S—H bond is easier to break (by an average of 17.5 kcal mol^{-1}) than the sulphinic O—H bond. In this comparison the energy of the hydrogen atom was taken as equal to −0.5 a.u. While the acid hydrogen atom dissociation energies increase approximately with the electronegativity nature of the X substituent, the S—H homolytic dissociation shows a more scattered behaviour with the nature of X.

Analogously, the formation of XSO_2^- by heterolytic dissociation from either XSO_2—H or XS(O)O—H can be compared. Again, proton dissociation from oxygen is harder (in this case), also by an average 17.5 kcal mol^{-1} compared to S—H. As expected, the more electronegative the nature of X, the easier (in terms of energy) is proton removal relative to radical formation, for breaking either the S—H and the O—H bonds. Homolytic and heterolytic O—H dissociation will be discussed in more detail later.

Tables 12 and 13 also allow a more extensive comparison of properties such as bond lengths and atomic charges in going from the sulphinic acids to the dissociated radicals and anions, along the lines discussed somewhat in Reference 1 for sulphinic compounds and derivatives and, more extensively, in Reference 2 for sulphones. Analogously, trends in the energies and geometries of radicals and anions between XSY and XS(O)Y systems can also be compared.

IV. METHYLSULPHONYL DERIVATIVES

A comprehensive discussion of sulphonic acids, sulphones and their radicals and anions from a computational point of view has recently been given[2]. That chapter should be referred to for the basic references, to which we will add here[25–29]. The Tables presented there of neutral parents, radicals obtained from them by homolytic dissociation of a hydrogen atom (even from a methyl group) and anions generated by deprotonation[2] are augmented here with larger molecules, and the discussion is expanded accordingly. All the new structures contain one or more methyl groups. The same calculational procedures (RHF gradient optimization of the geometry using the 6-31G* basis set for the parent compounds and radicals, and the 6-31+G* basis for the anions) described for the XSY and XS(O)Y compounds were used here, as well as in the previous studies[1,2], for compatibility. For all systems the MP2/6-31+G* energy was calculated as a single point using the RHF or UHF optimized geometry. The properties of the neutral parents are summarized in Tables 15–17 and shown selectively in Figures 12 and 13, the radicals in Tables 18–21 and Figures 14–20 and the anions in Tables 22–24 and Figures 21–28.

Four CH_3SO_2X compounds have been added in Tables 15–17, none of them acids. The geometric and electronic structural trends discussed previously can be extended to include these species. The optimized geometries are shown only for CH_3SO_2F (**75**) and $CH_3SO_2OCH_3$ (**78**) in Figures 12 and 13, respectively. However, all the geometries with a methyl group of the $CH_3—SO_2X$ form show a staggered conformation of the $S(O_2X)$ group relative to $C(H_3)$ with respect to the S–C bond. This structural aspect has been reviewed by Hargittai[28] using experimentally determined structures, who also consistently found staggered conformations. In addition, we also find here that the methyl group C—H bond *trans* or anti to the C—X bond is slightly longer than the other C—H bond lengths. This differential C—H bond distance effect is very small (0.001–0.003 Å) and could even be considered to be too close to the accuracy or convergence level of the gradient optimization criteria in the computer codes to be significant. However, the effect is consistent for all the $CH_3—SO_2X$ systems studied here, unless X is a group with potential hydrogen bonding (donor) properties where internal hydrogen bond interaction effects can dominate. The slightly longer C—H bond length in the *trans* position should mean that dissociation of that bond is more facile than the other methyl C—H bonds.

Experimental evidence supporting the lability of one of the C—H bonds comes from steric stability studies at the chiral carbon atom (in $XSO_2—CRR'H$) where H/D exchange reaction rates have been compared with racemization kinetics in basic solution. It is found that the ratio of exchange to racemization rates is consistently much larger than one (by at least an order of magnitude) which implies that the exchange reaction proceeds through an intrinsically asymmetric carbon with retention of configuration. This result correlates with the remarkable stability of α-sulphonyl carbanions which stubbornly retain their original configuration in electrophilic attack. The lengthened *trans* C—H bond distance is the precursor to the stable α-sulphonyl carbanions. These kinetic studies and their structural implications have been comprehensibly reviewed by Oae and Uchida[26].

TABLE 15. Energies and dipole moments of neutral CH_3SO_2X derivatives[a]

Molecule	6-31G*			6-31 + G*		
	Energy (a.u.)		RHF dipole moment (*D*)[b]	Energy (a.u.)		RHF dipole moment (*D*)[b]
	RHF	MP2[b]		RHF[b]	MP2[b]	
75 CH_3SO_2F	−686.212681	−687.006167	4.347	−686.222059	−687.029940	4.462
76 CH_3SO_2Cl	−1046.238666	−1046.993443	4.306	−1046.247134	−1047.014535	4.389
77 $CH_3SO_2NH_2$	−642.385777	−643.167194	3.869	−642.394865	−643.190237	4.017
78 $CH_3SO_2OCH_3$	−701.243527	−702.167557	3.454	−701.252363	−702.191313	3.586

[a]Geometry RHF/6-31G* optimized with no symmetry or equivalence constraints.
[b]In the RHF/6-31G* optimized geometry.

TABLE 16. Calculated bond lengths for CH_3SO_2X derivatives[a]

Molecule	Bond lengths (Å)				
	C—S	S=O	X	S—X	C—H
75 CH_3SO_2F	1.760	1.413[b]	F	1.564	1.080[c]
76 CH_3SO_2Cl	1.771	1.420[b]	Cl	2.031	1.081[c]
77 $CH_3SO_2NH_2$[f]	1.766	1.431[b]	N	1.651	1.081[c]
78 $CH_3SO_2OCH_3$	1.761	1.427[b]	O	1.579[e]	1.080[c] 1.078[c,d]

[a]From the RHF/6-31G* optimized geometries.
[b]Two equivalent values.
[c]Average value.
[d]H—C(—S); see Figure 13.
[e]S—O. O—C = 1.433 Å.
[f]N—H = 1.001 Å.

TABLE 17. Mulliken atomic charges and orbital occupancies on S in CH_3SO_2X derivatives[a].

Molecule	Atomic charges					d-Orbital occupancy on S
	S	C(—S)	O	X[g]	H(—C)	
75 CH_3SO_2F	1.737	−0.770	−0.638[b]	−0.441	0.250[c]	0.670
76 CH_3SO_2Cl	1.439	−0.743	−0.640[b]	−0.178	0.254[c]	0.624
77 $CH_3SO_2NH_2$[h]	1.647	−0.734	−0.703[b]	−1.031	0.231[c]	0.646
78 $CH_3SO_2OCH_3$	1.720	−0.757 −0.206[f]	−0.688[b]	−0.729[d]	0.209[c,e]	0.665

[a]From RHF/6-31G* basis optimized geometries.
[b]Two equivalent values.
[c]Average value.
[d]O(—C).
[e]H(—C—O).
[f]C(—O).
[g]Defined in Table 16.
[h]q[H(—N)] = 0.415[b].

Sulphonyl radicals having the unpaired electron spin located primarily on the oxygen and/or sulphur atoms were discussed previously[2]. Here, we address the radicals produced by the homolytic cleavage of a methyl C—H bond in the α-position to the central sulphur atom. The general formula of these radicals is $XSO_2CH_2\cdot$, and they are discussed here for X = F (**79**, Figure 14), Cl (**80**, Figure 15), OH (**81**, Figure 16), NH_2 (**82**, Figure 17) and CH_3 (**83**, Figure 18). There are also two radical structures of the $XSO_2OCH_2\cdot$ type, with $X = CH_3$ (**84**, Figure 19) and H (**85**, Figure 20). There is also one $XSO_2CH_2\cdot$ structure with X = H in Reference 2 (**27**, Tables 4–7, Figure 29). As can be seen from Table 21, the unpaired electron spin in these methylene radical systems is localized mainly on its carbon atom.

A comparison of trends in bond-length changes from the neutral parents (Table 16 and Reference 2) to the corresponding methylene radical species (Table 19 and

TABLE 18. Energies and dipole moments of $XSO_2\dot{C}H_2$ and $XSO_2O\dot{C}H_2$ radicals[a]

Molecule	6-31G*			6-31 + G*		
	Energy (a.u.)		UHF dipole moment (*D*)[b]	Energy (a.u.)		UHF dipole moment (*D*)[b]
	UHF	MP2[b]		UHF[b]	MP2[b]	
79 $FSO_2CH_2\cdot$	−685.575259	−686.340503	4.249	−685.584739	−686.364005	4.312
80 $ClSO_2CH_2\cdot$	−1045.601591	−1046.328267	4.214	−1045.610454	−1046.349822	4.264
81 $HOSO_2CH_2\cdot$	−661.577622	−662.347078	4.084	−661.586758	−662.369795	4.150
82 $NH_2SO_2CH_2\cdot$	−641.748585	−642.502189	3.801	−641.757795	−642.525145	3.905
83 $CH_3SO_2CH_2\cdot$	−625.752466	−626.474858	5.104	−625.760087	−626.494812	5.260
84 $CH_3SO_2OCH_2\cdot$	−700.609230	−701.509432	4.528	−700.618735	−701.533859	4.554
85 $HSO_2OCH_2\cdot$	−661.553675	−662.322172	3.303	−661.563305	−662.344997	3.415

[a]Geometry UHF/6-31G* optimized with no symmetry of equivalence constrains.
[b]In the UHF/6-31G* optimized geometry.

TABLE 19. Calculated bond lengths for $XSO_2\dot{C}H_2$ and $XSO_2O\dot{C}H_2$ radicals[a]

Molecule	Bond lengths (Å)								H_2CS angle[e]
	C—S	S=O	S—H	C—H	X	S—X	X—H	C—O	
79 $FSO_2CH_2\cdot$	1.730	1.412[b]	—	1.071[b]	F	1.563	—	—	174.2
80 $ClSO_2CH_2\cdot$	1.735	1.418[b]	—	1.071[b]	Cl	2.032	—	—	170.2
81 $HOSO_2CH_2\cdot$	1.734	1.426 1.417	—	1.071[b]	O	1.589	0.955	—	173.6
82 $NH_2SO_2CH_2\cdot$	1.738	1.430[b]	—	1.071[b]	N	1.647	1.001[b]	—	168.4
83 $CH_3SO_2CH_2\cdot$	1.748 1.748	1.435[b]	—	1.082[c] 1.072[b,d]	C	1.773	—	—	178.2
84 $CH_3SO_2OCH_2\cdot$	1.765	1.425 1.418	—	1.081[c] 1.071[b,d]	O	1.592[f]	— —	1.382	145.9
85 $HSO_2OCH_2\cdot$	—	1.416 1.419	1.316	1.070[b,d]	O	1.584	—	1.389	145.9

[a]From the UHF/6-31G* optimized geometries.
[b]Two equivalent values.
[c]Average value.
[d]Hydrogen on radicalic carbon.
[e]Angle between CH_2 bisector and C—S bond.
[f]S—O.

TABLE 20. Mulliken atomic charges and d-orbital occupancies on S in $XSO_2\dot{C}H_2$ and $XSO_2O\dot{C}H_2$ radicals[a]

Molecule	Atomic charges						d-Orbital occupancy on S
	S	C	O(=S)	H(—C)	X[f]	H(—X)	
79 $FSO_2CH_2\cdot$	1.754	−0.593	−0.632[b]	0.263[b]	−0.434	—	0.685
80 $ClSO_2CH_2\cdot$	1.454	−0.554	−0.634[b]	0.269[b]	−0.170	—	0.641
81 $HOSO_2CH_2\cdot$	1.714	−0.587	−0.692	0.261	−0.810	0.511	0.684
			0.649	0.252			
82 $NH_2SO_2CH_2\cdot$	1.664	−0.582	−0.694	0.243	−1.024	0.416[c]	0.662
			−0.693	0.255			
83 $CH_3SO_2CH_2\cdot$	1.562	−0.597[e]	−0.704[b]	0.231[c]	−0.753	—	0.612
84 $CH_3SO_2OCH_2\cdot$	1.735	−0.759	−0.654	0.239[c]	−0.686[g]	—	0.671
		−0.089[e]	−0.697	0.216[d,c]			
85 $HSO_2OCH_2\cdot$[h]	1.565	−0.066	−0.637	0.218[c]	−0.679	—	0.682
			−0.671				

[a] From UHF/6-31G* optimized geometries.
[b] Two equivalent values.
[c] Average value.
[d] Hydrogen on radicalic carbon.
[e] Radicalic carbon.
[f] Defined in Table 19.
[g] O(—C).
[h] q[H(—C)] = 0.051.

TABLE 21. Spin populations[a] in $XSO_2\dot{C}H_2$ and $XSO_2CH_2^{\cdot}$ radicals[a]

Molecule	C				H[c]
	s	p_x	p_y	p_z	s
79 $FSO_2CH_2\cdot$	0.130			0.942	−0.176
80 $ClSO_2CH_2\cdot$	0.136	0.864	0.124	0.035	−0.174
81 $HOSO_2CH_2\cdot$	0.177	0.136	0.236	0.699	−0.180
82 $NH_2SO_2CH_2\cdot$	0.135	0.136	0.035	0.863	−0.180
83 $CH_3SO_2CH_2\cdot$	0.137	0.460		0.550	−0.180
84 $CH_3SO_2OCH_2\cdot$	0.180	0.040	0.807	0.093	−0.152
85 HSO_2OCH_2	0.180	0.125	0.248	0.602	−0.158

[a] From UHF/6-31G* optimized geometries.
[b] Only values higher than 0.035 are included.
[c] Total spin population for both hydrogen atoms on the methylene carbon atom.

Reference 2) shows that, for a given X, the C—S, C—H and S=O bond lengths shorten, while the S—X bond distance remains essentially unchanged. In Table 19 the orientation of the $CH_2\cdot$ plane relative to the C—X axis is defined by the angle that the CH_2 bisector makes with the C—S bond (called H_2CS angle). For the $XSO_2CH_2\cdot$ systems this angle is seem to be consistently close to 180°, making the H_2CS grouping very nearly planar. The corresponding value of this angle for $HSO_2CH_2\cdot$, for example, is 179.3°. The unpaired spin in these radicals is thus in a mainly carbon atom p-type orbital (with about 10%

TABLE 22. Energies and dipole moments of $XSO_2CH_2^-$ and $XSO_2OCH_2^-$ anions[a]

Molecule	Energy (a.u)		RHF dipole moment (D)[b,c]
	RHF	MP2[b]	
86 $FSO_2CH_2^-$	−685.640538	−686.463325	1.947
87 $ClSO_2CH_2^-$	−1045.684684	−1046.461807	4.775
88 $HOSO_2CH_2^-$	−661.624507	−662.451046	3.320
89 $NH_2SO_2CH_2^-$	−641.784490	−642.593487	2.830
90 $CH_3SO_2CH_2^-$	−625.787115	−626.563298	3.128
91 $CH_3SO_2OCH_2^-$	−700.616081	−701.564178	3.488
92 $HSO_2OCH_2^-$	−661.559548	−662.371072	5.070
93 $CH_3OSO_2CH_2^-$	−700.647954	−701.604319	5.474

[a] Geometry RHF/6-31 + G* optimized with no symmetry or equivalence constraints.
[b] In the RHF optimized geometry.
[c] Origin dependent.

TABLE 23. Calculated bond lengths for $XSO_2CH_2^-$ and $XSO_2OCH_2^-$ anions[a]

Molecule	Bond lengths								H_2CS angle[f]
	C—S	S=O	S—H	C—H	X	S—X	X—H	C—O	
86 $FSO_2CH_2^-$	1.631	1.440[b]	—	1.075[b]	F	1.660	—	—	146.2
87 $ClSO_2CH_2^-$	1.594	1.429[b]	—	1.070[b]	Cl	2.607	—	—	154.1
88 $HOSO_2CH_2^-$	1.646	1.451[b]	—	1.077[b]	O	1.666	0.952	—	139.8
89 $NH_2SO_2CH_2^-$	1.684	1.461[b]	—	1.081[b]	N	1.687	1.003[c]	—	128.8
90 $CH_3SO_2CH_2^-$	1.791	1.466[b]	—	1.083[b]	C	—	—	—	132.0
	1.687[d]			1.078[e,b]				1.620	
91 $CH_3SO_2OCH_2^-$	1.772	1.442	—	1.081[c]	O	1.512	—		102.5
		1.446		1.092[e,b]				1.691	
92 $HSO_2OCH_2^-$	—	1.438[b]	1.328	1.092[c]	O	1.500	—	1.394	98.1
93 $CH_3OSO_2CH_2^-$	1.649	1.451	—	1.085[c]	O	1.669	—		144.7
		1.443		1.076[e,c]					

[a] From the RHF/6-31 + G* optimized geometries.
[b] Two equivalent bonds to the accuracy of the table.
[c] Average value.
[d] Methylene carbon.
[e] C—H on the methylene carbon.
[f] See footnote *e* in Table 19.

s character—see Table 21), approximately perpendicular to the H_2CS plane. The S—X bond is also roughly perpendicular to the H_2CS plane and therefore lies nearly parallel to the radical orbital. Because of the near-planarity of the H_2CS grouping, radical reactions involving methylene in a sulphonyl compound are not expected to retain configuration around the carbon atom.

The trends in bond shortening or lengthening in going from the neutral parent compounds to the radical species have been interpreted in terms of either two MO,

TABLE 24. Mulliken atomic charges and d-orbital occupancies on S for $XSO_2CH_2^-$ and $XSO_2OCH_2^-$ anions[a]

Molecule	Atomic charges							d-Orbital occupancy on S
	S	C	O	H(—C)	H(—S)	X[f]	H(—X)	
86 $FSO_2CH_2^-$	1.858	−0.971	−0.851[b]	0.179[b]	—	−0.544	—	0.622
87 $ClSO_2CH_2^-$	1.200	−0.719	−0.642[b]	0.227[b]	—	−0.651	—	0.563
88 $HOSO_2CH_2^-$	1.771	−0.986	−0.865[b]	0.169[b]	—	−0.887	0.494	0.620
89 $NH_2SO_2CH_2^-$	1.611	−0.987	−0.851[b]	0.163	—	−1.090	0.424	0.599
				0.175			0.406	
90 $CH_3SO_2CH_2^-$	1.402	−0.959[d]	−0.863[b]	0.209[c]	−0.017	−0.701	—	0.571
91 $CH_3SO_2OCH_2^-$	1.969	−0.826	−0.819	0.119[e,c]	—	−0.708	—	0.666
		−0.726[d]	−0.850	0.243[c]				
92 $HSO_2OCH_2^-$	1.684	−0.609	−0.791[b]	0.108[b]	—	−0.693	—	0.689
93 $CH_3OSO_2CH_2^-$	1.798	−0.977	−0.871	0.173[c]	—	−0.633	—	0.629
		−0.328[d]	−0.849	0.113[e,c]				

[a] From RHF/6-31+G* optimized geometries.
[b] Two equivalent values.
[c] Average value.
[d] Anionic carbon.
[e] Hydrogen on anionic carbon.
[f] Defined in Table 23.

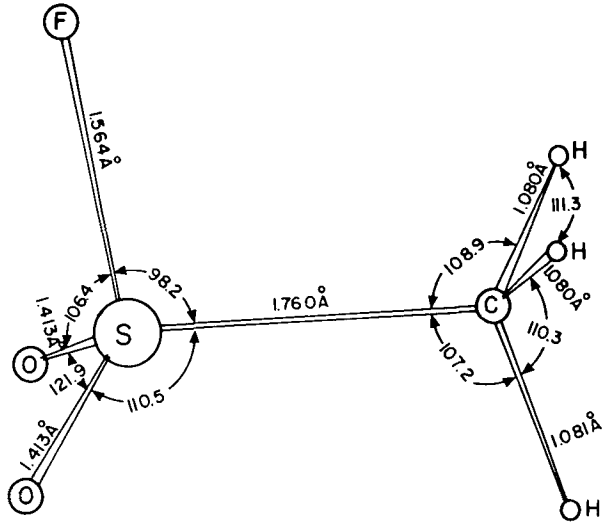


FIGURE 12. CH_3SO_2F, structure **75** in Tables 15–17

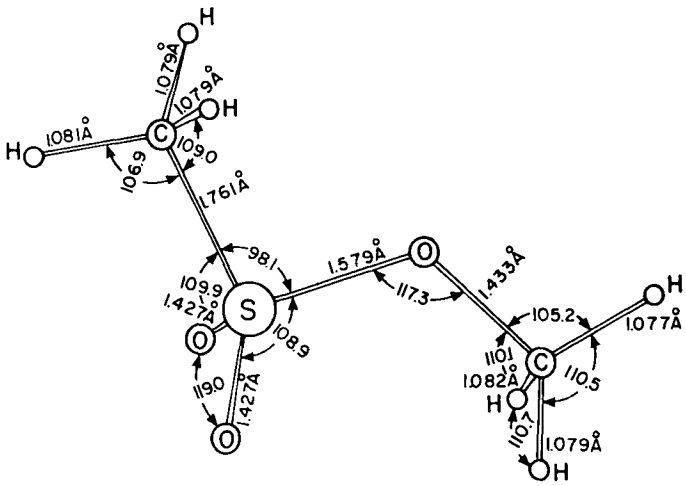


FIGURE 13. $CH_3SO_2OCH_3$, structure **78** in Tables 15–17

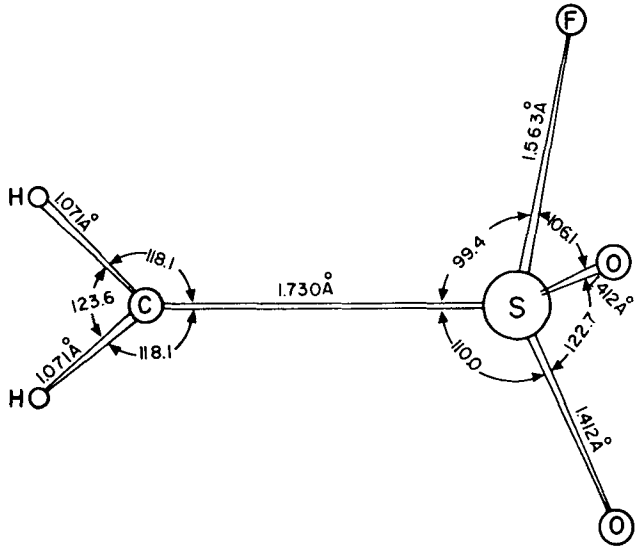


FIGURE 14. $FSO_2CH_2\cdot$ radical, structure **79** in Tables 18–21

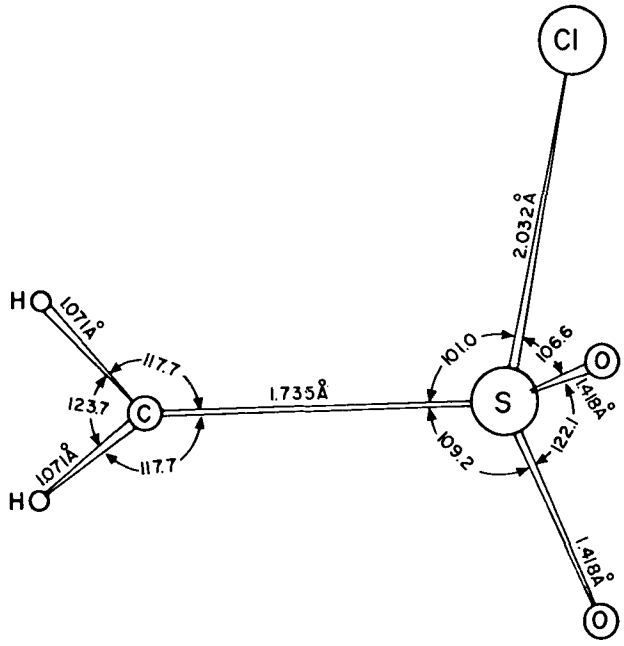


FIGURE 15. $ClSO_2CH_2\cdot$ radical, structure **80** in Tables 18–21

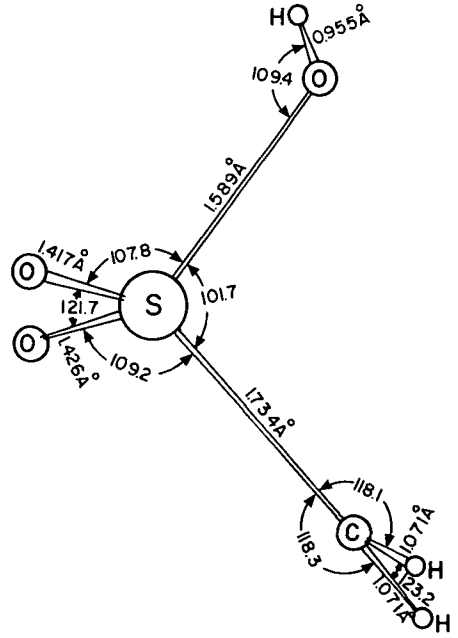


FIGURE 16. $HOSO_2CH_2\cdot$ radical, structure **81** in Tables 18–21

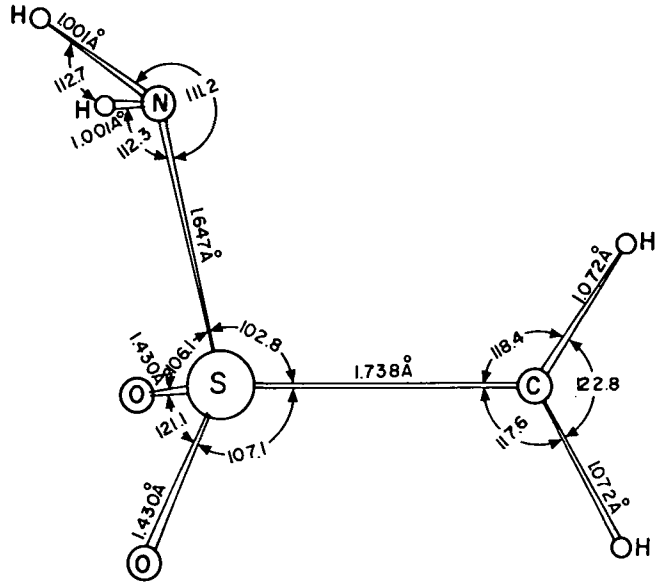


FIGURE 17. $NH_2SO_2CH_2\cdot$ radical, structure **82** in Tables 18–21

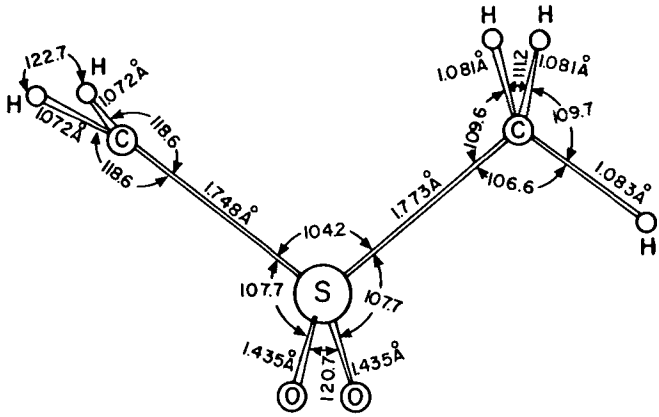


FIGURE 18. $CH_3SO_2CH_2\cdot$ radical, structure **83** in Tables 18–21

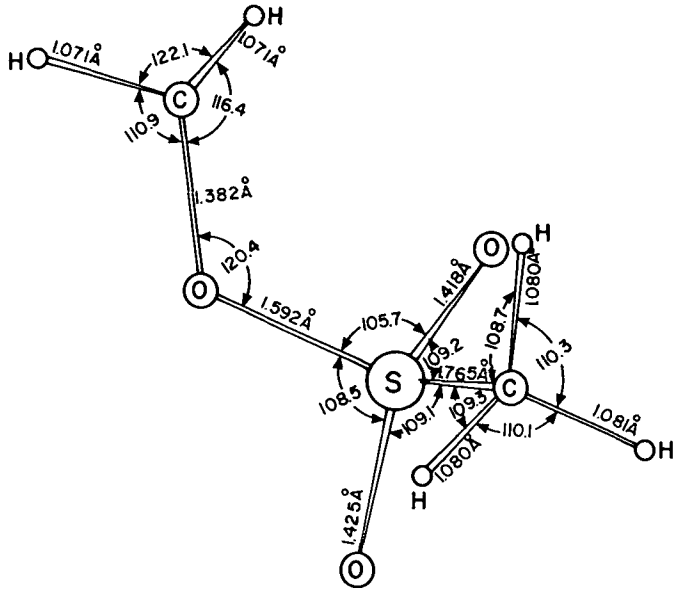


FIGURE 19. $CH_3SO_2OCH_2\cdot$ radical, structure **84** in Tables 18–21

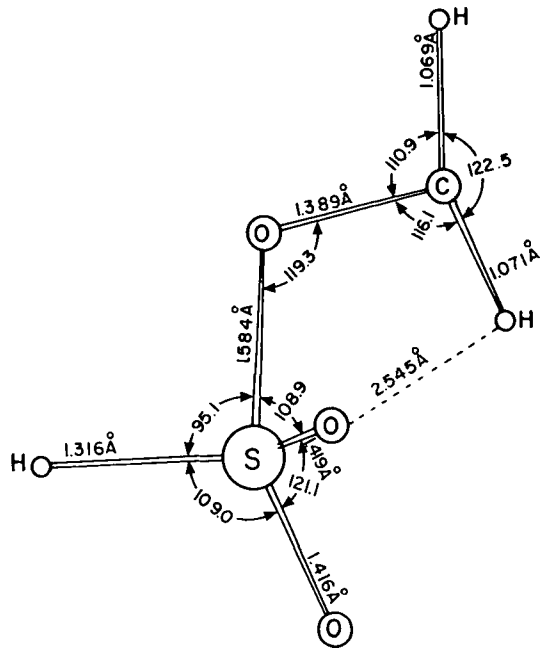


FIGURE 20. $HSO_2OCH_2\cdot$ radical, structure **85** in Tables 18–21

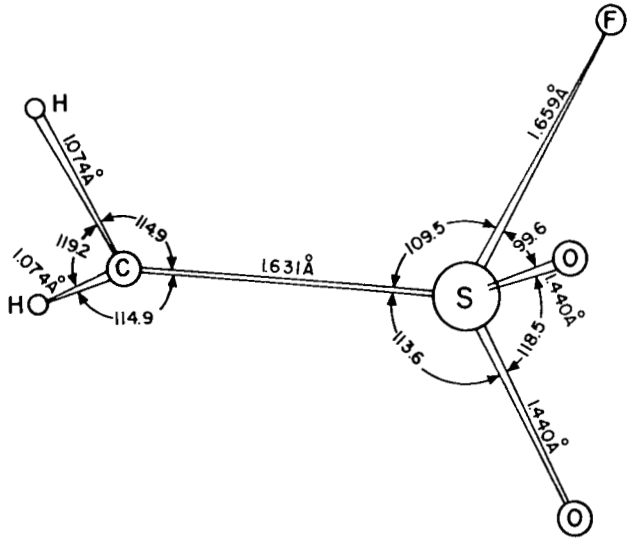


FIGURE 21. $FSO_2CH_2^-$ anion, structure **86** in Tables 22–24

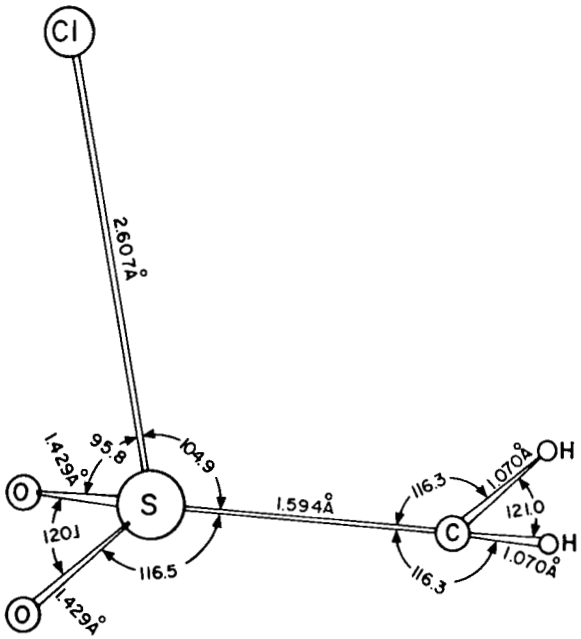


FIGURE 22. $ClSO_2CH_2^-$ anion, structure **87** in Tables 22–24

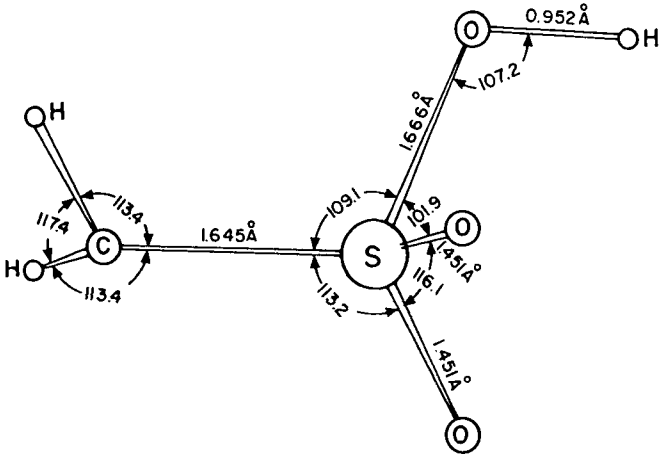


FIGURE 23. $HOSO_2CH_2^-$ anion, structure **88** in Tables 22–24

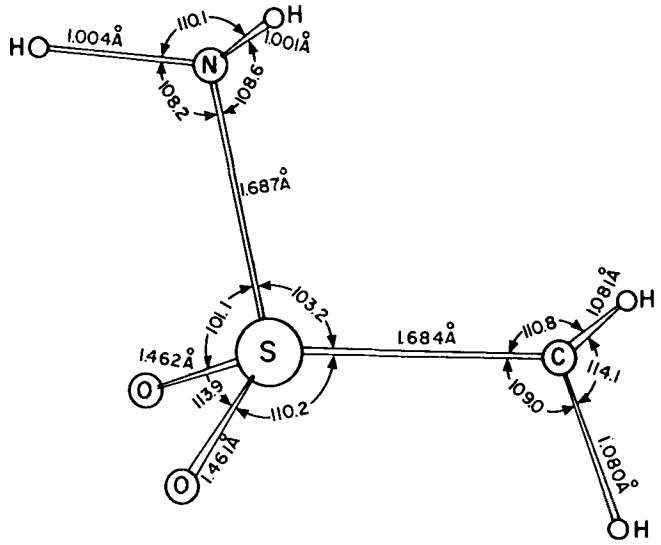


FIGURE 24. $NH_2SO_2CH_2^-$ anion, structure **89** in Tables 22–24

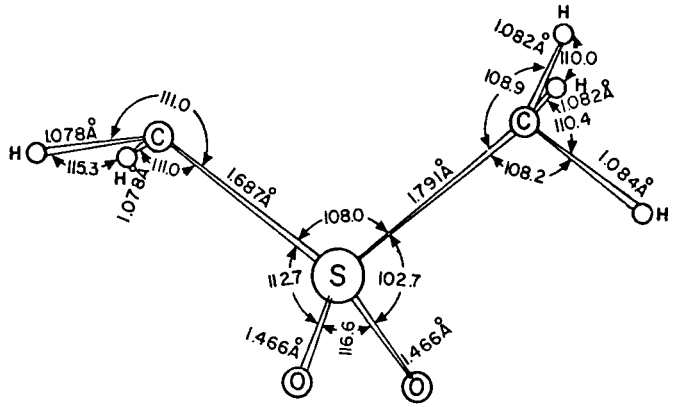


FIGURE 25. $CH_3SO_2CH_2^-$ anion, structure **90** in Tables 22–24

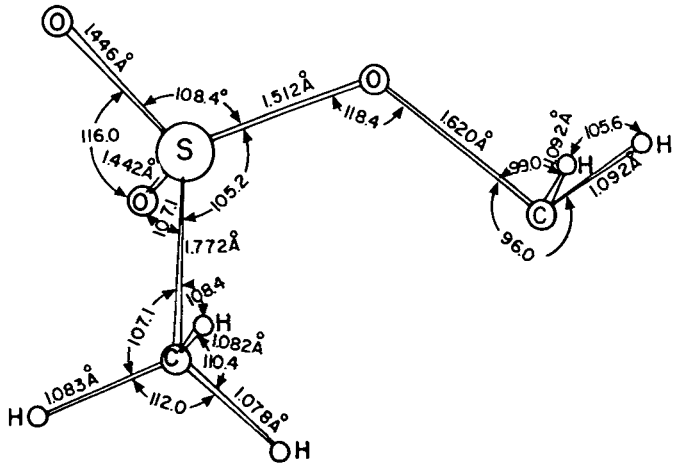


FIGURE 26. $CH_3SO_2OCH_2^-$ anion, structure **91** in Tables 22–24

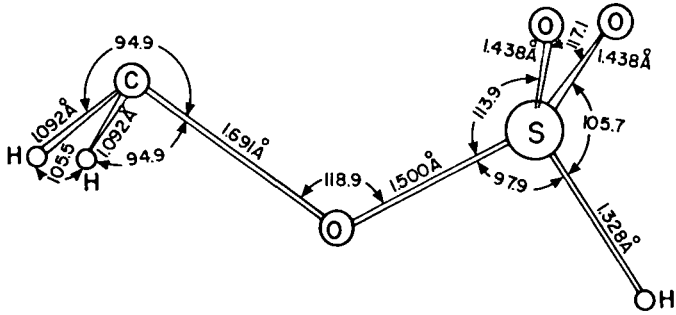


FIGURE 27. $HSO_2OCH_2^-$ anion, structure **92** in Tables 22–24

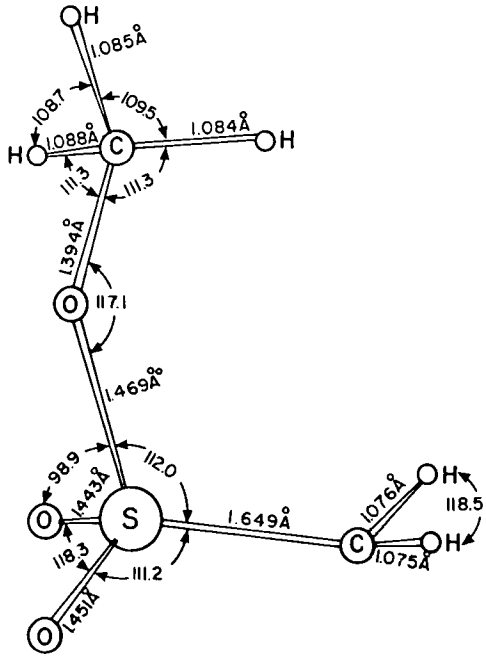


FIGURE 28. $CH_3OSO_2CH_2^-$ anion, structure **93** in Tables 22–24

three-electron interactions or two MO, one-electron interaction[2]. In the former case, X—Y bonding MO mixes with the radical MO to stabilize and shorten the X—Y bond length. In the second case the MO containing the unpaired electron is stabilized by interacting with an antibonding MO (S—X in this case) which stabilizes the radical centre and delocalizes a small amount of spin population into the S—X bond via its antibonding σ MO. In a Valence Bond language, CH_2 can form a partial double bond with the central sulphur atom if one of the other sulphur bonds (to O or X) is ruptured. The S—X bond is usually weaker than S=O and, being parallel to the radical MO, is well oriented for inducing such an incipient partial double-bonded structure of sulphur with methylene. The S—X bond is therefore expected to be weakened (and longer) in the radical relative to the neutral parent compound. These opposing shortening and lengthening effects for the S—X bond apparently are either individually not significant or approximately cancel each other since the S—X bond lengths remain essentially unchanged with hydrogen atom dissociation. The calculated spin population on X is always less than 0.001 and about −0.05 on sulphur. On the other hand, the S—C bond is apparently strengthened by some induced partial double-bond character in the radical and consequently shortens somewhat relative to the neutral parent.

The geometries of those radicals with potential hydrogen bonding donor properties (X = OH, NH_2) have additional features. In projection along the S—O axis the O—H bond in $HOSO_2CH_2\cdot$ is preferentially oriented to lie parallel with one of the S=O bonds. The H···O distance is 2.35 Å and this S=O bond has a length of 1.426 Å, compared to the other S=O bond distance of 1.417 Å (Figure 16). Analogous evidence of internal hydrogen bonding is found also in $NH_2SO_2CH_2\cdot$ where the two N—H bonds are eclipsed with the two S=O bonds for a double N···H interaction distance of 2.46 Å.

Evidence of intramolecular hydrogen bonding in sulphonyl compounds was discussed previously[2].

It is interesting to use the energies tabulated in Tables 15, 18 and Reference 2 to calculate the homolytic bond dissociation energies for C—H to form the substituted methylene radical. When this is done, it is found that for the XSO_2CH_3 structures the HF/6-31G* dissociation energies cluster closely around 86 kcal mol^{-1} (MP2/6-31+G* gives 103.5 kcal mol^{-1}), while for XSO_2OCH_3, the corresponding binding energies are about 84 (and 99) kcal mol^{-1}. A reasonable conclusion is that an oxygen atom α to the methylene radical centre is more effective in stabilizing the radical (or is less destabilizing) than an α-SO_2 group. Another conclusion is that the specific nature of X in a given generic-type structure is not very important to the homolytic C—H bond dissociation process.

The geometries of the corresponding $XSO_2CH_2^-$ sulphonyl anions in Table 23 and Figures 23–28 show a non-planar angle between the S—C bond and the CH_2 bisector (H_2CS angle in Table 20). The anion lone pair occupies the space of the dissociated proton for retention of configuration. For X = F (**86**), Cl (**87**), OH (**88**) and CH_3 (**90**) the S—X bond exactly bisects the CH_2 angle in projection along the S—C axis, as expected, while for X = NH_2 (**89**) the bCSN (b = CH_2 bisector) dihedral angle is 35.5°. Neither the flip nor the rotation barriers were probed, but each should be large enough to prevent racemization, as is observed experimentally. Thus calculated geometric structures are consistent with and reinforce the kinetic experiments cited above[26].

For the anions the C—S bonds decrease and the S—X bonds increase in length substantially compared with the neutral species. Here the potentially stabilizing two MO, three-electron interaction in the radical becomes a destabilizing two MO, four-electron interaction. The incipient dissociation of X^- to give the partially double-bonded $SO_2{=}CH_2$ structure is very favourable for electronegative X and results in the increased S—X and decreased S—C distances. The calculated deprotonation energies (comparing the energies in Tables 15 and 22) are consistent with these trends. Thus, the $XSO_2OCH_2^-$ anions (**91** and **92**), where the asymptotic S=C structure is not possible, have proton affinities that are at least 20 kcal mol^{-1} larger than any of the other ($XSO_2CH_2^-$) methylene anions where the CH_2 group is directly bound to sulphur. In these latter systems, the methyl deprotonation energies are also found to vary roughly with the electronegativity of X in the order, X = Cl < F < OH < CH_3 = NH_2. The Cl—S bond length in $ClSO_2CH_2^-$ (**87**, Figure 22) is an unusually large 2.067 Å (Table 23), indicating an incipiently dissociated Cl^-. Finally, the H_2CS angles are much larger for the $XSO_2CH_2^-$ type anions than the $XSO_2OCH_2^-$ anions. The relative stabilization of carbanions by sulphenyl and sulphonyl groups has been reviewed by several authors.[25–27].

Contrary to the other $XSO_2CH_2^-$ species, $CH_3SO_2CH_2^-$ (**90**, Figure 25) is found to have the methyl group *cis* to the methylene lone pair of electrons across the $(H_2)C$—S bond. The H_3C—S bond length at 1.791 (Table 23) is only slightly longer than normal (see Section 6). X = CH_3 is also anomalous here in its deprotonation energy, referred to above. Having the same value as the NH_2 group places methyl out of its accepted place in the electronegativity scale.

In a final look at the CH_3SO_2X compounds, we can compare the experimental[29] and RHF/6-31G* optimized geometric structure for CH_3SO_2F (**75**, Figure 12). With the calculated values in parenthesis, an electron diffraction study gives r(S=O) = 1.410 Å (1.413 Å), r(S—C) = 1.759 Å (1.760 Å), r(S—F) = 1.561 Å (1.564 Å), ⟨C—S—F = 98.2 (98.2), ⟨O=O=S—F = 106.2 (106.4) and ⟨O=S=O = 123.1 (121.9). The uncertainty in the experimental angles is typically ±1.5. As has been noted before,[1,2], such consistently good agreement for the S=O bond length supports the semi-polar (S^+—O^-) description of this bond as the preferred representation in place of the conventional double-bond

pictorial (S=O) characterization (also used here to avoid confusion). RHF/6-31G* does not usually do this well for conventional double bonds. The substantial difference in S=O and S—O(Y) bond lengths (see Section 6) must just affect the additional ionic interaction due to the charge transfer component, of the S=O bond. Hargittai and Hargittai[28,29] have also discussed the trends in CH_3SO_2X bond lengths and angles as a function of the electronegativity of X. The observed trends are completely adhered to by the calculated structures.

V. AROMATIC COMPOUNDS

The XSY, XS(O)Y and XSO_2Y compounds discussed in the previous chapters[1,2] and earlier sections of this review refer to non-aromatic systems. In fact, most experimental work involves aromatic sulphur compounds. We therefore review here a computational study

TABLE 25. Energies and dipole moments of aromatic sulphur compounds[a]

Molecule	Energy (a.u)		RHF dipole moment (*D*)
	RHF	MP2[b]	
94 PhSH	−628.208190	−629.074772	1.930
95 PhSOH	−703.037369	−704.085024	2.364
96 $PhSNH_2$	−683.219685	−684.252286	1.275
97 PhS(O)H	−702.995345	−704.047393	4.476
98 PhS(O)OH	−777.866411	−779.101571	4.131
99 $PhS(O)NH_2$	−758.038547	−759.258254	3.259
100 $PhSO_2H$	−777.845003	−779.080416	5.623
101 $PhSO_2OH$	−852.721936	−854.136383	4.931
102 $PhSO_2NH_2$ I	−832.891676	−834.290441	4.290
103 $PhSO_2NH_2$ II	−832.889830	−834.288664	6.623

[a] Geometry RHF/6-31G* optimized with no symmetry or eqivalence constraints.
[b] In the RHF optimized geometry.

TABLE 26. Calculated bond lengths of aromatic sulphur compounds[a]

Molecule	Bond length (Å)						
	C—C	C—H	C—S	S=O	X	S—X	X—H
94 PhSH	1.387[c]	1.075[c]	1.792	—	H	1.328	—
95 PhSOH	1.387[c]	1.075[c]	1.777	—	O	1.655	0.950
96 $PhSNH_2$	1.385[c]	1.075[c]	1.782	—	N	1.698	0.999[b]
97 PhS(O)H	1.386[c]	1.075[c]	1.792	1.483	H	1.341	—
98 PhS(O)OH	1.386[c]	1.075[c]	1.789	1.461	O	1.623	0.956
99 $PhS(O)NH_2$	1.385[c]	1.075[c]	1.790	1.473	N	1.679	1.004[c]
100 $PhSO_2H$	1.386[c]	1.074[c]	1.763	1.432[b]	H	1.329	—
101 $PhSO_2OH$	1.386[c]	1.074[c]	1.761	1.428 1.420	O	1.591	0.955
102 $PhSO_2NH_2$ I	1.386[c]	1.074[c]	1.768	1.431[b]	N	1.651	1.001[b]
103 $PhSO_2NH_2$ II	1.386[c]	1.074[c]	1.774	1.428[b]	N	1.640	1.000[b]

[a] From RHF/6-31G* optimized geometry.
[b] Two equivalent values.
[c] Average value.

TABLE 27. Mulliken atomic charge and d-orbital occupancies on S[a] in the aromatic sulphur compounds

Molecule	Atomic charges								d-Orbital occupancy on S
	S	H(—C)[b]	X(—S)[g]	H(—C)[c]	C(—S)	O(=S)	H(—O)	C(—C)[c]	
94 $PhSH$[f]	−0.023	0.224	—	0.209	−0.217	—	—	−0.175– −0.199	0.078
95 PhSOH	0.457	0.235 0.217	−0.820	0.208–0.210	−0.214	—	0.481	−0.186– −0.207	0.118
96 $PhSNH_2$	0.336	0.239	−0.980	0.202–0.208	−0.162	—	—	−0.184– −0.207	0.108
97 PhS(O)H	0.879	0.268[d] 0.219	0.043	0.214–0.217	−0.304	−0.787	—	−0.180– −0.199	0.326
98 PhS(O)OH	1.272	0.267[d] 0.232	−0.834	0.216–0.217	−0.337	−0.775	0.480	−0.181– −0.201	0.344
99 $PhS(O)NH_2$	1.148	0.267[d] 0.231	−1.005	0.212–0.213	−0.318	−0.791	—	−0.171– −0.202	0.326
100 $PhSO_2H$	1.409	0.264[e]	0.054	0.212–0.223	−0.344	−0.695[e]	—	−0.167– −0.205	0.609
101 $PhSO_2OH$	1.753	0.264[d] 0.259	−0.813	0.222–0.223	−0.334	−0.707 −0.664	0.507	−0.176– −0.206	0.667
102 $PhSO_2NH_2$ I	1.717	0.256[e]	−1.024	0.218	−0.318	−0.712[e]	—	−0.176– −0.205	0.646
103 $PhSO_2NH_2$ II	1.711	0.258[e]	−0.995	0.220	−0.338	−0.701[e]	—	−0.185– −0.203	0.659

[a] From RHF/6-31G* basis SCF optimized geometries.
[b] *Ortho* to S.
[c] Other ring (*meta, para*) atoms.
[d] *Syn* to O.
[e] Two equivalent values
[f] H(—S) = 0.108.
[g] Defined in Table 26.

of the aromatic systems: the first of its kind, to the best of our knowledge. Tables 25–27 and Figures 29–38 show the properties of three phenyl sulphenyl compounds (PhSY), the three sulphinyls (PhS(O)Y) and four sulphonyls ($PhSO_2Y$), where Y = H, OH and NH_2. The sulphonamide is found in two conformations of NH_2 relative to SO_2.

Computationally, the same procedure was carried out as for the aliphatic sulphur compounds: gradient optimization of the geometric structure at the RHF/6-31G* level, followed by a single point MP2/6-31G* calculation. However, the single point MP2/6-31+G* calculations were not carried out because of the large sizes of these systems.

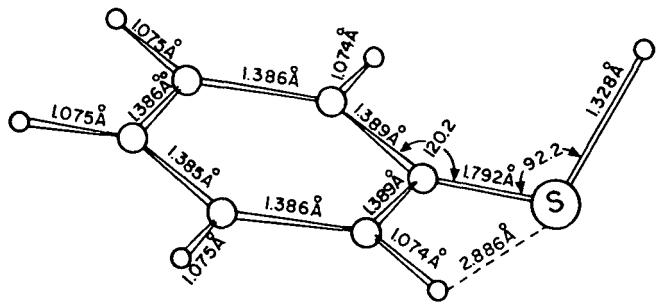


FIGURE 29. C_6H_5SH, structure **94** in Tables 25–27

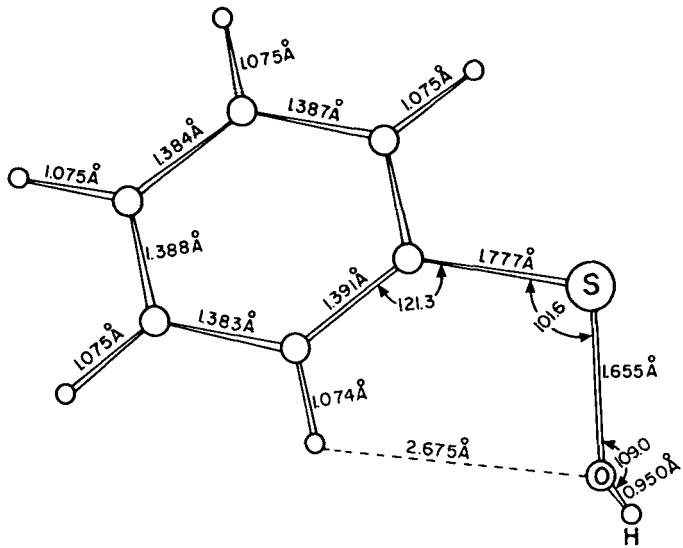


FIGURE 30. C_6H_5SOH, structure **95** in Tables 25–27

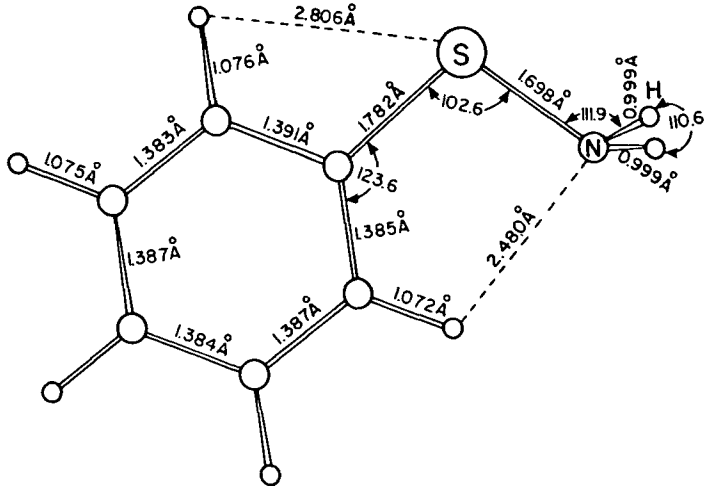


FIGURE 31. $C_6H_5SNH_2$, structure **96** in Tables 25–27

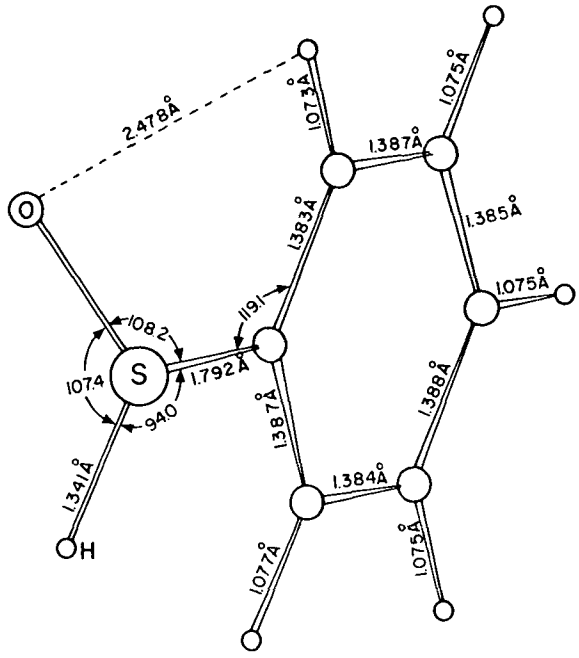


FIGURE 32. $C_6H_5S(O)H$, structure **97** in Tables 25–27

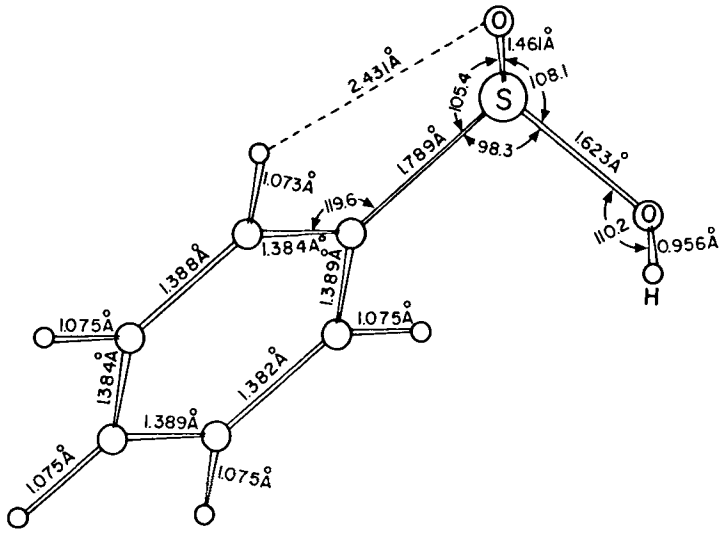


FIGURE 33. $C_6H_5S(O)OH$, structure **98** in Tables 25–27

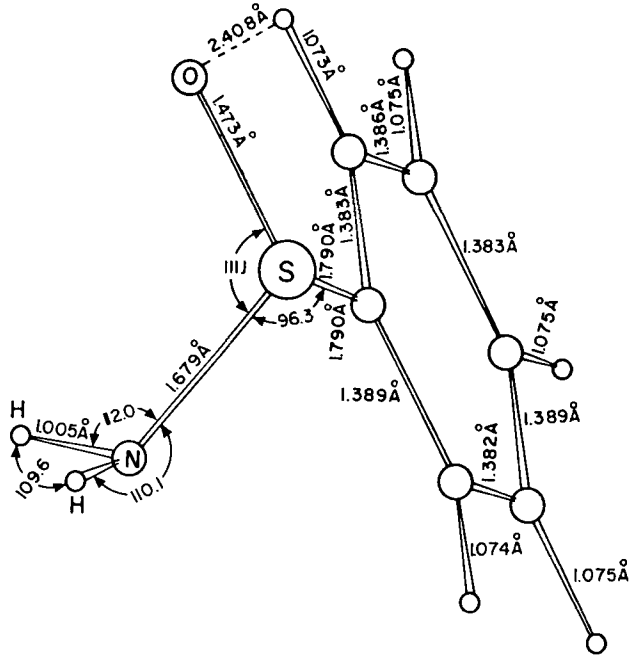


FIGURE 34. $C_6H_5S(O)NH_2$, structure **99** in Tables 25–27

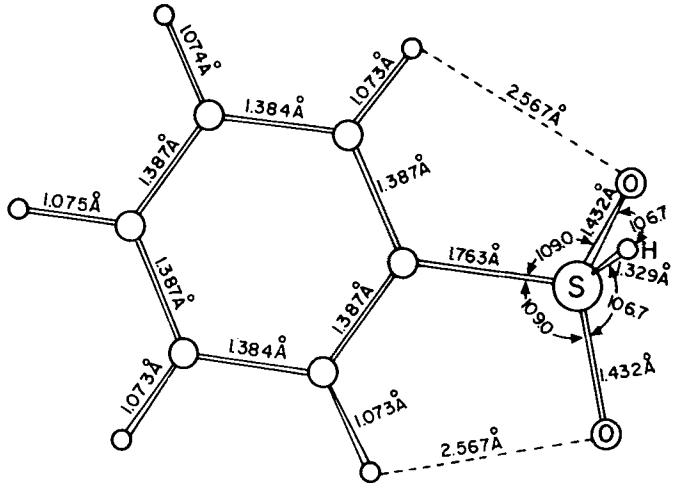


FIGURE 35. $C_6H_5S(O_2)H$, structure **100** in Tables 25–27

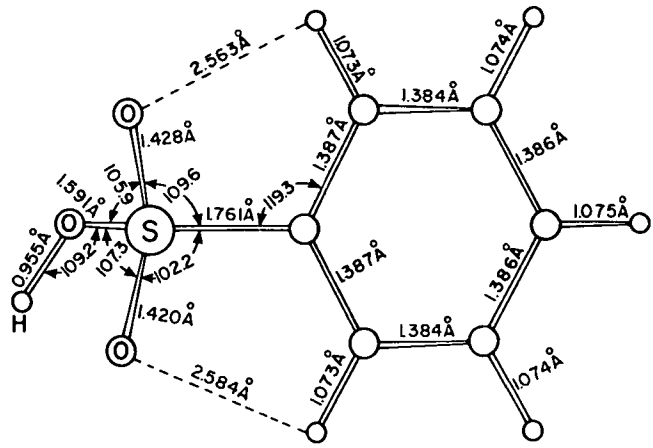


FIGURE 36. $C_6H_5SO_2OH$, structure **101** in Tables 25–27

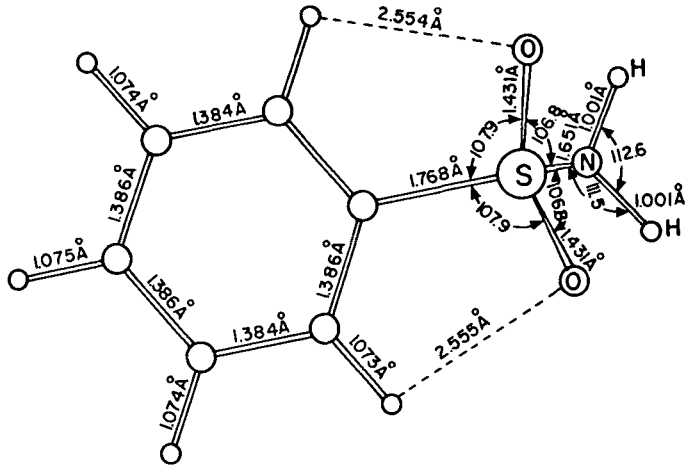


FIGURE 37. $C_6H_5SO_2NH_2$ I, structure **102** in Tables 25–27

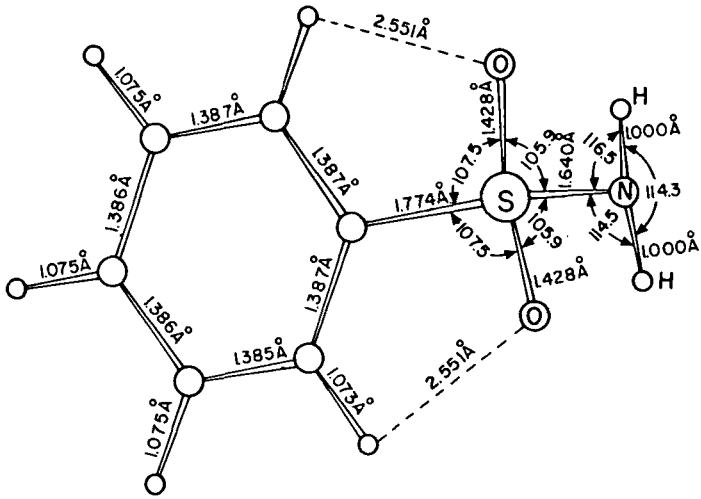


FIGURE 38. $C_6H_5SO_2NH_2$ II, structure **103** in Tables 25–27

The geometric structures of the $PhSO_2X$ compounds can be characterized by both the spatial/conformational relationship between the nuclear SO_2 group and the Y substituent, and the orientation of the SO_2 group relative to the aromatic ring. In $PhSO_2H$ (**100**) the ring C—S—H plane is perpendicular to the aromatic ring, placing the two sulphonyl oxygen atoms in closest possible contact (2.57 Å distance) with the two ring *ortho* hydrogen atoms. This attractive interaction between the ring hydrogen atoms and the semi-polar S=O bond oxygen atoms determines the structure. In $PhSO_2OH$ (**101**) the (C—)H···O(=S) interactions are joined by a simultaneous (O—)H···O(=S) internal hydrogen bond at 2.34 Å distance with a H—O—S=O dihedral angle that is very close to zero. The parallel alignment of the O—H and one S=O bond for maximum attractive interaction has been noted previously as a generally occurring motif in sulphonyl and sulphinyl acids[2].

Benzenesulphonamide has two stable structures, both of which show the *ortho* hydrogen atoms of the aromatic ring interacting with the SO_2 oxygen atoms at a distance of 2.55 Å. In the more stable structure (**102**) the NH_2 group aligns itself parallel with the SO_2 group for minimum (N—)H···O(=S) distances of 2.47 Å each, forming a sloping parallel V structure where the SO_2 angle (121.5°) is, of course, larger than for NH_2 (112.6°). The second sulponamide structure (**103**) can be approximately obtained from the first by 180° rotation of NH_2 about the S—N bond or inversion at the nitrogen atom. The energy difference between the rotamers is only 1.2 (RHF) or 1.1 (MP2) kcal mol^{-1} (Table 25) and here the (N—)H···O(=S) distance is 2.64 Å. Two different such rotamers were obtained also for the aliphatic HSO_2NH_2 molecule[2] with similar small energy differences. Although not shown in Table 27, the aromatic ring *ortho* hydrogen atoms are in all these cases (**100–103**) more positively charged by 0.04 units of positive charge (e) than the *meta*- and *para*-position hydrogen atoms, in accord with the former's intramolecular hydrogen-bonding interactions with the sulphonyl oxygen atoms.

Hargittai[28] has also reviewed the experimental structural data that are relevant to the internal hydrogen bonding effects discussed above. Experimentally, the 'perpendicular' model for $PhSO_2Y$, where the C—S—Y plane is perpendicular to the phenyl ring, is favoured structurally for Y = Cl, CH_3 and vinyl when hydrogen atoms are attached to the ring carbon atoms. Substitution of fluorine for the ring hydrogen atoms which eliminates the (C—)H···O(=S) interaction, results in a different conformational geometry around the C—S bond.

The extent of double-bond character in the C—S bond of the aromatic sulphones can be measured by the quinonoid alternation of C—C bond lengths in the ring to give four 'long' and two 'short'. This differential is seen (**100–103**) consistently to be only 0.002–0.003 Å, which can be taken as indicating not much double-bond character in C—S. A possibly related property is the atomic charge on sulphur in the aromatic sulphones (Table 27) compared to the aliphatic compounds. Using the numbers in Table 17 and previous chapter[2] for comparisons shows that the atomic charge on sulphur in $PhSO_2Y$, CH_3SO_2Y and HSO_2Y for a given Y substituent is consistently largest for the aromatic sulphone. This may indicate some additional π-type interaction involving the phenyl ring not possible in the aliphatic systems, although the C—S bond length is not much different between the aromatic and aliphatic systems (compare Table 26 with Tables 2, 12, 16 and References 1–2).

$XS(O)Y$ compounds, where $X = C_6H_5$, Figures 32–34 can also be discussed structurally in terms of the relationship between Y (= H, OH, NH_2) and the S=O bond on one hand, and the orientation of S=O with respect to the aromatic ring, on the other hand. Both benzenesulphinic acid (**98**) and benzenesulphinamide (**99**) have orientations of their Y substituent relative to S=O similar to that in the corresponding aliphatic $XS(O)Y^1$ (X = H, for example). The projection of XS(O)OH along the S—O bond

has the conformation shown in footnote b, Table 14 for both X = H (angle $a = 32.0°$) and X = C_6H_5 ($a = 41.2°$). These dihedral angles allow a substantial (O—)H···O(=S) internal hydrogen bond interaction at a 2.58 Å distance, while simultaneously accommodating the lone-pair interactions (between the singly-bonded S and O atoms) for minimum repulsion. Because the sulphur lone pair is located *trans* to the O—H bond, the type *a* orientation also allows a stabilizing interaction between the non-bonding (nb) electron pair on sulphur and the O—H σ^* MO. Although the intramolecular hydrogen bond between (O—)H and (O=)S is still possible in the types *b* and *c* rotamers (Table 14), these later orientaions are not favourable for the nb-σ^* interaction and, perhaps, this is the reason that types *b* and *c* are not found here. These considerations have recently been discussed in a different context[30].

In $XS(O)NH_2$ for both X = H[(1)] and X = C_6H_5 (**99**) the optimized structures have the S=O bond located between the two N—H bonds in projection along the S—N axis. This allows a maximum number of (S=)O···H(—N) interactions at a 2.76 Å distance. There could be other stable rotamer structures but these are expected to be of higher energy, for the reasons enumerated above, and were not probed. For example, a possible rotamer geometry for both the hydrogen and benzenesulphinamides has the lone pairs on nitrogen and sulphur *trans* to each other across the S—N bond. Besides allowing only one (S=)O···H(—N) interaction, this conformer would not have any nb pair of electron *trans* to a bond (S—H, N—H or S=O), which is considered to be a stabilizing stereoelectronic arrangement.

As was found in the $PhSO_2X$ compounds, the S=O bond in the aromatic sulphines, PhS(O)Y, orients itself to be approximately parallel to the aromatic ring for maximum interaction between (S=)O and one *ortho* ring H(—C). The O···H distance is in the 2.41–2.48 Å range (Y = H, OH and NH_2) and the atomic charge on the affected hydrogen atoms is larger than on the rest of the ring hydrogen atoms. This difference is usually around 0.05 e, except for the other *ortho* hydrogen atom in the cases of Y = OH and NH_2. In these latter systems there is evidence for an additional hydrogen-bond-type interaction between the electronegative atom of the Y group and the other ring *ortho* hydrogen atom. In these cases the charge difference between the two ortho hydrogen atoms is only 0.03e. Thus, in $C_6H_5S(O)NH_2$ for example, there are three intramolecular hydrogen-bond interaction distances: (N—)H···O(=S) at 2.76 Å, (S=)O···H(—C) at 2.41 Å and (S—)N···H′(—C) at 2.41 Å. The *ortho H′* interaction is undoubtedly weak but is sufficient to determine the final rotameric structure of these simple aromatic sulphinamides.

Although never large, the actual dihedral angle that the S=O bond in PhS(O)Y makes with the plane of the aromatic ring depends on the nature of Y. The largest angle is for Y = H (Figure 32), apparently due to crowding with the nb electron pair on S which prefers to be perpendicular to the ring plane. This can be considered to be the 'normal' case. For Y = OH (Figure 33) and NH_2 (Figure 34) the O=S—C—C(*ortho*) dihedral angle is very close to zero. In these cases there are two addtional weak interactions which must be accommodated: Z···H(—C)$_{ortho}$ and (Z—)H···O(=S), with Z=O(H) and $N(H_2)$.

In all the aromatic sulphur compounds studied here (**94**–**103**) the sulphur atom lies in the plane of the aromatic ring. The S—C—C$_{(ortho)}$—C$_{(meta)}$ and S—C—C$_{(ortho)}$—H dihedral angles never deviate from planarity by more than 4°, and usually less. In the PhSX compounds (**94**–**96**) the net charges on the ring *ortho* hydrogen atoms are consistently larger than on the *meta*- and *para*-position hydrogen atoms. This property is again indicative of a weak internal hydrogen-bond interaction between the *ortho* hydrogen atoms and the lone-pair electrons on the sulphur atom. For Y = H and NH_2 in PhSY there are two such equivalent interactions, but for Y = OH there is one such interaction of (C—)H with O(—H) and one with the sulphur atom. The (C—)S···H(—C) distances

lie in the narrow range of 2.885–2.889 Å, while (S—)O···H(—C) in **95** is 2.675 Å. S···H(—C) and S···H(—O) interactions in XSY compounds will be seen again in Section 7.

The angle between the C—S—Z plane having Z = H, O(H) or $N(H_2)$ and the ring plane in aromatic PhS(O)Y compounds then depends on these extra intramolecular interactions. For Z = H, S—H is perpendicular to the aromatic plane. In both benzenesulphenic acid and benzenesulphenamide **96** the angle is near 30°. Kost and Raban[31] have emphasized the interaction of the sulphur lone pair of electrons with the aromatic ring in *ortho*-substituted benzenesulphenamides in determining the local conformation around the (ring) C—Z bond.

VI. COMPARISON OF PROPERTIES

The XSY, XS(O)Y and XSO_2Y compounds are characterized by zero, one, and two S=O bonds, respectively. In comparing properties among these types of sulphur compounds the focus will be on geometric and electronic structural trends and their possible energetic (thermodynamic) implications. As was briefly expounded in the Introduction, a great deal of our understanding of electronic structure and bonding comes from a knowledge and comparison of molecular geometries. Geometric structure determination can be a difficult experimental task. The collection of structures and energies compiled here and previously[1,2] represents a substantial data base of simple sulphur-containing compounds in a common basis set and level of theory. These computational results allow a comparison and understanding of trends and effects in geometric and electronic structure descriptions, and the connection between them.

A relatively trivial example of the use of this data base for over 70 neutral closed-shell electronic structure XSY, XS(O)Y, XSO_2Y systems has recently been given[32]. The Koopmans' theorm[33] frozen orbitals ionization energy of the easily identified sulphur atomic 2s electron, represented by (the negative of) its RHF orbital energy in the molecule, was plotted against the Mulliken atomic charge on the sulphur atoms for the whole series of compounds. A least-squares fit of the data to a straight line gave a correlation coefficient of 0.930. This approximately linear fit express simultaneously the general environmental dependence of core electron binding energies[34], the 'chemical shift' effect[35] and the more subtle factors that are missing from the simple, linear relationship and must be taken into account for quantitative accuracy[36].

The most straightforward comparison among these sulphur compounds involves the purely structural aspect, where the variation in geometric parameters is compared across function type SO_n, $n = 0$, 1 or 2. A number of reviews and papers have addressed these trends[18,28,29,37]. In these analyses we will only use the data on the neutral, non-radical molecules. The first question that can be asked is: how do the S=O and S—O(H) or S—O(Y) bond lengths vary as a function of the other substituents (absence, presence and type) in the series. For the S—O(H) and S—$O(CH_3)$ bond distances taken together in XSO_nOY compounds the average S—O bond length of 13 members having $n = 0$ is 1.651 Å, 22 bonds with $n = 1$ average to 1.614 Å and 12 distinct bond lengths in $n = 2$ systems have a 1.577 Å average. The trend is therefore definitely for a shorter S—O bond length with increased oxidation or coordination state of the central sulphur atom. It should, however, be recalled that the S—O bond length is also a function of the other substituents on sulphur (X) within a given structure type. As has been pointed out previously[2], the equilibrium S—O distance roughly decreases with increased electronegativity of X. Thus FSOH (2.9) for example, although belonging to the $n = 0$ category, has a S—O bond length of 1.612 Å, which statistically belongs to the $n = 1$ structure-type category. Intramolecular interactions can also affect bond distances, as, for example, to elongate the O—H bond in the $n = 1$ and $n = 2$ acid systems. Therefore, the trends described above for S—O, and for all the other geometric parameters analyzed

here, are true only in an average or statistical sense. Exceptions to the category values can be found for cases that are at the boundaries of the parameter ranges, because they involve an extreme substituent type or because of special intramolecular interactions.

The S=O bond length is also found to shorten with n increasing from 1 (XS(O)Y) to 2 (XSO_2Y). The average of 21 S=O distances in XS(O)OY (Y = H and CH_3) is 1.446 Å. Likewise, for XSO_2OY 24 distinct S=O bond lengths have an average 1.417 Å value. If the more general generic types XS(O)Y and XSO_2Y from the appropriate tables and previous work[1,2] are included in the statistical analysis, then 32 XS(O)Y compounds give a somewhat larger average S=O distance of 1.454 Å and 50 distinct S=O bonds in XSO_2Y compounds have a longer average 1.421 Å bond length. We see from this increase in average S=O bond length in each category that the acid and methoxy sulphur compounds usually have somewhat shorter S=O bonds than the other, general substituents in this study. However, the difference between XS(O)Y and XSO_2Y compounds is maintained at about −0.03 Å on the average. In addition, the average difference between S—O and S=O is about 0.16 Å, in both the XS(O)Y and XSO_2Y systems.

The other two bond lengths involved in the SOH and $SOCH_3$ functional groups are O—H and O—C. The average of 9 XS(O)Y compounds O—H bonds is 0.951 Å, of 18 sulphines is 0.956 Å and of 10 XSO_2Y compounds is 0.955 Å. It is reasonable to attribute the uniformly longer O—H bond distance in S=O containing compounds, at least partially, to internal hydrogen bonding with the semi-polar O(=S) atom. This interaction has been noted in a number of cases[2,38] and is supported by the differential S=O bond lengths in the sulphonic acids. Interestingly, the maximum deviation from the respective O—H bond-lengths averages is only 0.002 Å for each distinct value of n in $XS(O_n)OH$. Thus, the degree of internal hydrogen bonding in the sulphinic and sulphonic acids is nearly independent of the X substituent.

The O—C bond distance in the $XS(O_n)OCH_3$ compounds increases by about 0.01 Å for every unit increase in n. Indications of intramolecular (S=)O···H(—C) hydrogen bonding have also been found in the XS(O)Y and XSO_2Y systems[1,2] but it is not clear that they cause these computed variations in the O—C bond length in the methoxy compounds. Hydrogen-bonding effects involving the methyl effect in XS(O)Y and XSO_2Y systems will be discussed in the next Section.

The calculated behaviour of the other bond distances (X—S) in the generic $XS(O_n)Z$ compounds, where Z is any singly-bonded atom subtituent, as a function of n can be summarized as follows. In all available cases (X = H, C, N, F, S, Cl) the X—S bond length decreases from $n = 1$ to $n = 2$. For example, for the S—C bond eleven $n = 0$ members give an average 1.799 Å distance, nine $n = 1$ bonds have an average 1.792 Å length and twelve $n = 2$ contributors average to 1.767 Å. Along with carbon, both fluorine, oxygen (in OH, from above) and nitrogen (in NH_2) also show a modest decrease in their respective equilibrium bond distances with sulphur in going from $n = 0$ to $n = 1$. However, S—H, S—S and S—Cl increase their bond lengths in going from XS(O)Y and XSO_2Y systems. Here we must caution that the number of contributing bonds to these last averages is small (3–6 each) for N, F, S and Cl bonded to the central sulphur atom. Recall also that the S—X bond distance is typically a function of the electronegativity of Z within each class. Nonetheless, although presented without explanation or interpretation, the fact that the bond lengths of S with first-row atoms behave differently from sulphur- Z (= second-row atom) distances in a consistent fashion is not intrinsically unreasonable. The S—H bond, which also behaves differently from the first-row atoms, has 10 members with $n = 0$ and an average of 1.327 Å distance, 13 cases with $n = 1$ giving a 1.340 Å average and 10 bonds for $n = 2$ averaging to 1.324 Å. All these trends can usually be followed not only statistically, but also for specific X, Y substituents in XSO_nY as n varies through 0, 1 and 2. Some of these trends in bond-length changes with increased oxygen content have also been noted by Hargittai[37] in his analysis of experimentally determined

geometric structures. The decrease in N—S bond length with n in XSO_nNH_2 compounds has been interpreted as due to increased $N \rightarrow S$ π bonding when sulphur becomes more electropositive as the value of n increases[39].

Another property whose behaviour can be traced as a function of n is the atomic charge, obtained here by the Mulliken population analysis and the d orbital population on the central sulphur atom. A word of caution needs to be injected here again about populations. The charge on an atom in a molecule is not a quantum mechanical observable and its definition is therefore arbitrary. Some definitions are probably better than others in terms of serving the needs of such a definition. All methods require a partitioning of either real space or wave function (Hilbert) space into atomic regions. Partitioning the physical space-may be the least arbitrary but it is complicated and time consuming. In addition, the physical boundaries are not always automatically obtained and their interpretation is not always unambiguous.

The Mulliken population analysis has the advantage of simplicity, long usage and wide experience, and the absence of any other method that has also no flaws or failures. Its known defects include a basis set dependence and a tendency to give poor results (when compared to chemical experience and intuition) with an extended basis set, especially with diffuse basis functions. The 6-31G* basis set used for the population analysis Tables here for the neutral (parent and radical) species has no diffuse basis orbitals. A comparison of q(X), the atomic charge on atom X, and d(S), the d orbital population on sulphur, in the same valence basis set for similar classes of molecules should give useful information. However, caution should be exercised in drawing unambiguous conclusions that are unsupported by other evidence. The values for q(X) and d(S) for the anions in the 6-31+G* basis set are even more susceptible to uncertainties in interpretation.

The clearest and most outstanding feature of the calculated values of q(S) and d(S) is their joint uniform increase with n in XSO_nY. Even though there is a range of q(S) values for a given n due to q(S) increasing with increased electronegativity of X or Y, there is no overlap in q(S) values (in units of positive charge = e) between XSY type compounds (average of 26 values = 0.315e), XS(O)Y type compounds (average of 31 values = +1.135e) and XSO_2Y type compounds (average of 26 values = +1.582e) in this database (Tables 3, 13, 17, 27 and References 1–2). This is true even for those molecules that contain both divalent and tetravalent sulphur atoms in S—S bonds. An analogous statement can be made about d(S) whose ranges (averages) are 0.07–0.16 (0.114) for $n = 0$, 0.28–0.42 (0.350) for $n = 1$ and 0.60–0.75 (0.665) for $n = 2$ using the 6-31G* basis set. The calculated trends are completely general. Both in their behaviour within a given structure type (specific n) and as n varies, q(S) and d(S) move together. Thus, d orbitals on the central sulphur atom are of increased importance as valence atomic electron density is removed by electronegative substituents, or the oxidation state and coordination number increase. The 3d atomic subshell is, presumably, stabilized by the higher atomic charge. It can then serve simultaneously to provide greater spatial flexibility as a polarizing function and as an empty valence orbital for back-bonding electron transfer to S[1,2]. The calculated behaviour of q(S) as a function of substituent is shown in Figure 39. This is a very expanded version of Figures presented by Hargittai[28].

The general decrease in S=O, S—X and S—Y bond lengths in XSO_nY as n and as the electronegativity of X or Y increase could be attributed to a valence shell contraction effect due to the increased atomic charge q(S); although, as noted, the more diffuse d(S) increases correspondingly.

As expected, both types of oxygen atom, O(=S) and O(—S), have their atomic charges reduced (in absolute value) in going from $n = 1$ to $n = 2$ in XSO_nY by 0.07e and 0.08e, on the average, respectively. This seems to be the general trend also for N, F, S and Cl attached to the central sulphur atom and is predicted on the basis of simple electrostatics. The addition of an electron-withdrawing oxygen atom to the central

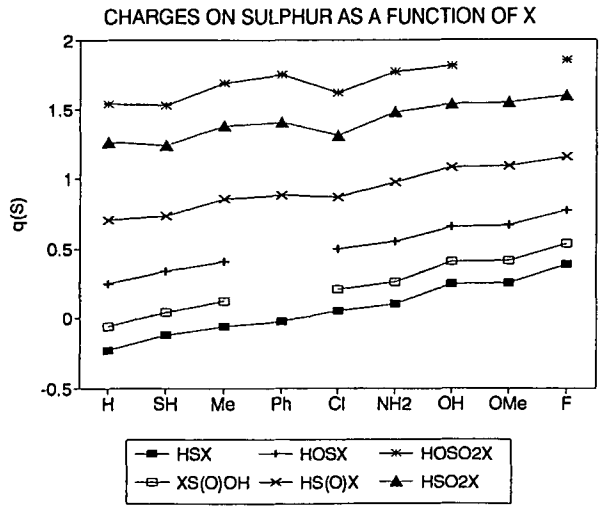


FIGURE 39. Charges on S as a function of substituent X

sulphur atom in XS(O)Y to give an additional semi-polar S=O bond is expected to draw charge from all the other atoms. However, O(—S) becomes more negative in going from $n = 0$ (14 examples with an average charge of -0.722) to $n = 1$ (21 cases with an average q of -0.802). Again, N, F, S and Cl, although with many fewer examples, seem to follow this same trend. Thus, the XSY compounds are generally more ionic than the XS(O)Y compounds in all their S—Z (Z = O, X, Y) bonds (except, perhaps, for Z = Hydrogen). The additional electron density comes from the sulphur atom whose atomic charge jumps by an average of 0.82e from $n = 0$ to $n = 1$, of which an average of only 0.74e go into the new O(=S) atom and the rest divides among the other atoms bonded to sulphur. In contrast, q(S) increases, on the average, by only 0.45e from XS(O)Y to XSO_2Y.

The H(—O) atom in $XS(O_n)OH$ has maximum q(H) for $n = 2$, making the sulphonic acids the best proton donors. This is well known-experimentally[39]. We can compare the calculated deprotonation energies for the $XS(O)_nOH$ systems as a function of n (= 0, 1, 2) to determine quantitatively the relative acidities of the different classes of sulphur compounds. Using the MP2/6-31 + G* energies from the appropriate parent neutral and anion tables, the XSY compounds ($n = 0$), with X = F, Cl, NH_2, SH, CH_3, H and CH_3O, have an average calculated proton affinity of 350.1 kcal mol^{-1}. The XS(O)Y compounds ($n = 1$), with X = F, Cl, NH_2, SH, CH_3, H and OH, average to 321.3 kcal mol^{-1} and the XSO_2Y compounds ($n = 2$), including X = F, Cl, NH_2, SH, CH_3, H and OH, have an average proton affinity of 307.9 kcal mol^{-1}. As with all the electronic energy differences between molecular species quoted here, it is necessary to add other small thermodynamic terms (like vibrational, rotational, translational, etc.) to compare these numbers to experimental results[1-3,6]. These correction terms, however, are small (of the order of several kcal mol^{-1}, at most) and tend to reduce the calculated number accordingly.

From the average O—H deprotonation energies calculated for the XSY, XS(O)Y and XSO_2Y systems, the lowest value is for the sulphonic acids, as determined experimentally[30]. Within each of the three classes the order of heteronuclear ionization approximately follows the electron-withdrawing properties of X, as expected based on simple arguments. The more electronegative the substituent, the more ionic the O—H bond, the smaller the deprotonation energy.

The correlation can also be examined for the calculated homonuclear dissociation of the hydrogen atom from the different acid groups (O—H). For $n=0$, the average dissociation energy is 65.8 kcal mol^{-1}, for the XS(O)Y ($n=1$) it is 81.4 kcal mol^{-1} and for $n=2$ the average homonuclear binding energy is 113.4 kcal mol^{-1}. This trend (with n value) is exactly the opposite of that found for the proton dissociation energies, and the sulphonic acids have the smallest proton affinities and highest hydrogen-binding energies (absolute values). The reason for this complementary opposite behaviour is that the more ionic the character of the O—H bond, the easier will its ionic (heterolytic) splitting be, but the more ready will be the covalent (homolytic) splitting. The behaviour of the hydrogen atom dissociation energy with the character of X for a given group (n value) in $XS(O_n)OH$ is not as simple as for deprotonation and the calculated values have different orderings for $n=0$ compared to $n=1$ and $n=2$. In these latter two cases, the (homolytic) hydrogen atom binding energy increases with the electronegativity of X, as expected from the increased ionic character of the O—H bond. For $n=0$ (XSY), however, both hydrogen atom and proton dissociation energies are calculated to approximately decrease with the increasing electron-withdrawing property of X.

In Section 3 we compared the homolytic and heterolytic dissociations of H from XS(O)O—H and XSO_2—H to form the same respective $XSO_2\cdot$ radicals and XSO_2^- anions. We can extend these comparisons in parallel with the XS(O)OH and XSO_2OH relative O—H dissociation properties, to the analogous XS(O)H and XSO_2H systems with respect to breaking the S—H bond. Comparing the seven (X) substituents in the XSO_2Y system with eight (X = F, Cl, NH_2, SH, CH_3, H, OH and OCH_3) XS(O)Y type compounds, the average S—H deprotonation energy is 28.6 kcal mol^{-1} lower in the XSO_2Y system. This is almost exactly the same average difference (28.8 kcal mol^{-1}) as for the relative O—H deprotonation from the corresponding acids XS(O)OH and XSOH. Here, also, the proton dissociation energy for S—H parallels the electronegativity of X in both the XSO_2Y and XS(O)Y systems. The homolytic dissociation of a hydrogen atom from the central sulphur shows the expected complementary behaviour to the heterolytic dissociation and is also, on the average, 15.8 kcal mol^{-1} lower (but) in XS(O)H relative to XSO_2H. Each S—H dissociation in XS(O)H and XSO_2H, of course, is smaller than the corresponding O—H (homolytic) binding energy in XS(O)OH and XSO_2OH. Again, for the $XSO_2H \rightarrow XSO_2\cdot + H\cdot$ process the energy dependence on X is opposite to that for $XSO_2H \rightarrow XSO_2^- + H^+$, while both $XS(O)H \rightarrow XSO\cdot + H\cdot$ and $XS(O)H \rightarrow XSO^-$ and H^+ have the same energy dependence on the character of the substituent X.

The relative hydrogen atom and proton dissociation energies for S—H from XS(O)H and O—H from the isoelectronic XSOH, respectively, have the same properties already described in Section 3 for these same processes with respect to XSO_2H and XS(O)OH. The consistently smaller binding energies calculated for S—H dissociation relative to O—H from different precursor types, when both processes give the same products, means that the acid form is always intrinsically more stable when comparing isoelectronic systems. Thus, directly comparing the energies of XS(O)H (Table 11) with those of XSOH (Table 1) for a given X substituent shows the latter to be consistently more stable and, not surprisingly, to have the lower dipole moment. Similarly, comparing isoelectronic XS(O)OH (Table 11) to XSO_2H (Reference 2), for the lowest-energy conformer in each case, shows the former to have the respective lower energies and smaller dipole moments for a given X. These are general trends for comparing isomeric XSO_nY to $XSO_{n-1}OY$, where the systems with the fewer number of S=O bonds are intrinsically more stable. This has been noted also for the anions[25-27]. It should also be noted that because the higher-energy isomer has the larger dipole moment, these calculated stability orders could be affected by interaction with solvent which could preferentially stabilize the larger dipole moment isomer. We will return to this latter point in the next Section.

VII. DIMERS, WATER COMPLEXES AND HYDROGEN BONDING

The hydrogen bond (H-bond) takes many forms, involves a variety of atoms (A—H···B) and spans a modestly wide range of chemical energies (2-37 kcal mol^{-1})[40-43]. As a flexible type of chemical bond occurring in a variety of molecular and metal complexes, with a pervasive presence in biochemical systems and a dominating influence on their activity, the H-bond is attracting increased specific attention both experimentally and theoretically.

The classical H-bond situation usually involves the oxygen or nitrogen atoms as the donor(A) and acceptor(B). Recent attention has been focused on the involvement of the C—H group in hydrogen bonding situations. These observed or inferred interactions usually involve the more acidic alkyne C—H bond[44-47], although the association of the less acidic alkenes (> C—H) with strong bases have also been reported[48-49]. Such an *intra*molecular H-bond interaction has also been proposed to exist for a vinyl sulphone (> C—H···O=S) in the gas phase from an electron diffraction study[50]. This type of association reflects the relatively strong ionicity of the S=O group which is now well recognized[1,2,38,51].

The general hydrogen bonding properties of the sulphoxide (> S=O) and sulphone (> SO_2) groups have recently been reviewed[38,39,51], highlighting the influence of the A—H···O=S interaction on *intra*molecular conformation and *inter*molecular association in solutions, particularly those involving phenol. The structures of cyclical 1:1 hydrogen bonded complexes formed by sulphinic acids with water and methanol have been studied by *ab initio* theoretical methods.[1] Here, as expected, the O—H···O=S interaction is prominent. However, evidence of *intra*molecular (methyl)C—H···O=S hydrogen bonding has also been noted in *ab initio* structure study of a series of methyl-substituted sulphones[2]. Intermolecular association involving the methyl C—H bond with the S=O group in dimers and its influence on the chemical and physical properties of liquid methylsulphonyl compounds has been emphasized by Robinson[52,53].

In general, the bulk properties of certain sulphones and especially sulphoxides have been interpreted as indicating a degree of mutual association in the liquid phase and in aprotic solution[38,52,53]. Two types of *inter*molecular interactions have been proposed in explanation of these observations: the S=O···S=O association[38] and, as mentioned above, C—H···O=S bonding[52,53]. Both type structures can also take on cyclic forms with double or multiple interactions. With regard to the former type of non-bonded structure, *intra*molecular S···O interactions based on the spatial proximity of the sulphur and oxygen atoms in molecules have been noted in a wide variety of sulphur compounds, including sulphones and sulphoxides[54,55]. Thus, both the S···O=S···O and (methyl)C—H···O=S type interactions have been identified or proposed in both *intra* and *inter*molecular situations.

The nature of the experimental evidence offered in support of these proposed interactions divides into the molecular and the bulk-type properties. On the molecular level unusually short interatomic distances between formally non-bonded atoms, eclipsed dihedral alignment of bonds as the preferred conformation, and shifts in the characteristic frequency of the affected bond(s) as well as changes in their bond length(s), are taken as indicative of an operative interaction. On the bulk property level, boiling points that are either high compared to similar systems where substitution (fluorine for methyl, for example) precludes such non-bonded interactions, or are comparable to obviously hydrogen bonded systems (hydroxyl in place of methyl, for example) are offered as evidence of an associative interaction. However, although experimentally determined molecular structure may be used to infer the existence of both types of *intra*molecular interactions[31,37,38,51,54,55], there seems to be no direct structural evidence on the molecular level for the *inter*molecular cases.

We have therefore extended our previous *ab initio* computational studies of sulphinic and sulphonic acid derivatives[1,2], which included structural evidence of the

*intra*molecular (methyl)C—H···O=S interactions, to include both the *inter*molecular hydrogen bonded and the interacting S=O type dimer associations. For comparison purposes, the corresponding (sulphone and sulphoxide) monomer–water (1:1) complexes have also been determined, as well as a number of analogous carbonyl–water and dimer carbonyl structures. The importance of electron correlation from a higher level theory on the calculated water complex and dimer binding energies has also been examined. Finally, in all cases, the effect of basis set superposition error (BSSE)[56,57] on the calculated binding energies has been taken into account quantitatively. A preliminary report of some of these results has been given elsewhere[32].

All calculations were carried out using the GAUSSIAN set of computer programs[15,16]. Geometry optimization at the RHF self-consistent field (SCF) level was carried out using the standard 6-31G* basis set (with 5 d-type atomic orbitals) for all atoms. This was followed by a MP2[6] single point calculation at each RHF optimized geometry. BSSE was taken into account in the usual fashion of calculating the dimer and water complex binding energies using reference monomer and water energies obtained in the full dimer and water complex basis set, respectively, including the basis functions on the 'ghost' atoms. The possible effect on BSSE of changes in the monomer and water geometries from the isolated molecule to the *in situ* dimers and complexes (extra polarization effects) was also taken into account. Each calculated (RHF and MP2) dimer or water complex binding energy was adjusted by the difference in the calculated water and monomer energies of the asymptotic and full complex or dimer basis sets, at the optimum complex or dimer geometry, respectively. This correction is assumed to somewhat over-estimate the true BSSE but takes into account BSS in the actual bonded monomer and water complex geometries[57,58]. Both the RHF and MP2 binding energies are reported here, both before and after BSSE correction.

Generally, no attempt was made to test these minimum energy (zero energy gradient) structures for stability by examining the curvature of the second derivative energy matrix (vibrational frequencies). Therefore, it may be that, especially where there is more than one geometry for a given dimer or water complex combination, one or more structures could be a transition state rather than a stable equilibrium structure. Since the purpose of this computational survey was to obtain qualitative information on the (possible hydrogen bonding interactions and geometries in these systems, the extra effort of systematically testing each stationary state structure was not deemed worthwhile. Also, although possibly giving some idea of dimer association in the neat liquid or water–monomer complexation in solution, the 1:1 interaction model may not be a completely realistic representation of three-dimensional bulk matter with multiple simultaneous interactions in all directions.

It is also possible that there are other minimum energy structures for the given dimer and water complex types than those presented here. The potential surface is very flat and the possibility of other local minima cannot be ruled out. A number of initial relative monomer–monomer and monomer–water orientations and conformations were explored that led to many of the structures presented here. Experience gained with the obtained structures suggested new initial relative orientations for analogous systems which were tried, some of which gave new structures while others either dissociated or rearranged to give previously obtained geometries. Although the set presented here cannot claim to be exhaustive, given the wide geometric explorations, there is a high probability that it contains the lowest-energy cyclic structure for a given dimer and water complexes type.

Weak hydrogen bonded systems need a large basis set and relatively high level of theory for a quantitatively accurate description of the geometry and binding energy. Correlation (from post-HF methods like MP2) shortens the hydrogen bond distance and increases the binding energy. Improving the basis set at the RHF level usually lengthens the hydrogen bond distance and decreases the binding energies due to reduced

TABLE 28. RHF and MP2 total energies[a] and binding[b] energies of dimers

Monomer	Energies (a.u.)		RHF Dipole moment[b]	Binding energy (kcal mol^{-1})			
						After BSSE[b,c]	
	RHF	MP2[b]		RHF[b]	MP2[b]	RHF	MP2
104 HS(O)H I	−946.883013	−947.492214	8.806	7.3	7.8	6.0	5.5
105 HS(O)H II	−946.875509	−947.485867	0.003	2.5	3.8	0.9	1.0
106 HS(O)H III	−946.887451	−947.497811	0.430	10.0	11.3	7.4	10.8
107 $CH_3S(O)H$ I	−1024.987804	−1025.863141	1.494	16.6	19.4	13.4	14.0
108 $CH_3S(O)H$ II	−1024.987205	−1025.861651	1.924	16.2	18.5	13.1	13.8
109 $CH_3S(O)H$ III	−1024.985284	−1025.858723	0.019	15.0	16.7	12.9	12.8
110 $CH_3S(O)H$ IV	−1024.986531	−1025.862033	0.017	15.8	18.7	12.9	13.4
111 $CH_3S(O)CH_3$ I	−1103.082286	−1104.222871	0.300	8.2	11.1	5.7	6.4
112 $CH_3S(O)CH_3$ II	−1103.078219	−1104.216708	9.590	5.6	7.2	4.3	4.7
113 $CH_3S(O)CH_3$ III	−1103.086658	−1104.229428	0.012	10.9	15.2	7.3	8.6
114 $CH_3S(O)F$	−1222.724162	−1223.953670	3.163	7.4	9.0	5.2	5.1
115 HSO_2H	−1096.568658	−1097.546821	3.897	9.6	10.5	7.7	7.2
116 CH_3SO_2H I	−1174.680352	−1175.922202	0.284	6.9	8.8	5.5	5.9
117 CH_3SO_2H II	−1174.684559	−1175.926277	3.415	9.5	11.3	7.6	7.6
118 CH_3SO_2H III	−1174.684494	−1175.926405	4.652	9.5	11.4	5.0	5.1
119 $CH_3SO_2CH_3$	−1252.791240	−1254.298495	6.001	8.9	11.9	7.2	8.3
120 CH_3SO_2F	−1372.436420	−1374.026498	0.078	6.9	8.9	5.6	6.1
121 H_2S	−797.332918	−797.573087	1.693	0.9	1.4	0.8	1.2
122 HSOH	−946.983568	−947.580947	3.012	5.9	7.8	4.7	5.7
123 HC(O)H I	−227.736968	−228.329195	0.002	3.5	4.5	2.1	2.2
124 HC(O)H II	−227.735247	−228.326060	2.278	2.4	2.6	1.8	1.7
125 $CH_3C(O)H$ I	−305.836248	−306.685749	2.193	3.7	5.0	2.4	2.8
126 $CH_3C(O)H$ II	−305.836700	−306.686251	1.438	4.0	5.3	2.6	3.1
127 $CH_3C(O)CH_3$	−383.929797	−385.040366	0.028	4.6	7.0	2.7	4.2

[a]Geometries RHF/6-31G* optimized with no symmetry or equivalence constraints.
[b]In the RHF/6-31G* optimized geometry.
[c]See text.

TABLE 29. Calculated bond lengths (Å) for dimers[a]

Monomer	C—H···O=S	S—H···O=S	S=O		C—H		S—H	
			H-bonded	other	H-bonded	other	H-bonded	other
104 HS(O)H I	—	2.548 2.577	1.486	1.484	—	—	1.338[b]	1.340 1.341
105 HS(O)H II	—	—	—	1.483 1.482	—	—	—	1.345
106 HS(O)H III	—	2.205 2.543	1.492 1.494	—	—	—	1.333 1.334	1.341 1.343
107 $CH_3S(O)H$ I	2.393 2.551	2.477	1.493 1.494	—	1.080[b]	1.083[c]	1.333	1.341
108 $CH_3S(O)H$ II	2.507	2.468 2.528	1.494[b]	—	1.080	1.083[c]	1.331 1.333	— 1.341
109 $CH_3S(O)H$ III	—	2.455 2.443	1.497[b]	—	—	1.083[c]	1.331	—
110 $CH_3S(O)H$ IV	2.415 2.420	—	1.493[b]	—	1.079[b]	1.083[c]	—	1.341[b]
111 $CH_3S(O)H$ I	2.387 2.374	—	1.495[b]	—	1.080[b]	1.083[c]	—	—
112 $CH_3S(O)H$ II	2.453 2.548	—	1.492	1.490	1.081	1.082	—	—
113 $CH_3S(O)CH_3$ III	2.455[b] 2.477 2.449	—	1.497[b]	—	1.082[b]	1.083[c]	—	—
114 $CH_3S(O)F$	2.341 2.523	—	1.450 1.452	—	1.081[b]	1.082[c]	—	—

115 HSO_2H	—	2.348 2.576 2.664	1.437 1.435	1.426 1.427	—	—	1.322 1.323 1.324	1.327
116 CH_3SO_2H I	2.352 2.362	—	1.437	1.432	1.082	1.082[c]	—	1.330
117 CH_3SO_2H II	2.620	2.600	1.442	1.432	1.080	1.083[c]	1.325	—
118 CH_3SO_2H III	—	2.398 2.486	1.441 1.440	1.434[b]	—	1.082[c]	1.323 1.324	—
119 $CH_3SO_2CH_3$	2.476 2.310 2.478	—	1.441[b]	1.439	1.082[b]	1.082[c]	—	—
120 CH_3SO_2F	2.427[b]	—	1.419[b]	1.413[b]	1.080	1.080[c]	—	—
121 H_2S	—	—	—	—	—	—	1.326	1.326
122 HSOH[f]	—	—	—	—	—	—	—	3.327 1.329
123 HC(O)H I	—	2.576[b,d]	1.188[b,e]	—	—	—	1.087[b,g]	1.092[g]
124 HC(O)H II	—	3.025[b,d]	1.186[b,e]	—	—	—	1.090[g] 1.091[g]	1.090[g]
125 $CH_3C(O)H$ I	2.702[d] 2.844[d]	—	1.191[b,e]	—	1.081 1.085	1.082 1.087	1.092[g]	1.095[g]
126 $CH_3C(O)H$ II	2.884[d]	2.650[d]	1.191[b] 1.192	—	1.085 1.087	1.082	1.091[g]	1.093[g]
127 $CH_3C(O)CH_3$	2.908[d] 2.946[d] 2.970[d] 2.981[d]	—	1.196[b,e]	—	1.086	1.085 1.082	—	—

[a] From the RHF/6-31G* basis optimized geometries.
[b] Two equivalent bonds to the accuracy of the table.
[c] Average value.
[d] O=C—H···O=C.
[e] —H···O=C.
[f] O—H···O—S 1.976 Å; S—O 1.648 Å.
[g] C—H bond lengths.

TABLE 30. Mulliken atomic charges in dimers[a]

Monomer	S	C	O	H(—S) bonded	H(—S) other	H(—C) bonded	H(—C) other
104 HS(O)H I	0.707	—	−0.797[b]	0.057	0.052	—	—
				0.555	0.054		
105 HS(O)H II	0.736[b]	—	−0.785[b]	—	0.245	—	—
106 HS(O)H III	0.716	—	−0.827	0.127	0.024	—	—
	0.655	—	−0.819	0.081	0.040	—	—
107 $CH_3S(O)H$ I	0.825[b]	−0.738	−0.833[b]	0.083	0.018	0.263	0.193–0.210
		−0.747				0.281	
108 $CH_3S(O)H$ II	0.829	−0.741	−0.837	0.081[b]	—	0.266	0.191–0.220
	0.854	−0.734					
109 $CH_3S(O)H$ III	0.845[b]	−0.732[b]	−0.835[b]	0.087[b]	—	—	0.194–0.224
110 $CH_3S(O)H$ IV	0.869[b]	−0.746[b]	−0.826[b]	—	0.019[b]	0.280[b]	0.188–0.215
111 $CH_3S(O)CH_3$ I	1.028[b]	−0.749[b]	−0.848[b]	—	—	0.288[b]	0.184–0.211
		−0.726[b]					
112 $CH_3S(O)CH_3$ II	0.990	−0.745[b]	−0.827[b]	—	—	0.244	0.204–0.229
	1.009	−0.729[b]				0.240	
113 $CH_3S(O)CH_3$ III	0.998[b]	−0.757[b]	−0.843[b]	—	—	0.278	0.190–0.231
		−0.757[b]					
114 $CH_3S(O)F$[g]	1.304	−0.788	−0.755[b]	—	—	0.309	0.213–0.230
	1.310	−0.765				0.255	
115 HSO_2H	1.252	—	−0.737[b]	0.107	0.048	—	—
			−0.670[b]	0.070			
116 CH_3SO_2H I	1.392[b]	−0.781[b]	−0.720[b,d]	—	0.035[b]	0.312	0.223–0.229
			−0.690[b]				

117 CH_3SO_2H II	1.408[b]	−0.770[b]	−0.692[b] −0.752[b,d]	0.071[b]	—	0.259[b]	0.232–0.241
118 CH_3SO_2H III	1.392[b]	−0.752[b]	−0.686[b] −0.688[b]	0.032[b]	—	0.253[b]	0.224–0.225
119 $CH_3SO_2CH_3$	1.555[b]	−0.779[b] −0.784 −0.751	−0.715 −0.749 −0.732[b]	—	—	0.317 0.277[b]	0.214–0.248
120 CH_3SO_2F[i]	1.754[b]	−0.790[b]	−0.676[b,d] −0.637[b]	—	—	0.296[b]	0.245–0.248
121 H_2S	−0.247 −0.236	—	—	0.132 0.119	0.110	—	—
122 HSOH[f]	0.217[b]	—	−0.850 −0.845	—	0.076 0.090	—	—
123 HC(O)H I	0.132[b,e]	—	−0.458[b]	—	—	0.142[b,h]	0.184[b,h]
124 HC(O)H II	0.156[b,e]	—	−0.452[b]	—	—	—	0.151–0.145[h]
125 $CH_3C(O)H$ I	0.374[b,e]	−0.610 −0.621	−0.510 −0.503	—	—	0.218 0.246	0.182–0.201 0.144[h]
126 $CH_3C(O)H$ II	0.340[e] 0.380[e]	−0.603 −0.608	−0.511 −0.517	—	—	0.216 0.178[h]	0.181–0.209 0.142[h]
127 $CH_3C(O)CH_3$	0.560[b,e]	−0.602[b] −0.600[b]	−0.558[b]	—	—	0.218[b] 0.221[b]	0.179–0.202

[a] From RHF/6-31G* basis optimized wave functions.
[b] Two equal values.
[c] Averaged.
[d] Hydrogen bonded.
[e] C(=O).
[f] H(—O) bonded = 0.540 other 0.500.
[g] $q(x) = -0.487; -0.496$.
[h] H(—C=O).
[i] $q(F) = -0.441; -0.440$.

TABLE 31. RHF and MP2 and binding energies[a] of water complexes[a]

Monomer	Energies (a.u.) RHF	Energies (a.u.) MP2[b]	RHF dipole moment[b]	Binding energy[c] (kcal mol^{-1}) RHF[b]	Binding energy[c] (kcal mol^{-1}) MP2[b]	After BSSE[b,c] RHF	After BSSE[b,c] MP2
128 HS(O)H	−549.458610	−549.949013	2.671	8.5	10.0	6.6	6.8
129 $CH_3S(O)H$	−588.510345	−589.133065	2.914	12.7	15.0	10.6	11.2
130 $CH_3S(O)CH_3$ I	−627.549827	−628.303568	5.987	3.7	5.0	2.6	3.1
131 $CH_3S(O)CH_3$ II	−627.557669	−628.312371	4.637	8.6	10.5	6.6	6.9
132 HS(O)OH	−624.334727	−625.008114	1.212	13.5	16.6	10.8	12.0
133 $CH_3S(O)OH$	−663.386443	−664.192484	3.591	12.7	15.9	9.7	10.8
134 $CH_3S(O)OCH_3$	−702.403845	−703.335562	2.272	7.1	8.5	5.3	5.2
135 HSO_2H	−624.298806	−624.972308	4.956	8.0	8.9	6.6	6.5
136 CH_3SO_2H	−663.356305	−664.162002	4.187	7.7	9.3	6.1	6.4
137 $CH_3SO_2CH_3$	−702.410471	−703.349686	5.379	7.9	10.6	5.2	5.7
138 CH_3SO_2F I	−762.232497	−763.212617	2.786	6.6	8.4	4.9	5.3
139 CH_3SO_2F II	−762.233640	−763.214106	2.428	7.3	9.3	4.9	5.2
140 H_2O	−152.027884	−152.397456	3.104	5.8	7.1	4.7	5.2
141 H_2S	−474.678977	−474.984003	0.875	2.4	3.5	1.3	1.5
142 HSOH	−549.992687	−549.992687	3.503	7.5	9.7	6.1	7.2
143 HOSOH	−624.356622	−625.025326	1.976	9.2	12.6	6.6	8.1
144 CH_3SOH	−588.548676	−589.165437	3.148	7.3	9.6	5.8	7.0
145 CH_3SOCH_3	−627.572737	−628.317280	2.118	6.0	8.6	3.9	4.9
146 CH_3OSOH	−663.383485	−664.179791	2.081	9.2	12.8	6.5	8.0
147 HC(O)H	−189.883582	−190.364895	2.295	5.4	6.8	3.7	4.0
148 $CH_3C(O)H$	−228.934145	−229.544473	3.194	6.1	7.8	4.2	4.7
149 $CH_3C(O)CH_3$	−267.980763	−268.720774	3.793	5.7	8.2	3.9	5.0

[a]Geometries RHF/6-31G* optimized with no symmetry or equivalence constraints.
[b]In the RHF/6-31G* optimized geometry.
[c]See text.

BSSE in the more complete basis. The monomer geometries are not changed to significant degree by hydrogen bonding in the complex. Thus, RHF/6-31G* geometry optimization is expected to give hydrogen bond lengths that are too long, relative to exact theory or experiment, and underestimate the binding energy. A single point MP2/6-31G* calculation at the RHF geometry will still give too small a binding energy because the hydrogen bond distances are too long. Because the dissociation potential for the dimers and water complexes is relatively shallow, even around the energy minimum, large (several tenths Å) changes in the hydrogen bond length can amount to only tenths of kcal mol^{-1} difference in the binding energy. These are the uncertainties that are attached to the energies and geometries presented here[59,60]. We take it as given that the hydrogen bond distances are overestimated (by up to 0.1–0.2 Å for the longer-range interactions) at the RHF/6-31G* level.

Further, along these lines, for a given basis set size, MP2 is expected to give a larger binding energy than RHF. If the contrary is calculated at the RHF optimized geometry, then it could indicate a significant difference in equilibrium hydrogen bond distance predicted by those two levels of theory, and/or steep curvature at the energy minimum. The latter indicates a relatively strong hydrogen bond with a respectable binding energy. It should then be possible to use the relative binding energies calculated at the MP2 and RHF levels at the latter's optimized geometry, as well as the magnitude of the binding energy itself, as a criterion for assessing these two effects. An alternative explanation for a decreased hydrogen bonding energy at the MP2 level relative to RHF

TABLE 32. Calculated bond lengths for water complexes[a]

Monomer	Hw···O=S	Ow···H—C	Ow···H—S	(O—H)w bonded	(O—H)w other	S=O bonded	S=O other	C—H bonded	C—H other	S—H bonded	S—H other
128 HS(O)H	1.962	—	2.659	0.955	0.947	1.492	—	—	—	1.338	1.340
129 $CH_3S(O)H$	1.931	2.574	3.080	0.957	0.947	1.494	—	1.081	1.083[b]	1.338	—
130 $CH_3S(O)CH_3$ I	—	2.701[c]	—	—	0.948[c]	—	1.487	1.082[c]	1.083[b]	—	—
131 $CH_3S(O)CH_3$ II	1.967	2.657	—	0.956	0.947	1.497	—	1.081	1.083[b]	—	—
132 HS(O)OH	2.029	—	1.890[d]	0.957	0.948	1.470	—	—	—	—	1.340
133 $CH_3S(O)OH$	2.016	—	1.908[d]	0.957	0.947	1.474	—	—	1.083	—	—
134 $CH_3S(O)OCH_3$	2.044	2.614	—	0.953	0.947	1.473	—	1.082	1.082[c]	—	—
135 HSO_2H	2.442	—	2.613 2.612	0.950	0.947	1.432	1.429	—	—	1.324[c]	—
136 CH_3SO_2H	2.203	2.592	2.690	0.951	0.947	1.439	1.433	1.080	1.082[b]	1.326	—
137 $CH_3SO_2CH_3$	2.447 2.476	2.543	—	0.950[b]	—	1.441[c]	—	1.082	1.081[b]	—	—
138 CH_3SO_2F I	2.687 2.690	—	—	0.950[c]	—	1.416[c]	—	—	—	—	—
139 CH_3SO_2F II	2.224	2.397	—	0.951	0.948	1.419	1.413	1.080	1.081	—	—
140 H_2O	—	2.017	—	0.952 0.949[b]	0.947	—	—	—	—	—	—
141 H_2S	3.346[e]	—	2.875	0.948	0.948	—	—	—	—	—	—
142 HSOH	3.400[e]	—	1.918[d]	—	0.949[c]	—	—	—	—	—	1.329
143 HOSOH	2.936[e]	—	1.991[d]	0.952	0.949	—	—	—	—	—	—
144 CH_3SOH	3.340[e]	1.938	—	—	0.949[c]	—	—	—	1.083[b]	—	—
145 CH_3SOCH_3	2.049[f]	2.652	—	0.951	0.948	—	—	1.081	1.083[b]	—	—
146 CH_3OSOH	2.273[f]	—	2.002[d]	0.952	0.948	—	—	—	1.082[b]	—	—
147 HC(O)H	2.095[g]	—	—	0.951	0.947	1.189[h]	—	—	1.089[b]	—	—
148 $CH_3C(O)H$	2.068[g]	2.651	—	0.952	0.947	1.192[h]	—	1.081	1.087	—	—
149 $CH_3C(O)CH_3$	2.046[g]	2.663	—	0.952	0.947	1.197[h]	—	1.080	1.086	—	—

[a] From RHF/6-31G* optimized geometries.
[b] Average value.
[c] Two equivalent bonds within the accuracy of the table.
[d] Ow···H—O.
[e] Hw···S.
[f] Hw···O—S.
[g] Hw···O=C.
[h] C=O.

TABLE 33. Mulliken atomic charges in water complexes[a]

Molecule	S	C	O(—S) bonded	O(—S) other	H(—S) bonded	H(—S) other	H(—C) bonded	H(—C) other	H(—O) bonded	H(—O) other	X[h]	Ow
128 $HS(O)H$	0.677	—	0.805	—	0.091	0.058	—	—	0.506	0.444	—	−0.971
129 $CH_3S(O)H$	0.843	−0.748	−0.824	—	0.058	—	0.270	1.198–0.222	0.509	0.444	—	−0.973
130 $CH_3S(O)CH_3$ I	0.985	−0.739[b]	—	0.819	—	—	0.225	0.209–0.215	—	0.462[b]	—	−0.908
131 $CH_3S(O)CH_3$ II	1.013	−0.745 −0.724	−0.846	—	—	—	0.267	0.195 0.230	0.510	0.439	—	−0.967
132 $HS(O)OH$	1.089	—	−0.801	—	—	0.028	—	—	0.543[b] 0.508	0.465	−0.868	−0.963
133 $CH_3S(O)OH$	1.250	−0.742	−0.822	—	—	—	—	0.212–0.219	0.510 0.546[g]	0.462	−0.879	−0.969
134 $CH_3S(O)OCH_3$	1.276	−0.768 −0.195[f]	−0.832	—	—	—	0.262	0.165–0.219	0.502	0.445	−0.738	−0.956
135 HSO_2H	1.272	—	−0.722	−0.689	0.067 0.066	—	—	—	0.485	0.465	—	−0.942
136 CH_3SO_2H	1.405	−0.770 −0.753	−0.739	−0.695	0.655	—	0.263	0.226–0.243	0.490	0.458	—	−0.947
137 $CH_3SO_2CH_3$	1.549	−0.774	−0.734[b]	—	—	—	0.290	0.220–0.250	0.473[b]	—	—	−0.933
138 CH_3SO_2F I	1.750	−0.796	−0.676	−0.637	—	—	0.300	0.245[b]	0.489	0.455	−0.441	−0.935
139 CH_3SO_2F II	1.762	−0.791	−0.665[b]	—	—	—	—	0.244[b] 0.294	0.470[b]	—	−0.441	−0.920

140 H_2O	—	—	—	—	—	—	—	—	0.496	0.465[b] 0.437	—	−0.957
141 H_2S	−0.256	—	—	—	0.140	0.102	—	—	0.458	0.458	—	−0.902
142 HSOH	0.213	—	—	−0.858	—	0.074	—	—	0.473 0.544[g]	0.468	—	−0.913
143 HOSOH	0.646	—	—	−0.841	—	—	—	—	0.490 0.532	0.463 0.486[g]	—	−0.932
144 CH_3SOH	0.372	−0.659	—	−0.870	—	—	—	0.187–0.210	0.473 0.537[g]	0.467	—	−0.913
145 CH_3SOCH_3	0.407	−0.683 −0.144[f]	−0.740	—	—	—	0.246	0.162–0.197	0.501	0.444	—	−0.948
146 CH_3OSOH	0.656	−0.162[f]	−0.850	−0.735	—	—	—	0.173–0.187	0.490 0.530[g]	0.462	—	−0.934
147 HC(O)H	—	0.141[c]	−0.464[d]	—	—	—	0.180[e]	0.157[e]	0.488	0.444	—	−0.946
148 $CH_3C(O)H$	0.358[c]	−0.625	−0.511[d]	—	—	—	0.247	0.153[e] 0.193 0.198	0.494	0.441	—	−0.949
149 $CH_3C(O)CH_3$	0.555[c]	−0.615 −0.594	−0.557[d]	—	—	—	0.244	0.187 0.215	0.499	0.439	—	−0.953

[a]From RHF/6-31G* optimized geometries.
[b]Two equivalent values.
[c]C(=O).
[d]O(=C).
[e]H(—C=O).
[f]C(—O).
[g]H(O—S).
[h]X = O, F.

would be a calculated decrease in dipole moment and/or local bond ionicity, which should affect the electrostatic nature of the hydrogen bond. Although correlation does cause changes in this direction, they would have to be substantial to overcome the natural tendency of the electron correlation to improve the molecular bonding interaction. We will not explore these issues in this chapter any further.

The calculated binding energies at both the RHF/6-31G* and MP2/6-31G* levels for the RHF geometry optimized dimers are presented in Table 28, with and without BSSE correction. Since one of the objectives of this study was to compare S···O and S···H(methyl) *inter*molecular interactions, it should be noted that all the sulphur dimers in Table 28 except for HS(O)H II, **105**, Figure 41 are of the H-bonding type. All attempts to start with an initial dimer geometry which maximized *inter*molecular S···O interactions lead either to dissociation or rearranged to give a hydrogen bonded structure, except **105** which has the smallest calculated binding energy (MP2/6-31G* after BSSE correction) at 1.0 kcal mol^{-1}. Thus, the anti-parallel, double S···O interaction is found to be substantially weaker than the (S—)H···O(=S) and (C—)H···O(=S) association. It should be noted that the SO_2 dimer has been identified experimentally as not having the anti-parallel structure[61]. Electrostatic calculations of the Buckingham–Fowler type[62] predict the anti-parallel structure to have a binding energy of only 1.0 kcal mol^{-1}[61]. It should also be noted, however, that a recently analysed microwave structure of the acetylene-SO_2 complex in the gas phase[63] showed the dominant interaction to be between the sulphur atom and the π electrons of C_2H_2.

The RHF/6-31G* optimized dimer geometries involving sulphur are shown in Figures 40–57. The bond lengths are tabulated in Table 29 for comparison purposes and the Mulliken atomic charges are displayed in Table 30. The tables also include some carbonyl dimer property results which can, by contrast, be used to emphasize the special hydrogen bonding properties of the S=O bond. Analogously, the water complexes with XSY, XS(O)Y, XSO_2Y monomers are shown in Figures 58–78. The corresponding properties are tabulated in Tables 31–33, including, again, for comparison, some water–carbonyl complexes. Table 34 tabulates the interatomic distances between the heavy atoms involved in *inter*molecular hydrogen bonding, both in the dimers and in the monomer–water complexes. The H_2O and H_2S dimers and mixed complexes are included in the tables for completeness.

The generally outstanding features of the dimer structure are their multiple hydrogen bonded interactions involving both the (S—)H···O(=S) and (C—)H···O(=S) associations, where possible. The first question we can ask is whether the binding energy numbers in Table 28 indicate which of these two hydrogen bonds is intrinsically stronger. The best comparison here is within a given dimer composition where both types of bonds are possible, such as $CH_3S(O)H$ (**107–110**) and CH_3SO_2H (**116–118**). Thus comparing **109** with **110** (Table 28 and Figures 45 and 46) shows that the former structure with two (S—)H···O(=S) bonds has an MP2/6-31G* binding energy (after BSSE correction) of 12.8 kcal mol^{-1} while **110**, also with two (C—)H···S(=O) hydrogen bonds, has the higher binding energy of 13.4 kcal mol^{-1}. Analogously, for CH_3SO_2H, the hydrogen bond energy increases from 5.1 kcal mol^{-1} for two (S—)H···O(=S) bonds in structure **118** to 5.9 kcal mol^{-1} in structure **113**, with one of each type of association. The differences are not large but seem to show consistently that (C—)H···O(=S) is stronger than (S—)H···O(=S). The other two $CH_3S(O)H$ dimer structures, **107** and **108**, as well as **117** for the CH_3SO_2H dimer, involve multiple hydrogen bonding to given oxygen atom and these are more difficult to resolve in terms of the two different hydrogen donors, C—H and S—H.

The complexes of the simple sulphoxides [XS(O)Y] and sulphones [XSO_2Y] with water (Tables 31–33) for X,Y = H, CH_3 (structures **128–131**, **134–137** and Figures 58–61, 64–66, respectively) also indicate a role for the interaction of a methyl hydrogen atom

TABLE 34. Interatomic distances between heavy atoms with hydrogen bonds in dimers and water complexes[a]

Dimers	C···O	S···O	Water complexes	O···O	O···C	O···S
104 HS(O)H I		2.938	**128** HS(O)H	2.820		3.253
105 HS(O)H II			**129** $CH_3S(O)H$	2.825	3.370	3.375
106 HS(O)H III		2.907	**130** $CH_3S(O)CH_3$ I		3.494[d]	
		3.151	**131** $CH_3S(O)CH_3$ II	2.878	3.446	
107 $CH_3S(O)H$ I	3.205	3.251	**132** HS(O)OH	2.780		
	3.300			2.814		
108 $CH_3S(O)H$ II	3.276	3.012	**133** $CH_3S(O)OH$	2.799		
		3.239		2.796		
109 $CH_3S(O)H$ III		3.044	**134** $CH_3S(O)OCH_3$	2.909	3.387	
		3.063	**135** HSO_2H	2.893		2.936
110 $CH_3S(O)H$ IV	3.221		**136** CH_3SO_2H	2.877	3.324	3.157
	3.225		**137** $CH_3SO_2CH_3$	3.124[b]	3.364	
111 $CH_3S(O)CH_3$ I	3.252		**138** CH_3SO_2F I	2.991	3.293	
	3.256		**139** CH_3SO_2F II	3.135[b]		
112 $CH_3S(O)CH_3$ II	3.389		**140** H_2O	2.980		
	3.462		**141** H_2S			3.275
113 $CH_3S(O)CH_3$ III	3.442		**142** HSOH	2.856		
	3.438		**143** HOSOH	3.264		
	3.442		**144** CH_3SOH	2.868		
	3.434		**145** CH_3SOCH_3	2.968	3.510	
114 $CH_3S(O)F$	3.283		**146** CH_3OSOH	3.047		
	3.334			2.835		
115 HSO_2H		3.172	**147** HC(O)H	2.949		
		2.972		3.213		
		2.972	**148** $CH_3C(O)H$	2.986	3.530	
116 CH_3SO_2H I	3.335		**149** $CH_3C(O)CH_3$	2.972	3.549	
117 CH_3SO_2H II	3.348	3.195				
118 CH_3SO_2H III		3.199				
		3.100				
119 $CH_3SO_2CH_3$	3.499					
	3.329					
120 CH_3SO_2F	3.314					
121 H_2S[e]						
122 HSOH[c]						
123 HC(O)H I	3.397					
124 HC(O)H II	3.020					
125 $CH_3C(O)H$ I	3.704					
	3.479					
	3.110					
126 $CH_3C(O)H$ II	3.371					
	3.436					
	3.008					
127 $CH_3C(O)CH_3$	3.546					
	3.515					
	3.555					
	3.551					

[a] From RHF/6-31G* optimized geometries.
[b] Average of two close values.
[c] O···O distance is 2.892 Å.
[d] Two equivalent values.
[e] S···S distance is 4.505 Å.

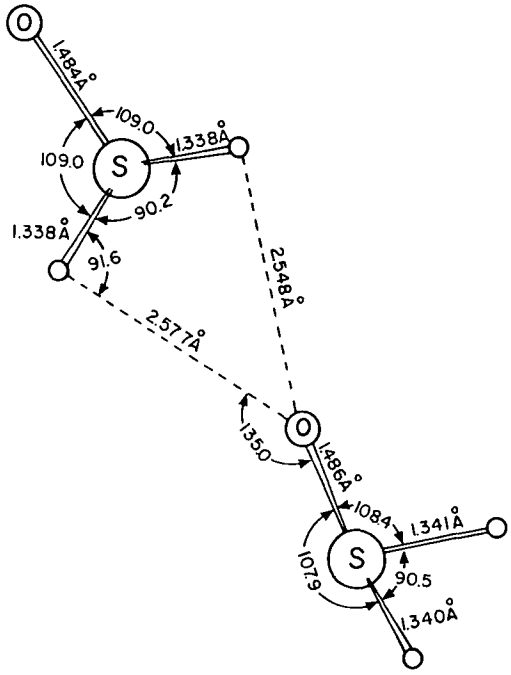


FIGURE 40. HS(O)H dimer I, structure **104** in Tables 28–30

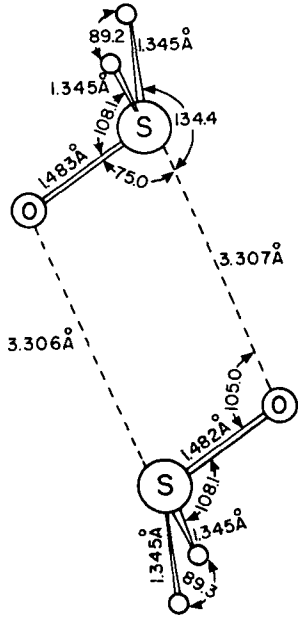


FIGURE 41. HS(O)H dimer II, structure **105** in Tables 28–30

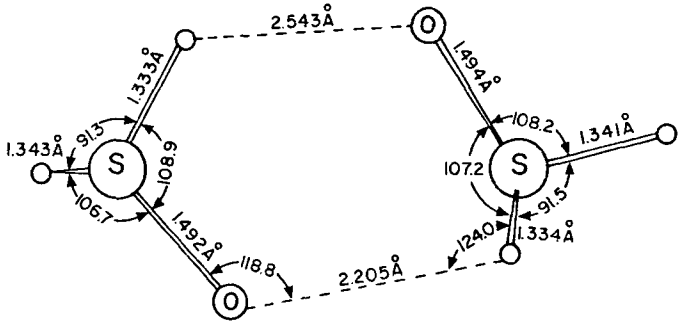


FIGURE 42. HS(O)H dimer III, structure **106** in Tables 28–30

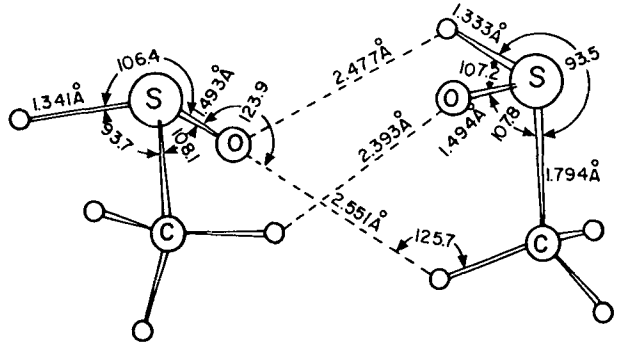


FIGURE 43. $CH_3S(O)H$ dimer I, structure **107** in Tables 28–30

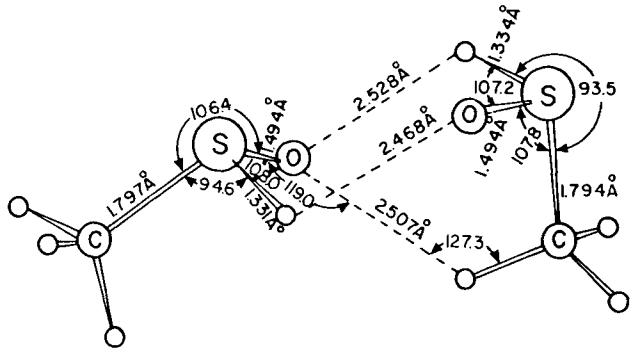


FIGURE 44. $CH_3S(O)H$ dimer II, structure **108** in Tables 28–30

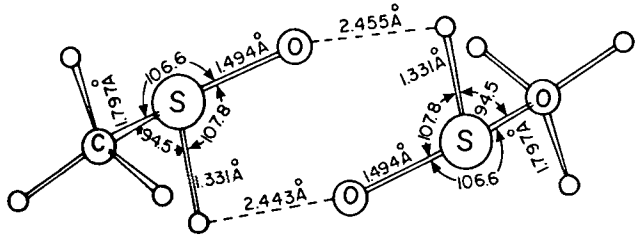


FIGURE 45. $CH_3S(O)H$ dimer III, structure **109** in Tables 28–30

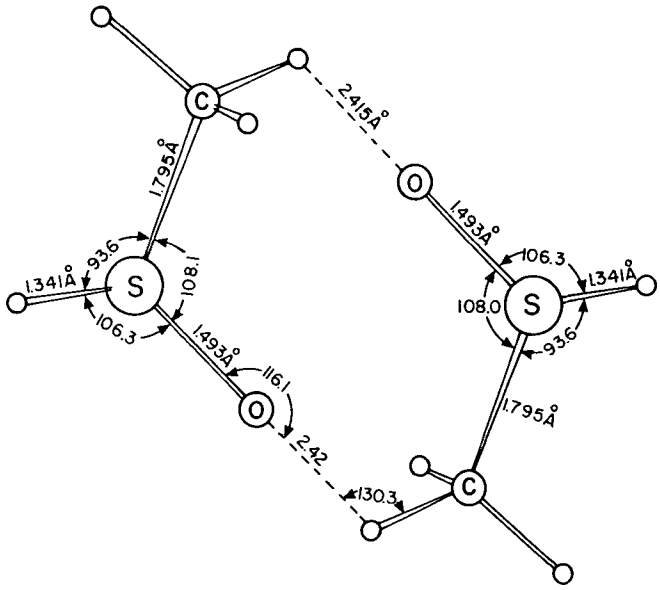


FIGURE 46. $CH_3S(O)H$ dimer IV, structure **110** in Tables 28–30

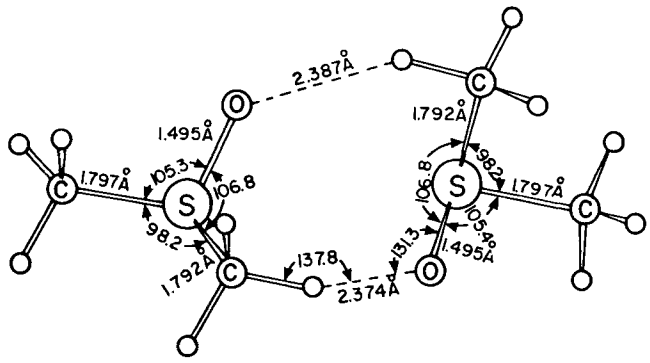


FIGURE 47. $CH_3S(O)CH_3$ dimer I, structure **111** in Tables 28–30

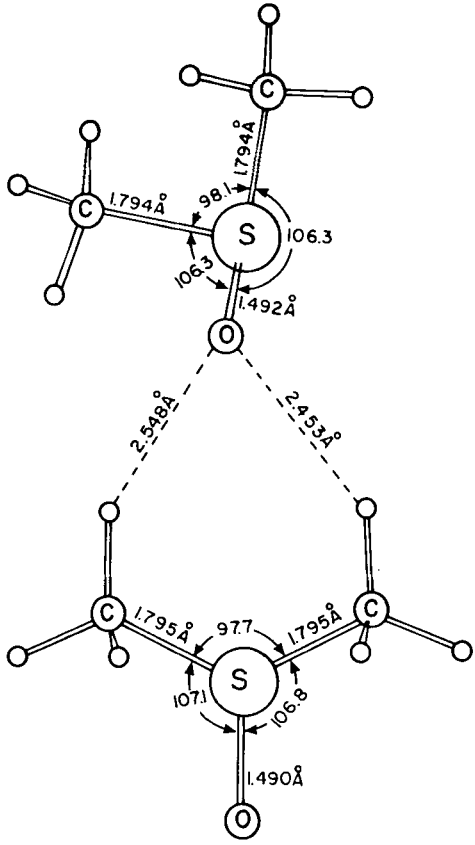


FIGURE 48. $CH_3S(O)CH_3$ dimer II, structure **112** in Tables 28–30

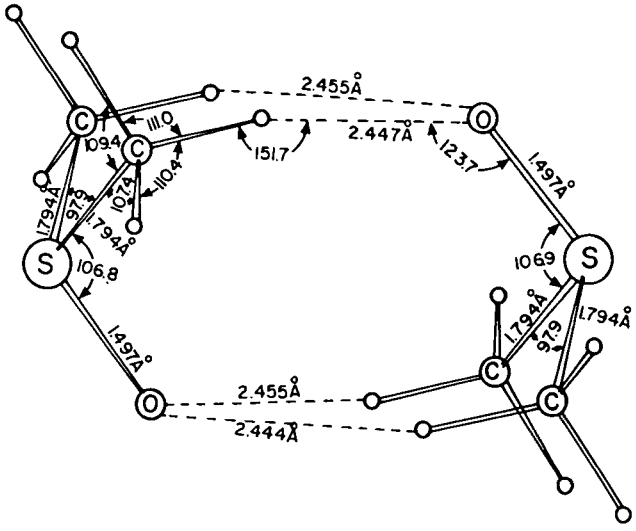


FIGURE 49. $CH_3S(O)CH_3$ dimer III, structure **113** in Tables 28–30

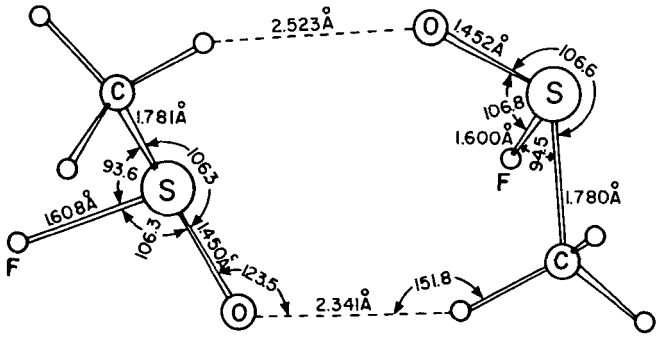


FIGURE 50. $CH_3S(O)F$ dimer, structure **114** in Tables 28–30

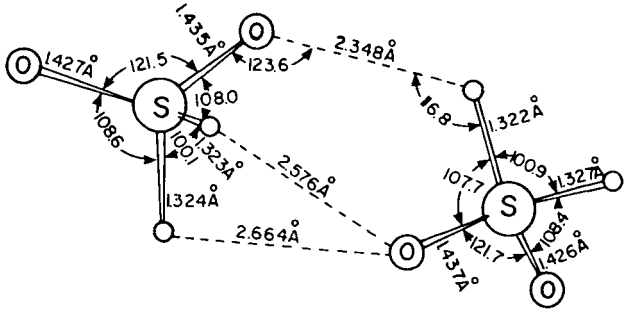


FIGURE 51. HSO_2H dimer, structure **115** in Tables 28–30

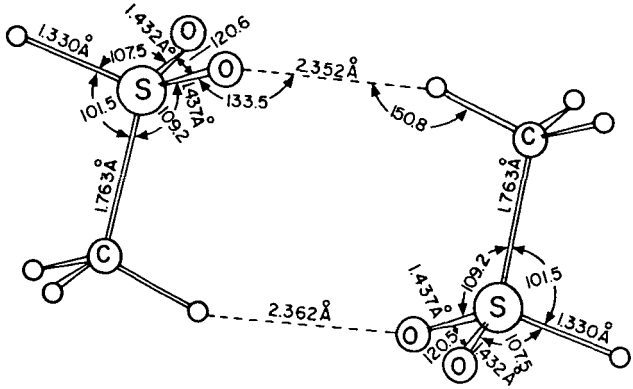


FIGURE 52. CH_3SO_2H dimer I, structure **116** in Tables 28–30

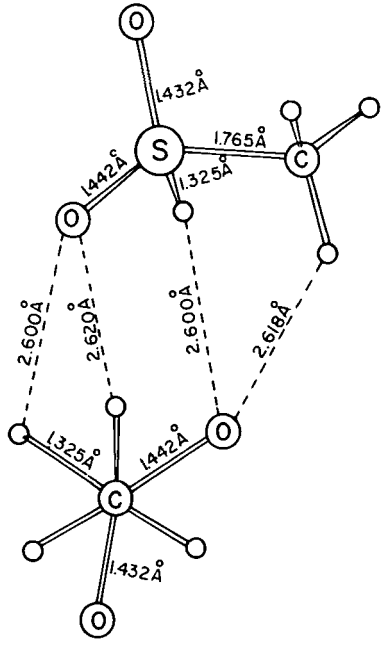


FIGURE 53. CH_3SO_2H dimer II, structure **117** in Tables 28–30

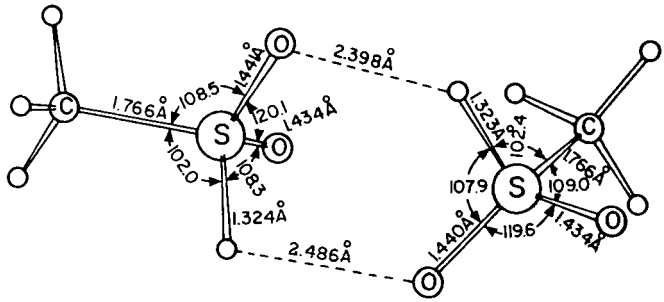


FIGURE 54. CH_3SO_2H dimer III, structure **118** in Tables 28–30

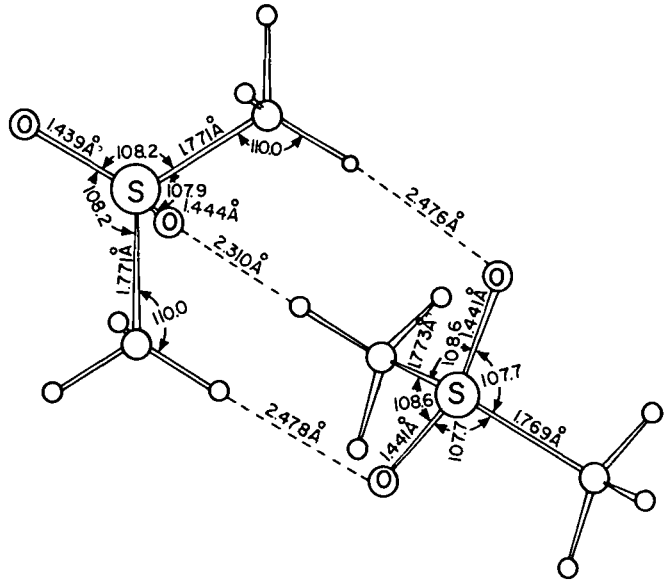


FIGURE 55. $CH_3SO_2CH_3$ dimer, structure **119** in Tables 28–30

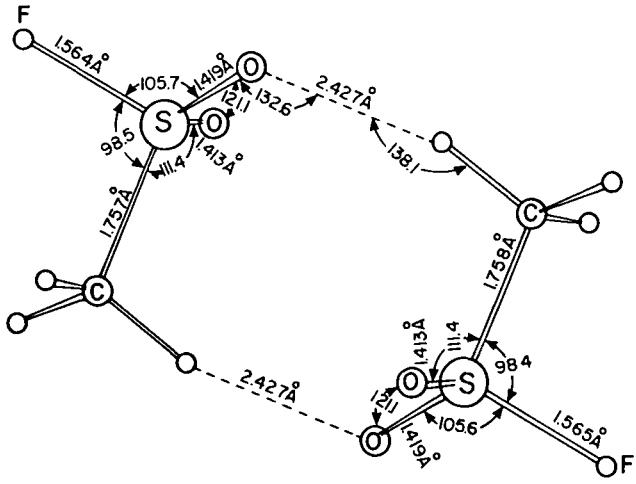


FIGURE 56. CH_3SO_2F dimer, structure **120** in Tables 28–30

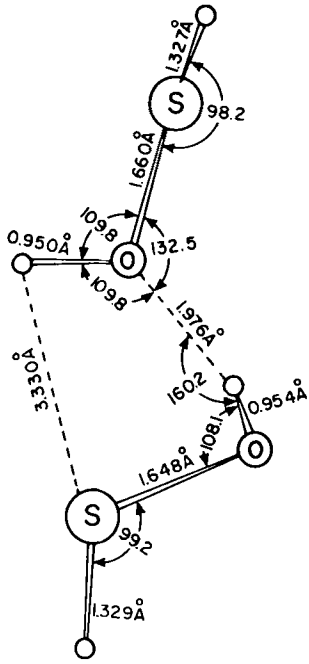


FIGURE 57. HSOH dimer, structure **122** in Tables 28–30

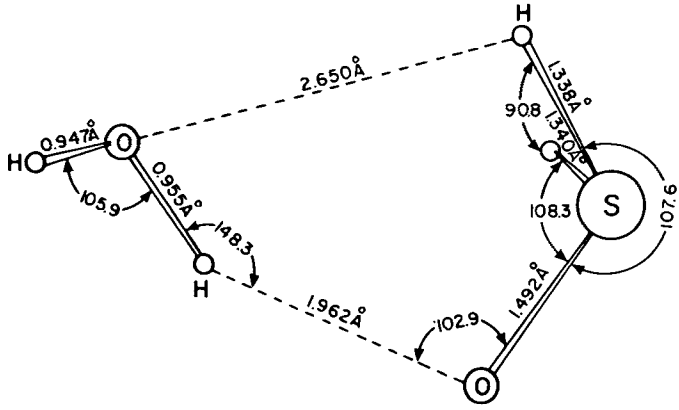


FIGURE 58. HS(O)H···water complex, structure **128** in Tables 31–33

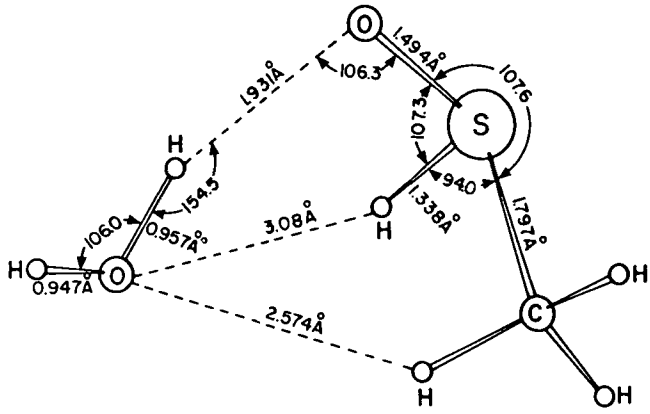


FIGURE 59. $CH_3S(O)H\cdots$water complex, structure **129** in Tables 31–33

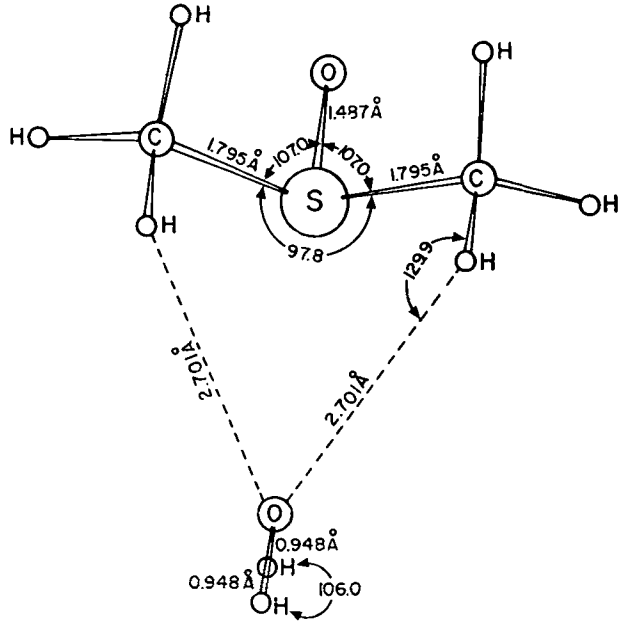


FIGURE 60. $CH_3S(O)CH_3\cdots$water complex I, structure **130** in Tables 31–33

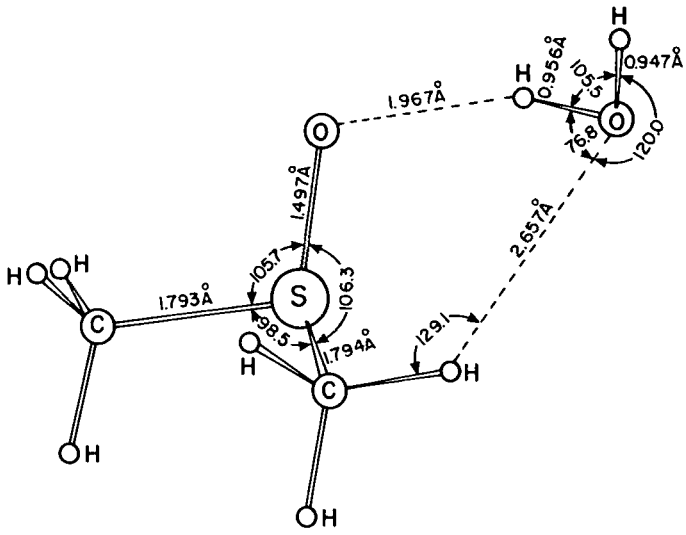


FIGURE 61. $CH_3S(O)CH_3\cdots$water complex II, structure **131** in Tables 31–33

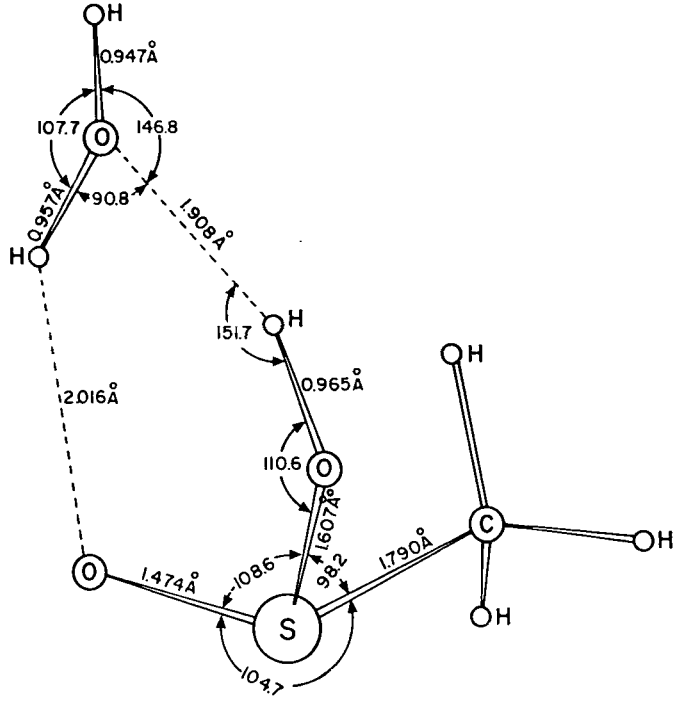


FIGURE 62. $CH_3S(O)OH\cdots$water complex, structure **133** in Tables 31–33

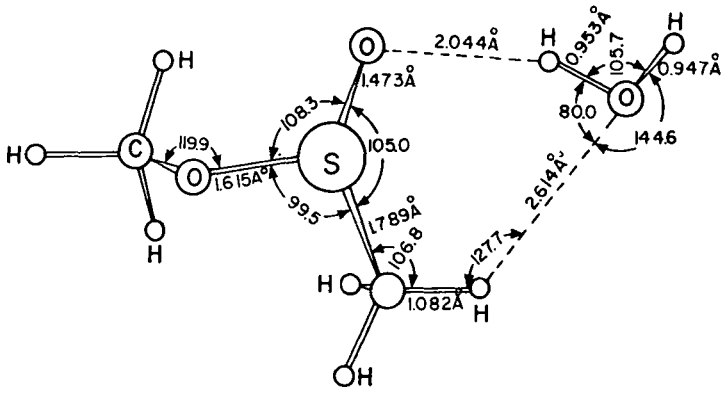


FIGURE 63. $CH_3S(O)OCH_3\cdots$water complex, structure **134** in Tables 31–33

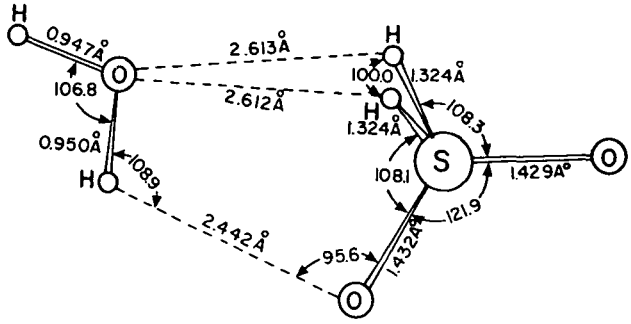


FIGURE 64. $HSO_2H\cdots$water complex, structure **135** in Tables 31–33

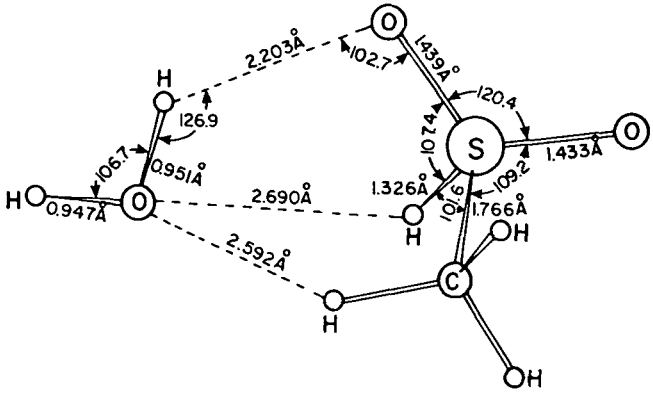


FIGURE 65. $CH_3SO_2H\cdots$water complex, structure **136** in Tables 31–33

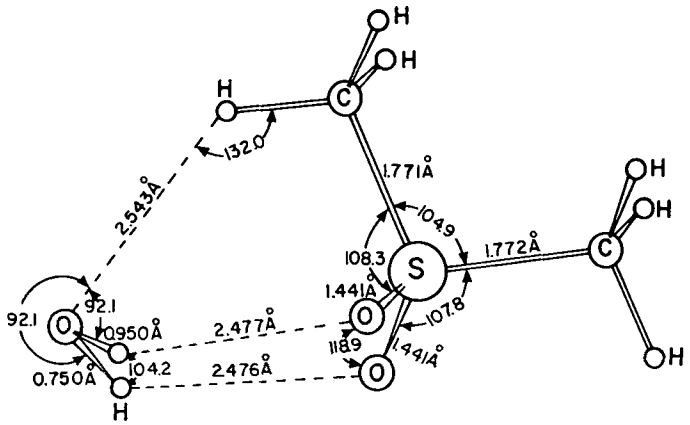


FIGURE 66. $CH_3SO_2CH_3\cdots$water complex, structure **137** in Tables 31–33

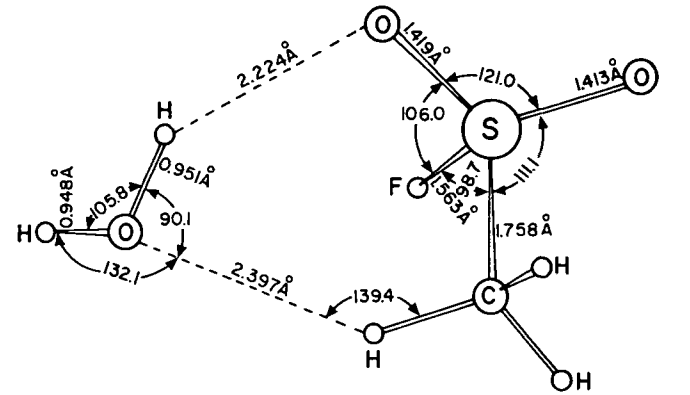


FIGURE 67. $CH_3SO_2F\cdots$water complex I, structure **138** in Tables 31–33

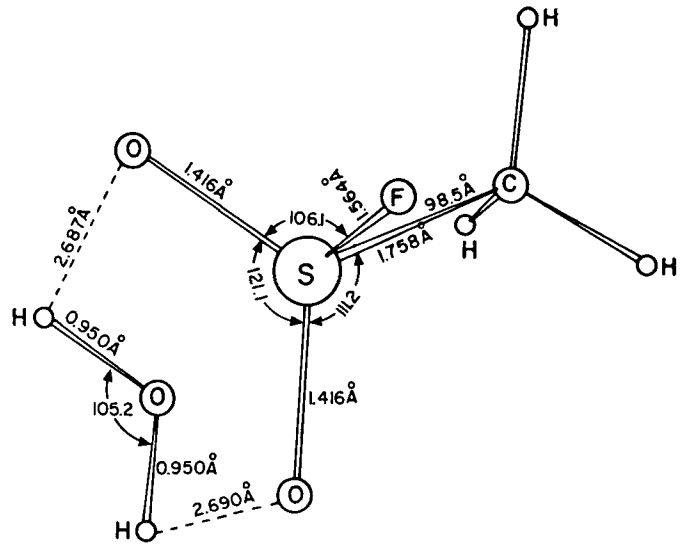


FIGURE 68. $CH_3SO_2F\cdots$water complex II, structure **139** in Tables 31–33

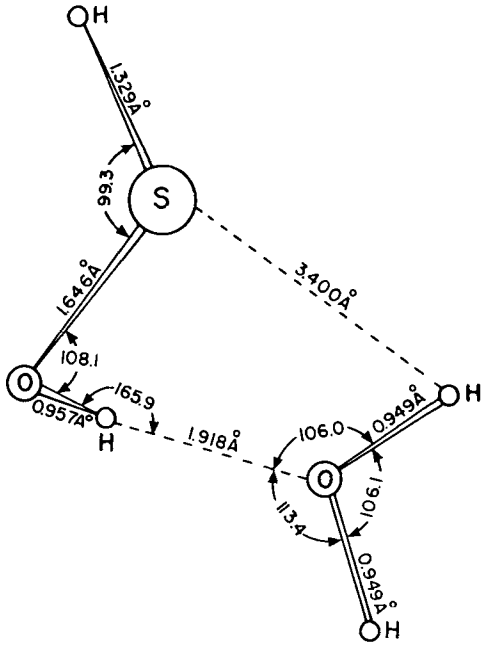


FIGURE 69. HSOH···water complex, structure **142** in Tables 31–33

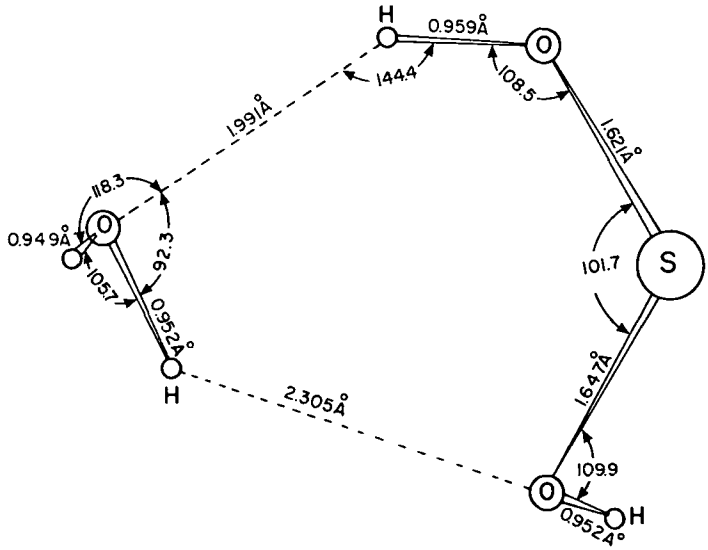


FIGURE 70. HOSOH···water complex, structure **143** in Tables 31–33

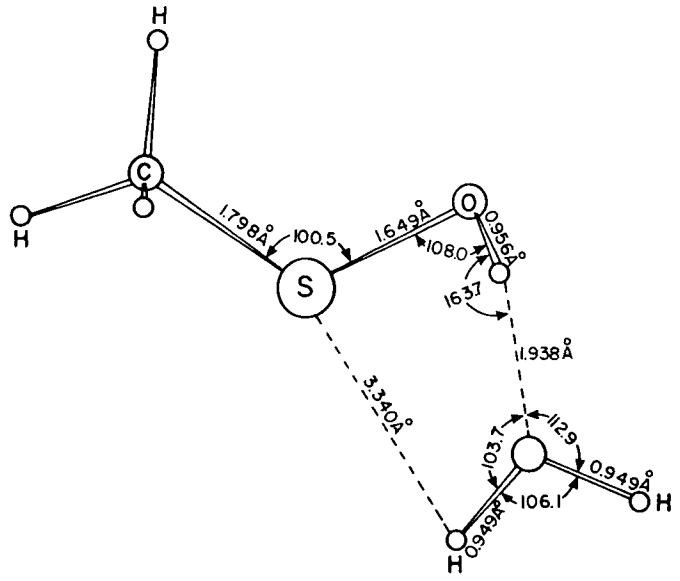


FIGURE 71. $CH_3SOH\cdots$water complex, structure **144** in Tables 31–33

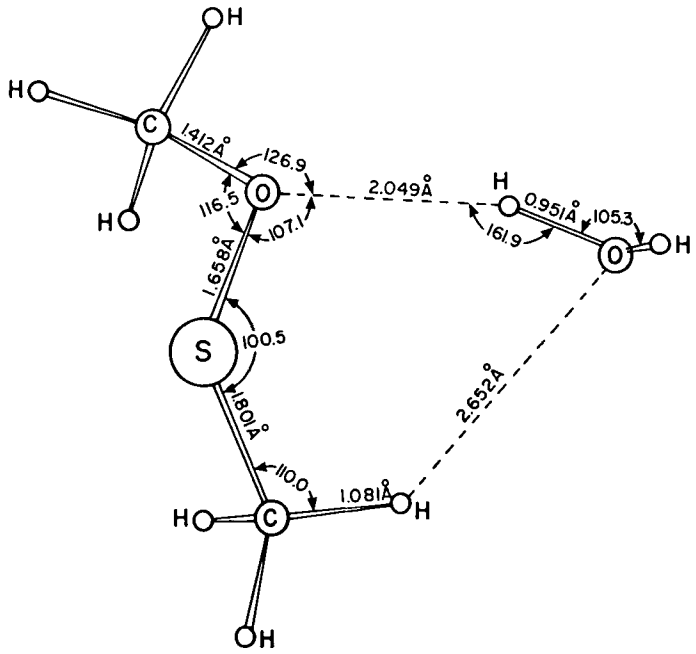


FIGURE 72. $CH_3SOCH_3\cdots$water complex, structure **145** in Tables 31–33

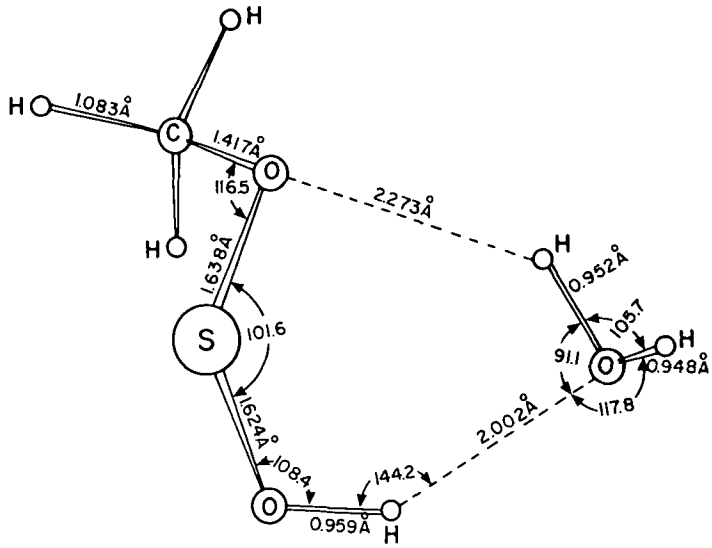


FIGURE 73. $CH_3OSOH\cdots$water complex, structure **146** in Tables 31–33

with the water oxygen atom (O_w). The analogous $CH_4\cdots$water interaction has also seen investigated[64]. It is difficult to assess the relative importance of the (S—)H$\cdots O_w$. (C—)H$\cdots O_w$ and (O_w—)H$\cdots$O(=S) interaction energies from the relatively few unique structures found. In the two $CH_3S(O)CH_3$–water complexes (**130**, Figure 60 and **131**, Figure 61), the former structure has a double (C)—H$\cdots O_w$ interaction with the same oxygen atom for a binding energy of 3.1 kcal mol^{-1} (after BSSE correction), and the latter structure has one (C—)H$\cdots O_w$ and one (O_w—)H$\cdots$O(=S) association and a binding energy of 6.9 kcal mol^{-1}. This certainly seems to establish the weaker strength of (C—)H$\cdots O_w$ relative to (O_w—)H$\cdots$O(=S). In addition, the (O_w—)H$\cdots$O(=S) bond distance is consistently shorter by a significant amount (about 0.6 Å) than the other two types of hydrogen bond lengths in the water complexes and the conventional correlation of bond distance with bond strength would also favour the (O_w—)H$\cdots$O(=S) interaction.

However, because many of these hydrogen bonds in both the dimers and the monomer–water complexes are bent to different degrees, a more consistent measure of hydrogen bond strength might be the distance between the heavy atoms Y$\cdots$O (Y = C, O, S) in the (Y—)H$\cdots$O bonds[60,65]. On that basis, in the dimers, the small differences in (Y—)H$\cdots$O(=S) distances between the two different types of hydrogen bonds (Y = C and Y = S) are usually somewhat reduced in the Y$\cdots$O distances. The effect is not great because the difference in hydrogen bond lengths is already small. In the water complexes (Tables 32 and 34), however, the difference between the $H_w\cdots$O(=S) and $O_w\cdots$H(—Y) distances is substantial, especially for the sulphoxides. This difference is generally somewhat reduced in the Y$\cdots$O distances, but comes nowhere close to eliminating it.

Another question with regard to the sulphoxides and sulphones centres about the relative basicity of the O(=S) atoms as measured by relative hydrogen bond strengths. The resolution of this question is based on comparing the relative dimer and water complex binding energies for the XSO_nY series, with X, Y = H, CH_3 and $n = 1, 2$. Again, on the basis of Tables 28 and 31 it is clear that, generally, the sulphoxides ($n = 1$) are more

basic than the sulphones ($n = 2$). The difference is small for both X = Y = H or CH_3, but very large (almost a factor of 2 larger in binding energy) for the mixed compounds, $CH_3S(O)H$ compared to CH_3SO_2H. In these comparisons, the largest binding energy structure of a given dimer or water complex composition was adopted as the reference. Although this generally larger hydrogen binding energy for the sulphoxides is more pronounced in the dimers relative to the water complexes, the large difference in hydrogen bond length between the sulphoxides and the sulphones is actually in the water complexes for the $(O_w—)H\cdots O(=S)$ interaction distance (Table 32). Here, however, comparing the sulphoxides to the sulphones, the heavy atom distances, $O_w\cdots O(=S)$ in Table 34, substantially reduce the differences in bond lengths involving the hydrogen atom in Table 32.

Given that the atomic charge on the S=O oxygen atom in XS(O)Y is consistently (absolute value) larger that on each S=O oxygen in XSO_2Y, as documented in Section 6, the better hydrogen bonding properties of the XS(O)Y systems are no surprise. However, the difference in atomic charge on oxygen between XS(O)Y and XSO_2Y is calculated to be only 0.076e, on the average. The actual specific charge difference between oxygen atoms in CH_3SOH (Table 13) and $CH_3SO_2H^2$ is actually closer to 0.1e. Nonetheless, the difference in atomic charge on the oxygen atoms in bare HS(O)H (Table 13) and HSO_2H^2 is also 0.1e, and between $CH_3S(O)CH_3$ (Table 13) and $CH_3SO_2CH_3{}^2$ is the same 0.1e. In addition, as was pointed out previously in this chapter, the atomic charge on O(=S) on both sulphoxides and sulphonyls varies linearly with methyl substitution for H in XSO_nY, with no maximum (negative) value for CH_3SO_nH. Although the atomic charges on oxygen are enhanced by the hydrogen bonding (see Tables 30 and 33), the change is roughly the same for all the compounds. Clearly, then, the outstandingly better hydrogen bonding properties of $CH_3S(O)H$ in dimer and water complex formation relative to the dihydro and dimethyl sulphoxides, and to all three types of the sulphones, cannot be explained only by the relative Mulliken atomic charges on the S=O bond oxygen atom.

Substitution of fluorine for hydrogen or methyl bound to sulphur in the sulphoxide and sulphone dimers also gives different trends. Thus, replacing H in $CH_3S(O)H$ IV (**110**, Figure 46) or CH_3 in $CH_3S(O)CH_3$ I (**111**, Figure 47) with F to give $CH_3S(O)F$ (**114**, Figure 50) results in a decrease in dimer binding energy. These three dimers all have the same number and types of hydrogen bonds. On the other hand, replacing hydrogen in CH_3SO_2H I (**116**, Figure 52) with fluorine to give CH_3SO_2F (**120**, Figure 55) leads to a small (0.2 kcal mol^{-1}) increase in dimer binding energy. Here, again, both dimers have the same cycle structure with two $(C—)H\cdots O(=S)$ hydrogen bonds.

The sulphinic acid dimer (**122**, Figure 57) and water complex (**39**, Figure 69) form the same type of structure involving a hydrogen bond between (SO)—H and O_w. The acid–water complex has a larger binding energy, shorter hydrogen bond distance and larger (negative) charge on the hydrogen bonded oxygen atom. Substituting OH for H to give the HOSOH–water complex (**143**, Figure 70) increases the binding energy through a second $(O_w—)H\cdots O$ interaction at 2.305 Å. Replacing (S)H with CH_3 (**144**, Figure 71) slightly reduces the HSOH binding energy with water while maintaining the same hydrogen bonded structure. If CH_3O is substituted for OH in CH_3SOH to give CH_3SOCH_3 (**145**, Figure 72), the $(O_w—)H\cdots O$ hydrogen bond is considerably weakened. When CH_3O replaces CH_3 in CH_3SOH or OH replaces CH_3 in CH_3SOCH_3, to give CH_3OSOH (**146**, Figure 73) a second hydrogen bond is formed which strengthens the monomer–water interaction in both cases. This is also equivalent to replacing an H in HOSOH with the CH_3 group where the calculated hydrogen binding energy is only slightly reduced.

Analogously, replacing the (S)H in HS(O)OH (**132**) with CH_3 to form $CH_3S(O)OH$ (**133**, Figure 62) reduces the water complex binding energy. Both acids form a cyclic, double hydrogen bonded water complex with $(S=)O\cdots H(—O_w)$ and $(O—)H\cdots O_w$ interactions. Continuing the hydrogen → methyl substitution to form $CH_3S(O)OCH_3$

(**134**, Figure 63) gives a lower binding energy water complex with a $(C—)H\cdots O_w$ association replacing the acid group's interaction with water. As noted before, methyl substitution for hydrogen generally increases the calculated atomic charge on sulphur (Tables 30 and 33) and these trends are also found in the dimers and water complexes.

For comparison purposes, Tables 28–33 also show dimer and water complex properties of the carbonyl compounds, XC(O)Y, that correspond to the sulphoxides discussed above (X, Y = H, CH_3). As expected, the hydrogen bonded carbonyls generally have smaller binding energies, larger hydrogen bond distances, and, of course, smaller (negative) charges on the oxygen atoms. An interesting trend regarding the carbonyls is that, in contrast to the sulphur compounds, increased methyl substitution increases both the dimer and water complex binding energies, with no maximum at the monomethyl stage. A general observation about both the sulphoxide, sulphones and carbonyl complexes is that, whenever there are two or more structures for a given dimer or water complex combination, the hydrogen bonded structure with the lowest dipole moment is the most stable. Another consideration favouring the sulphur dimers and water complexes is the steric factor. Carbonyls are intrinsically planar while the sulphoxides and sulphone monomers are three dimensional. The steric crowding and/or bending that usually accompanies the hydrogen bond associations probably imposes a degree of strain on the carbonyl planarity which adversely affects their dimer and water complex stabilities.

In the previous Section the stability and more relative dipole moments of XSOH was compared to the isomeric XS(O)H. We can examine this comparison here for X = H, for both the dimer and the water complex using the common MP2/6-31G* energies. For the monomer complexes with water, before BSSE correction, HSOH is only 0.3 kcal mol^{-1} less stable (Table 31) than HS(O)H (each referenced to its own asymptotes). After BSSE correction the HSOH–water complex is preferentially stabilized by 0.4 kcal mol^{-1}. Therefore, water will probably not reverse the natural stability of bare HSOH relative to HS(O)H (by 27.8 kcal mol^{-1}—Tables 1 and 11). For the respective dimers, using **106**, the most stable of the $[HS(O)H]_2$ structures for the comparison, before BSSE correction HS(O)H improves by 3.5 kcal mol^{-1} (Table 28) relative to HSOH while after BSSE correction the recovery margin increases to 5.1 kcal mol^{-1}. These preferential dimer stabilizations, however, are probably insufficient to overcome a (double) monomer difference of 57.6 kcal mol^{-1} between HSOH and HS(O)H. Analogously, for the water complexes of HS(O)OH and HSO_2H, the intrinsically more stable XS(O)Y monomer (Table 11 and Reference 2) has the larger binding energy by 8.7 kcal mol^{-1} (before BSSE correction) or 4.3 kcal mol^{-1} (after BSSE correction), which only reinforces its already preferred stability. The disproportionation reaction of two XSY monomers to form XS(O)Y + water[39] can also be analysed using the monomer, dimer and water complex energies generated in this study.

Finally, at the beginning of this Section we discussed the effect of MP2 on the hydrogen bond length and binding energies of the dimers and water complexes. As a demonstration, the HSOH I dimer (**104**, Figure 40) and the water complex (**128**, Figure 58) were directly MP2/6-31G* optimized. The comparison is with the corresponding RHF/6-31G* optimized geometries and energies, and the RHF and MP2 energies calculated at those geometries. For the dimer, the two $(S—)H\cdots O(=S)$ distances are reduced from 2.577 Å and 2.548 Å (Table 29) to 2.529 Å and 2.508 Å, respectively. The RHF(MP2) binding energies decrease (increase) from 7.3 (7.6) kcal mol^{-1} (Table 28) to 7.0 (8.0) kcal mol^{-1}, before BSSE correction. For the water complex the equilibrium $(O_w—)H\cdots O(=S)$ distance decreases from 1.962 Å (Table 32) to 1.906 Å, but the longer range $O_w\cdots H(—S)$ interaction decreases in length from 2.659 Å to 2.466 Å. At the same time, the RHF (MP2) binding energy decreases (increases) from 8.5 (10.0) kcal mol^{-1} (Table 31) to 8.4 (10.2) kcal mol^{-1}, again before BSSE correction. This exercise nicely demonstrates the quantitative effect of MP2 on the hydrogen bond distances and binding energies.

VIII. METAL ION COMPLEXES AND PROTONATED SPECIES

The coordination of metal cations to XSY, XS(O)Y and XSO_2Y compounds is expected to affect their geometric and electronic structural properties. The experimental literature deals with these kinds of complexes either from the point of view of the metal, with XSO_nY as a ligand[66–68], or from the point of view of the sulphur compound as a substrate, where the metal ion is used for detection of, or as a catalytic agent inducing change in, the substrate[62,69,70]. Our point of view here is the latter. The XSO_nY series offers a particularly rich prospect of interesting chemistry and properties because of the potential availability of multiple sites for metal ion attachment. This is especially true of the amide derivatives (sulphenamide, sulphinamide and sulphonamide) which offer the oxygen, sulphur and nitrogen atoms as possible receptors of metal ions.

As was noted previously[3], the interaction of bare cations with single or multiple ligands in the gas phase has developed into a very active research area, both experimentally and theoretically. The determination of metal ion–substrate binding energies by the various spectrometric and spectroscopic techniques[71] offers an opportunity to analyse the nature of the metal–ligand bond. By comparing the variation of the binding energy with the nature of the metal ion and the ligand(s) much can be learned about the mechanism of bond formation. However, these methods give no direct information on the structure of the complexes or on preferred site attachment where the substrate offers the possibility of several coordination and conformational possibilities for complexation, as is found here.

Because the coordination of metal ions to XSO_nY compounds as isolated complexes is only in the very earliest stages of investigations, we have undertaken a preliminary computational study of the Au^+ interactions with $HOSNH_2$, $HS(O)NH_2$ and HSO_2NH_2 in the gas phase. Metal ion interactions with sulphur–oxygen compounds in condensed phase have recently been reviewed[38,39,51]. These three compounds are taken as prototypes of the XSY, XS(O)Y, XSO_2Y systems reviewed in this chapter. For comparison purposes, the analogous protonated species were also generated. The complexation process described here involves perturbation of the sulphur compounds by the metal ion, but not disruption of any existing chemical bond in the sulphur compound substrates. Properties of interest include preferred binding site locations and conformations, metal–substrate binding energies and equilibrium bond lengths, ligand geometric structure and its progressive change upon complexation and protonation, and the relative energetic effects of complexation vs protonation. The gold cation was chosen as the representative metal ion because its closed-shell electronic structure ($\cdots 5d^{10}6s^0$) leads us to expect a mainly electrostatic (charge–dipole) interaction with XSO_nY. However, experience has shown that Au^+ complexes also show detectable covalent interaction effects[3,72].

The details of the calculations and the results are as follows. The geometries of the M—XSO_nY complexes (M = Au^+ and H^+) were gradient optimized at the RHF level. *Ab initio* relativistic compact effective potentials (RCEP) and basis sets were used for Au^+ [73]. Basis sets and CEPs for the main group elements (N, O and S) were taken from a standard tabulation[74]. The transition metal RCEP includes the semi-core 5s and 5p (along with the valence 5d) electrons in the valence region. The basis set, crafted to represent accurately the 5s, 5p, 5d and any 6s, 6p electron density, is ($7^{sp}5^d$) contracted down to [$4^{sp}3^d$]. The crucial valence 5d sub-shell is thus represented by a triple-zeta set of basis functions. Analogously, for the main group elements, the valence (s,p) + polarization (d) CEP-211G* basis set was used, split from the tabulated valence CEP-31G distribution[74]. The single-zeta polarization d exponents were 0.8 (O), 0.8 (N) and 0.49 (S). The valence region is expected to be better described by the CEP-211G basis than the all-electron (AE) 6-31G basis because of the greater flexibility (three basis functions

instead of two in the latter case) and smaller outer valence exponent in the former case. For the hydrogen atom the standard valence 31G basis set[15,16] was used.

Although discussed previously (Reference 1, Reference 2 and structures **12, 66–67**), the three prototypical amine and amide ligands ($n = 0$, 1 and 2, with $Y = NH_2$ and $X = OH$ or H in XSO_nY) were recalculated in the CEP basis set for consistency. The RHF/CEP energies and dipole moments of the bare ligands are shown in Table 35, as well as the MP2/CEP energies which were single point calculated for the RHF/CEP equilibrium geometry of only the most stable conformer complexes of each (n value) type substrate. Table 36 shows the RHF energies of all the gradient optimized structures obtained here. The corresponding bond distances and Mulliken population data are tabulated in Tables 37 and 38, respectively. Again, for only the most stable complexes of a given n value in XSO_nNH_2 the MP2 energies at the RHF optimized geometries were (single point) calculated and these are also listed in Table 36. In addition, for these same

TABLE 35. Total energies and dipole moments of substrate sulphur compounds[a]

Molecule	Energy (a.u)		RHF dipole moment (D)[b]
	RHF	MP2[b]	
150 $HS(O)NH_2$ I	−37.182065	−37.676954	2.869
151 $HS(O)NH_2$ II	−37.174664		4.904
152 HSO_2NH_2 I	−52.663057	−53.345535	3.610
153 HSO_2NH_2 II	−52.659857		5.454
154 $HOSNH_2$ I	−37.215734	−37.703704	2.454
155 $HOSNH_2$ II	−37.212581		2.361

[a]Geometry RHF optimized with no symmetry or equivalence constraints using the CEP basis set described in the text.
[b]In the RHF/CEP optimized geometries.

TABLE 36. Total energies of Au^+–Substrate complexes[a].

Substrate	Energies (a.u.)			Substrate binding site atom
	RHF	MP2[b]	MP2[c]	
156 $Au^+—HS(O)NH_2$	−172.124393	−172.755235	−172.756238	O
157 $Au^+—HS(O)NH_2$	−172.121215			O
158 $Au^+—HS(O)NH_2$	−172.095530			S
159 $Au^+—HS(O)NH_2$	−172.089138			S
160 $Au^+—HS(O)NH_2$	−172.096974			N
161 $Au^+—HS(O)NH_2$	−172.120866			O
162 $Au^+—HSO_2NH_2$	−187.589843			O
163 $Au^+—HSO_2NH_2$	−187.590818	−188.407440	−188.408680	O
164 $Au^+—HSO_2NH_2$	−187.577518			N
165 $Au^+—HOSNH_2$	−172.145018	−172.781774	−172.783830	S
166 $Au^+—HOSNH_2$	−172.149251	−172.784679	−172.786792	S

[a] Geometries RHF optimized with no symmetry or equivalence constraints, using the CEP basis set described in the text.
[b] In the RHF/CEP optimized geometries.
[c] After one-dimensional MP2/CEP optimization of the $Au^{(+)}$–Substrate site atom. See text.

TABLE 37. Calculated optimized bond lengths of Au^+–Substrate complexes[a]

Complex	Bond lengths (Å)							
	Au—O	Au—S	Au—N	S=O	S—N	N—H[b]	H—S	H—O
156 Au^+—$HS(O)NH_2$	2.196[d]	3.471[d]	4.771	1.536	1.710	1.024	1.346	—
157 Au^+—$HS(O)NH_2$	2.197	3.439	4.020	1.529	1.719	1.024	1.350	—
158 Au^+—$HS(O)NH_2$	3.364	2.467	3.409	1.460	1.712	1.026	1.350	—
159 Au^+—$HS(O)NH_2$	3.332	2.467	3.417	1.461	1.718	1.026	1.356	—
160 Au^+—$HS(O)NH_2$	4.722	3.536	2.230	1.461	1.802	1.024	1.359	—
161 Au^+—$HS(O)NH_2$	2.203	3.419	3.441	1.521	1.746	1.026	1.350	—
162 Au^+—HSO_2NH_2	2.277	3.382	4.544	1.478 1.433	1.623	1.007	1.338	—
163 Au^+—HSO_2NH_2	2.277[e]	3.362[e]	4.293	1.474 1.431	1.622	1.008	1.342	—
164 Au^+—HSO_2NH_2	3.382	3.234	2.329	1.429	1.720	1.015	1.344	—
165 Au^+—$HOSNH_2$	3.282	2.439[f]	3.360	1.615[c]	1.755	1.025	—	0.960
166 Au^+—$HOSNH_2$	3.108	2.449[g]	3.522	1.622[c]	1.735	1.024	—	0.961

[a] From RHF/CEP optimized geometries.
[b] Average value lengths.
[c] S—O bond lengths.
[d] Au—O = 2.117 Å, Au—S = 2.388 Å after MP2/CEP optimization of the Au—O distance; see text.
[e] Au—S = 3.252 Å, Au—O = 2.174 Å after MP2/CEP optimization of the Au—O distance; see text.
[f] Au—S = 2.321 Å after MP2/CEP optimization of the Au—S distance; see text.
[g] Au—S = 2.329 Å after MP2/CEP optimization of the Au—S distance; see text.

TABLE 38. Mulliken atomic charges and d-orbital occupancies on S in Au^+–Substrate complexes[a]

Complex	Atomic charges					d-Orbital occupancy on S
	S	O	N	H(—S)	Au	
156 Au^+—$HS(O)NH_2$	0.631	−0.768	−0.565	0.166	0.851	0.356
157 Au^+—$HS(O)NH_2$	0.644	−0.754	−0.582	0.159	0.851	0.353
158 Au^+—$HS(O)NH_2$	0.594	−0.555	−0.558	0.167	0.640	0.485
159 Au^+—$HS(O)NH_2$	0.647	−0.574	−0.545	0.147	0.635	0.475
160 Au^+—$HS(O)NH_2$	0.756	−0.576	−0.815	0.099	0.774	0.402
161 Au^+—$HS(O)NH_2$	0.713	−0.735	−0.620	0.135	0.833	0.351
162 Au^+—HSO_2NH_2	1.156	−0.702	−0.803	0.173	0.879	0.814
163 Au^+—HSO_2NH_2	1.147	−0.564 −0.690	−0.788	0.162	0.879	0.821
164 Au^+—HSO_2NH_2	1.169	−0.558 −0.551	−0.965	0.170	0.846	0.844
165 Au^+—$HOSNH_2$	0.453	−0.549 −0.633	−0.563	—	0.577	0.230
166 Au^+—$HOSNH_2$	0.389	−0.644	−0.540	—	0.615	0.204

[a] From RHF/CEP optimized geometries.

complexes, a one-dimensional stepwise optimization at the MP2 level was carried out for the metal-binding atom distance, with all the other (metal complex) geometric parameters held fixed at their RHF optimized values. The resultant MP2 energies are also found in Table 36.

The RHF optimized geometries of the three most stable complexes are shown in Figures 74–76. In contrast, with the formic acid– and formamide–Au^+ complexes[3], the structures here are intrinsically non-planar, irrespective of the coordination site. No attempt was made to test the stability of these structures as absolute minima.

The RHF energies of the protonated XSO_nNH_2 species, in their gradient optimized structures, are given in Table 39. The corresponding equilibrium bond lengths, and

TABLE 39. RHF total energies of protonated substrates[a]

Protonated species	RHF energy (a.u.)	Protonated at
167 $HS(OH)(NH_2)^+$	−37.520063	O
168 $HS(OH)(NH_2)^+$	−37.516121	O
169 $HS(OH)(NH_2)^+$	−37.513828	O
170 $HS(O)NH_3^+$	−37.488963	N
171 $H_2S(O)(NH_2)^+$	−37.448612	S
172 $H_2S(O)(NH_2)^+$	−37.442460	S
173 $HS(O)(OH)(NH_2)^+$	−52.960852	O
174 $HSO_2NH_3^+$	−52.955538	N
175 $HOSNH_3^+$	−37.536663	N
176 $H_2O)S(NH_2)^+$	−37.513574	O

[a]Geometry RHF/CEP optimized with no symmetry or eqivalence constraints.

TABLE 40. Calculated bond lengths for protonated substrates[a]

Protonated Species	Bond lengths (Å)					
	H—O	H—S	H—S[b]	S—O	S—N	N—H[d]
167 $HS(OH)(NH_2)^+$	0.963	1.340	2.157	1.600	1.693	1.024
168 $HS(OH)(NH_2)^+$	0.963	1.344	2.147	1.592	1.707	1.024
169 $HS(OH)(NH_2)^+$	0.965	1.347	1.162	1.580	1.739	1.027
170 $HS(O)NH_3^+$	3.541	1.361	2.434	1.444	1.906	1.023
171 $H_2S(O)(NH_2)^+$	2.336	1.348	1.348	1.432	1.681	1.028
172 $H_2S(O)(NH_2)^+$	2.524	1.353	1.349	1.431	1.685	1.028
173 $HSO(OH)(NH_2)^+$	0.969	1.342	2.137	1.416 1.546[c]	1.601	1.011
174 $HSO_2NH_3^+$	2.796	1.344	2.362	1.414	1.856	1.021
175 $HOSNH_3^+$	0.961	—	2.412	1.607	1.819	1.021
176 $(H_2O)S(NH_2)^+$	0.966[e]	—	2.452	1.853	1.659	1.016

[a] From RHF/CEP optimized geometries.
[b] New H—S bond lengths.
[c] S—O bond length.
[d] Average value lengths.
[e] The new O—H has the same bond length.

Mulliken atomic charges and d orbital population on the sulphur atom are shown in Tables 40 and 41, respectively. The calculated RHF dissociation energies for both the complexes and protonated substrates are listed in Table 42. Finally, the BSSE corrected RHF/CEP and MP2/CEP binding energies for the most stable of each type complex are found in Table 43.

The bare sulphinamides (**150** and **151**) (structures **66** and **67**), and have been treated previously[1,75,76]. The RHF dipole moments in the CEP basis (Table 35) are consistently

TABLE 41. Mulliken atomic charges and d-orbital occupancies on S in protonated substrates[a]

Protonated species	Atomic charges					d-Orbital occupancy on S
	S	O	N	H(—S)	H[b]	
167 $HS(OH)(NH_2)^+$	0.656	−0.623	−0.544	0.233	0.523	0.307
168 $HS(OH)(NH_2)^+$	0.658	−0.607	−0.541	0.220	0.527	0.304
169 $HS(OH)(NH_2)^+$	0.710	−0.593	−0.570	0.202	0.521	0.301
170 $HS(O)NH_3^+$	0.852	−0.508	−0.729	0.137	0.406	0.388
171 $H_2S(O)(NH_2)^+$	0.766	−0.468	−0.546	0.232	0.232	0.601
172 $H_2S(O)(NH_2)^+$	0.823	−0.477	−0.534	0.208	0.216	0.591
173 $HSO(OH)(NH_2)^+$	1.126	−0.454 −0.572	−0.785	0.220	0.547	0.784
174 $HSO_2NH_3^+$	1.175	−0.461	−0.874	0.200	0.483	0.840
175 $HOSNH_3^+$	0.514	−0.628	−0.647	—	0.414	0.810
176 $(H_2O)S(NH_2)^+$	0.504	−0.746	−0.641	—	0.551	0.151

[a] From RHF/CEP optimized geometries.
[b] The added proton.

TABLE 42. Bond dissociation energies for Au^+ complexes and protonated substrates[a]

Complex or protonated species	Atom bonded to cation		
	O	S	N
	Binding energy (structure no.)		
$Au^+—HS(O)NH_2$[b]	40.7 (**156**) 38.7 (**157**) 38.5 (**161**)	22.6 (**158**) 18.6 (**159**)	23.5 (**160**)
$Au^+—HSO_2NH_2$[c]	31.6 (**163**) 31.0	—	23.3 (**164**)
$Au^+—HOSNH_2$[d]	— —	35.2 (**166**) 32.6 (**165**)	
$H^+—HS(O)NH_2$[b]	212.1 (**167**) 209.6 (**168**) 208.2 (**169**)	167.3 (**171**) 163.4 (**172**)	192.6 (**170**)
$H^+—HSO_2NH_2$[c]	186.5 (**173**)	—	183.5 (**174**)
$H^+—HOSNH_2$[d]	186.9 (**176**)	191.0 (**167**)	201.4 (**175**)

[a] In kcal mol^{-1}, from RHF/CEP optimized geometries.
[b] Relative to conformer **150**.
[c] Relative to conformer **152**.
[d] Relative to conformer **154**.

TABLE 43. Bond dissociation energies for Au^+ complexes after BSSE correction[a]

Complex	Strcture number	Binding energy HF	MP2
Au^+—$HS(O)NH_2$[b]	**156**	39.8	45.4
Au^+—HSO_2NH_2[c]	**163**	30.9	33.3
Au^+—$HOSNH_2$[d]	**166**	34.5	46.6

[a] In kcal mol^{-1}, from the RHF/CEP optimized geometries.
[b] Relative to conformer **150**.
[c] Relative to conformer **152**.
[d] Relative to conformer **154**.

0.15*D* larger than the all-electron basis set results (Table 11), and the RHF energy differences between rotamers is smaller (by less than 1 kcal mol^{-1}) in the CEP basis, out of a 5 kcal mol^{-1} average difference between the rotamers. These small differences in results between the CEP and AE methods probably reflect variations in the valence part of these basis sets more than they are the result of the different core electron representations.

In projection along the S–N bond, the more stable of the two bare sulphinamide rotamers [**150** (CEP) and **66** (AE)] has the sulphoxide oxygen atom located between the two amine nitrogen atoms and *trans* to the nitrogen lone pair of electrons. Thus, the H, O and lone pair of electrons on the sulphur atom are staggered with the two hydrogen atoms and lone pair on nitrogen. This allows for maximum (N—)H···O(=S) intramolecular hydrogen bond interactions, non-maximal electron-pair replusions, gives the smaller dipole moment (Table 35), and apparently allows an effective interaction

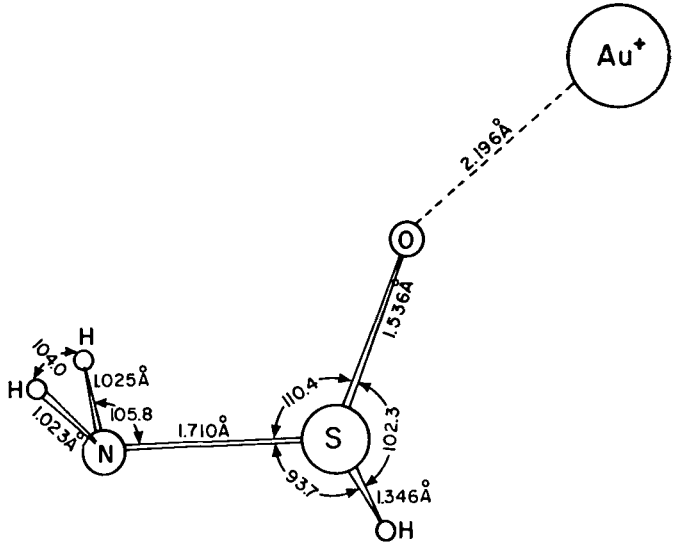


FIGURE 74. Au^+—$HS(O)NH_2$, structure **156** in Tables 36–43

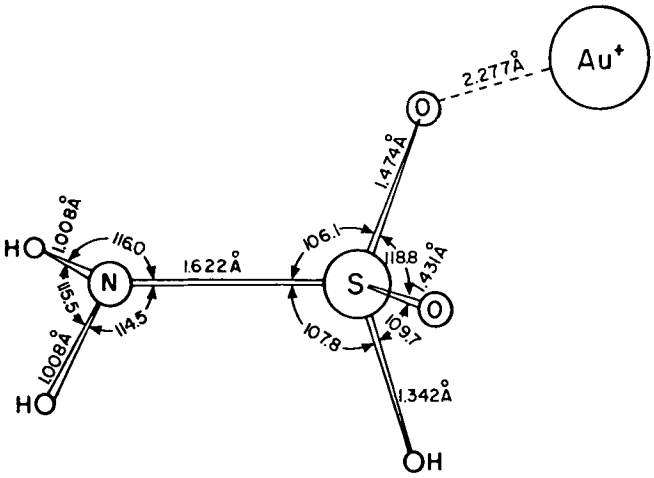


FIGURE 75. Au^+—HSO_2NH_2, structure **163** in Tables 36–43

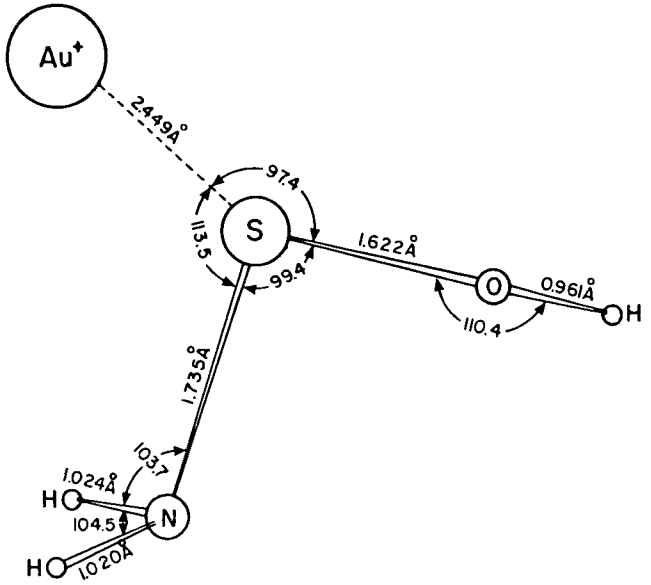


FIGURE 76. Au^+—$HOSNH_2$, structure **166** in Tables 36–43

between the non-bonding (nb) pair on nitrogen and the parallel σ(S=O)* MO. This latter mixing results in a marginally slightly longer S=O bond length in **66** (1.468 Å) relative to **67** (1.465 Å), which is shown in Table 12. Also, because the sulphur atom lone pair is *trans* to one of the two (otherwise equivalent) N—H bonds, its N—H bond length (1.026 Å) is calculated to be slightly longer than its partner's (1.023 Å). Conformer

151 (or **67**) has only one internal (N—)H···O(=S) hydrogen bond, where S—H straddles the two N—H bonds (in projection along the S—N axis) and the nitrogen atom lone pair is *trans* to S—H. This induces a nb–σ^*(S—H) interaction which should lengthen the S—H bond in **67** (**151**) relative to **66** (**150**). This is, in fact, observed computationally in Table 12. These types of stereoelectronic effects have been discussed with regard to carbonyl systems[30,37]. A third possible staggered conformer (III), with the S and N lone pair *trans* to each other, rotated spontaneously to the **150** structure in geometry optimization.

The bare sulphonamides (**152** and **153**) have also been discussed previously[2,76,78–82]. The lower-energy conformer, **152**, is 1.9 (RHF/6-31G*) or 2.0 (MP2/6-31G*)[2,78] kcal mol^{-1} more stable than **153**, compared to the RHF/CEP-211G* 2.0 kcal mol^{-1} difference in Table 35 [79,82]. It should be noted that at the RHF/6-31 + G*//6-31G* level this difference is reduced to 1.5 or (MP2) 1.6 kcal mol^{-1}. The AE and CEP calculated dipole moments agree to 0.03*D* for **152** but only to 0.21*D* for structure **153**. The conformation of **152** viewed along the S—N axis has the two S=O bonds eclipsed with the two N—H bonds, and the S—H bond aligned with the nitrogen lone pair. Rotamer **153**, on the other hand, has the corresponding 180° rotated staggered conformation. The former rotamer allows stronger internal hydrogen bond interactions which presumably endow its preferred stability. In both rotamers the two N—H bonds are stereoelectronically equivalent. In **153**, as in **151** for the sulphinamide, the nitrogen atom lone pair is *trans* to the S—H bond and the resultant S—H lengthening (relative to **152**) is again observed[2]. These interactions work in the opposite direction for the S—N bond which is longer in **150** relative to **151** (Table 12) and **152** relative to **153** [2,77]. A third possible rotamer (IV), with the S—H bond *trans* to one of the N—H bonds, reverted spontaneously to **153** in geometry optimization.

Aminesulphenic acid (**154** and **155**) is also found in two conformers. Previously (Reference 1 and Tables 1–3, structure **12**) only the more stable rotamer was reported. The RHF/CEP-211G* dipole moment for **154** agrees to 0.07*D* with the AE calculated value. The two conformers in Table 35 differ in the orientation of the two lone pairs of electrons on sulphur, relative to the lone pair on nitrogen. Projected along the S—N axis, **154** has the nb electron pair on N *cis* to, or eclipsing, the S—O bond, with the two S atom nb pairs eclipsing the two N—H bonds. This places maximum distance between the nb electron pairs on the different centres in accord with the principles of Valence Shell Electron Repulsion theory[83]. Rotamer **6** has the amine group inverted, forcing maximum proximity of lone pairs of electrons on the different centres across the S—N bond, and places **155** (Table 35) 2.0 kcal mol^{-1} above **154** in energy at the RHF level.

Six stable (zero gradient) structures were found for the Au^+—$HS(O)NH_2$ complex (**156–161**, Tables 36–38). The most stable, **156**, shown in Figure 74. All the calculated geometric structures of these complexes can be associated with one of the rotamers, **150**, **151** or III, described above. Analogously, the equilibrium geometries for the six protonated structures (**167–172**, Tables 39–42) were found to have corresponding sulphinamide rotamer parentages. The most stable protonated structure is **167** with the proton attached to the XS(O)Y oxygen atom of rotamer **150**; this is also the sulphine conformation and metal ion coordination site of complex **156**. Two other oxygen bound complex (protonated) structures are **157** (**168**) and **161** (**169**), with rotamer parentages **151** and III (see above). There are two sulphur bound complexes (protonated species), **158** (**171**) and **159** (**172**) with origins in conformers **150** and **151**, respectively, and one geometry with Au^+ and a proton attached to the nitrogen atom (structure **160** and **170**, respectively) with the **150** parent rotamer structure.

The optimum RHF Au^+—O equilibrium distance in **156** (Table 37) is 2.196 Å, which is very similar to the length (2.203 Å) in that same coordination site calculated for the Au^+–formamide complex[3] in the same basis set. This is somewhat surprising if the oxygen atom in the S=O bond is considered to be more negative than in C=O. The

RHF binding energy, however, is slightly larger for $HS(O)NH_2$ (Table 42) than for $HC(O)NH_2$[3]. The S=O bond length in **150** is 1.488 Å, which increases to 1.536 Å upon complexation with Au^+ in **156** (Table 37) and expands to 1.600 Å in **167** (Table 40) upon protonation. This is the expected order of change which correlates with increased binding energy and perturbation of the S=O bond. In the protonated species (**167**) the O—H bond distance is a normal 0.963 Å and the S—O bond distance (1.600 Å) is almost a regular single bond length. Complex **157** (protonated, **168**), with conformer **151** for the sulphinamide, having an S=O distance of 1.485 Å (1.592 Å), shows the same S=O characteristics as **156** (**167**). Complex **161** (protonated, **169**) stabilizes conformer III of the sulphinamide because of an additional interaction with the nitrogen lone pair. In both the complex and protonated species the cation is tilted towards the nitrogen atom.

In these cation-oxygen atom bound sulphinamides, the S—N bond distance decreases progressively in going from the free rotamer to the complex to the protonated species. Thus, for **150** (**151**) the S—N bond length is 1.738 Å (1.741 Å) which progressively shortens to 1.710 Å (1.719 Å) in the complex and 1.693 Å (1.707 Å) upon protonation. In these two conformations the tilt of the amine hydrogen atoms prevents a long-range interaction between the cation and the nitrogen lone pair of electrons. The behaviour of the S—N bond here is consistent with previous results[3] and is expected on the basis of increased π character of the S—N bond from the nitrogen atom lone pair due to the polarizing effect of the cation. Increased π character on the S—N bond is also expected to enhance its reactivity. However, in **161** (and **169**) the S—N bond is larger, 1.746 Å (and 1.739 Å), than in the other cation-oxygen coordinated sulphinamides. This increase presumably reflects the reduced ability of the nitrogen atom nb electrons to enhance the double bond character of S—N due to its long-range interaction with the cation. In **169** the (O—)H···N distance is only 2.57 Å.

In complexes **158** and **159** (protonated species **171** and **172**) the cation is bound directly to the sulphur atom with conformations **150** and **151**, respectively, for the sulphinamide. Here, the S=O bond length progressively decreases with increasing cation binding strength by 0.02–0.03 Å per step. This shortening is presumably due to cation induced back-donation of electron density from the oxygen atom to sulphur, which enhances the covalent double-bond character of the S=O bond compared to its original semi-polar nature. Tables 38 and 41 confirm the reduced negative charge on the oxygen atom in these cases, compared to the cation-oxygen bonded systems. For comparison, the calculated atomic charges on oxygen in rotamers **150** and **151** are −0.685 and −0.683, respectively. Complexes **158** and **159** have the smallest atomic charge on Au which probably reflects a more covalent interaction of the metal ion with the sulphur atom relative to oxygen or nitrogen coordination.

The S—N bond length in the sulphinamides (1.738 Å and 1.741 Å in **150** and **151**, respectively) is also found to progressively decrease upon Au^+ complexation and protonation at the sulphur atom, again by about 0.03 Å per step. Here too, the explanation involves increased double-bond character of the S—N bond when cation attachment to the sulphur atom attracts electron density from the adjacent nitrogen lone pair of electrons. The nitrogen atom atomic charge (−0.610 and −0.585 in **150** and **151**, respectively) is found (Tables 38 and 41) to decrease progressively in going from the bare sulphinamides to the complexes and protonated species.

Finally, cation attachement to the nitrogen atom in sulphinamide **150** to give structures **160** and **170** is, of necessity, *trans* to the S=O bond across the S—N axis. The S—N bond length increases (1.738 Å → 1.802 Å → 1.906 Å) upon Au^+ complexation and protonation, respectively, as expected. The cation localizes the electron density on the nitrogen atom, reducing any contribution it may make to the double bond character of the S—N bond. The S=O bond length is seen to decrease (1.488 Å → 1.461 Å → 1.444 Å) with increased cation bonding strength ($Au^+ \rightarrow H^+$). As mentioned above, interaction

between the nb electrons on nitrogen and the σ(S=O)* MO is invoked to explain certain steroelectronic effects[3]. Thus, when this interaction is strongly reduced because of direct cation attachment at the nitrogen atom the S=O bond is strengthened, and hence shortens.

Three Au^+—HSO_2NH_2 complexes were found. The most stable in RH optimization is the oxygen coordinated structure **163** shown in Figure 75. The sulphonamide conformation is actually the (Table 35) higher-energy **153** parent form. Structure **162**, also oxygen coordinated, is only 0.6 kcal mol^{-1} above **163** (Table 36) and has the lower-energy rotamer geometry (**152**) with the N—H and S=O eclipsed bonds. This latter conformation has the amine group hydrogen atoms pointing parallel to the S=O bonds in the complex where the Au^+ is located. In both complexes the Au^+ tilts away from the amine group and the more remote location of the amine hydrogen atoms from the Au^+ in **163** compared to **162** may account for the former's slight energy advantage. This should be investigated further at a higher level of theory. A third Au^+ complex, **164**, has the cation attached to the nitrogen atom in the parent sulphonamide **153** conformation which allows an additional equivalent interaction with both S=O oxygen atoms. In both oxygen coordination complexes **162** and **163**, the cation interaction with oxygen is local to a single oxygen atom and not bridging symmetrically to both oxygen atoms. On the other hand, two protonated structures of sulphonamide are found, both having the **153** rotamer geometry. At lower energy, **173** is attached to one oxygen atom (with a long 2.87 Å interaction distance with N) while in **174** the amine nitrogen atom is protonated.

Protonation at either the (second) or nitrogen atom shortens the S=O bond length for the different reasons enumerated above (see Tables 37, 40 and Reference 2). Au^+ coordination at one oxygen atom or at nitrogen slightly increases the other S=O bond length, probably due to long-range interaction of its oxygen atom with the cation. Complexation or protonation at the oxygen atom decreases the S—N bond length, while cation attachment at the amine nitrogen atom lengthens it.

Protonation of the aminesulphenic acids (**154** and **155**) at the sulphur atom gives the XS(O)Y structures **167–169**, which have already been discussed above with regard to oxygen protonation of the sulphinamides. Protonation of rotamer conformation **154** at the oxygen atom gives structure **176**, while protonation at the nitrogen atom of rotamer **155** results in structure **175**. In each case the alternative atom site protonation of the parent rotamer is unfavourable because of the proximity of other hydrogen atoms. As usual, the oxygen protonated species is the more stable. Complexation of Au^+ to the aminesulphenic acids was found to take place preferentially at the sulphur atom of rotamer **154**. Two equilibrium structures were found at the RHF level (**165** and **166**) and the latter, which is calculated more stable, is shown in Figure 76. The two Au^+–sulphur attached structures differ essentially in the orientation of the hydroxyl group hydrogen atom to Au^+, which is spatially more remote in **166**. The smaller Au^+—S—O angle in **166** (97.4°, Figure 76) compared to 106.3° in **165** suggests a residual $Au^+ \cdots O(-H)$ stabilizing interaction which is supported by the more negative atomic charge calculated on the oxygen atom for **166** compared to **165** (Table 38).

Of course, in the divalent sulphides the charge on the sulphur atom (Table 38) is relatively low (+0.23 and +0.25, respectively, for **154** and **155**). The covalency of the Au^+–sulphur bonding is reflected in the low atomic charge on Au in the complexes (Table 14). This covalent interaction with the more polarizable sulphur atom is apparently stronger than the more electrostatic interactions with the acidic oxygen or amine nitrogen atoms. It thus seems that in XSY system the preferred site of metal cation coordination is at the sulphur atom.

The N-protonated sulphenamide (**175**) has a longer S—N bond (1.819 Å) and shorter S—O bond (1.607 Å) length (Table 40) than its parent (**154**) conformer (1.727 Å and

1.662 Å, respectively). The O-protonated structure (**176**) has shorter S—N and longer S—O bond lengths than its parent (**154**) conformer (1.750 Å and 1.647 Å, respectively). The three types of sulphur compounds, XSY, XS(O)Y, XSO_2Y behave consistently in their geometry changes upon metal ion complexation or protonation.

Table 42 allows a cross comparison of calculated protonation and Au^+ coordination binding energies (at the RHF level without BSSE correction) to a XSY, XS(O)Y and XSO_2Y systems, for the different possible attachment sites of oxygen, nitrogen and sulphur. As with the hydrogen-bonded dimer and water complex (Section 7) systems, the largest calculated binding energy is for the XS(O)Y, both for protonation and metal ion coordination. Here, persumably, this preference is due to the higher ionicity of the S=O oxygen atom. Cation attachment at the sulphur atom is favoured in XSY over XS(O)Y and is not found at all for XSO_2Y. This latter result can be attributed to the strong increase in the atomic charge on the sulphur atom in XSO_nY with increasing value of n, as well as the decreasing availability of lone-pair electrons on sulpur[39]. The dissociation energy of a cation from the nitrogen atom is largest for XSY and smallest for XSO_2Y. This trend correlates with the availability of the nitrogen lone pair of electrons for interaction with the cation, in competition with its contributing to the partial double-bond character of the N—S bond. The order of site attachment preference for XSY and XSO_2Y is oxygen > nitrogen > sulphur. For XSY the order is sulphur > nitrogen > oxygen, which can be explained by a combination of low positive charge on sulphur (together with its large polarizability), smaller negative atomic charge on oxygen and the more concentrated lone pair of electrons on the nitrogen atom.

As was mentioned in the previous section on hydrogen bonding, MP2 (correlation) usually reduces the equilibrium bond length for weak interactions. To gauge the magnitude of this effect the Au^+–atom bond distance was MP2 optimized for the lowest-energy complex of a given class, fixing all the other geometric parameters at the RHF (metal complex) optimized values. The results are given in the footnotes to Table 37. For the metal–sulphine the reduction in Au—O distance in **156** is 0.08 Å and a further (MP2) stabilization of 0.6 kcal mol^{-1}. For the sulphone (**163**) the Au—O distance decreases by 0.10 Å and the binding energy increases by 0.8 kcal mol^{-1}. Both metal ion complexes of the sulphene were optimized in this way. The Au—S bond decreases by 0.12 Å in both cases (**165** and **166**) and the MP2 dissociation energies are enhanced by 1.3 kcal mol^{-1} each. These results can serve as guidelines for estimating the effect of MP2 optimization on the cation–substrate equilibrium distance and interaction energy.

Table 43 shows the effect of correcting the RHF binding energies for BSSE and also presents the MP2 binding energies at the RHF optimized geometries, after BSSE correction. Only the lowest-energy complex of each type sulphur compound is listed. On the RHF level, comparing with Table 42, BSSE correction reduces the calculated complex binding energies by only 0.7–0.9 kcal mol^{-1}. The increase in binding energy in going to the MP2 level is more substantial, especially for Au^+—$HOSNH_2$ (**166**), with the metal ion coordinated to the sulphur atom, where the increase is 11.1 kcal mol^{-1}. The Au^+–substrate dissociation energies for the oxygen (O=S) coordinated sulphine (**156**) and sulphone (**163**) increase by only 2.4 – 4.6 kcal mol^{-1} in going from the RHF to MP2 levels. The much larger effect of MP2 specifically on the sulphur coordinated sulphene complex was also seen in one-dimensional optimization of the Au^+-coordination site atom bond distance discussed above. For the sulphinamide, where metal ion complexation to sulphur was also found (**158** and **159**), the RHF energy differences between (the lower energy) **158** and the most stable oxygen bound complex (**156**) in Table 42 is 18.1 kcal mol^{-1}. This gap is probably too large to be overcome by MP2. Nonetheless, metal ion coordination to sulphur needs to examined further at the MP2 level.

IX. ACKNOWLEDGEMENTS

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CHAPTER 2

Structural chemistry of organosulfur compounds

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Supplement S: The chemistry of sulphur-containing functional groups,
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I. INTRODUCTION

This review treats the geometrical aspects of molecular structure, which are quantitatively described in terms of bond lengths, bond angles and torsional angles. Experimental results are surveyed; theoretical calculations are involved only when they are used in conjunction with experimental techniques or for the interpretation of results. Two qualitative models have been widely used to understand and even predict molecular structure and the trends in its changes: the Valence-Shell Electron-Pair Repulsion (VSEPR) model[1,2] and considerations of nonbonded intramolecular interactions[3].

The structures of different classes of organic sulfur compounds have been reviewed in previous volumes of this series[4-9]. Some data on their molecular geometry are also found in other chapters and in volumes on analogous compounds (functional groups with O, Se, Te). A recent chapter[8] and monographs have reviewed the structures of sulfur-containing free molecules[10-14].

This chapter focuses on results of recent gas-phase studies, first because these include the simplest molecules of fundamental importance, and also because it is the free molecules where the structure is governed solely by intramolecular forces. As to the structures of molecules in the crystal, studying the effect of intermolecular interactions is of principal interest and helps to understand real structures and processes in solid and liquid phases, in chemical and biological systems. All this motivates studies of subtle changes in molecular structure, effects of substituents and crystal environment[15].

There is a vast amount of structural data. Through 1991 the Cambridge Structural Database contains about 90,000 organic and organometallic structures from X-ray and neutron crystallographic studies, and 19% of the entries involves a sulfur atom. One must be content with some subjectivity in the choice, and I attempted to include mainly basic and characteristic molecules from X-ray-diffraction studies. Reference to gas-phase studies from 1987 through 1991 should be nearly complete. The start of the period has been partly adapted to the coverage of previous reviews, first of all in this series, on a given class of compounds, to minimize overlap and produce a self-contained text at the same time.

The three basic experimental methods of structure determination and the nature of structural parameters obtained and their uncertainties were discussed briefly in a previous review in this series[5]. These are electron diffraction (ED) and microwave spectroscopy (MW) for the gas phase and X-ray diffraction (XD) for crystal structures. Further details on these and other experimental and computational techniques of structure elucidation and on the physical meaning of parameters can be found in some more recent books[1,15-19]. The different representations of molecular geometry (r_e, r_a, r_g, r_α, r_0, r_s, r_z etc.) will be indicated in the following sections, and they have to be taken into account for exact comparisons. However, we shall usually not be concerned with the different physical meanings of structural parameters. Error estimates will be given in parentheses in units of the last digit quoted; the original papers have to be consulted to ascertain their different definitions.

Torsional angles (dihedral angles) and their signs are defined in different ways in the publications reviewed. All such data have been transformed here, when possible, to meet the IUPAC convention[20] (Figure 1). SI units are preferred. The Ångström seems to be more commonly used in structural work than pm, $1\ \text{Å} = 100\ \text{pm} = 10^{-10}\ \text{m}$. The calorie has been converted into joule, $1\ \text{cal} = 4.184\ \text{J}$; this has changed the meaning of significant digits in the original data. Energy difference is often given as the wave number of the associated radiation, $1\ \text{cm}^{-1}$ for $11.96\ \text{J mol}^{-1}$. Following recent recommendations, the spelling 'sulfur' is used[21].

Structures will be discussed and classified according to the bonding situation around the sulfur atom, its coordination number first of all[12]. Of course, not each structure fits unequivocally into this scheme.

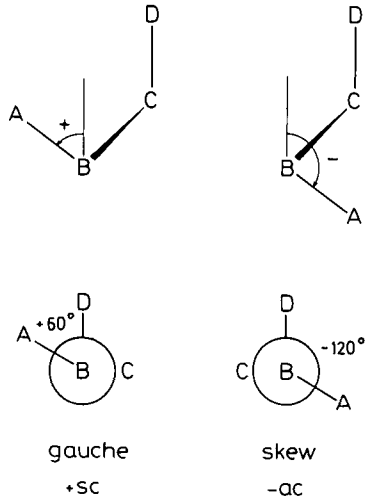


FIGURE 1. Conformations of the A—B—C—D chain: examples of a *gauche*, $+sc$ (*synclinal*) form with a dihedral angle of $+60°$ and a *skew*, $-ac$ (*anticlinal*) form with $-120°$. Simplified perspective views (above) and Newman projections (below)

II. ONE-COORDINATED SULFUR

A. Thiocarbonic Acid Derivatives

The structures of free thiocarbonyl halides and other simple derivatives have been discussed in detail in Reference 12. Bond lengths and bond angles, including some more recent data, are summarized in Table 1.

The C=S bond is shorter for more electronegative substituents, and the bond angles are also in accord with the postulates of the VSEPR model[1]. When oxygen replaces sulfur, no definite trends in the other bond lengths and in the bond angles can be observed because of the similar electron distributions around the carbon atom in the thiocarbonyl and the carbonyl groups[12,30].

Thiourea forms honeycomb-like channels in crystalline adducts, which may house guest molecules in different types of disorder. The structure of the adduct $CCl_4 \cdot 3SC(NH_2)_2$ has been determined at 170 K by XD[31]. The thiourea molecules are connected by N—H···S hydrogen bonds with angles from 156 to 169° (Figure 2). A Coulombic interaction is proposed between coplanar atoms involving the CCl_4 carbon and the three sulfur atoms pointing to it. The threefold disorder of CCl_4 within the thiourea channels is shown in Figure 3. Bond length C=S is 1.727(5) Å, angle S=C—N 120.5(4), 120.2(3)°. The mean C=S bond length in thioureas is 1.681 Å with a sample standard deviation of 0.020 Å over a sample of 96 observations, based on a comprehensive statistical analysis of bond lengths in organic molecules in the Cambridge Structural Database[32]. Honeycomb structures are also found in selenourea adducts[33].

TABLE 1. Structural parameters[a] of thiocarbonyl derivatives $X^1C(S)X^2$

Molecule		C=S(Å)	X^1—C=S(deg)	X^2—C=S(deg)	X^1—C—X^2(deg)	Reference
HC(S)H	r_z	1.6138(4)	[121.86]	[121.86]	116.27(10)	22
HC(S)H	r_e	1.6110(8)	[122.05]	[122.05]	115.9(11)	18, 23
FC(S)F	r_z	1.587(2)	[126.5]	[126.5]	106.89(11)	24
FC(S)Cl	r_g	1.593(1)	123.6(1)	127.3(1)	[109.1]	25
ClC(S)Cl	r_z	1.602(5)	[124.4]	[124.4]	111.2(3)	26
BrC(S)Br	r_a^0	1.597(5)	[124.2]	[124.2]	111.6(4)	27
$HC(S)NH_2$	r_s	1.626(2)	127(5)	125.3(3)	108(5)	28
HC(S)OMe	r_a	1.612(3)	[126.7]	126.6(5)	106.7(28)	29

[a]Parameters in brackets have been calculated from the original data.

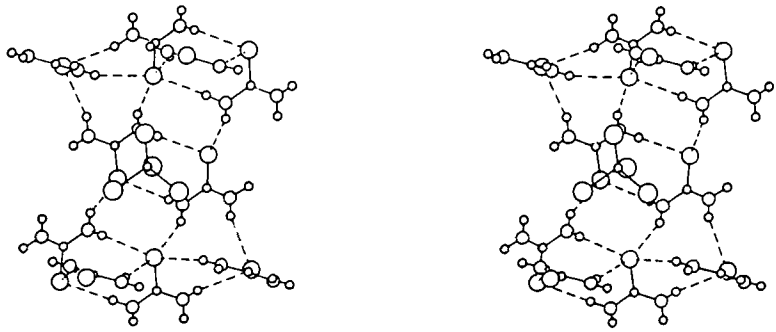


FIGURE 2. Hydrogen bonding in the channel wall of the adduct $CCl_4 \cdot 3SC(NH_2)_2$ and one of the CCl_4 orientations. Stereoview, reproduced by permission of the International Union of Crystallography from Reference 31.

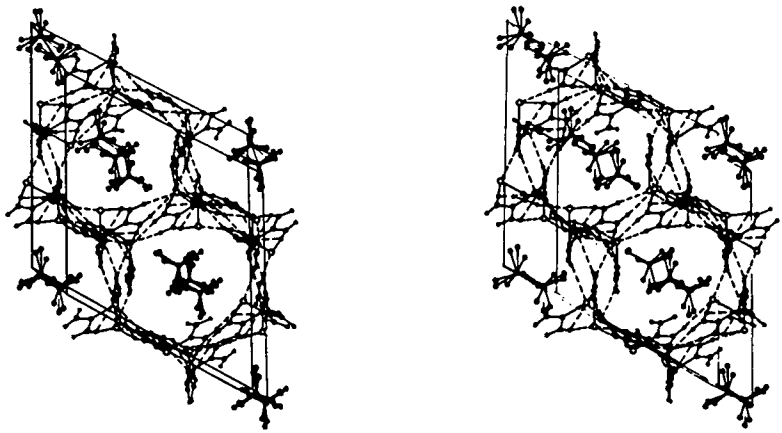


FIGURE 3. Thiourea channels and the threefold disorder of CCl_4 in the trigonal $R\bar{3}$ crystal of $CCl_4 \cdot 3SC(NH_2)_2$. Stereoview tilted about 20° from the threefold symmetry axis. Reproduced by permission of the International Union of Crystallography from Reference 31

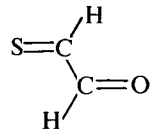
B. Thioaldehydes and Thioketones

Since existing data were reviewed[12], there have been only few gas-phase experimental studies on simple, often unstable molecules.

Thioacrolein, $CH_2{=}CHCHS$, has a planar structure with *anti* position of the double bonds[34]. The C=S bond length could be determined by MW spectroscopy with large uncertainty, r_s 1.61(2) Å.

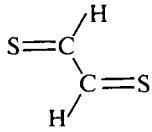
Thiopropynal, HC≡CCHS, was generated by the pyrolysis of dipropargyl sulfide and studied by MW spectroscopy[35]. The C=S bond length is 1.620 Å.

The *anti* form of thioglyoxal (**1**) has been identified by MW, and two of its parameters could be estimated[36]. The C=S bond is relatively short, 1.589 Å, angle C—C=S is 122.7°. A nearly *syn* form with higher energy and an S=C—C=O dihedral angle of about 10° is also predicted by *ab initio* 6-31G** calculations[36]. Glyoxal, the oxygen analog, exists

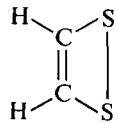


(1)

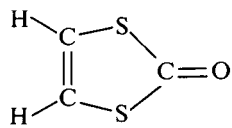
in *syn* and *anti* form, and the C=O bond length in the latter, r_g 1.212(2) Å[37], is the same as in propynal, r_g 1.214(5) Å[38]. High-level *ab initio* calculations predict[39] that the *anti* form of dithioglyoxal (ethanedithial) (**2**) is more stable than the *gauche* form and their cyclic valence isomer, 1,2-dithiete (**3**). Matrix IR, PES and MW studies of the pyrolysis of 1,3-dithiole-2-one (**4**) indicate, however, that **3** is produced and not the open-chain isomers[39a]. In *anti* **2**, bond C=S is 1.631 Å, angle C—C=S 123.3° from MP2/6-31G* calculations[39b].



(2)

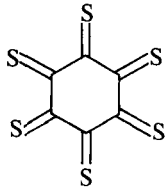


(3)



(4)

Analogously, the dithiete-like quinonoid **6** or symmetric isomers **7** are more stable than the planar or chair-form cyclic hexathioketone **5** expected in mass spectrometric, photolytic or pyrolytic processes[40]. Geometries and energies of C_6S_6 and C_6O_6 isomers have been obtained from *ab initio* calculations[40]. On the other hand, the planar hexaketo form is the most stable isomer of C_6O_6[40a].



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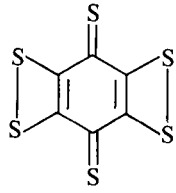

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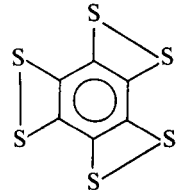
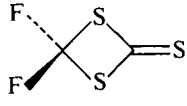


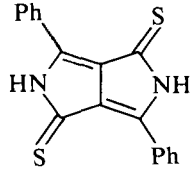
(7)

In 4,4-difluoro-1,3-dithietane-2-thione (**8**), the C=S bond r_a 1.598(5) Å is shorter than in acyclic derivatives as the S—C(S)—S angle closes to 99.2(6)° and carbon hybridization changes upon formation of a planar ring[41].

Evaporated films of 3,6-diphenylpyrrolo[3,4-*c*]pyrrole-1,4-dithione (**9**) find application,



(8)



(9)

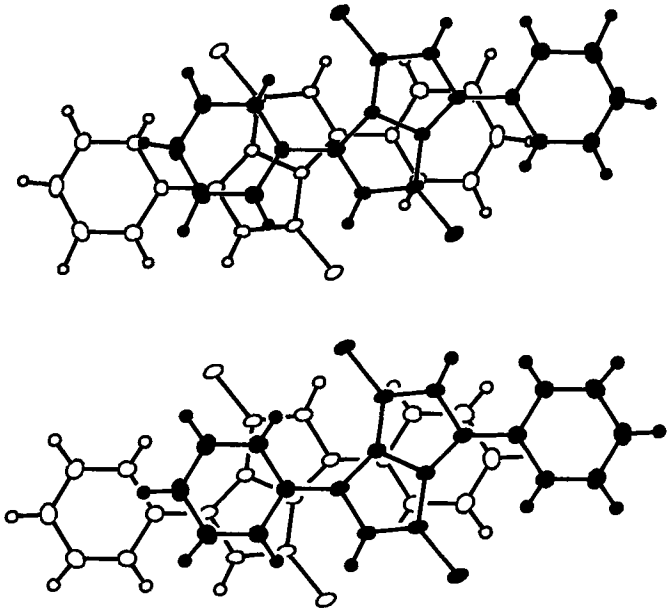


FIGURE 4. The overlap of two molecules along the stacking axis in the crystals of **9**: modification I (above) and modification II (below). Reproduced by permission of the International Union of Crystallography from Reference 42

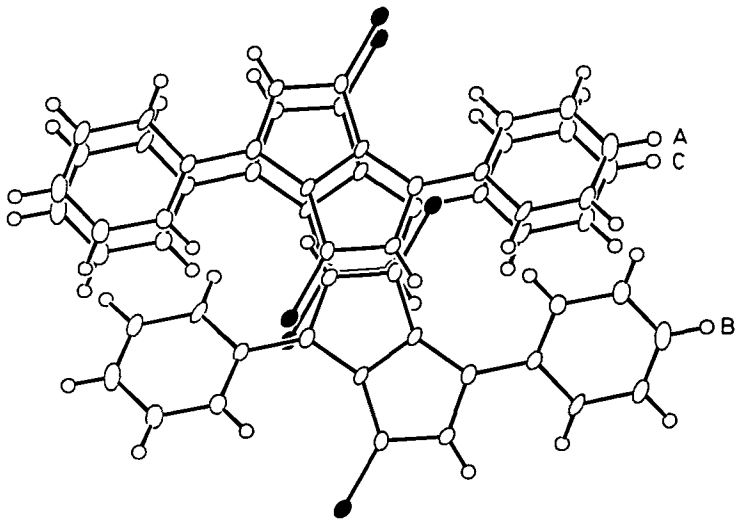


FIGURE 5. The overlap of molecules A, B and B, C along the *b* axis in modification III of **9**. Reproduced by permission of the International Union of Crystallography from Reference 43

among others, as excellent photoconductors for laser printers (see References 42 and 43 and references cited therein). There are slight differences in the molecular dimensions in the three modifications studied by XD[42,43]. Bond C=S is 1.660(3), 1.664(3) and 1.654(5) Å in modifications I, II and III[43], respectively. The molecules possess C_i crystallographic symmetry in I and II, C_2 symmetry in III. The phenyl rings are rotated by 13.3(5), 6(1) and 30.1(2)° in I, II and III from the plane of the fused heterocyclic rings, which are slightly nonplanar in the latter case[43] with a dihedral angle of 5.4(1)°. The N—H···S angles in the intermolecular hydrogen bonding are 162(3), 150(4) and close to 180° in I, II and III[43]. Molecules within the stacks lie parallel in I and in a zigzag fashion in II, and in both modifications the heterocyclic core of a molecule overlaps with the phenyl rings of neighboring molecules along the stacking axis (Figure 4). Modification III, which is obtained by solvent-vapor treatment, is the only phase that exhibits a drastically increased photoconductivity and near-IR absorption. The molecular packing in III is strikingly different from that in I and II. Molecules in the columns along the *b* axis overlap at the bonds S=C, (S)C—N, N—C(Ph) and N—H of the heterocyclic system (Figure 5), and hydrogen bonding is stronger than in I and II as seen from the bonding angles above.

C. Carbon Disulfide, Thioketene and Related Structures

Structural data of CS_2 and its O, Se, Te analogs have been compiled[12,18,33]. Only C=S bond lengths should be cited[18] here, in CS_2 r_g 1.5592(22) Å and r_e 1.55256 Å, in OCS r_e 1.5606(20) Å.

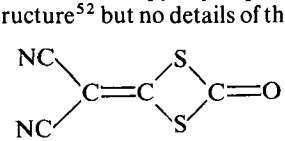
The bond lengths in propadienonethione, O=C=C=C=S (**10**), from a MW study[44] are in turn: r_s 1.1343, 1.2696, 1.2540 and 1.5825 Å. The C=C bond at the carbonyl group is longer. One of the aims of studying this molecule, like many other types of simple organic molecules, was to identify it in interstellar space[45].

Molecules S=(C=)$_n$S and oxygen analogs with cumulated double bonds have been characterized in spectroscopic and *ab initio* studies[46]. The electronic structure changes with the number of carbon atoms. An interesting finding is that, contrary to Hund's rule, the singlet state of S=C=C=S seems to be lower in energy than the triplet state[46a]. The calculated C=S bond lengths are 1.562 and 1.573 Å for the two states, respectively.

Ketene and thioketene belong to the most extensively studied simple molecules. Their zero-point average structures (r_z) have been reported recently[47,48]. Here corrections were applied to the ground-state inertial constants: vibrational and centrifugal distortional corrections from new experimental and *ab initio* force fields, and even electronic corrections to account for off-axis π-bond and lone-pair electrons! The C—H bonds lengthen from ketene to selenoketene[49] (Figure 6), implying increasing p character[48], while concomitant trends of closing H—C—H angles and shortening C=C bonds may be partly concealed by uncertainties or different meanings of the parameters. For comparison, the r_0 parameters of allene[50] are: C=C 1.3084 Å, C—H 1.087 Å and H—C—H 118.2°.

Three sets of parameters have been reported in a MW study of methylthioketene, $CH_3CH=C=S$; r_0 (C=S) 1.5576, 1.5520 or 1.5627 Å with different assumptions[51].

Dicyanothioketene, $(NC)_2C=C=S$, is a pyrolysis product of **11**. Its MW spectrum is consistent with a planar C_{2v} structure[52] but no details of the geometry could be obtained.



(**11**)

Propadienethione, $H_2C=C=C=S$ (**12**), has a linear skeleton according to a MW study and in good agreement with results of *ab initio* MP3/6-31G** calculations[53]. Its

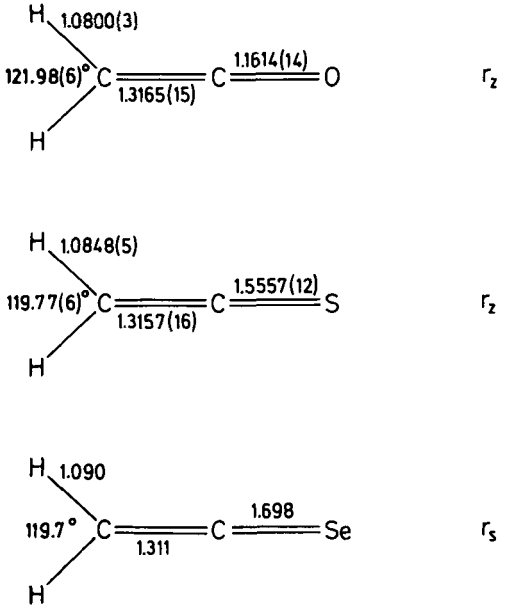
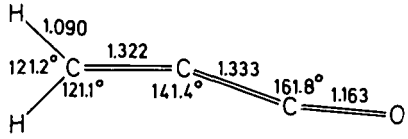
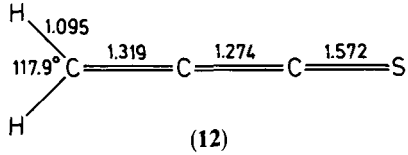


FIGURE 6. Structural parameters (Å, deg) of ketene[47], thioketene[48] and selenoketene[49]

oxygen analog, propadienone (**13**), is kinked on the other hand[54], contrary to the classical expectation for cumulated double bonds. The double-bonded chain is linear again in butatrienone[55]. A high level of *ab initio* calculation with electron correlation is needed to account for these features properly[53]. Structural parameters of **13** and **12** are shown in Figure 7. The C=C(=O) bond is longer than the C=C(=S) bond, similarly to the case of **10**. As the number of carbon atoms increases, the dipole moment alternates parallel in the oxo and thioxo series[53], indicating an alternating change in the electronic structure.



(**13**)



(**12**)

FIGURE 7. r_s parameters (Å, deg) of **13** and **12**, both from Reference 53

D. Isothiocyanates

A comprehensive review on the structures of free and crystalline isocyanates and isothiocyanates was published in this series[5]. Gas-phase structures were discussed in detail in a more recent book[12]. Interest in these systems has continued: new molecules have been studied and several structures have been redetermined.

The puzzling disagreement between conclusions from spectroscopic and ED studies of silyl pseudohalides used to attract much attention[5,12]. H_3SiNCO and H_3SiNCS, e.g., have linear skeletons according to vibrational[56,57] and MW spectroscopic studies[58,59] but are found by ED to be bent at nitrogen[60].

Pseudohalides RNCY (as well as RNNN), Y = O, S, Se, perform low-frequency large-amplitude bending vibrations at the nitrogen attached to R. The behavior of the molecule depends on the form of the bending potential function and on the positions of the vibrational energy levels (Figure 8). Even if a molecule is linear in equilibrium, i.e. at the minimum of potential energy (Figure 8a), it appears bent by ED, due to the very short time-scale (10^{-20} s) of electron scattering and the averaging (apparent shortening, 'shrinkage') of nonbonded internuclear distances over the large-amplitude bending vibrations of the linear chain. A molecule with two potential minima and a sufficiently high barrier between them (Figure 8c) is definitely bent. Figure 8b shows an example of an intermediate case.

Molecules H_3MNCY can be positioned, even quantitatively, between the two extremes 'linear' and 'bent' on the basis of their characteristic rotational spectra[61]. A recent model of quasi-symmetric top molecules includes bending of the M—N=C chain and internal rotation of the H_3M group about the M—N axis[61]. Parameters of the bending potential functions may serve the classification of molecules (Table 2).

In accord with an analysis of the potential function from ED data (in 1972), H_3SiNCS is a linear molecule with harmonic bending vibration; H_3SiNCO is quasi-linear, i.e. albeit it has a double minimum in the potential energy, the hump at Si—N=C of 180° is about as high as the ground-state vibrational level[60] (Figure 8b). The shrinkage effect completely explains the apparent deviation from linearity found in both molecules[60]. H_3CNCSe is another typical quasi-linear molecule (Table 2). H_3CNCS represents different cases in itself: in the ground vibrational state it behaves like a bent molecule, while from the second

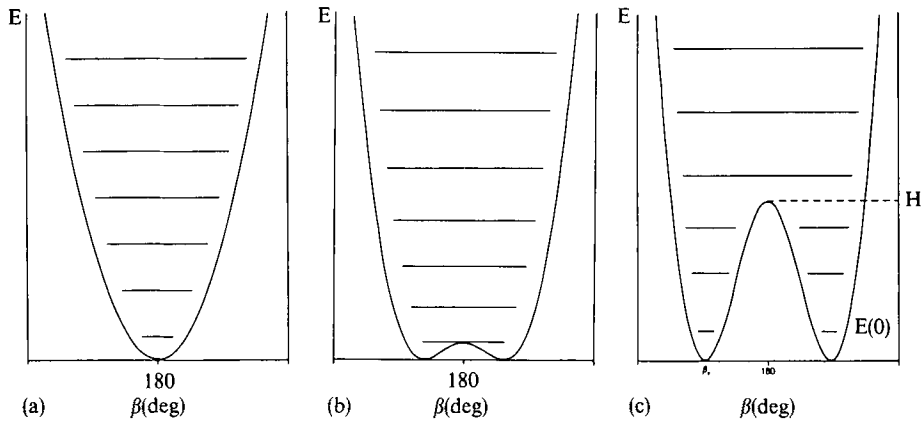


FIGURE 8. Schematic bending potential energy (E) curves and vibrational energy levels of a (a) linear, (b) quasi-linear and (c) bent molecule. ($180° - \beta$) is the angle of bending, β_e the equilibrium bond angle, H the height of the potential barrier, $E(0)$ the energy of the ground vibrational state. Drawn after Reference 61

TABLE 2. Some characteristics of the large-amplitude bending vibration in H_3MNCY molecules[a]

	H_3SiNCS	H_3SiNCO	H_3CNCSe[b]	H_3CNCS[c]	H_3CNCO[d]
H (cm^{-1})	0[e]	20[g], 32[e]	25	193	928
$E(0)$ (cm^{-1})		22[g]	28	53	90
ν_{10} (cm^{-1})	66[f]	15[h]	29		
V_3 (cm^{-1})	0[e]	0[e]	3	2	21
β_e (deg)	180[e]	159[i]	162	151	140
β(ED) (deg)	164[g]	152[g]		142[j]	140[j]

[a] H is barrier to linearity, $E(0)$ energy of ground vibrational state above minimum, ν_{10} wave number of M—N=C bending fundamental vibration, V_3 barrier to internal rotation, β_e equilibrium bond angle M—N=C (at the minimum of potential energy), β(ED) effective bond angle from ED (shrinkage effect not considered). Rounded values from the original data.
[b] Reference 62.
[c] Reference 63, one of two models.
[d] Reference 64, one of two models.
[e] Reference 61.
[f] Reference 57, observed.
[g] Reference 60.
[h] Reference 56.
[i] Reference 65.
[j] Reference 66.

excited state upwards, which lies higher than the barrier to bending, it approaches the linear case[61]. The rotational spectrum of H_3CNCO, in its lower vibrational states, is close to that of a bent molecule. It may be noted that kT/hc is about 210 cm^{-1} at 300 K, and hence several excited bending vibrational states in these molecules are populated at normal experimental conditions (cf. Table 2). In this series of molecules, the torsional barrier V_3 increases as the barrier to linearity H gets higher (Table 2). For a really bent molecule, methylthiocyanate, H_3CSCN, H is estimated[61] to be 6300 cm^{-1}, V_3 is 560 cm^{-1} and angle CSC 99.0(1)°[67].

Structural data of free isothiocyanate molecules and oxygen and selenium analogs are compiled in Figure 9 and Table 3.

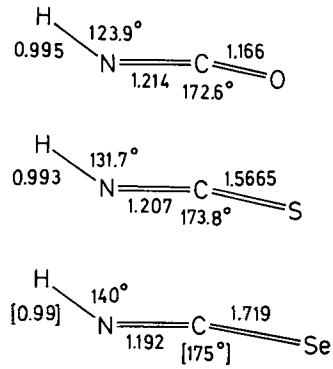


FIGURE 9. The r_s structures (Å, deg) of free isocyanic[68,69], isothiocyanic[70] and isoselenocyanic acid[71]. Assumed values are in the brackets [ ]

TABLE 3. Bond lengths and bond angles in isocyanates, isothiocyanates and isoselenocyanates from gas-phase studies

R—N=C=Y		C=Y(Å)	N=C(Å)	R—N(Å)	R—N=C (deg)	Reference
		C=O		C—N	C—N=C	
MeNCO[a]	r_a	1.202(5)	1.168(5)	1.450(4)	140.3(4)	66
EtNCO[b]	r^*_{av}	1.174(4)	1.218(5)	1.448(9)	132.2(22)	72
i-PrNCO	r_a	1.184(4)	1.214(6)	1.460(8)	132.6(10)	73
ClC(O)NCO	r_a	1.139(16)	1.218(23)	1.384(6)	127.1(16)	74
				Si—N	Si—N=C	
H_3SiNCO[c]	r^*_s	1.160(6)	1.221(12)	1.706(9)	180	58
MeH_2SiNCO	r_a	1.169(18)	1.213(23)	1.718(2)	151.7(16)	75
$Me_2HSiNCO$	r_a	1.155(4)	1.218(4)	1.719(5)	153.5(13)	76
Me_3SiNCO	r_a	1.176(10)	1.202(16)	1.740(4)	156.9(30)	77
				Ge—N	Ge—N=C	
H_3GeNCO	r_0	1.182(20)	1.168(27)	1.826(15)	143.2(34)	78
				P—N	P—N=C	
F_2PNCO[d]		1.175(5)	1.218(6)	1.678(4)	132.0(12)	79
		C=S		C—N	C—N=C	
MeNCS	r_a	1.597(5)	1.192(6)	1.479(8)	141.6(4)	66
EtNCS[b]	r^*_{av}	1.580(4)	1.187(5)	1.438(7)	147.4(20)	72
i-PrNCS	r_a	1.598(5)	1.201(6)	1.459(13)	135.9(17)	73

C_3H_5NCS[e]						
anti	r_{av}	1.574(3)	1.193(3)	1.387(5)	149.1(15)	80
syn	r_{av}	1.574(3)	1.193(3)	1.413(5)	150.8(17)	80
				Si—N	Si—N=C	
H_3SiNCS	r_s	1.5745	1.2208	1.6725	180	59
MeH_2SiNCS	r_a	1.578(3)	1.195(4)	1.724(6)	156.4(16)	75
$Me_2HSiNCS$	r_a	1.579(5)	1.212(5)	1.723(8)	154.7(22)	76
Me_3SiNCS	r_a	1.587(4)	1.191(6)	1.743(6)	158.2(10)	81
				Ge—N	Ge—N=C	
H_3GeNCS	r_s	1.542(20)	1.144(15)	1.817(15)	180	82
				P—N	P—N=C	
F_2PNCS[d]		1.522(7)	1.248(4)	1.690(7)	138.7(6)	79
		C=Se		C—N	C—N=C	
MeNCSe	r_0	1.708[f]	1.205(10)	1.447(9)	157.0(40)	83
EtNCSe	r_0	1.709[f]	1.210(10)	1.444(10)	158.0(30)	84
				P—N	P—N=C	
F_2PNCSe	r_α	1.681(10)	1.212(8)	1.649(12)	149.0(15)	85

[a] Bond lengths C=O and N=C are possibly interchanged[72,73], see text.
[b] From ED + MW data, corrected for the effects of zero-point torsional vibration.
[c] Corrected for the effects of large-amplitude Si—N=C bending.
[d] From combined ED and liquid-crystal NMR data, without vibrational corrections.
[e] C_3H_5 = cyclopropyl.
[f] Assumed.

The structures of the free acids HNCO, HNCS and HNCSe have been determined by MW spectroscopy (Figure 9). The three molecules are bent at =C= with *E (trans)* configuration of the chain, and they tend to be more linear, both at =C= and at —N=, from the O through the Se derivative. It seems, too, that the slightly bent structure of N=C=Y (with the *E* form of R—N=C=Y), where it has been determined at all, is real in alkyl isocyanates and isothiocyanates[73,80], and is not only an artifact due to shrinkage effects.

H_3SiNCO has been found to be bent by matrix IR spectroscopy[86]. From an XD study at 140 K, angle Si—N=C is 158.4(5)° and the N=C=O chain is slightly bent with 176.4(6)° in a *trans* Si—N=C=O sequence[87]. Vibrational spectra of the trimethylsilyl derivatives have been interpreted in terms of C_{3v} symmetry with a linear Si—N=C chain[88]. However, Me_3SiNCO is bent in the crystal at −90 °C with Si—N=C 163.7(6)° and N=C=O 177.6(8)°[89]. The apparent bending at nitrogen in silyl and in some alkyl derivatives, as obtained by ED, is consistent[73,75,77,81] with a linear or a quasi-linear molecule performing large-amplitude bending vibrations. It should be noted that gas-phase ED yields the thermal averages of structural parameters and cannot really distinguish between a linear equilibrium structure and a quasi-linear molecule with a small hump in the potential function. (The ED study of SiH_3NCO and SiH_3NCS is a rare exception[60].)

Quantum chemical calculations reflect the features of these flexible molecules adequately only when electron correlation is considered and rigorous convergence criteria are used at geometry optimization[74,90,91]. Photoelectron spectra and the molecular geometries of methyl and methylsilyl derivatives have been interpreted by *ab initio* MP2/4-31G* calculations[91a,92]. In good agreement with experimental MW data, the equilibrium geometries of MeNCY, Y = O, S, Se, and EtNCO are bent. The change in the electronic structure from O to S and Se can be expressed[91a] by formulae **14a** and **14b**:

(14a) **(14b)**

The data in Table 3 indicate a widening of the R—N=C angle, indeed, from Y = O to Se but the decreasing trend in the N=C bond lengths, present in the calculated values[91a] and in the acids HNCY (Figure 9), is not clear in the experimental data. (Similar internuclear distances like N=C and C=O in isocyanates are not well determined from ED because of parameter correlation[12]. Thus, magnitudes of N=C and C=O in MeNCO[66], Table 3, should probably be reversed[72,73].) The Si—N bonds lengthen with the increasing number of Me substituents on silicon[75] (Table 3).

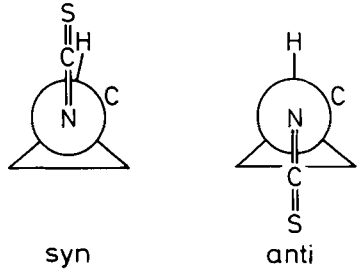
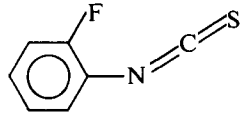


FIGURE 10. The conformers of cyclopropyl isothiocyanate with N=C=S and C—H in *syn* position (*trans* form in the original paper[80]) and in *anti* position (*cis* in the original)

Alkyl and silyl derivatives seem to have different conformational properties. In EtNCY and *i*-PrNCY, Y = O, S, the N=C bond tends to eclipse one of the C—C bonds[72,73]. The effective conformation of the apparently bent methylsilyl derivatives, on the other hand, is close to forms with an eclipsed Si—H and N=C bond[75]. Cyclopropyl isothiocyanate exists at 35 °C as a mixture of *syn* and *anti* form, with 72(5) percent *syn*[80] (Figure 10). The *syn* conformer is more abundant in 2-fluorophenyl isothiocyanate (**15**) and the C—N=C angle is estimated to 147° from a low-resolution MW study[93]. Only the *syn* form is present in the corresponding isocyanate, due to an electrostatic intramolecular interaction[94].



(**15**)

E. Thiocarboxylic Acid Derivatives

Parameters of two thioformic acid derivatives are shown in Table 1 (Section II.A). The structure of thioacetamide, $CH_3C(S)NH_2$, has been determined both in the gas phase[95] and in the crystal[96]:

	C=S(Å)	C—N(Å)	C—C(Å)	N—C=S(deg)	C—C=S (deg)
ED	1.647(3)	1.356(3)	1.512(4)	122.3	122.9(3)
XD	1.713(6)	1.324(8)	1.494(8)	121.6(4)	120.7(4)

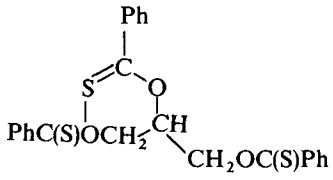
Apart from the uncertainties and different physical meanings of the parameters, a lengthening of the C=S bond and corresponding changes in adjacent bonds and angles occur in the crystal, due to N—H···S hydrogen bonds[95]. Similar structural changes and formation of N—H···O bonds are observed in acetamide upon crystallization[97]. The CH_3 group eclipses the double bond in both molecules.

Silyl *O*-thioacetate, $MeC(S)OSiH_3$ (**16**), has been studied by XD at 130 K and by ED at room temperature[98]. The heavy-atom skeleton is nearly planar with *syn* S=C—O—Si and a short S···Si distance. Parameters:

	C=S(Å)	O—C=S(deg)	C—C=S(deg)	C—C—O(deg)	S···Si(Å)
ED	1.615(8)	127(2)	122	111.4(8)	3.143(9)
XD	1.627(3)	123.0(2)	125.2(2)	111.8(3)	3.185(9)

Intermolecular contacts in the crystal are rather long but directional, e.g., an angle C=S···Si of 100.8(4)° is typical of bond angles in sulfides[98].

An XD study of monothiobenzoic acid *O*-esters **17**[99a], **18**, **19** and **20**[99b] sought to explain why only **17** undergoes a solid-state isomerization to the *O,S,S*- or (at 80 °C almost exclusively) to the *S,S,S*-ester. The S=C—O—C fragments are all practically planar and



(**17**)

$PhC(S)OCH_2CR_2CH_2OC(S)Ph$

	R
(**18**)	H
(**19**)	Me
(**20**)	$CH_2OC(S)Ph$

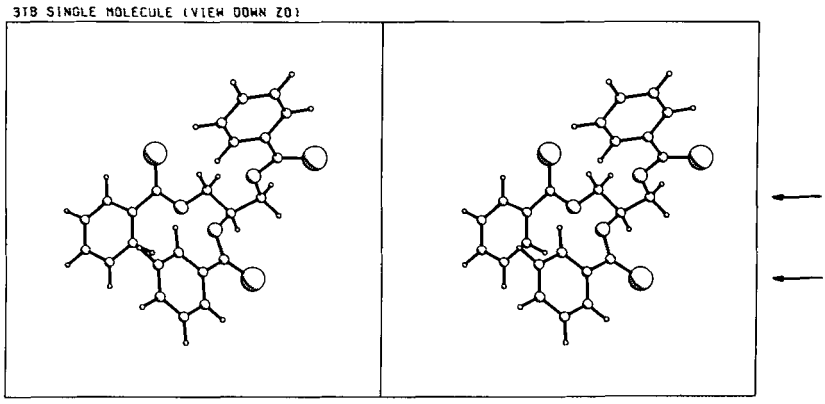


FIGURE 11. Stereoview of a molecule of 1,2,3-propantriyltris(*O*-thiobenzoate) (**17**) in the crystal. Atoms forming the short S···C distance of 3.44 Å are marked by arrows. Reproduced from a drawing kindly provided by Professor Rex A. Palmer

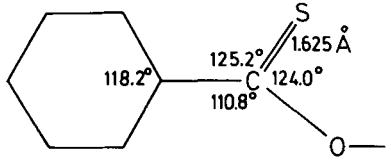


FIGURE 12. Mean values of parameters calculated from the data of *O*-thiobenzoates **17**, **18**, **19** and **20**, Reference 99

syn (*sp*, *synperiplanar*) in the four structures, and the mean planes of the attached rings are inclined by 5 to 20° to these planes. Only one of the S=C—O—C—C chains in **17** has an (*sp*, *sp*) conformation with a C—O—C—C dihedral angle of 25° and a short S···C distance of 3.44 Å (Figure 11), while all other equivalent chains in the four molecules have the (*sp*,*ap*) form and much longer S···C distances. The short S···C contact in **17** indicates a possible initial step and an *intra*molecular mechanism for the isomerization reaction. This rotational form corresponds at the same time to minimal potential energy with respect to rotation about the SC—O and O—CH bonds[99a]. Mean values of some bond lengths and bond angles (Figure 12) compare well with those in other molecules, e.g. in **16** above, and meet qualitative expectations from the VSEPR model[1]. The mean endocyclic *ipso* C—C—C bond angle is compatible with an electronegativity of the —C(S)OR substituent close to that of the carbon atom[100,101].

F. Other Structures

Some molecules, partly inorganic, will be mentioned here, in which one-coordinated sulfur is bonded to other atoms than carbon.

The pyramidal isomer of disulfur difluoride, $S{=}SF_2$, has a double bond with (p–p)π overlap, and its structure is satisfactorily described by *ab initio* SCF calculations[102]. The

molecular geometry has been determined by MW[103] (r_z) and from combined ED and rotational spectroscopic data[102] (r_{av}):

	S=S(Å)	S—F(Å)	S=S—F(deg)	F—S—F(deg)
r_z	1.8571(12)	1.6074(8)	108.02(4)	91.72(6)
r_{av}	1.856(2)	1.608(2)	108.1(2)	91.7(3)

Structural variations in molecules of the type $X_3M{=}Y$, where X is halogen or Me, Y is O, S, Se, BH_3 or a lone pair, and M is P or As, have been analyzed in Reference 12 in terms of the VSEPR model[1]. An asymmetrically substituted derivative, $CH_3CH_2P(S)Cl_2$, is a mixture of two conformers with the C—C bond either *gauche* or *anti* to the P=S bond[104]. Bond lengths, r_a P=S 1.897(2) Å among others, are similar to those in related molecules[12]. The bond angles at phosphorus are consistent with the expectations from the VSEPR model for electronegative substituents and for double bonds[1], Cl—P—C 103.1(5), Cl—P—Cl 102.0(4), C—P=S 116.1(12) and Cl—P=S (calculated from the original data) 115.2°. The r_0 parameters of the related fluoride, $CH_3CH_2P(S)F_2$, have been obtained in a MW study[105]: P=S 1.880(3) Å, F—P—C, 102.0(2), C—P=S 119.4(4) and dihedral angle C—C—P=S 56.9(2)° for the *gauche* form; P=S 1.861(7) Å for the *anti* form, which is more stable by 63(37) cm^{-1}.

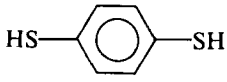
Methyl thioborine[106], MeB=S, has a linear skeleton and B=S bond length r_s 1.6028(45) Å similar to that in HB=S[107], r_e 1.5978(3) Å and in ClB=S[108], r_s 1.606(1) Å.

III. TWO-COORDINATED SULFUR

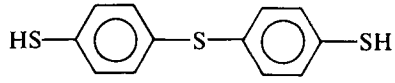
A. Thiols

The structures of thiols were reviewed in this series two decades ago[4], and later gas-phase studies in the monographs cited[12,14]. Transition-metal thiolates are discussed in Reference 109.

Recent data of trifluoromethanethiol, *p*-benzenedithiol (**21**) and 4,4′-thiobis(benzenethiol) (**22**) are collected in Table 4, and data of CH_3SH for comparison.



(**21**)



(**22**)

Triphenylmethanethiol, Ph_3CSH, crystallizes in the triclinic $P\bar{1}$ space group[114]. The phenyl rings are in propeller-like conformations with S—C—C—C dihedral angles of 42 to 61° in the two independent molecules, and the S—H bond staggers the (S)C—Ph bonds. The sulfur bond lengths and bond angle are C—S 1.873(4), 1.866(4), S—H 1.31(4), 1.40(5) Å, C—S—H 100(2), 98(3)°.

TABLE 4. Structural parameters of the thiol group from gas-phase studies

Molecule		C—S(Å)	S—H(Å)	C—S—H (deg)	Reference
H_3CSH	r_0	1.819(5)	1.335(10)	96.5(5)	110
F_3CSH[a]	r_z	1.801(10)	1.347(4)	91.99(13)	111
21	r_g	1.775(4)	1.359(11)	96.5(20)	112
22	r_g	1.778(4)[b]	1.388(19)	94.6(31)	113

[a]Approximate zero-point average structure with an assumption on *r*(C—F).
[b]Mean value.

The position of the thiol hydrogen atom is not well determined from ED and XD because of its relatively small contribution to the scattering, and some of the parameters may have to be assumed. The problem can be solved by using ED and MW experimental data together, as well as vibrational spectroscopic data for the necessary conversion of different representations of molecular geometry in such a joint analysis[15].

Ethenethiol, CH_2=CHSH, exists in two forms (Figure 13). Potential function and framework relaxation during rotation, as well as geometric parameters have been deduced from *ab initio* and MW data[115]. The *syn* form is in a true energy minimum but the *anti*, which is separated by a torsional barrier of 800 cm^{-1} and lies higher by 50 cm^{-1}, is a quasi-planar form with a small energy maximum at the planar position of the S—H group. The nature of the potential function is strongly affected by *trans* substituents in ethenethiol. Bond lengths and angle obtained for the *syn* form: C—S 1.761 Å, S—H 1.336 Å and C—S—H 95.8°.

The C—S bond is shorter, the C—S—H angle smaller in trifluoromethanethiol, F_3CSH, than in H_3CSH (Table 4). Other C—S—H bond angles are in a narrow range. There are short F···H distances in F_3CSH (2.70 Å as calculated from coordinates in Reference 111), and the F_3C group is tilted away by 3° from the staggered S—H bond (Figure 14). Tilt and the rotational barrier $V_3 = 448(4)$ cm^{-1} are similar to those in H_3CSH[110], whereas the barrier decreases when F_3C replaces H_3C attached to carbon or nitrogen[111]. Variations in S—H bond lengths may be partly due to the different physical meanings of the parameters. The mean C—S bond length in alkanethiols is 1.808 Å with a standard deviation of 0.010 Å in a sample of 6 observations[32].

The benzene ring is practically undistorted in **21**[112] and **22**[113], the C—C(S)—C endocyclic bond angles being 120.1(2)° and 120.4(3)°, respectively. This is consistent with 119.9(1)° in thiophenol found by low-temperature XD[116] and 120.2(6)° in diphenyl sulfide[117a], and with the correlation line between the electronegativity of third-period substituents and *ipso* bond angle in monosubstituted benzenes[100,101].

The importance of possible intramolecular hydrogen bonding in conformational equilibria has often been demonstrated. Repulsive forces alone tend to stabilize the *anti* form of 1,2-disubstituted ethanes. Reinvestigations of ethane-1,2-dithiol, $HSCH_2CH_2SH$ (**23**)[118], and 2-aminoethanethiol, $H_2NCH_2CH_2SH$ (**24**)[119], by joint analyses of ED intensities, rotational constants and dipole-moment components from MW studies, as well as vibra-

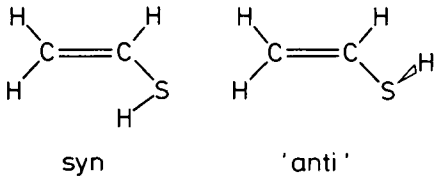


FIGURE 13. The *syn* and the quasi-planar *anti* form of CH_2=CHSH

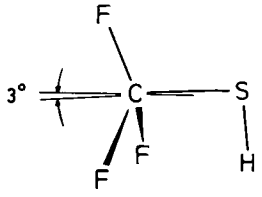


FIGURE 14. Tilt of the F_3C group in trifluoromethanethiol

TABLE 5. Structural parameters of ethane-1,2-dithiol (**23**)[118] and 2-aminoethanethiol (**24**)[119]

Parameter	**23** 350 K r_g (Å), $\angle_\alpha$ (deg)	**24** 372 K r_g (Å), $\angle_\alpha$ (deg)
C—S	1.824(2)	1.828(3)
S—H	1.373(15)	1.371(12)
C—C	1.537(6)	1.526(2)
C—C—S	113.1(4)	113.1(4)
C—S—H	94.0[d]	90.0[d]
gauche I		
S—C—C—S	69.0(15)	63.4(24)[e]
C—C—S—H	−40(30)	−21(28)
H—S—C—C	−141(22)	−49(18)[a]
gauche II		
N—C—C—S		63.8(13)
C—C—S—H		−72(11)
e—N—C—C[a]		47(19)[a]
anti[b]		
⟨S—C—C—S⟩	14.9(52)	
x	0.541(86)	0.227(54)
$\Delta E^{\circ c}$	1.1(36)[f]	0.8(18)
$\Delta S^{\circ c}$	−4.2(92)	6.3(38)

[a] Dihedral angle e—N—C—C, e is the lone pair of nitrogen, lying in the bisector plane of angle H—N—H.
[b] Staggered conformation assumed. ⟨S—C—C—S⟩ is the root-mean-square torsional amplitude (deg), x is the mole fraction of the *anti* form.
[c] Energy (kJ mol^{-1}) and entropy (J K^{-1} mol^{-1}) difference between *gauche* form(s) and *anti* form, $\Delta E^\circ = E_g - E_a$, $\Delta S^\circ = S_g - S_a - R \ln 2$.
[d] Assumed.
[e] Dihedral angle N—C—C—S.
[f] Corrected value, 0.26(86) kcal mol^{-1}, from footnote 5 in Reference 119.

tional spectroscopic data confirm the main conclusions from earlier ED[120] and MW studies[121,122] and give more detailed information concerning the presence and energy difference of conformers and the positions of thiol and amino protons. Some results are presented in Table 5.

The bond lengths C—S and S—H and angle C—C—S are the same in the two molecules; the C—C bond is shorter in the amino derivative.

From ED data at two temperatures, the energy (ΔE°) and entropy differences (ΔS°) between conformers have been obtained (Table 5). The *gauche* form of **23** is barely higher in energy than the *anti* form, due to a stabilizing, albeit weak, S—H···S hydrogen bond in the *gauche* conformer with favorable positions of the S—H bond and the lone electron pair of the other sulfur atom (Figure 15). The wave number of the torsional vibration about the C—C bond is estimated[118] at 87(24) cm^{-1} from the torsional amplitude ⟨S—C—C—S⟩. Two *gauche* conformers of **24** have been identified in a MW study[122] but *ab initio* calculated energies and the weakness of spectra[123] indicate the presence of other forms. The ED analysis[119] reveals three conformers indeed, one of the *gauche* forms having an intramolecular S—H···N hydrogen bond (Figure 16).

For larger molecules, MW spectroscopy may yield valuable information on the geometry and energetics of coexisting conformers, even if the number of rotational constants obtained for one or more isotopic species is far from enough to give a detailed geometric

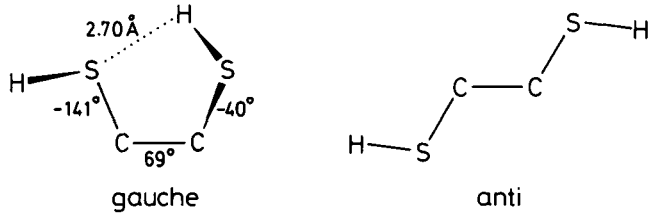


FIGURE 15. Heavy-atom skeletons of $HSCH_2CH_2SH$ (**23**) conformers with refined torsional angles[118]. There is an intramolecular S—H···S hydrogen bond in the *gauche* form

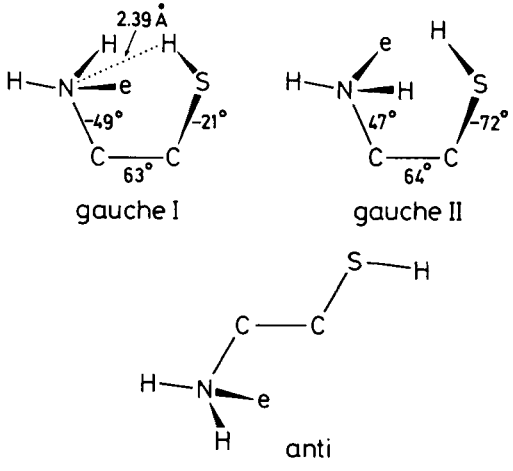


FIGURE 16. The three forms of $H_2NCH_2CH_2SH$ (**24**), found by ED[119], with refined torsional angles. Torsion about the C—N bond is given by the e—N—C—C dihedral angle, e being the lone pair of nitrogen. Conformer *gauche* I is characterized by an S—H···N hydrogen bond

structure. Often, parameters are taken from parts of related molecules, and 'plausible structures' are constructed that are consistent with the observed rotational spectra.

The conformation of 1-mercapto-2-propanol, $CH_3CH(OH)CH_2SH$ (**25**), has been studied by MW and IR spectroscopy and *ab initio* calculations[124]. Only one conformer is present in the vapor with an all-*gauche* (+*sc*, +*sc*, −*sc*) H—S—C—C—O—H chain and an O—H···S hydrogen bond (Figure 17). The H···S distance is 2.66 Å in the 'plausible structure', the sum of van der Waals radii 3.05 Å. This form of **25** is similar to the unique or more stable form of other hydrogen-bonded 1,2-disubstituted propanes,

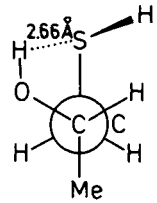


FIGURE 17. The structure of $CH_3CH(OH)CH_2SH$ (**25**) with an O—H···S hydrogen bond. Newman projection along the (O)C—C(S) bond. The O—C—C—S dihedral angle is 58(2)°

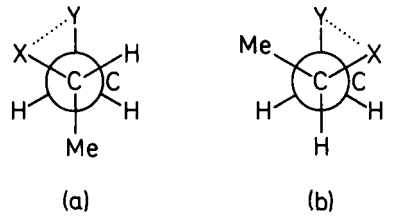
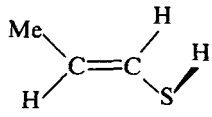


FIGURE 18. Hydrogen-bonded conformers of 1,2-disubstituted propanes $MeCHXCH_2Y$, X, Y = OH, NH_2 and F

$MeCHXCH_2Y$, X, Y = some combinations of OH, NH_2 and F, inasmuch as the Me—C and the C—Y bonds are in *anti* position (Figure 18a). A hydrogen bond of the type S—H···O is not realized in **25**, neither in 2-mercaptoethanol, because it would involve a long O···H distance. (See references cited in Reference 124.)

The MW spectrum of (*E*)-propene-1-thiol (**26**) indicates a thiol group *skew* to the double bond but a *syn* form, which is in a higher energy minimum, can also be present[125].



(**26**)

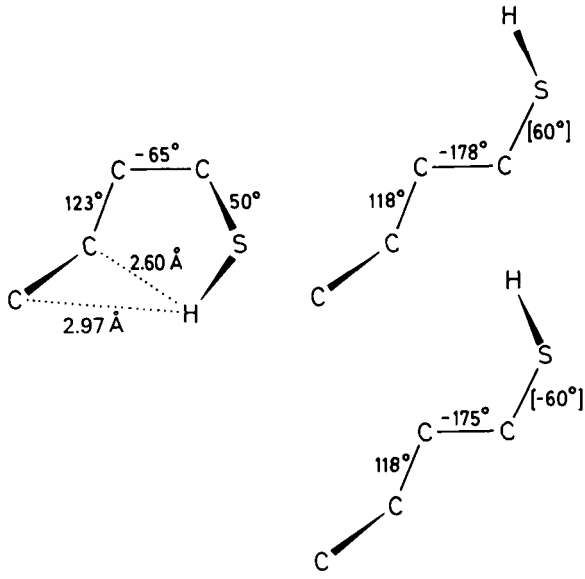


FIGURE 19. The three conformers of $H_2C{=}CHCH_2CH_2SH$. Relative signs of the torsional angles are given; assumed values are in brackets. Uncertainty for C—C—S—H is ±5°, for the other angles ±3°. Drawn from the data in Reference 126

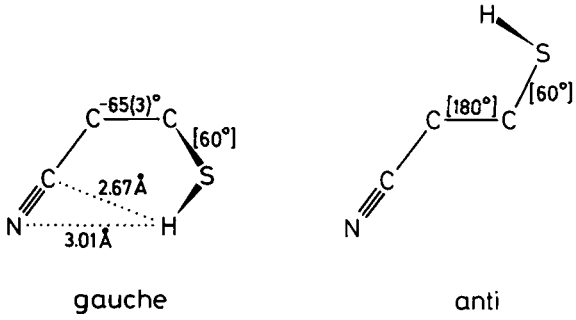


FIGURE 20. The two conformers of $NCCH_2CH_2SH$ with dihedral angles shown

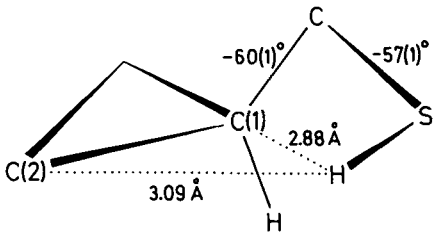


FIGURE 21. The conformation of cyclopropylmethanethiol and dihedral angles S—C—C(1)—H and H—S—C—C(1) from MW spectroscopy[128]. Short H···C distances are indicated

Three conformers of 3-butene-1-thiol, $H_2C{=}CHCH_2CH_2SH$, exist at $-60\,^{\circ}C$ according to MW spectra[126]. One of the forms is stabilized by a weak intramolecular hydrogen bond between the sulfur atom and the C=C π electrons (Figure 19), the other two forms are higher in energy by 2.9(5) and 3.6(5) kJ mol^{-1}. The hydrogen bond is weaker than in the corresponding single conformer of 3-buten-1-ol[126]. It can be seen from the torsional angles (Figure 19) that the C=C bond eclipses one of the methylene C—H bonds, and the conformation is staggered about the $H_2C—CH_2$ and the C—S bonds.

A similar hydrogen bond occurs in one of the two conformers of 3-mercaptopropionitrile, $NCCH_2CH_2SH$ (Figure 20), as found in a MW study[127]. The mercapto group can also act as a proton donor to the quasi-π-electron system of cyclopropane in the single conformer of cyclopropylmethanethiol[128], $C_3H_5CH_2SH$ (Figure 21).

B. Open-chain Sulfides

A review on sulfides in this series[6] was followed by detailed discussions of gas-phase structures[11,12,14]. Some recent results will be given here, including those on silyl sulfides.

Ethyl methyl sulfide, $CH_3CH_2SCH_3$, has been repeatedly investigated. The ED study established the presence of 75(15) percent *gauche* form in the mixture (Figure 22), assuming equal bond lengths and bond angles for the two conformers[129]. From the MW spectra, the r_s parameters were determined separately for the two forms[130]. Recently, the torsional potential function (Figure 23) has been obtained from the analysis of high-resolution

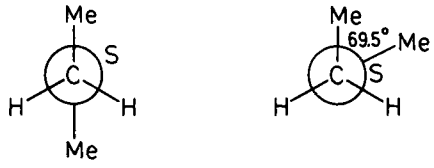


FIGURE 22. The two conformers of ethyl methyl sulfide. Newman projections down the H_2C—S bond

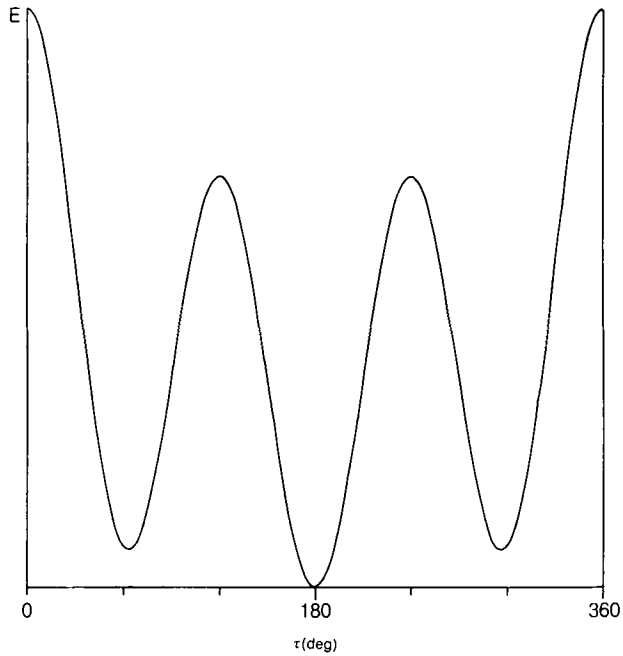


FIGURE 23. The form of the torsional potential function of ethyl methyl sulfide: rotation about the H_2C—S bond. Drawn after Reference 131

far-infrared spectra and from *ab initio* calculations[131], considering the geometry relaxation during internal rotation. The energy difference is small, 131(45) cm^{-1}, the *anti* form being more stable, and the torsional barriers are: *gauche* to *gauche* 1184(9), *gauche* to *anti* 881(21) and *anti* to *gauche* 1012(17) cm^{-1}. Some results are compared in Table 6. The bond angles are markedly wider in the *gauche* conformer.

The geometry of the most stable conformer of diisopropyl sulfide has been determined from ED data with constraints from *ab initio* calculations[132]. The molecule has C_2 symmetry and C—S—C—H dihedral angles of 59(7)° (Figure 24).

Sulfur bond lengths and bond angles in some sulfides change parallel with the size of the alkyl groups (Table 7). As in the two conformers of EtSMe, steric effects also appear

TABLE 6. Important structural parameters of ethyl methyl sulfide

	Et—S (Å)	Me—S (Å)	C—C (Å)	C—S—C (deg)	S—C—C (deg)	C—S—C—C (deg)
gauche						
ED, r_α[a]	1.816(27)	1.804(27)	1.534(8)	97.1(11)	114.0(5)	66(9)
MW, r_s[b]	1.806(2)	1.802(2)	1.524(2)	100.22(12)	114.70(12)	69.43(83)
MW, r_0[c]	1.810(2)	1.805(1)	1.526(2)	100.40(4)	114.52(6)	69.47(7)
anti						
MW, r_s[d]	1.804(4)	1.804(4)	1.530(4)	99.00(22)	109.48(28)	180[e]
MW, r_0[c]	1.814(7)	1.803(7)	1.526(12)	99.08(25)	109.47(13)	180[e]

[a]Reference 129, bond lengths and bond angles in the *gauche* and *anti* conformers assumed to be equal.
[b]Reference 130b.
[c]Reference 131, adjusted parameters using rotational constants and *ab initio* 6-31G* calculations.
[d]Reference 130a.
[e]Assumed.

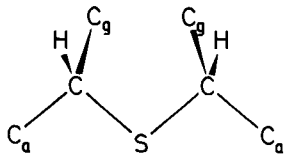


FIGURE 24. The conformation of diisopropyl sulfide, $(Me_2CH)_2S$. Bonds C—C_a and C—C_g are *anti* and *gauche* to the farther C—S bond

TABLE 7. Sulfur bond lengths and bond angles in alkyl sulfides (r_g, $\angle_a$)

	C—S (Å)	C—S—C (deg)	Reference
Me_2S	1.807(2)	99.05(4)	133
EtSMe[a]	1.813(4)	97.1(11)	129
i-Pr_2S	1.829(3)	102.9(17)	132(b)
t-Bu_2S	1.854(5)	113.2(12)	134

[a]Mean values from ED.

in the S—C—C angles within one molecule of *i*-Pr_2S (see Figure 24): S—C—C_g 112.0(7)°, S—C—C_a 106.5(7)° and in the tilt of the Me_3C groups in *t*-Bu_2S, 7(2)°. Similar variations are observed[136b] in the series of analogous ethers Me_2O, EtOMe, *i*-Pr_2O[135] and *t*-BuOMe[136].

The structures of some sulfides with sp^2 carbon have been determined by gas-phase ED (Table 8). (Other data of **22** are listed in Table 4, Section III.A.) The C—S bonds are shorter than in Me_2S, following the trend observed for sp, sp^2 and sp^3 carbon atoms; there seems to be a trend, too, that C(sp^2)—S bonds are shorter for alkyl than for aryl carbon[11,12,32,139] (see Section V.B). The shortening is about the same in the O and Se analogs[33] (Table 9). The C—Y—C bond angles are wider in the divinyl derivatives and decrease from O to Se.

TABLE 8. Bond lengths (r_g) and bond angles of sulfides with sp^2 carbon

	C—S (Å)	C—S—C (deg)	Reference
$(CH_2{=}CH)_2S$	1.758(4)	101.8(21)	137
Ph_2S	1.772(5)	103.7(13)	117
22	1.778(4)[a]	103.5(13)	113
27 C_{ar}—S	1.774(6)	104.6(7)	138
C_{me}—S	1.809(6)		

[a]Mean value.

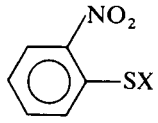
TABLE 9. Parameters of methyl and vinyl chalcogenides

	Y = O	Y = S	Y = Se
Me_2Y			
C—Y (Å)	1.415(1)	1.811(4)	1.945(0.4)
C—Y—C (deg)	111.8(2)	99.2(6)	96.32(8)
Reference	140	361	141
$(CH_2{=}CH)_2Y$			
C—Y (Å)	1.389(2)	1.758(4)	1.916(4)
C—Y—C (deg)	118.8(2)	101.8(21)	100.3(10)
Reference	142	137	143

A single conformer has been found in divinyl sulfide, although other forms may also be present[137]. The C—S—C=C dihedral angles, τ_1 32(9)° and τ_2 −148(7)°, are similar to those in the more abundant (80 percent) form of divinyl ether[142]. Two models of **22** are consistent with the ED experimental data[113], with $[\tau_1, \tau_2]$ of [68(2)°, 5(7)°] and [69(2)°, −27(7)°] about the central C—S bonds. For Ph_2S, conformers with angles about [44°, 44°] and [55°, −55°] have been preferred, assuming C_2 or C_s symmetry[117b].

The structure of *p*-bis(phenylthio)benzene, *p*-$C_6H_4(SC_6H_5)_2$, has been determined by XD[144]. The molecule has a symmetry center in the crystal, and its conformation is given by dihedral angles C—S—C—C (central ring) 56.6(1)° and C—S—C—C (terminal rings) 14.0(4)°, both positive. The *ipso* C—C—C bond angles in the rings are 119.5(2)° and 119.0(1)°, respectively; the distortions from the regular hexagon are small. The sulfur bond lengths and bond angle are C—S 1.773(2), 1.769(2) Å and C—S—C 104.7(1)°, similar to those in gas-phase Ph_2S.

Two effects are said to counteract in the conformational choice of diphenyl sulfide derivatives: coplanarity of both rings with the C—S—C plane is favored by conjugation but is hindered by the proximity of *ortho* hydrogens or substituents. A search in the Cambridge Structural Database (CSD) indicates a tendency that one of the rings is nearly coplanar with C—S—C and the other is roughly perpendicular to it[145]. The conformation of **22**, both in the gas phase[113] and in the crystal[146], is consistent with this expectation. A recent analysis of diphenyl sulfide structures from the CSD, accompanied by molecular mechanics and *ab initio* energy calculations, was prompted by research on antidepressants[147]. Data points are clustered about $[\tau_1, \tau_2]$ of [0°, 90°] and [90°, 0°] and, in smaller density, along bands connecting such points and including the conformer C_2 [45°, 45°] with the lowest energy. The mean C—S bond length is 1.775 Å (estimated standard deviation 0.013 Å), and the mean C—S—C is 103.2(15)° in the sample studied[147].



(27) X = Me
(28) X = Cl

A remarkable feature of methyl 2-nitrophenyl sulfide (**27**) is the short nonbonded intramolecular S···O distance[138]. An even shorter distance has been found by ED[148] and XD[149] in the related sulfenyl chloride (**28**) (Figure 25). This change in the S···O distance

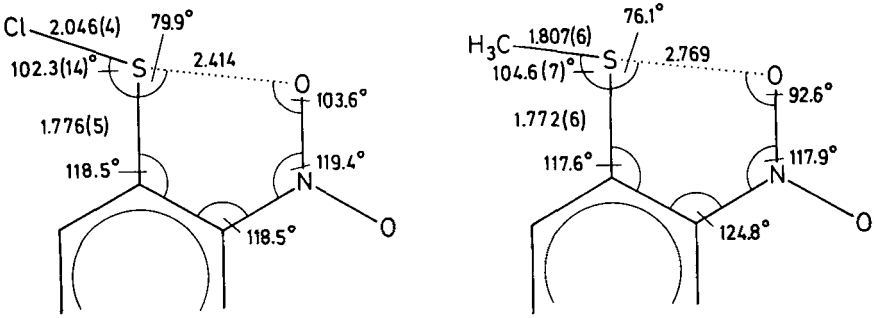


FIGURE 25. Intramolecular S···O interaction in 2-nitrobenzenesulfenyl chloride (**28**) and methyl 2-nitrophenyl sulfide (**27**). Distances (r_a) in Å. Drawn after Reference 138

FIGURE 26. The two conformers of ethyl vinyl sulfide

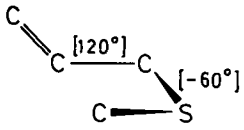


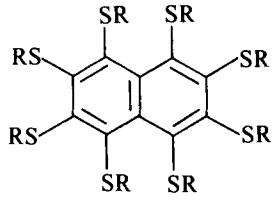
FIGURE 27. Allyl methyl sulfide, magnitude and relative sign of dihedral angles indicated

is associated first of all with changes in the angles C—C—N and N—O···S in the five-membered cyclic arrangement. Short sulfur(II)–oxygen intramolecular contacts occur in various structures[150,151], and one of the decisive factors in their geometry is the electronegativity of the substituent(s) on sulfur[152]. The effective torsional angles of the MeS and NO_2 groups in **27** from the ED study, Me—S—C(1)—C(2) 161° and O—N—C(2)—C(1) 32°, may indicate large-amplitude torsional vibrations, and are such that the Me—S···O sequence is nearly linear[138].

Two conformers of ethyl vinyl sulfide, $CH_2{=}CHSCH_2CH_3$, have been detected in a MW and *ab initio* study[153]. They differ in the rotation about the S—CH_2 bond but both have the double bond eclipsed with this bond (Figure 26). The *anti* form is more stable by 1.2(5) kJ mol^{-1}. The dihedral angle C—S—C—C is 77(2)° in the *gauche* form. The MW spectrum of allyl methyl sulfide, $CH_2{=}CHCH_2SCH_3$, on the other hand, is consistent with a form in which the CH_2—S bond is *skew* to the double bond and S—Me is in *gauche* position[154] (Figure 27). A similar form was found in allyl mercaptan[155].

Propargyl thiocyanate, $HC{\equiv}CCH_2SCN$, has been studied by ED and vibrational spectroscopy[156]. It consists of a *gauche* and an *anti* conformer with respect to rotation about the CH_2—S bond. The bond lengths (r_a) C(sp^3)—S 1.836(3) Å and C(sp)—S 1.689(3) Å are in accord with observations for these types of sulfur–carbon bonds[11,12,32,33]. The C—S—C angle is 97.4(10)°. The mean C(sp)—S bond length is 1.679(26) Å in a sample of $n = 10$ crystalline thiocyanates[32].

The new synthesis of octakis(cyclohexylthio)naphthalene (**29**) from perfluorodecalin



R = cyclohexyl

(**29**)

and its structure are equally remarkable[157]. The XD analysis and the ^{13}C solid NMR spectrum testify the unusual axial substituent position in one of the four independent cyclohexyl rings (Figure 28). The conformation and the endocyclic bond angles in the 2,6 positions (next to the S substituent) are different, too, from those in the other three

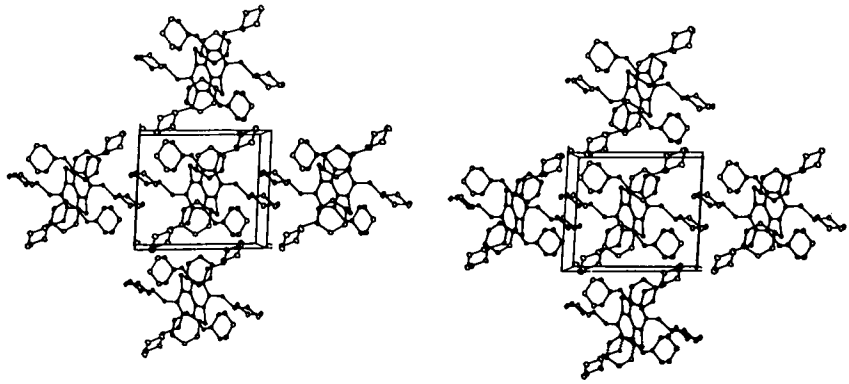


FIGURE 28. Stereoview of the molecular packing in the crystal of **29**. The molecule possesses a symmetry center in the triclinic crystal, space group $P\bar{1}$. One of the four independent cyclohexyl rings has the C—S bond in axial position. Reproduced by permission of the Royal Society of Chemistry from Reference 157a

cyclohexyl moieties. Mean sulfur bond lengths[157a] are C(sp^2)—S 1.775(1), C(sp^3)—S 1.819(2) Å, and angle C—S—C[157b] from 101.0(1) to 105.0(2)°.

Steric effects on the molecular geometry have been demonstrated in methyl-substituted disilyl sulfides (Table 10). In the latter two cases, molecular mechanics calculations were applied to eliminate symmetry constraints in the ED analysis, and the parameters cited are mean values. The Si—S bond is longer, the Si—S—Si angle is wider as the number of Me substituents increases. The Si—C bonds try to avoid eclipsing either of the Si—S and Si—C bonds in the other half of the molecule[159,160]. As a compromise, both groups are twisted about the Si—S bonds by about 30° or 90° from the *anti* Si—S—Si—C positions (Figure 29).

A plausible structure of methyl silyl sulfide, $MeSSiH_3$, has been determined from MW spectra of four isotopic species[161] (r_0): C—S 1.819 Å and S—Si 2.134 Å are similar to the

TABLE 10. Parameters of (methylsilyl) sulfides (r_a)

	Si—S (Å)	Si—S—Si (deg)	Reference
$(H_3Si)_2S$	2.136(2)	97.4(7)	158
$(MeH_2Si)_2S$	2.141(1)	97.9(5)	159
$(Me_2HSi)_2S$	2.146(1)	100.8(20)	159
$(Me_3Si)_2S$	2.154(1)	105.8(7)	160

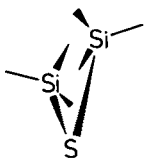


FIGURE 29. The conformation of bis(trimethylsilyl) sulfide, $(Me_3Si)_2S$

bond lengths in Me_2S and $(H_3Si)_2S$ (see above). The variation of sulfur bond angles is not as large as that of oxygen from ethers to siloxanes:

Me_2S	$MeSSiH_3$	$(H_3Si)_2S$	$(Me_3Si)_2S$
99.2(6)°	98.3°	97.4(7)°	105.8(7)°
Me_2O[140]	$MeOSiH_3$[162]	$(H_3Si)_2O$[163]	$(Me_3Si)_2O$[164]
111.8(2)°	120.6(10)°	144.1(9)°	148(3)°

The mean S—Si bond length from crystallographic data[32] is 2.145(20) Å, $n = 19$.

C. Disulfides

Disulfane, HSSH, the parent compound of disulfides, and the higher sulfanes H_2S_n have a long history in preparative chemistry and spectroscopy[165a,b]. It took more than twenty years to solve all the difficult experimental and theoretical problems and obtain a complete molecular structure of disulfane from high-resolution rotational spectra of its isotopic species[165]. The molecule has a C_2 symmetry axis, parallel to the dipole moment vector, and the two H—S—S planes are nearly perpendicular (Figure 30). Since estimated effects of the H—S—S—H torsional vibration have been removed, the parameters of HSSH in Table 11 characterize a 'partially corrected equilibrium structure' and are in good agreement with results of *ab initio* calculations[166].

The torsional potential function of HSSH has minima at about 90° dihedral angle (Figure 31). There are high and different maxima, although of the same magnitude, at the *syn* and *anti* forms of the H—S—S—H chain[174]: $V(syn)$ 2843(9) and $V(anti)$ 2037(12) cm^{-1}. The torsional barrier for the *anti* position in hydrogen peroxide[175], HOOH, is considerably lower: $V(syn)$ 2563(60) and $V(anti)$ 387(20) cm^{-1}. This feature leads to characteristic differences in the rotational spectra of the two molecules and indicates their distinct bonding structures[165]. It is interesting to note that HSSH is, by accident, a perfectly symmetric prolate top in its extrapolated equilibrium configuration[165c], i.e., two of its rotational constants are the same within estimated uncertainties: A_e 147 287.6(515), B_e 6984.72(48) and C_e 6984.92(94) MHz.

The MW spectrum of trisulfane[176], HSSSH, is consistent with C_s symmetry of the molecule having H—S—S—S dihedral angles of about 99° and −99° (Figure 30).

Gas-phase structural data of disulfanes and analogs are compared in Table 11. A considerable shortening of the central bond with increasing substituent electronegativity has been observed[12,33], and this is seen in the data of the Table. The O—O bond is short, the F—O bond is long in FOOF[167]. A significant (p–p) π component in the bonding explains the high torsional potential barrier in FSSF and the short S—S bond[102,177], which is close to the double bond in $S{=}SF_2$[102] (see Section II.F). The quantum chemical treatment of these relatively small molecules encounters severe problems[102,177,178].

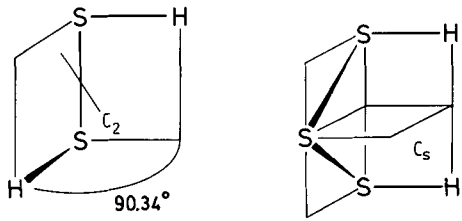


FIGURE 30. The models of disulfane (C_2 symmetry) and trisulfane (C_s)

TABLE 11. Structural parameters of disulfane derivatives and analogs X^1YYX^2 from gas-phase studies

X^1YYX^2		Y—Y (Å)	X^1 X^2	X—Y (Å)	Y—Y—X (deg)	X—Y—Y—X (deg)	Reference
FOOF	r_g	1.216(2)	F	1.586(2)	109.2(2)	88.1(4)	167
CF_3OOH	r_g	1.447(8)	CF_3	1.376(10)	107.6(8)	95[a]	168
			H	0.974(42)	100[a]		
CF_3OOF	r_g	1.366(33)	CF_3	1.419(24)	108.2(12)	97.1(60)	168
			F	1.449(15)	104.5(45)		
CF_3OOCF_3	r_g	1.419(20)	CF_3	1.399(9)	107.2(12)	123.3(40)	169
HSSH	r_e	2.0564(1)	H	1.3421(2)	97.88(5)	90.3(2)	165
FSSF	r_z	1.8931(5)	F	1.6339(3)	108.264(9)	87.526(16)	170
FSSF	r_{av}	1.890(2)	F	1.635(2)	108.3(2)	87.7(4)	102
CF_3SSH	r_g	2.038(5)	CF_3	1.806(6)	101.2(6)	91[a]	171
			H	1.34[a]	98[a]		
CF_3SSF	r_g	1.970(3)	CF_3	1.829(6)	102.0(6)	91(3)	171
			F	1.611(3)	105.7(8)		
CF_3SSCF_3	r_g	2.030(5)	CF_3	1.835(5)	101.6(6)	104.4(40)	172
MeTeTeMe	r_a	2.686(3)	CH_3	2.156(5)	98.9(4)	82(14)	173

[a] Assumed.

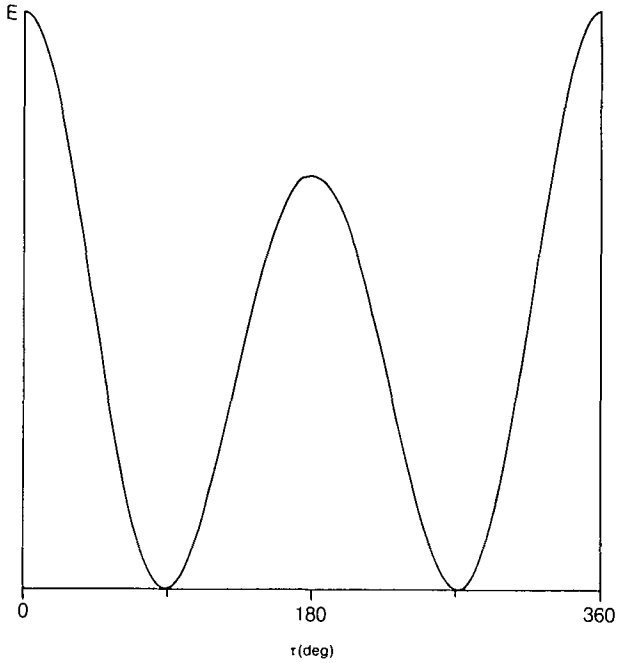
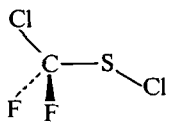


FIGURE 31. The form of the torsional potential function (E) of HSSH as a function of the dihedral angle τ. Drawn after Reference 165b

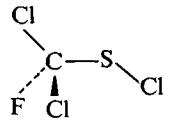
The mean bond lengths and their standard deviations in disulfides from n crystallographic observations[32]: (C)S—S(C) 2.048(26) Å, $n=99$; C(sp^3)—S(S) 1.833(22) Å, $n=59$; C(aromatic)—S(S) 1.777(12) Å, $n=47$.

D. Other Acyclic Structures

The structures of sulfenic acid derivatives have been reviewed very recently[9], and only some new results are mentioned here. Two methanesulfenyl chlorides have been studied by ED and *ab initio* calculations[179]. The conformation is staggered in both $CClF_2SCl$ (**30**) and CCl_2FSCl (**31**), and the predominant and more stable form has a C—Cl bond *anti* to the S—Cl bond. In (fluorocarbonyl)sulfenyl chloride, FC(O)SCl (**32**), the S—Cl bond is either *syn* (88 percent abundance) or *anti* to the C=O bond[180]. Parameters C—S, S—Cl (r_a/Å) and C—S—Cl (deg) in **30** 1.813(15), 2.014(3), 99.3(6), **31** 1.811(16), 2.004(3), 101.7(7) and **32** 1.756(5), 1.996(3), 100.3(5) are comparable to those in **28** (Figure 25, Section III. B).



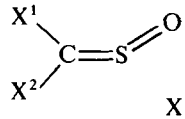
(30)



(31)

The sulfur bond configuration is similar in $(F_2P)SMe$[181], (r_a) C—S 1.822(5), S—P 2.085(3) Å, C—S—P 102.0(12)°, and in $(F_2P)SEt$[182], 1.825(6), 2.085(3) Å, 100.3(6)°, respectively. The S—P bond is longer, 2.132(4) Å, the sulfur bond angle P—S—P closes to 91.3(11)° in $(F_2P)_2S$[181].

Substituted sulfines have a planar X^1X^2CSO skeleton (**33**). Chlorine occupies the *cis* position in the mixed derivative, and in each case the *cis* S=C—X angle is larger than the *trans* angle[183]. Changes in the geometry of the CSO group are barely significant (r_a from ED):

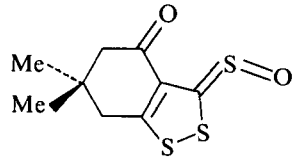


$X^1, X^2 = Cl, CF_3$

(**33**)

	C=S(Å)	S=O(Å)	C=S=O (deg)
Cl_2CSO	1.618(4)	1.453(3)	113.8(10)
$Cl(CF_3)CSO$	1.631(11)	1.457(5)	112.3(11)
$(CF_3)_2CSO$	1.634(7)	1.455(5)	111.3(20)

The *S*-oxide **34** exhibits a short intramolecular S···O distance of 2.81 Å between the S=O oxygen and the S atom of the nearly planar dithiole ring[184]. Parameters from the XD analysis are S=O 1.511(6) Å, C=S=O 104.6(4)°. The C=S bond length of 1.668(7) Å is similar to that in the related thione[184], 1.657(5) Å.



(**34**)

The structure of a thiazyl nitroxide, $(CF_3)_2NOSN$, has been determined in the gas phase by ED, and of its crystalline trimer by XD[185]. The O—S bond is long, r_a 1.751(7) Å from ED, the N—S bond is 1.423(9) Å, shorter than r_s in thiazyl fluoride[186], NSF, 1.448(2) Å and in thiazyl chloride[187], NSCl, 1.500 Å. The sulfur bond angle O—S—N 119.8 (32)° is of the same magnitude as in the thiazyl halides.

The free molecule of *N,N'*-bis(trimethylsilyl)sulfur diimide, $Me_3SiNSNSiMe_3$, possesses C_2 symmetry with effective Si—N=S=N dihedral angles of 42(1)°, measured from the *syn, syn* conformation[188] (Figure 32). Sulfur diimides with various conformations are

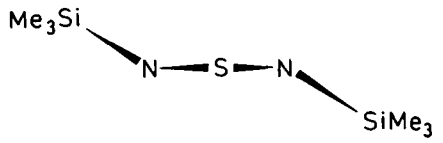


FIGURE 32. The projection of $Me_3SiNSNSiMe_3$ down the C_2 symmetry axis

known[188], e.g. MeNSNMe has a planar *syn, anti* heavy-atom skeleton in the gas-phase[189]. The N=S bond lengths (r_a) are similar but the N=S=N angle is wider in the Me_3Si than in the Me derivative, 1.536(3) and 1.532(10) Å, 129.5(16)° and 113.6(16)°, respectively. The empirical correlation between NSN angles and the associated NS bond distances[190] would give an N=S bond length of 1.50 Å for $Me_3SiNSNSiMe_3$. The relatively large deviation from the experimental value may arise from the overpassing of the validity range of NSN, 95 to 125°. The mean N=S bond length in N=S=N and N=S=S moieties from crystallographic data[32] is 1.541(22) Å, $n = 37$. A correlation has been also established between the lengths of sulfur–nitrogen bonds and the wavelengths of their stretching vibrations[191].

E. Carbon–Sulfur Heterocycles

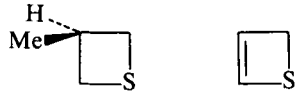
Cyclic sulfides, unsaturated rings and heterocycles with aromatic character will be discussed together, following, by and large, increasing ring size.

In three-membered rings with one heteroatom a shortening of the C—C bond with increasing heteroatom electronegativity has been observed[12]. This trend is present in the ring C—C bond lengths of (chloromethyl)thiirane or 3-chloropropylene sulfide[192] (**35**), r_a 1.492(23) Å and of its oxygen analog[193], 1.474(8) Å, although the uncertainties are large. According to the ED data, both have two coexisting conformers (Figure 33), and the more stable *gauche*-2 form is present in about 80 percent, while only the *gauche*-1 conformer with a short S···Cl distance has been identified from the MW spectra of **35**[194]. The ring geometry in **35**, C—S (mean) 1.822(13) Å, C—S—C 48.3(7)°, is very similar to that in thiirane (ethylene sulfide)[195]. The ring bonds are shorter in perfluorothiirane[196], $(CF_2)_2S$, r_g C—C 1.45(1), C—S 1.799(3) Å, C—S—C 47.5(5)°. The equatorial form of 1-thiaspiro-[2.5]octane (Figure 34) has been detected by MW[197], but molecular mechanics calculations and the study of the oxygen analog[198] indicate the presence of both the axial and the equatorial forms. The r_0 parameters of the thiirane ring are C—C 1.483, C—S 1.821 Å, C—S—C 48.05°. The chair-form ring is flattened compared to cyclohexane.

Four-membered rings have the longest bonds in the series of homologous cycloalkanes and some related heterocycles[12]. The smallest angular strain is achieved in the planar ring, which, however, is opposed by torsional strain. Depending on the two factors, the ring is planar, or has a puckered equilibrium structure, or, as an intermediate case, is quasi-planar with a small potential barrier at the planar configuration. Detailed analyses[199,200] of MW data of 3-methylthietane (**36**) yielded the bending potential function, which is

FIGURE 33. The two conformers of (chloromethyl)thiirane (**35**)

FIGURE 34. The equatorial form of 1-thiaspiro[2.5]octane



(36) (37)

asymmetric, with inversion barriers[200] V(equatorial) 305 cm^{-1} and V(axial) 169 cm^{-1}, i.e. the equatorial conformer is more stable by 136 cm^{-1}.

Thiete (**37**) has a definitely planar skeleton, its MW spectrum is that of a rigid rotor[201]. The bonds, r_s CH_2—S 1.853(3) Å, CH—S 1.770(3) Å, are longer than the corresponding bonds in the thiirane derivatives above and in Me_2S and $(CH_2{=}CH)_2S$ (Table 9, Section III. B). No such trend is observed in the carbon–carbon bonds. The C—S—C angle, 73.72(6)°, gets narrower than in thietane[202], 76.8(3)°, thus releasing angular strain at C=C.

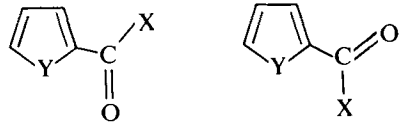
The rings in 4,4-difluoro-1,3-dithietane-2-thione (**8**) and in its 2-one analog have been found by ED to be planar or nearly planar[41]. Bond lengths and angles in the ring are $C(sp^2)$—S 1.758(6), 1.791(12)Å, $C(sp^3)$—S 1.823(6), 1.821(12)Å, C—S—C 83.1(5), 81.1(10)° in the two molecules, respectively.

1,2-Dithiete (**3**) is planar with C_{2v} symmetry and C=C 1.350 Å, C—S 1.753 Å, S—S 2.096 Å and C—S—S 77.7° from a MW study[203].

The structure of thiophene has been determined repeatedly[12]. A recent combined analysis of ED, MW and liquid crystal NMR data has demonstrated the usefulness of the latter technique for the more precise location of the H atoms[204]. Some of the parameters (r_a) obtained: C—S 1.7136(11), C=C 1.3783(15), C—C 1.4274(11) Å, C—S—C 92.56(8)°. The planar geometry of thiophene and of its O, Se, Te analogs and the different carbon–carbon bond lengths, resembling those in 1,3-butadiene, indicate a partially delocalized aromatic π-electron system[33]. Substituents have little effect on the geometries of these relatively rigid heterocycles. From the ED studies of carbonyl-substituted derivatives (**38–41**) only the conformational composition will be cited here.

	Y	X	*syn*, percent	Reference
38	O	H	31(9)	205
39	O	Cl	70(14)	206
40	S	H	81(8)	207
41	S	Cl	59(11)	208

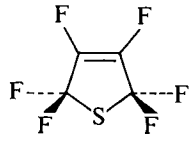
The reversed order in the O and S analogs is attributed to stabilizing effects of the O···H interaction in the *anti* form of **38** and of the S···O interaction in the *syn* form of **40**[207,208].



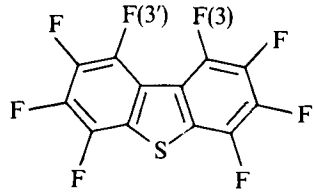
syn *anti*

(**38–41**)

The ring in perfluoro-3-thiolene (**42**) is planar as in thiophene. The sulfur bond angles are equal in the two rings, the C—S bond is longer in **42**[209], r_g C—S 1.809(4), C=C 1.382(14), C—C 1.456(5) Å, C—S—C 93.0(3)°. Perfluorotetrahydrothiophene (**106**) will be discussed with its dioxide in Section V. A.



(**42**)



(**43**)

The molecule of octafluorodibenzothiophene (**43**) has C_2 symmetry in the crystal and is planar[210]: C—S 1.737(3), C=C 1.404(4), C—C 1.470(6) Å, C—S—C 89.8(2)°. Bonds in the central ring seem to be longer than in free thiophene, but the different physical meaning of the parameters should also be considered. The short F(3)···F(3') distance, 2.55 Å, which is within the sum of van der Waals radii, 2.70 Å, is also apparent in the distortions of the F(3)—C—C angles.

The structures of 4,5-bis(methylthio)-2*H*-1,3-dithiole-2-one (**44**) and of the analogous 2-thione (**45**) (Figure 35) have been determined by XD[211]. The C—S bond lengths are again characteristic for sp^3 and sp^2 carbon; limits of values found in the two molecules: C(41)—S(4) 1.785(5) to 1.808(5), C(4)—S(4) 1.743(3) to 1.750(3), C(4)—S(3) 1.744(3) to 1.748(3) Å. The bonds adjacent to C=O in **44**, C(2)—S(1) 1.754(5) and 1.780(5) Å, are longer than the bonds next to C=S in **45**, 1.720(3) and 1.733(3) Å (cf. **13** and **12**, Section II.C). The C=S bond, 1.647(3) Å, is relatively long (see Table 1). Exocyclic and ring S atoms are involved in short S···S contacts in **44** (Figure 36).

The most important classes of organic metals, superconductors and semiconductors are based on sulfur-containing molecules, forming charge-transfer salts with a variety of stacking patterns in the crystal. The structures and properties of such systems have been reviewed[212–216]. The discussion of these structures goes beyond the scope of this chapter, and we list here just a few examples of XD studies to give an idea of the types of molecules and to provide sources for further references. One of the building blocks of these systems is tetrathiafulvalene (TTF) (**46**). Salts of the TTF donor with inorganic anions $[M_6O_{19}]^{2-}$, M = Mo, W, have been studied by XD[217]: $(TTF)_2[M_6O_{19}]$, as well as $(TTF)_3[Mo_6O_{19}]$. The molecules **44** and **45** and the related **47**[218] are precursors to bis(ethylenedithio)-tetrathiafulvalene, BEDT-TTF (**48**), a frequently used donor. Structures of salts of BEDT-TTF with a complex oxalato anion[219], $(BEDT\text{-}TTF)_4[Cu(C_2O_4)_2]$, and with the same

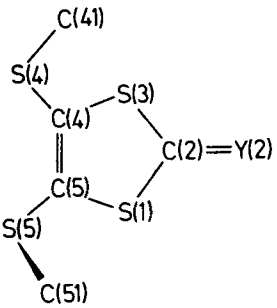


FIGURE 35. The conformation of **44** and the numbering of atoms in **44**(Y = O) and **45**(Y = S)

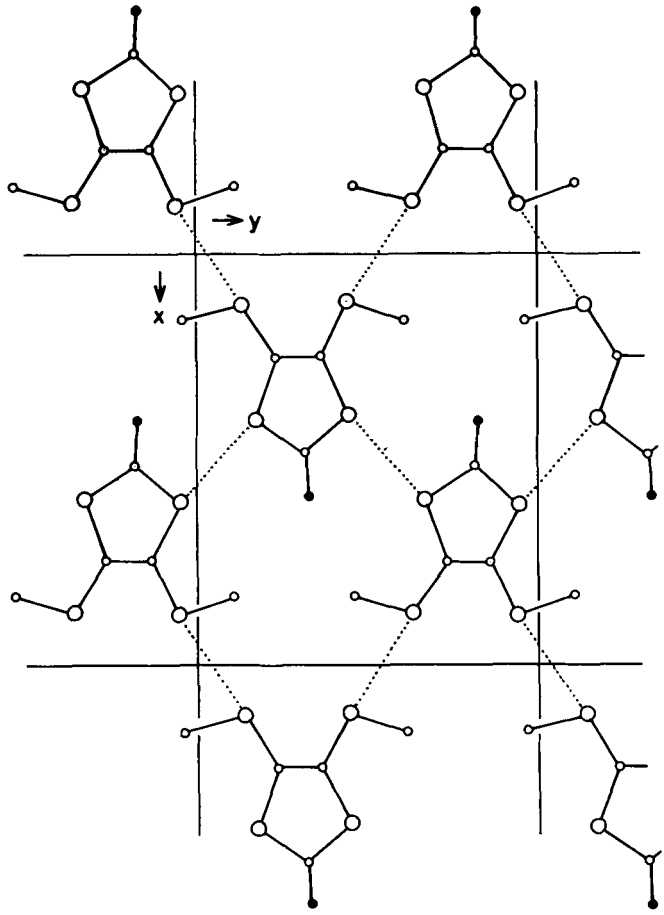
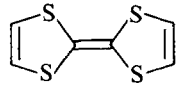
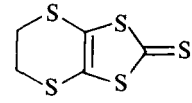


FIGURE 36. The crystal structure and S···S contacts in **44** projected down the *z* axis. Reproduced by permission of the International Union of Crystallography from Reference 211

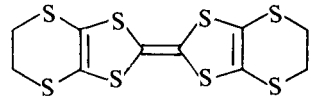


TTF

(46)



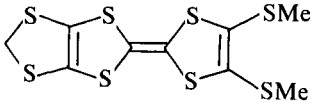
(47)



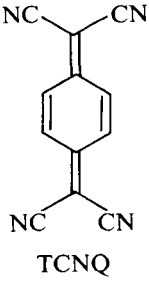
BEDT-TTF

(48)

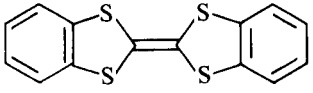
polyoxoanions[220] as above, (BEDT-TTF)$_2$ [M_6O_{19}], have been determined. A combination of methylthio substitution and fused ring is found in **49**, its acceptor partner is 7,7,8,8-tetracyano-*p*-quinodimethane (TCNQ) **50** in 2:1 ratio in a crystal[221]. The dibenzotetrathiafulvalene (**51**) donor and its salts with TCNQ and derivatives have been investigated[222]. Macrocyclic derivatives of TCNQ and TTF are known, e.g. **52**[223]. The aim of these studies is often to relate structure with electric properties of the crystal.



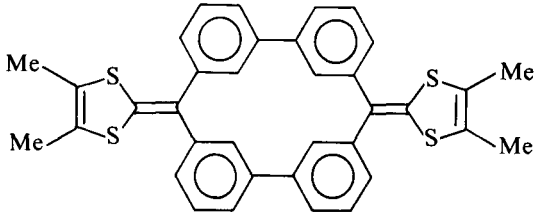
(**49**)



TCNQ (**50**)



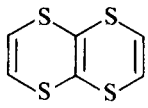
(**51**)



(**52**)

The six-membered rings of thiane[224], $\overline{CH_2(CH_2)_4S}$ (**53**), and 1,3,5-trithiane[225], $\overline{CH_2SCH_2SCH_2S}$ (**54**), have the chair conformation. The conformations of analogous heterocycles have been discussed[7,12,226], and it is observed[7,12] that the puckering of six-membered rings increases from cyclohexane with the increasing number of heteroatoms (O, S). Angular strain is thus released, and bond lengths and bond angles remain close to the values usual in acyclic molecules. Parameters C—S (r_g) and C—S—C from the ED studies: in **53** 1.811(4) Å, 97.6(8)°, in **54** 1.812(4) Å, 99.1(4)°.

The crystallographically independent molecules of **55** are exactly or nearly centrosymmetric, and the two fused dithiin rings, folded along the S···S lines, are composed into an overall chair form[227]. The fold angle is about 130°. Mean parameters of the symmetric molecule: C—S 1.762(3), C=C 1.331(6) Å, C—S—C 99.9(1)°.



(**55**)

Heterocyclic analogs of 9*H*,10*H*-anthracene are planar or mostly folded in the central ring, depending on several factors. In the perfluoro compounds, the degree of folding

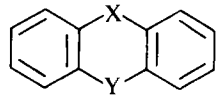
TABLE 12. Parameters (r_g) of the central ring of xanthene and related molecules[a]

	X	Y	C—X(Å)	C—X—C(deg)	C—Y—C(deg)	θ(deg)	Reference
56	O	C=O	1.367(8)	119.7(11)	115.7(8)	180	228
57	O	CH_2	1.357(5)	120.9(11)	112.7(7)	159.7(21)	229
58	S	C=O	1.751(2)	103.4(3)	119.4(6)	169.0(16)	230
59	S	CH_2	1.769(2)	100.0(7)	109.4(10)	131.3(13)	231
60	S	S	1.770(3)	104.1(1)	104.1(1)	131.4(3)	232

[a] θ is the fold angle of the central ring along the line X···Y.

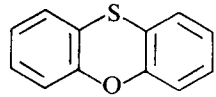
increases in the series of heteroatoms from O to Te[33]. Related molecules with a methylene or a carbonyl group in the central ring have been studied by ED (Table 12).

Bond lengths shown are similar to those in PhOMe[233], C_{ar}—O 1.361(15) Å and in Ph_2S[117], C_{ar}—S 1.772(5) Å, the C—O—C and C—S—C bond angles are wider than in Me_2O and Me_2S (Table 9). Angular strain leads to larger folding in the sulfur analogs, and a carbonyl group in the central ring wants to restore planarity: xanthone (**56**) is a planar molecule, while the folding in thioxanthene (**59**) is the same as in thianthrene (**60**) (Table 12). A deviation from planarity is observed within the halves of the 'butterfly' molecule in **59**[231] (Figure 37), like in other molecules of this type[33].



(56–60)

Phenoxathiin (**61**) has been studied in the crystal by XD[234]. The fold angle of the central ring, 142.3°, is slightly smaller than the angle between the mean planes of the fused benzene rings, 147.8°. Mean parameters of the heterocyclic ring are C—S 1.762, C—O 1.386, C=C 1.388 Å, C—S—C 97.7(1), C—O—C 117.4(2)°.



(61)

A derivative of thianthrene (**60**), the dication **62** with 14 π electrons is, contrary to expectation, not an aromatic ring system[235] but can be regarded rather as consisting of two chains MeO—CCC—S^+—CCC—OMe. The C—C bonds connecting these parts are elongated (XD)[235], 1.453(8) and 1.472(8) Å in the central and external rings, respectively, compared to those in **60**, C—C (mean) 1.400(2) Å.

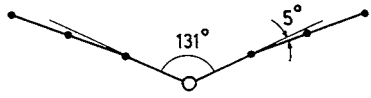
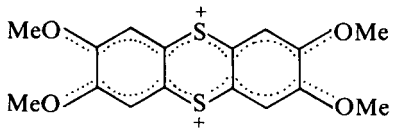
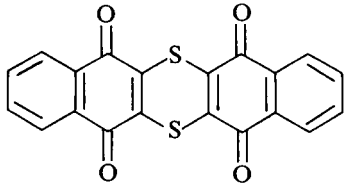


FIGURE 37. Projection of the thioxanthene (**59**) molecule, looking down the S···CH_2 line



(62)

The fused ring system is planar in the crystal of dinaphtho[2,3-*b*;2′,3′-*e*][1,4]dithiin-5,7,12,14-tetraone **(63)**[236]. The molecule combines donor sulfur and acceptor carbonyl functions, thus the pure substance shows the properties of a semiconductor charge-transfer complex[236]. Figure 38 illustrates the stacking of molecules. Stair-like stacks are linked by C—H···O hydrogen bonds (Figure 39). The mean C—S bond length is 1.754 Å, angle C—S—C 101.9(3)°.



(63)

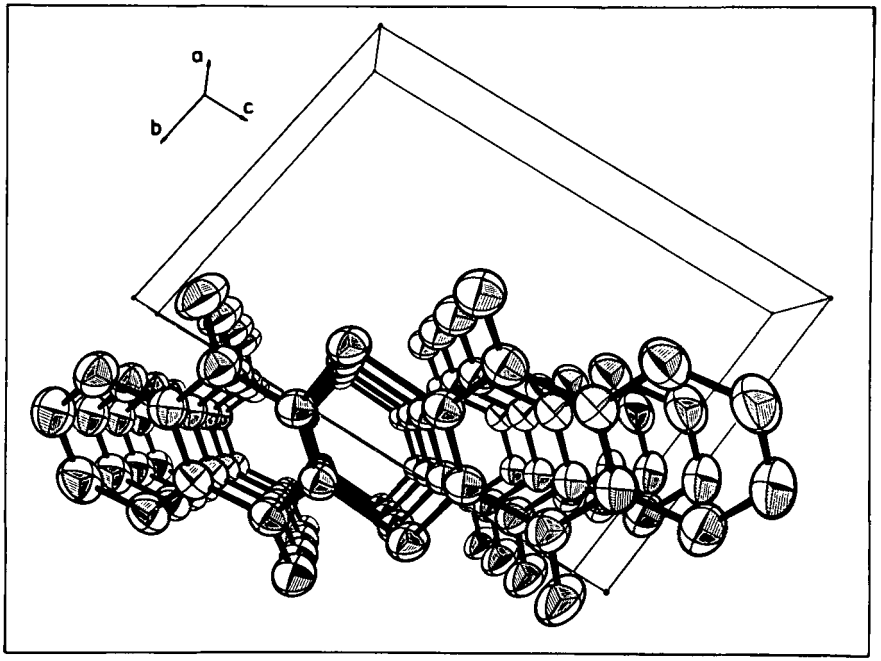


FIGURE 38. Perspective view of the molecular stacking in the crystal of **63**. Reproduced by permission of The Royal Society of Chemistry from Reference 236

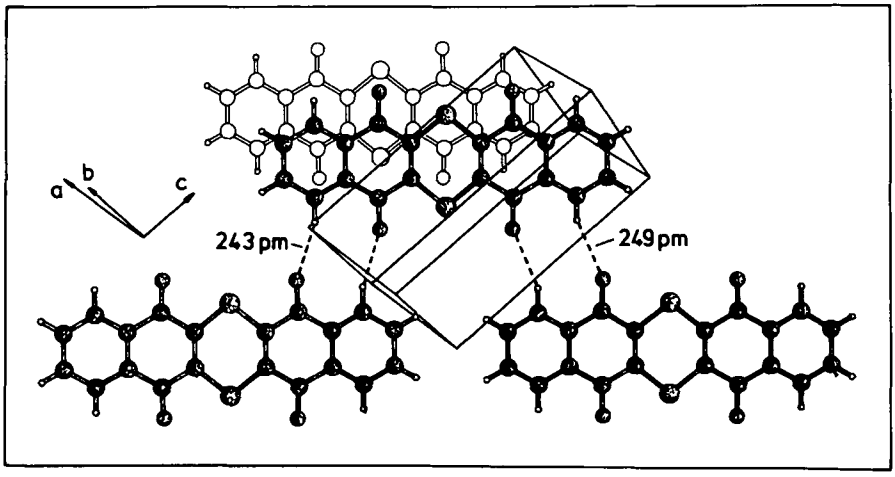


FIGURE 39. Adjacent stacks in the crystal of **63**. Reproduced by permission of The Royal Society of Chemistry from Reference 236

Macrocyclic thioethers have a rich coordination chemistry, a variety of structures of ligands and complexes[7,237–240]. One of the simplest ligands of this type is 1,4,7-trithiacyclononane, [9]aneS_3 (or 9S3 in other notation), which adopts the exceptional *endo* conformation with C_3 symmetry in the crystal[241]. Most crown thioethers prefer the *exo*dentate form and *gauche* arrangement at C—S bonds, *anti* at C—C bonds[238,242]. The gas-phase structure of [9]aneS_3 has been studied by ED and molecular mechanics calculations[243]. Two of the lowest-energy conformers, a C_2 [12222] and a C_1 [12222] form (Figure 40), were fitted equally well to the experimental data. (The numbers here in brackets [], according to Dale's notation[244], are the numbers of bonds between 'corner' atoms marking the form of the ring. A [333] form exists in the crystal[241].) Mean parameters in the C_1 ring are (r_a) C—S 1.820(1) Å, C—C 1.533(4) Å, C—S—C 103.8(7)° and C—C—S 115.0(5)°. The torsional angles about bonds (rounded values, starting from a C—S to the S—C bond), −127, 60, 75, −103, 74, −104, 130, −75 and 64°, do not resemble the usual pattern of *gauche* and *anti* sequence mentioned above. The D_3 [333] conformer (Figure 40), which is also in an energy minimum and makes one-third of cyclononane in the gas phase beside another C_2 form[245], is incompatible with the ED data[243] of [9]aneS_3.

Oxidation with H_2O_2 in glacial acetic acid gives the hexaoxide of [9]aneS_3, a sulfone. The molecule has an approximate C_3 symmetry in the crystal and the same conformation as the cyclic sulfide with *gauche* C—S and *anticlinal* C—C arrangements[246]. The bond lengths and angles are (rounded from the original data): C—S 1.782 to 1.788 Å, S=O 1.431 to 1.443 Å, C—C 1.525 to 1.533 Å, C—S—C 106.1 to 106.8°, C—C—S 112.6 to 115.9°, O=S=O 118.7 to 119.8°. Oxidation of [9]aneS_3 with Au(III) or [Ph_3C] [PF_6] leads through C—H bond cleavage to a bicyclic sulfonium cation (Figure 41). An XD study[247] of its salt [$C_6H_{11}S_3$] [BF_4] reveals a chair-form six-membered ring with torsional angles from 57° to 70°. The five-membered ring is an envelope. The bridging C—S bond, 1.8414(24) Å, is somewhat longer than the other C—S bonds from 1.798 to 1.817 Å. The

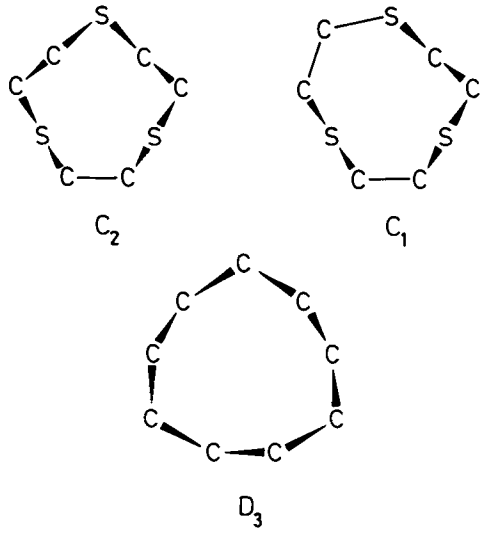


FIGURE 40. The C_2 and C_1 conformer of gas-phase [9]aneS_3 after Reference 243, and the D_3 form of cyclononane[245]

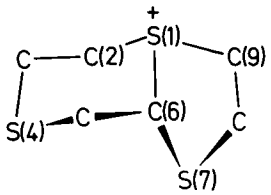
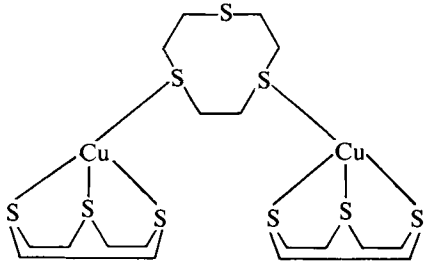


FIGURE 41. The conformation of the 4,7-dithia-1-thioniabicyclo-[4.3.0]nonane cation after Reference 247

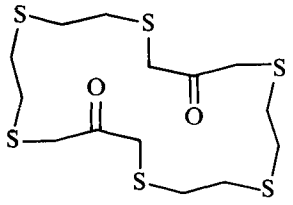
sulfur bond angles are smaller in the five-membered ring (rounded values): C—S (7) —C 91.0, C(6)—S(1)—C(9) 96.2, C(2)—S(1)—C(9) 102.4, C(2)—S(1)—C(6) 101.3 and C—S(4)—C 99.1°.

An unusual conformation and coordination of [9]aneS_3 occurs in the binuclear cation $[Cu_2(C_6H_{12}S_3)_3]^{2+}$ (**64**). In two $Cu(C_6H_{12}S_3)^+$ units, a tridentate ligand molecule binds the metal ion facially with minor changes from the free ligand's conformation, while the third ligand, adopting a different ring conformation, bridges these two units[248].

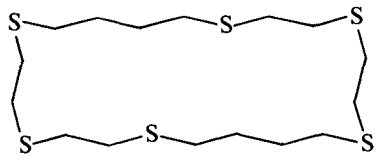


(64)

The molecule **65**, $C_{14}H_{24}O_2S_6$, has a center of symmetry in the crystal[249]. This large ring demonstrates the usual form of macrocyclic thioethers: the sulfur atoms occupy the *exo*dentate corner positions with *gauche* conformation about the C—S bonds and *anti* S—C—C—S moieties. The mean C—S bond length is 1.816 Å, the mean C—S—C angle 101.4°. The two C=O groups point inwards, above and below the mean ring plane.



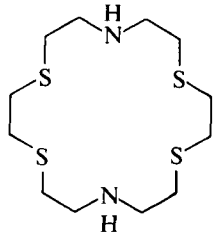
(65)



(66)

Dimethylene and tetramethylene chains connect the sulfur atoms in **66**[250], $C_{16}H_{32}S_6$. Sulfur bond lengths and bond angles are similar to those in **65** . The two sulfur atoms which are on the sides of the rectangle build *anti, anti* C—C—S—C—C linkages.

One example of a complex with the nitrogen-containing macrocycle [18]aneN_2S_4 (**67**) is shown in Figure 42. The coordination at Fe^{2+} is distorted octahedral[251]. The structures of the metal-free ligand[252] and of its diprotonated cation have been determined[253], too, by X-ray crystallography.



(67)

The conformations of 2,11-dithia[3.3]cyclophanes have been studied by XD, molecular mechanics and NMR methods[254]. The *ortho, meta* isomer (**68**) undergoes conformational interconversions in solutions, and adopts the *syn* chair–chair form in the crystal, with the aromatic rings in nearly parallel *syn* position. In **69**, the *para*-substituted benzene ring is slightly distorted to a boat form, and the substituent methylene carbon atoms also deviate

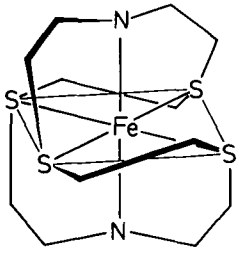
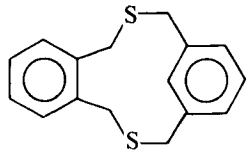
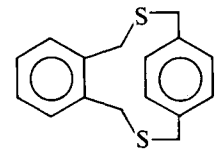


FIGURE 42. The coordination in the $[Fe(18]aneN_2S_4)]^{2+}$ cation after Reference 251



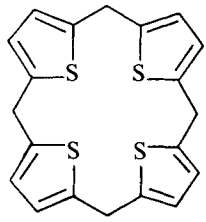
(68)



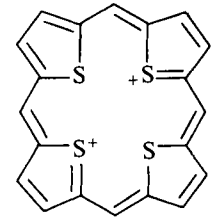
(69)

from the plane of its four central atoms by 0.44 Å. The C—S—C angles are relatively large, 106.4(2)° and 107.0(2)°.

Tetrathiaporphyrinogen (**70a**) has been prepared recently from its oxygen analog with H_2S and HCl[255], using a well-known reaction in furan chemistry. The molecule possesses a symmetry center in the crystal[255]. The thiophene rings are tilted from the plane of the CH_2 carbons by 19.6 and 78.6°, and their geometry, e.g. C—S (mean) 1.725 Å, C—S—C 92.9°, is similar to that of free thiophene (see above). The closest intramolecular S···S distance, 3.45 Å, is shorter than 3.70 Å, twice the van der Waals radius. The structures of a tetrathiaporphyrin dication salt[255] (**70b**) and of mono- and dithiaporphyrin derivatives[256] have been determined by XD.



(70a)



(70b)

Polyphenylene sulfides $(p\text{-}C_6H_4S)_n$, $n = 4$[257],5[258], 6[259], 7 and 8[260] have been studied by XD. The mean C—S bond lengths range from 1.775 to 1.784 Å in the series, the mean C—S—C angle opens with increasing ring size from 98.7° for $n = 4$ to 103.7° for $n = 8$[260]. The C—S bonds are slightly shorter, the C—S—C angles wider in the related acyclic $p\text{-}C_6H_4(SC_6H_5)_2$ (Section III. B). The flexibility of the heptameric macrocycle is indicated by the presence of four different conformations in the triclinic $P\bar{1}$ crystal (Figure 43). The octameric molecule, on the other hand, crystallizes in the tetragonal space group $P42_1c$, and has a rather symmetric (S_4) saddle-shaped ring (Figure 44).

F. Heterocycles with Sulfur and Other Heteroatoms

The plausible structure of thiazolidine, $\overline{CH_2NH(CH_2)_2S}$, has a twisted ring conformation with an axial N—H bond (Figure 45) and a presumably high barrier to pseudorotation, concluded from the vibrational energies (117 cm^{-1} in the first excited state)[261]. The torsional angles about the C—S bonds are 13.2°.

Isothiazole (**71**) as a compact molecule presents difficulties to ED analysis because of similar internuclear distances leading to high correlation between parameters. The utilization of rotational constants in the ED study helped to resolve ambiguities[262], and the parameters obtained are in good agreement with results of *ab initio* 6-31G* (6d) calculations. The complete substitution structure of 1,3,4-thiadiazole (**72**) has been determined from MW spectra of isotopic species[263]. Both molecules are planar. Some data are listed

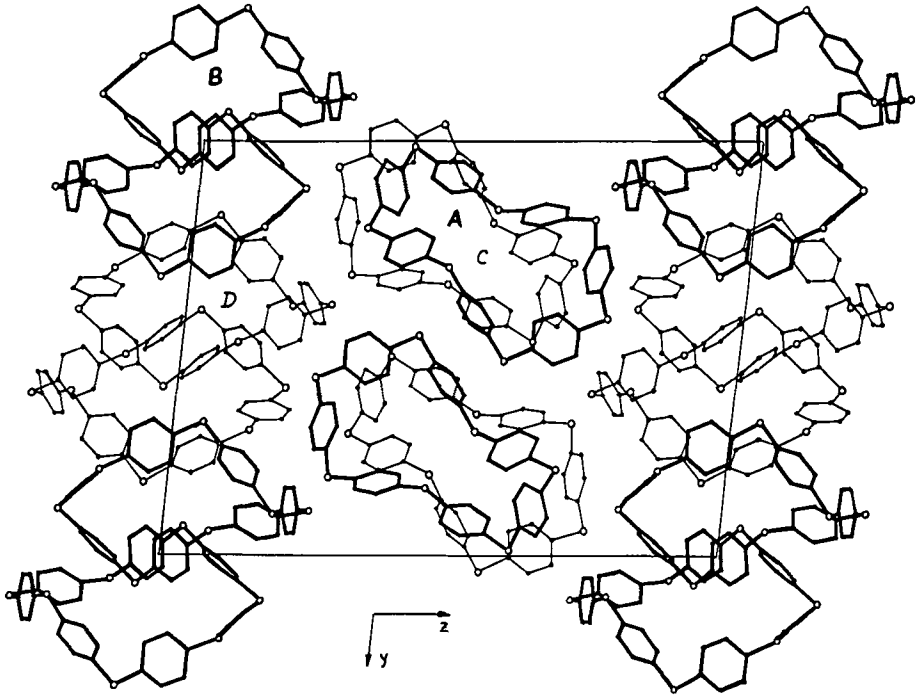


FIGURE 43. Projection of the crystal structure of $(p\text{-}C_6H_4S)_7$ on the *bc* plane. The geometries of the S_7 subsets are similar within pairs of symmetrically independent molecules A, C and B, D. Molecules are distinguished by thick and thin lines. Reproduced by permission of the authors from Reference 260

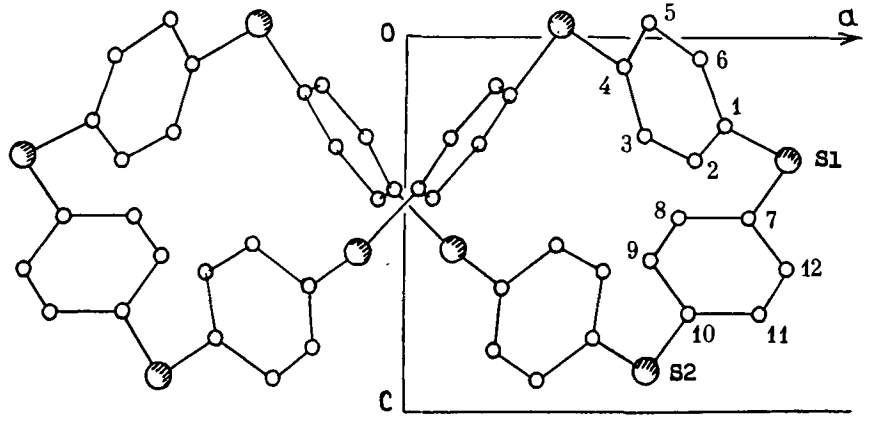


FIGURE 44. The projection of the $(p\text{-}C_6H_4S)_8$ molecule, S_4 symmetry, on the crystallographic *ac* plane. Reproduced by permission of the authors from Reference 260

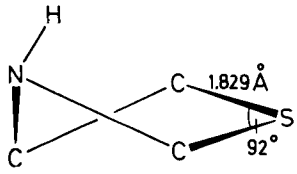


FIGURE 45. Plausible structure of thiazolidine from MW spectroscopy[261]

(71)

(72)

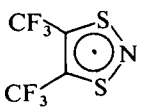
TABLE 13. Structural data of sulfur–nitrogen heterocycles[a]

		Bond		Angle	Reference
73[b]	C—S	1.749(5)	C—S—N	96.5(12)	268
	S—N	1.634(4)	S—N—S	117.3(9)	
74	C—S	1.743[c]	C—S—N	99.2[c]	268
	S—N	1.646[c]	S—N—S	113.9(1)	
75	C—S	1.713[c]	C—S—N	98.5[c]	269
	S—N	1.61[c]	S—N—S	117.1(2)	
76	C—S(1)	1.689(9)	C—S(1)—N	99.3(5)	270
	C—S(3)	1.712(9)	C—S(3)—N	98.7(4)	
	S(1)—N	1.617(9)	S—N—S	115.3(5)	
	S(3)—N	1.585(8)			
77	C—S	1.71(2)[c]	S—S—S	100.2(3)[c]	271
	S—S	2.026(8)[c]	C—S—S	98.8(5)[c]	
78	S—N	1.630[c]	S—S—N	94.6[c]	272
	S—S	2.087[c]	S—N—C	112.4[c]	
78[b]	S—N	1.623(3)	S—S—N	93.9(5)	272
	S—S	2.113(6)	S—N—C	113.9(6)	
79	$PhCN_2S_2$				273
	S—N	1.615[c]	S—S—N	94.8[c]	
	S—S	2.064(2)	S—N—C	114.8(3)[c]	
	S_3N_3				
	S^x—N(S^x)	1.620[c]	N—S^x—N	116.4[c]	
	S^x—N(S)	1.569[c]	N—S—N	113.4(2)	
	S—N	1.633[c]	S^x—N—S^x	122.6(2)	
			S^x—N—S	125.4[c]	
80	C—S	1.775(4)	C—S—N	97.0(2)	274
	S(1)—N(2)	1.632(4)	N—S—N	102.2(2)	
	S(3)—N(2)	1.659(4)	S—N—S	110.8(2)	
	S(3)—N(4)	1.646(4)	S—N—C	113.7(3)	
81	S(1)—N	1.590[c]	N—S—N	101.1(5)	275
	S(3)—N	1.532[c]	S—S—N	96.8[c]	
	S—S	2.093(5)	S—N—S	122.6[c]	

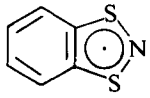
[a]Data from XD studies if not specially noted. Bond lengths in Å, bond angles in degrees.
[b]Gas-phase ED study.
[c]Mean value.
[x]Sulfur atom participating in S···S interaction (Figure 46).

here for **71**, r_g C—S 1.702(5), S—N 1.642(5), N=C 1.319(3) Å, C—S—N 96.1(2)°, and for **72**, r_s C—S 1.7200(3), N=C 1.3031(5) Å, C—S—C 86.38(2)°, but a meaningful discussion would require a systematic compilation of accurate data for related molecules.

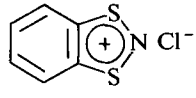
Many sulfur–nitrogen heterocyclic compounds, e.g. dithiadiazoles[264], are free radicals, neutral or ionic, and have unusual properties[265–267]. The free radical **73** is a paramagnetic liquid at room temperature[268]. Some of these species (**73**, **78**) have been studied in the gas phase by ED. Parameters from ED and XD investigations are shown in Table 13. The trithiolium ion of **77** is formally related to **73** by substituting S^+ for N. The crystal of **77** is orthorhombic, space group *Pnma* (or $Pna2_1$), and is built from layers, which are perpendicular to the *b* axis, and contain both cations and anions. The CN_2S_2 dithiadiazolyl rings are essentially planar. The variations in the S—S bond lengths of $PhCN_2S_2^+$ units in different structures have been explained by electron donation from the anionic species to the antibonding orbital of the cation[273]. Bond lengths in **80** between the rings and in the phenylene ring indicate larger contribution of the quinoid form (shown in the formula) than of zwitterionic forms. The structure of **79** is an example of strong S···S interactions in the crystal (Figure 46). Sulfur bond angles in the S_3N_3 ring are large. Bond lengths and angles in this six-membered ring show an interesting pattern: the two opposite angles N—S—N and S^x—N—S^x are narrower, the bonds forming them are longer than corresponding other angles and bonds in the ring (Table 13).



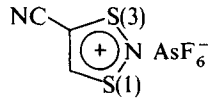
(**73**)



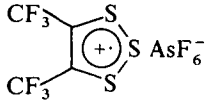
(**74**)



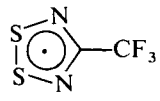
(**75**)



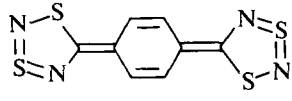
(**76**)



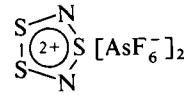
(**77**)



(**78**)



(**80**)



(**81**)

In aminotrithiadiazepines the lone pair of the amino nitrogen may have different orientations (Figure 47), due probably to packing effects in the crystal[276]. The lone pair of the NH_2 nitrogen is *antiperiplanar* to the C—S bond, which is slightly elongated to 1.720(4) Å, compared to 1.696(7) Å in the unsubstituted heteroring[276]. Stacks of planar molecules are linked by N—H···N hydrogen bonds (Figure 48), which are absent in the dimethylamino and morpholino derivatives.

Short nonbonded S···S contacts (2.666 Å) occur in the free S_4N_4 molecule (Figure 49), which has been studied by ED[277]. The S···S distances in the S—N—S fragments are somewhat longer (2.725 Å). The molecule possesses D_{2d} symmetry. Parameters r_α S—N

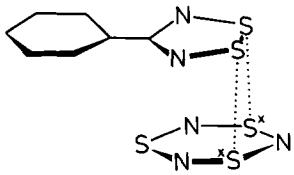


FIGURE 46. The structure of $[PhCN_2S_2][S_3N_3]$ (**79**), drawn after Reference 274. The mean S···S^x distance is 2.906(3) Å[273]

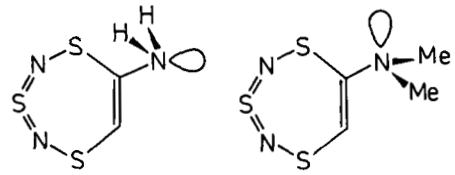


FIGURE 47. The conformation of aminotrithiadiazepines after Reference 276

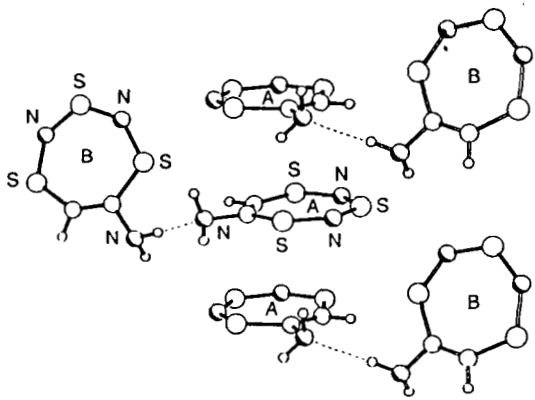


FIGURE 48. Stacking and N—H···N hydrogen bonds in the crystal of 6-aminotrithiadiazepine. Reproduced by permission of The Royal Society of Chemistry from Reference 276

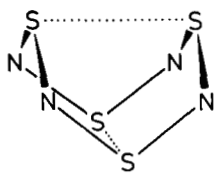


FIGURE 49. The structure of tetrasulfur tetranitride, with S···S distances of 2.666(14) Å indicated. Drawn after Reference 277

1.623(4) Å, N—S—N 105.3(7)° and S—N—S 114.2(6)° may be compared to those in Table 13.

Four- and five-membered rings with S and Si have been studied by ED. 3,3-Dimethyl-3-silathietane[278] (Figure 50) has a puckered ring with r_a C—S 1.853(4) Å, C—S—C 89.5(4)° and a S···Si distance of 2.67 Å, which is shorter than the sum of intramolecular 1,3

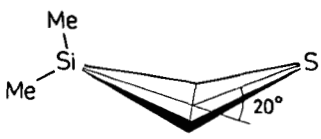
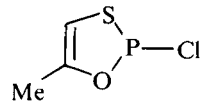


FIGURE 50. Ring puckering in 3,3-dimethyl-3-silathietane

FIGURE 51. The conformations of **82** (left) and **83** (right)



(**84**)

nonbonded radii[3c], 3.00 Å. As far as the conformation of a five-membered ring is governed mainly by torsional strain, the largest dihedral angle is expected at the bond where the torsional barrier is the highest[279]. This is observed in the half-chair ring of 3,3-dimethyl-3-silatetrahydrothiophene[280] (**82**) (Figure 51), with torsional angles S—C—C—Si 36, C—C—Si—C 28, C—Si—C—S 10° (dependent angles), Si—C—S—C 10(6) and C—S—C—C 29(6)°. Bond lengths and angles were determined with large uncertainties, C—S 1.86(3) Å, C—S—C 102(3)°. The ring of 2-methyl-1,3,2-dithiaarsolane[281] (**83**) has a similar shape with C_2 symmetry (Figure 51), r_a C—S 1.805(9), As—S 2.229(2) Å, As—S—C 100.5(8)°. The mean As—S bond length from crystallographic data[32] is 2.275(32) Å, $n = 14$. In 2-chloro-5-methyl-1,3,2-oxathiaphospholene (**84**), the envelope flap angle of the O—C=C—S and S—P—O planes is 15°, and the geometry at sulfur is given by r_a C—S 1.731(10), S—P 2.065(5) Å, P—S—C 95.6° if r(S—P) = r(P—Cl) is assumed[282].

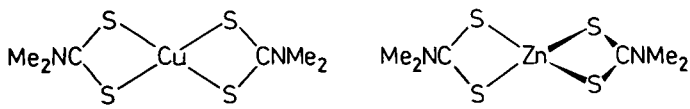


FIGURE 52. The structures of dithiocarbamato complexes $[M(S_2CNMe_2)_2]$. The coordination geometry is distorted square planar (D_{2h}) for M = Cu, and distorted tetrahedral (D_{2d}) for M = Zn

Organometallic compounds and metal complexes are not discussed in this chapter, but some structures are mentioned in various contexts. Two dithiocarbamato complexes, $[M(S_2CNMe_2)_2]$, M = Cu, Zn, have been studied in the gas phase by ED[283]. The coordination geometry is different in the two molecules (Figure 52). The square-planar arrangement around Cu is attributed to crystal field stabilization energy[283]. Parameters r_g C—S, S—M and the chelate angle S—M—S are for M = Cu 1.716(10), 2.284(9) Å, 78.8(7)°, for M = Zn 1.727(10), 2.348(8) Å, 79.7(6)°, respectively.

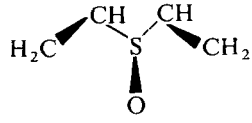
IV. THREE-COORDINATED SULFUR

A. Sulfoxides

There is little to add to the recent review on gas-phase structures of sulfoxide and sulfone molecules[8].

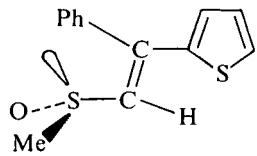
The ED investigation of divinyl sulfoxide (**85**) has detected the coexistence of at least two conformers[137]. Both C=C bonds eclipse the S=O bond in the form that is present

in 78(17) percent. This conformer has C_s symmetry and the C—S—C=C dihedral angles are 1(4)°. The C=C bonds seem to eclipse the S=O or S—C bond or the sulfur lone pair in the other form(s) present. Assuming that only the torsional angle varies between conformers, the following parameters have been obtained: r_g C—S 1.785(4), S=O 1.477(3) Å, C—S—C 99.2(18), C—S=O 107.5(14)°.



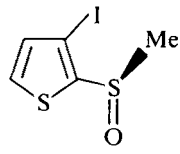
(85)

Vinyl sulfoxides and sulfones have some pharmacological importance because of their antianoxic activity[284]. The conformation of the vinyl sulfoxide **86** is characterized in the crystal[284] by dihedral angles C=C—S=O 133(1)° and C=C—S—Me −119(1)°, i.e. the C=C bond eclipses the lone pair of the S atom. The Ph and thienyl groups are rotated by about 60 and 25° from the respective C=C—C plane. The geometry at the S=O group: Me—S 1.788(7), C(sp^2)—S 1.767(6), S=O 1.509(4) Å, Me—S—C(sp^2) 95.5(3), Me—S=O 105.4(3), C(sp^2)—S=O 104.7(3)°.



(86)

Ab initio calculations indicate that eclipsed forms are preferred in vinyl[285] and phenyl[286] sulfoxides and in sufinyl derivatives of furan and thiophene[287]. The XD study of derivatives **87–91** revealed different conformations depending on the substitution position[288]. Unless a 2-halogeno substituent interferes, the *synperiplanar* orientation of the S=O group to the ring O or S atom is realized. Ranges of parameters are Me—S 1.770(12) to 1.81(2), C(ring)—S 1.754(8) to 1.79(3), Me—S being longer when their difference is significant; S=O 1.47(2) to 1.507(7) Å, Me—S—C(ring) 97.6(4) to 99(1), Me—S=O and C(ring) —S=O 104.6(7) to 107(1)°. The sulfinyl S atom is chiral in **87–91**. The crystals of these substances contain both enantiomers, and belong to one of the centrosymmetric space groups. The conformation of ring-substituted methyl phenyl sulfoxides in the crystal is similarly close to coplanarity of the ring and S=O group if at least one of the *ortho* positions is unsubstituted[289]. The ranges of parameters found: Me—S 1.779(6) to 1.803(4), C(ring)—S 1.786(4) to 1.820(3), S=O 1.478(3) to 1.499(3) Å, Me—S—C(ring) 95.7(2) to 98.6(2), Me—S=O and C(ring)—S=O 104.2(2) to 108.5(6)°.



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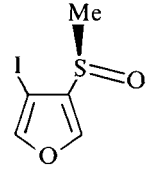

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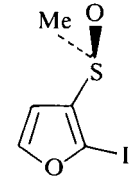

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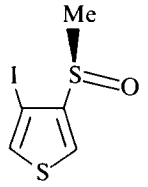

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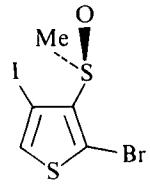
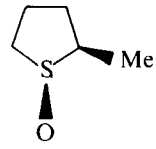


(91)

Simple five-membered saturated ring molecules, cyclopentane and tetrahydrofuran, perform large-amplitude out-of-plane vibration, pseudorotation. Tetrahydrothiophene-1-oxide (**92**) and *cis*-2-methyltetrahydrothiophene-1-oxide (**93**) are found by ED to have distinct conformations along the pseudorotation pathway[290]. **92** is characterized by an asymmetric half-chair ring, **93** lies between a half-chair and an envelope form with an equatorial Me group. The S=O bond is pseudoaxial in both molecules. Parameters r_g are the following:

	C—S (Å)	S=O (Å)	C—S—C (deg)	C—S=O (deg)
92	1.828(4)	1.484(3)	92.0(3)	110.0(4)
93	1.834(4)	1.485(3)	91.7(4)	105.3(3)

(92)



(93)

Thiane-1-oxide takes the chair conformation with axial S=O bond and C_s overall symmetry, according to an ED study[291] (Figure 53). The puckering is unevenly distributed in the ring, and is larger at the sulfur end than in thiane (**53**)[224]. Let us compare below the dihedral angles about bonds and the flap angles of the C(6)—S—C(2) and C(3)—C(4)—C(5) planes to the plane of C(6), C(2), C(3), C(5) in the two molecules (see Figure 53 for the numbering of atoms). Other structural parameters in thiane-1-oxide

	Dihedral angle			Flap angle	
	6–S–2–3	S–2–3–4	2–3–4–5	6–S–2	3–4–5
Thiane	55.4	−60.8	58.6	49.6	52.3°
Thiane-1-oxide	65.0	−64.4	51.8	56.8	47.0°

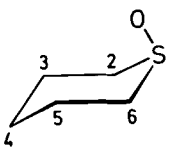


FIGURE 53. The conformation of thiane-1-oxide

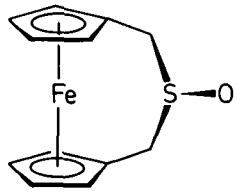


FIGURE 54. The conformation of **94**

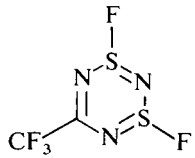
are r_g C—S 1.816(4), S=O 1.483(3) Å, C—S—C 91.1(7), C—S=O 108.1(3)°.

The structure of 2-thia[3]ferrocenophane *S*-oxide (**94**) (Figure 54) in the crystal[292] is similar to that of the parent sulfide[293]. The C—S—C—C dihedral angles in **94** are about 70°, C—S 1.826(2), S=O 1.501(2) Å, C—S—C 100.46(9) and C—S=O 105.2(1)°.

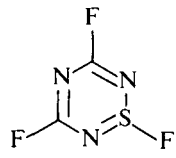
B. Other Structures

Two inorganic molecules will be mentioned first. SO_3 has the planar trigonal geometry exceptional for sulfur. A new equilibrium structure has been determined from the pure rotational spectrum[294], r_e S=O 1.4175 Å. Trithiazyl trifluoride, $(NSF)_3$, has a slightly puckered chair N_3S_3 ring of C_{3v} symmetry with axial *endo* S—F bonds. Parameters from the ED study[295], r_a S—N 1.592(2), S—F 1.619(4) Å, N—S—N 113.3(2), S—N—S 123.5(2) and N—S—F 101.8(2)°, agree well with *ab initio* and XD results.

Ring form and S—F positions in **95**[296] and **96**[297] are similar to those in $(NSF)_3$. The puckering at the N—C—N fragments is smaller than at N—S—N in $(NSF)_3$, and N and C atoms are even coplanar in **96**. Bond lengths r_a from ED are comparable in the three molecules, **95** S—N 1.580 (4), S—F 1.630(10) Å, N—S—N 111.3(12), S—N—S 121.7(2), N—S—F 98.6(21)°, **96** S—N 1.592(7), S—F 1.633(14) Å, N—S—N 109.8(17), N—S—F 100(3)°.

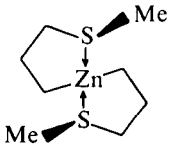


(**95**)



(**96**)

The ED study of bis(3-methylthiopropyl)zinc (**97**) gave C—S (mean) 1.813(5), Zn—S 2.732(12) Å, Zn—S—CH_2 91(2), CH_2—S—CH_3 112(5), S—Zn—S 173(12)° for a C_2 model. The geometry around Zn is nearly square planar, and the long and weak Zn—S coordinative bond is associated with a large mean vibrational amplitude[298].



(**97**)

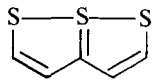
The history of problems[299] and structures[33,299] of 1,6,6aλ^4-trithiapentalene (**98**) and analogs have been surveyed in References 33 and 299. One of the basic questions is the

form of the potential function that governs the 'bell-clapper' motion of the central S atom. The structures of **99** and **100** have been determined by joint analyses of ED data and rotational constants[300]. The large vibrational amplitudes obtained and earlier information indicate a wide flat potential well. Amplitudes and bond distances in the nearly linear O—S—O and S—S—S chains of analogous molecules have been correlated. The C—S and S—O bonds get shorter in the aza derivative **100**:

	C—S(Å)	S—O(Å)	O—S—O(deg)
Y = CH	1.752(16)	1.865(9)	174.3(6)
Y = N	1.696(12)	1.827(8)	172.3(8)

The corresponding mean parameters in the pentalene parts of **101a–c** are[301]:

X = S	1.662	1.848	169.9(1)
X = SO	1.655(3)	1.853	168.1(1)
$X = SO_2$	1.662	1.85	168.8



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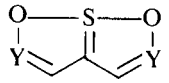
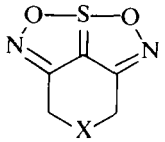


(99) Y = CH

(100) Y = N



(101a) X = S

(101b) X = SO

(101c) $X = SO_2$

The XD study of **101a–c** has been undertaken in order to find correlations of structure with electrochemical reduction potentials and, in fact, phytotoxic activities[301]. Apart from the sulfur atom at X, the ring atoms are nearly coplanar. The largest dihedral angle between the five-membered rings, 7.2°, occurs in the sulfoxide, which has the S=O bond in axial position. The three molecules present an example of comparing related sulfides, sulfoxides and sulfones (mean parameters):

	C—S(Å)	S=O(Å)	C—S—C(deg)	C—S=O(deg)	O=S=O(deg)
X = S	1.818		100.2		
X = SO	1.826	1.496(2)	97.7(1)	105.8	
$X = SO_2$	1.789	1.432	103.1	108.2	119.8

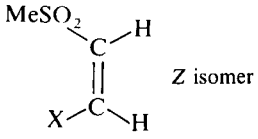
V. FOUR-COORDINATED SULFUR

A. Sulfones

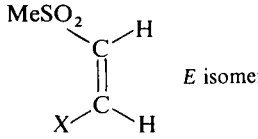
Gas-phase structures which were not discussed in the preceding review[8] include two vinyl sulfones. Both geometrical isomers of methyl 2-chloroethenyl sulfone[302], $MeSO_2CH{=}CHCl$ (**102**), and methyl 2-cyanoethenyl sulfone[303], $MeSO_2CH{=}CHCN$ (**103**), are mixtures of two conformers according to ED studies. The crystal structures of both isomers of

103 have also been determined[303], and molecular parameters are similar to those in the gas phase. The crystalline *E* isomer consists of the prevailing gas-phase conformer. The C=C bond is staggered, due to steric hindrance, to the $MeSO_2$ group in (*Z*)-**102**, but it tends to eclipse a bond in the other molecules. In (*E*)-**102**, which was reinvestigated by a joint ED and *ab initio* analysis, the more abundant conformer is stabilized by an intramolecular O···H hydrogen bond in the nearly planar *syn* O=S—C=C—H chain[302b]. The large substituents cause an opening of bond angles in the *Z* isomers of **102** and **103** (ED results, X = Cl, C≡N):

	O=S—C(=C)(deg)	S—C=C(deg)	C=C—X(deg)
E-**102**	109.2(6)	117.8(7)	123.0(13)
Z-**102**	111.1(7)	127.6(10)	124.3(10)
E-**103**	105.2(5)	114.9(6)	121.5(7)
Z-**103**	109.6(3)	124.7(4)	127.3(7)



Z isomer



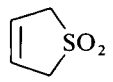
E isomer

(102) X = Cl

(103) X = C≡N

The structures and ring puckering potentials of **104**[304] and **105**[305] have been investigated by MW spectra and *ab initio* calculations. The equilibrium geometry is nonplanar in both rings, with dihedral angles of about 27° and 20°, respectively, between the C—S—C plane and the plane of the carbon atoms. The potential barrier at the planar configuration considerably decreases if an SO_2 group replaces a CH_2 group in the ring, from 515 cm^{-1} in cyclobutane to 140(35) cm^{-1} in **104**[304a] and from 232 cm^{-1} in cyclopentene to 50(11) cm^{-1} in **105**[305]. Making reasonable assumptions, C—S—C angles of 82.3° and 97.7° are consistent with MW spectra.

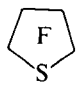
(104)



(105)

Perfluorotetrahydrothiophene, its 1-oxide and 1,1-dioxide (**106–108**) have strongly puckered half-chair ring conformation; symmetric C_2 rings fit well the experimental ED data[306]. Bond lengths and angles are influenced by ring formation and fluorine substitution, and demonstrate as well the changes so much characteristic for analogous sulfides, sulfoxides and sulfones (r_a):

	106	**107**	**108**
C—C(mean) (Å)	1.548(4)	1.553(5)	1.556(6)
C—S(Å)	1.822(4)	1.903(4)	1.882(7)
C—S—C(deg)	94.5(3)	89.4(4)	93.2(10)



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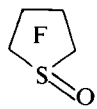

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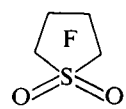
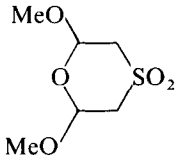


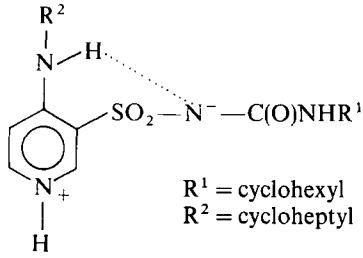
(108)

The 1,4-oxathiane ring of **109** has the chair conformation in the crystal with an equatorial and an axial MeO group[307]. The ring is more flattened at S than at O and is also less puckered at S than the ring of thiane (**53**): dihedral angles C—S—C—C are 55.4(12)° in **53**[224], and 49.6° (mean) in **109**. It is interesting that the C—S—C—C angle is the largest, 65.0°, in thiane-1-oxide among these three molecules (see Section IV.A). Mean sulfur bond parameters in **109** are C—S 1.774(5), S=O 1.435(4) Å, C—S—C 100.5(2), C—S=O 109.3, O=S=O 117.9(2)°.



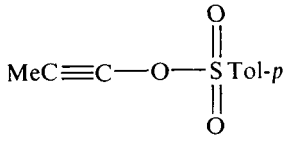
(**109**)

The bonding parameters and conformations of arylsulfonamides, this important class of molecules, were compiled and discussed in detail more than ten years ago[308]. It is not possible to review the development of this field here, only some structures will be mentioned. *N*-Methyltoluene-*p*-sulfonamide (**110**) and *N,N*-dimethyltoluene-*p*-sulfonamide (**111**) have been studied by NMR and XD[309]. Mean bond lengths are comparable with the usual values in sulfonamides[32,308]: C—S, S=O, S—N are 1.770(2), 1.439, 1.620(9) Å in **110**, and 1.762(2), 1.428, 1.614(2) Å in **111**; angles N—S—C are 107.6(5) and 107.5(1)°, respectively. **111** adopts an approximately symmetric conformation in the crystal: the C—S—N plane is nearly perpendicular to the ring plane, and the C—S—N—C sequences are in *gauche* form with dihedral angles of about 70°. The conformations of the four independent molecules of **110** are similar to each other, and may be obtained from this form by rotations about the C—S and S—N bonds by not more than 20°. The sulfonylurea **112** and related molecules are studied as ion transport inhibitors[310]. There is an intramolecular N—H···N hydrogen bond in **112** with a distance N to N of 2.881(3) Å. The protonated pyridinium structure is indicated by bond lengths and angles. The sulfur bond geometry is given by C—S 1.774(5), the relatively short S—N 1.575(5), S=O 1.439(4) and 1.458(3) Å, C—S—N 107.3(2), the very different N—S=O angles of 107.2(2) and 115.1(2), C—S=O 105.3(2) and 105.7(2), O=S=O 115.2(2)°.



(**112**)

The SO_2 group is found in sulfonic acid esters. The first alkynyl carboxylate, phosphate and sulfonate esters have been synthesized very recently[311]. Propynyl tosylate (**113**) exists in a *gauche* conformation in the crystal[312]; the dihedral angle C—O—S—C is 72.2(3)°. The C—C≡C—O chain is essentially linear. Parameters C—S 1.741(3), S=O (mean) 1.423 Å, O=S=O 121.8(2), C—S—O 102.4(1) and S—O—C 117.6(2)° are



(113)

similar to those in alkyl tosylates[312] and in sulfones[12]. The mean C_{ar}—S distance in arenesulfonyl derivatives C_{ar}—$S(O_2)OX$ is 1.752 Å (with a sample standard deviation of 0.008 Å and $n=27$)[32]. The C(sp)—O distance in **113**, 1.331(4) Å, is one of the first of its kind measured experimentally, and is shorter, as expected, than the mean $C(sp^3)$—O bond, 1.465(7) Å, in primary alkyl tosylates[312]. A remarkable phenomenon is the lengthening of the neighboring O—S bond from the mean 1.575(5) Å in alkyl tosylates, to 1.649(2) in **113**[312]. The shortening of the C—O bond from sp^3 to sp^2 to sp carbon and the concomitant lengthening of the adjacent O—S or O—C bond is observed in experimental and calculated *ab initio* geometries of sulfonate and carboxylate esters, and is interpreted on the basis of Bent's rule by the increasing electron-withdrawing ability of the groups from Me to CH_2=CH to CH≡C[311,312].

The crystals of *o*-toluenesulfonic acid dihydrate contain the deprotonated *o*-$MeC_6H_4SO_3^-$ anion and the $H_5O_2^+$ cation[313]. Anions and cations are linked by a network of hydrogen bonding along the *c* axis (Figure 55). The O···O distance within the $H_5O_2^+$ ion is very short, 2.425(3) Å. The S—O bond that is engaged in two hydrogen bonds is longer, 1.473(2) Å, than the other two S—O bonds, 1.447 Å. The C—S bond is 1.771(2) Å, the mean C—S—O angle 107.0°. One of the S—O bonds is nearly coplanar with the aromatic ring.

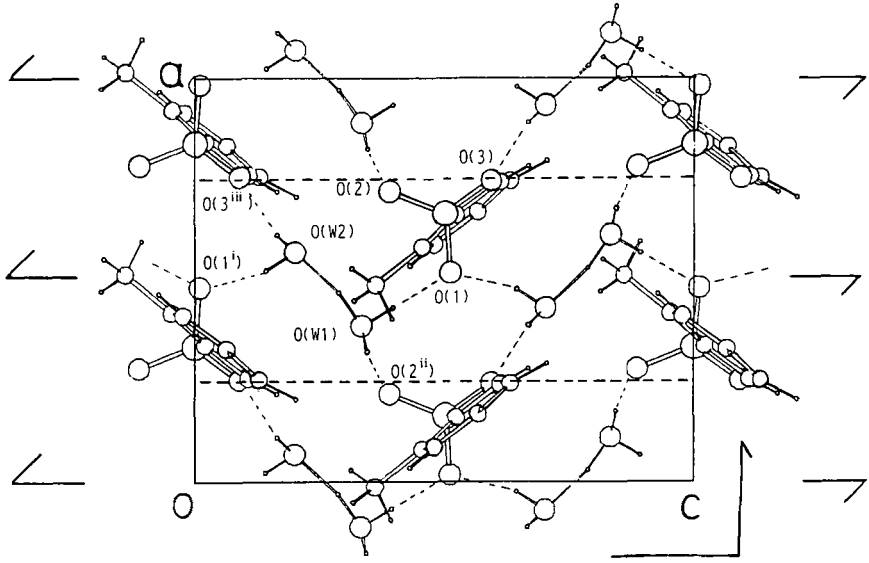


FIGURE 55. The crystal structure of *o*-$MeC_6H_4SO_3^- \cdot H_5O_2^+$ projected along the *b* axis. Reproduced by permission of the International Union of Crystallography from Reference 313

The nature of the S=O bond has been a matter of discussions.[17] O NMR studies on arylsulfinic and arylsulfonic acid derivatives[3,14] emphasize the importance of the polarized $S^+—O^-$ formulation against the π-bond character (with involvement of sulfur d orbitals), as well as the different character of the C=O double bond.

B. The Sulfur Bond Geometry in Sulfones, Sulfoxides and Sulfides

We quote here mean C—S and S=O bond lengths (in Å, with sample standard deviations in parentheses and the number of observations *n*) from a statistical analysis[32] of crystallographic data in the Cambridge Structural Database. (We follow the notation in the reference to specify the environment of the bond: The atoms forming the target bond are in bold type; C* is an sp^3 carbon whose other bonds are to C or H only; C_{ar} is an aryl carbon in a six-membered ring and is treated separately from other sp^2 carbon atoms.)

	n		*n*		*n*
C*—SO_2—C		**C*—S(=O)—C**		**C*—S—C***	
1.779(20)	94	1.809(25)	88	1.819(19)	242
C_{ar}—SO_2—C		**C_{ar}—S(=O)—C**		**C_{ar}—S—C_{ar}**	
1.763(9)	96	1.790(10)	41	1.768(10)	158
				C(sp^2)—S—C*	
				1.751(17)	61
C—SO_2—C		**C—S(=O)—C**			
1.436(10)	316	1.497(13)	90		

Trends in the variations of molecular geometry have been touched on in the preceding sections. The structures of sulfones, sulfoxides and sulfides are discussed and compared in References 1, 8 and 10–12, and it will be sufficient to summarize the most important findings here.

The C—S single bond in sulfides shortens as the carbon hybridization changes[11,12,33] from sp^3 to sp^2 to sp, but the effect is smaller or not significant in sulfoxides and sulfones[8,11]. Although ranges overlap, there seems to be a trend that C—S is shorter for aliphatic than for aromatic sp^2 carbon.

Sulfones, sulfoxides and sulfides are termed in the VSEPR model as AX_4, AX_3E and AX_2E_2 systems, respectively, with a tetrahedral arrangement of bonding and nonbonding electron pairs around sulfur[1,8,12]. Here A is the central atom, X are the ligands, E the lone pairs. Since a lone pair requires larger space than a bonding pair in the valence shell of A, a closing of bond angles and a lengthening of bonds is expected when going from AX_4 to the related AX_3E molecule. Predicting the changes from the AX_3E to the AX_2E_2 case is, however, not at all straightforward[1]. All interactions between bonding and lone pairs in the valence shell must be considered, and there are bond/bond, bond/lone-pair and lone-pair/lone-pair repulsions in an AX_2E_2 molecule. The space requirement of a bonding or nonbonding electron pair may be characterized by the average of the angles it forms with all adjacent pairs[1,12,33].

The closing of bond angles X—S—X and the lengthening of bonds from an X_2SO_2 sulfone to the related X_2SO sulfoxide agree with qualitative expectations from the VSEPR model[8,11,12]. The X—S—X angle opens again, on the other hand, in the corresponding X_2S sulfide, and the changes in the S—X bond lengths from X_2SO to X_2S are small and of different signs. In line with the VSEPR model, the X—S—X angle closes with increasing electronegativity of X in X_2SO_2, X_2SO and X_2S, and the angles X—S—X, X—S=O

and O=S=O increase in this order in a given molecule[8,11,12]. Observed trends in geometries of molecules with a tetrahedral electron-pair arrangement are well reproduced and interpreted by model *ab initio* calculations[1,12,315], which yield also 'angles' describing the positions of lone pairs.

The trends of bond length variations observed in gas-phase data are reflected, too, in the crystallographic mean values cited above.

The remarkably small variation of the O···O distance in sulfones (the mean is about 2.48 Å) indicates the importance of nonbonded interaction in these molecules beside electron-pair repulsions, and explains the correlation found between S=O bond lengths and O=S=O angles in sulfones[1,8,11,12].

Correlations of S=O bond lengths with wave numbers of S=O stretching vibrations in sulfones and sulfoxides[12], or with wavelengths of S=O stretching in sulfones[191] may be used to predict bond lengths from vibrational data. Group electronegativities have been estimated from their correlations with S=O stretching wave numbers and with S=O bond lengths in $XYSO_2$ sulfones[11,12].

The M—Y—M angle, M = C, Si, Ge, closes from Y = O to S and to Se. The oxygen bond angle changes in a wide range; it opens from C—O—C to C—O—Si and to Si—O—Si; the bond angles of two-coordinated S and Se have a smaller variability[1,11,12,33].

C. Trimethyloxosulfonium and Alkylidynesulfur Derivatives

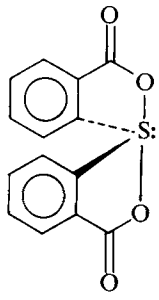
The common structural characteristics of the two title classes is the trigonal-pyramidal arrangement of the four sulfur bonds.

The crystal structures of trimethyloxosulfonium salts have been reported recently in a series of publications[316]. The $(CH_3)_3SO^+$ cation possesses $3m$ (C_{3v}) crystallographic symmetry in the cubic crystals of $[(CH_3)_3SO]Cl \cdot H_2O$, space group $P2_13$ (b). The same cation has an approximate C_{3v} symmetry in the orthorhombic crystals of its Br^-, I^- (a), NO_3^- (c), CrO_4^{2-} (d), $[CdCl_3]^-$, $[CdBr_3]^-$ (e) and SCN^- salts (f), and a crystallographic symmetry plane in some of these cases. (The letters in parantheses refer to items in Reference 316.) The geometrical parameters of the $(CH_3)_3SO^+$ cation are in ranges C—S 1.732(4) to 1.756(3), S—O 1.433(2) to 1.440(4) Å, C—S—C 105.5(1) to 107.8(3) and C—S—O 111.6(2) to 113.6(1)°. The trimethylsulfonium ion has a symmetry plane in crystalline $[(CH_3)_3S]$ I and an approximate C_{3v} symmetry[317], with longer C—S bonds of 1.785(3) and 1.805(6) Å and narrower C—S—C angles of 101.1(2) and 101.8(1)°.

Alkylidynesulfur trifluorides are a new class of molecules which contain the $C{\equiv}SF_3$ moiety. An exceptional feature of these molecules is that they are bent at sp carbon. Vibrational spectra of (trifluoroethylidyne)sulfur trifluoride, $F_3CC{\equiv}SF_3$, have been assigned on the basis of C_{3v} symmetry with a linear C—C≡S chain[318]. The molecule is found by ED[318] to be bent in the gas phase with a C—C≡S angle of 155(3)°, and also in the crystal[319] with C—C≡S 171(2)°. The ED study[320] of $F_5SC{\equiv}SF_3$ gives S—C≡S 159(3)°. *Ab initio* calculations reproduce the 'nonclassical' behavior of these molecules[318], showing a shallow minimum in the bending potential functions near 150°. $F_5SC{\equiv}SF_3$, however, lies on a threefold symmetry axis, and is thus linear in the crystal[321], according to an XD study at −168 °C. Packing effects seem to act toward linearity in both molecules. Other important parameters (r_a from ED) are in $F_3CC{\equiv}SF_3$, C≡S 1.434(14), S—F 1.561(3) Å, F—S—F 93.2(9)°; in $F_5SC{\equiv}SF_3$, C≡S 1.401(9), S—F (mean) 1.559(2) Å, F—S—F (SF_3) 93.9(6)° (see also Section VI).

D. Sulfuranes

Sulfuranes may be regarded as derivatives of the hypothetical SH_4 molecule with an S(IV) atom. The syntheses and structures of the first stable organic spirosulfuranes **114**[322]



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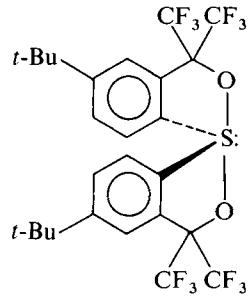

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and **115**[323] were reported in the early seventies. Subsequent studies on the chemistry and structures of organic sulfuranes are reviewed in References 324 and 325. Only the gas-phase structures of some fluorosulfuranes will be discussed briefly in this section.

The general shapes of sulfur tetrafluoride and related molecules comply with the expectations from the VSEPR model[1]. The five electron pairs around sulfur are arranged in a trigonal-bipyramidal fashion, and the lone pair occupies an equatorial position (Figure 56). As the data in Table 14 illustrate, the axial S—F_a bonds are longer than S—F_e, and are bent away from the lone pair. The bond angle in the equatorial plane is smaller than 120°. Less electronegative substituents are placed in an equatorial site (Figure 56). However, when comparing parameters, we may find apparent (or sometimes real?) discrepancies with the VSEPR model. It has been pointed out that the VSEPR model involves the consideration (i) of all angles at the central atom, including those formed by the lone pair(s), and (ii) of all electron-pair interactions in the valence shell, viz. bond/bond, bond/lone-pair and lone-pair/lone-pair repulsions[1,12]. Lone-pair angles are usually not accessible to experiment unless they can be obtained from symmetry considerations. Thus, e.g., the smaller C—S—C angle in $(CF_3)_2SF_2$ than F_e—S—F_e in SF_4 (Table 14) seems to disagree[329] with the predictions of the VSEPR model. The bond angle, however, can vary only at the expense of bond to lone-pair angles in the equatorial plane, and is the result of a balance between bond/bond and bond/lone-pair interactions. Taking all this into account, the apparent contradiction is resolved[1,12]. On the other hand, the C—Se—C angle[332] in $(CF_3)_2SeF_2$, 118.7(17)°, is wider than the F_e—Se—F_e angle[18,333] in SeF_4, 100.6(7)°.

The C—S bond lengthens by about 0.10 Å if CH_3 in CH_3SF_3 is replaced by CF_3 or by CF_2 in other derivatives (Table 14). The ED experimental geometries of CY_3SF_3, Y = H, F, are well reproduced by *ab initio* calculations[327]. One C—Y bond eclipses the S—F_e bond. It still awaits an explanation why in the series SF_4, CF_3SF_3, $(CF_3)_2SF_2$ the

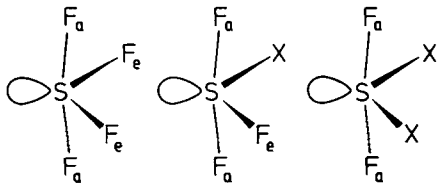

FIGURE 56. The trigonal-bipyramidal arrangement of axial and equatorial ligands and of the lone electron pair in SF_4 and in its derivatives

TABLE 14. Structural parameters[a] of SF_4 derivatives XSF_3 and X_2SF_2

	S—F_a	S—F_e	S—X	F_a—S—F_a	F_e—S—X X—S—X	Reference
					F_e—S—F_e	
SF_4[b]	1.646(3)	1.545(3)		173.1(5)	101.6(5)	326
			S—C		F_e—S—C	
CH_3SF_3	1.689(1)	1.575(5)	1.790(13)	174.6(8)	102.9(8)	327
CF_3SF_3	1.679(4)	1.596(11)	1.911(7)	165.2(25)	100.7(16)	327
$CF_2(SF_3)_2$[c]	1.664(4)	1.562(6)	1.888(7)	173.1(15)	97.2(11)	328
					C—S—C	
$(CF_3)_2SF_2$	1.681(3)		1.888(4)	173.9(8)	97.3(8)	329
			S—N		F_e—S—N	
Me_2NSF_3	1.670(7)	1.563(9)	1.639(13)	174.0(12)	104.6(10)	330
			S—S		F_e—S—S	
$FSSF_3$[d]	1.624(6)[e] 1.722(8)[f]	1.569(8)	2.040(5)	167.0	104.9(14)	331

[a] Distances in Å, angles in degrees. r_a parameters unless noted.
[b] r_0 parameters.
[c] r_g distances.
[d] r_a parameters.
[e] *Syn* to the S—F group.
[f] *Anti* to the S—F group.

smallest F_a–S—F_a angle occurs in CF_3SF_3[327]. The trigonal bipyramid is highly distorted in $FSSF_3$. The S—F group eclipses one of the S—F_a bonds in this molecule, and the *anti* S—F_a bond is considerably longer and forms a short $F_a \cdots S$ contact (2.33 Å) with the S—F group. *Ab initio* calculations[331] indicate that this weak bonding interaction may be important in the dissociation process $FSSF_3 \rightarrow 2SF_2$. The S—S bond is longer than in $FSSF$[102], 1.890(2) Å (Table 11, Section III.C).

Alkylsulfuranyl radicals are transition states in alkyl radical displacement reactions and have been studied by *ab initio* calculations[334]. The sulfur is three-coordinated but exhibits the trigonal-bipyramidal arrangement, a lone pair and the unpaired electron occupying equatorial positions. The axial Me—S—Me grouping is linear in $Me_2HS^{\bullet}$, the angle of the axial bonds is 170° in $H_3S^{\bullet}$ and $Me_3S^{\bullet}$. Axial bonds are longer; *ab initio* calculated values[334] in $H_3S^{\bullet}$ S—H_a 1.529, S—H_e 1.319 Å; in $Me_2HS^{\bullet}$ S—C_a 2.138, S—H_e 1.322 Å; in $Me_3S^{\bullet}$ S—C_a 2.215, S—C_e 1.814 Å.

VI. FIVE- AND SIX COORDINATED SULFUR

The five ligands of sulfur have the trigonal-bipyrimidal arrangement. The doubly-bonded group occupies an equatorial site, and the S—F_a bonds are tilted away from it (Figure 57). The S—F_a bonds are longer than the S—F_e bonds.

Four models of sulfur tetrafluoride oxide, OSF_4, were found to fit the ED experimental data[335]. A choice between them was suggested, using arguments based on the VSEPR model and on nonbonded interactions[12,336]. The re-analysis[337] of ED and MW data yielded a structure very similar to the preferred one[12,336]. Geometrical data of related molecules are listed in Table 15.

There is a large asymmetry in MeN=SF_4 and FN=SF_4. The C—N and F—N bonds lie in the axial plane, eclipsing one of the S—F_a bonds, and the *anti* S—F_a bonds are even

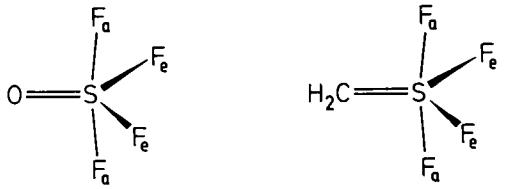

FIGURE 57. The structures of OSF_4 and $CH_2{=}SF_4$

TABLE 15. Structural parameters of $X{=}SF_4$ molecules[a]

	$O{=}SF_4$ ED + MW r_a	$CH_2{=}SF_4$ ED r_a	$MeN{=}SF_4$ ED + MW r_α^0	$FN{=}SF_4$ ED + MW r_{av}
X	O	CH_2	MeN	FN
X=S	1.409(4)	1.55(2)	1.480(6)	1.520(9)
S—F_a	1.596(3)	1.595(15)	1.643(4)[b]	1.615(7)[b]
S—F_a			1.546(7)[c]	1.535(12)[c]
S—F_e	1.539(3)	1.575(15)	1.567(4)	1.564(5)
F_a—S—F_a	164.6(6)	170(2)	167.0(6)	172.5(7)
F_e—S—F_e	112.8(4)	97(2)	102.6(2)	99.8(3)
Reference	337	338	339	340

[a]Distances in Å, angles in degrees.
[b]The S—F_a bond *syn* to N—C or N—F, respectively.
[c]The *anti* S—F_a bond.

shorter than the S—F_e bonds. The N=S bond lengthens from the methyl to the fluoro derivative.

The orientation of the CH_2 group is similarly axial in $CH_2{=}SF_4$ (Figure 57). The structure and electron density distribution of a derivative, (2,2,2-trifluoro-1-methyl-ethylidene)sulfur tetrafluoride, $CF_3(CH_3)C{=}SF_4$, has been determined[341] by XD at −151 °C. The $C_2C{=}SF_2$ skeleton (with the axial fluorines) is approximately planar, and also coplanar with one of the C—F bonds eclipsing the C—CH_3 bond (cf. Figure 58). Bond lengths and angles (in one of the two crystallographically independent molecules), C=S 1.599(3), S—F_a (*syn* to CF_3) 1.593(2), S—F_a (*anti*) 1.586(2), S—F_e 1.569(4) and 1.570(5) Å, F_a—S—F_a 170.40(5), F_e—S—F_e 98.4(2)°, compare well with those in gas-phase $CH_2{=}SF_4$, considering the large uncertainties in the latter case (Table 15). The chemical bonds in $CF_3(CH_3)C{=}SF_4$ and especially the noncylindrical character of the C=S double bond are clearly seen in the electron deformation density maps in Figure 58.

The equatorial fluorines of OSF_4 are substituted by CF_3 groups in $(CF_3)_2S(O)F_2$. Important parameters from an ED study[342] are, r_a C—S 1.891(5), S=O 1.422(7), S—F_a 1.641(4) Å, F_a—S—F_a 173.1(6), C—S—C 97.8(8)°.

Ring formation in a 1,2,4-oxadithiete derivative[343] (Figure 59) diminishes the bond angle at five-coordinated sulfur, and fluorine is expelled from one of the axial positions. The endocyclic bond angle at the SO_2 group, 84.8(3)°, is also narrower than in acyclic sulfones. The ring is strictly planar in one of the three independent molecules which lies on a symmetry plane in the orthogonal *Pbnm* crystal, and the other two molecules have practically the same parameters[343]: S=C 1.573(6), C—S 1.723(6), (O_2)S—O 1.626(5), O—S(F_3) 1.715(5), S—F_a 1.565, S—F_e 1.525 Å (both calculated from atomic coordinates given in Reference 343), O—S=C84.8(9), O—S—F_a 179.5(2) and F_e—S—F_e 98.8(2)°.

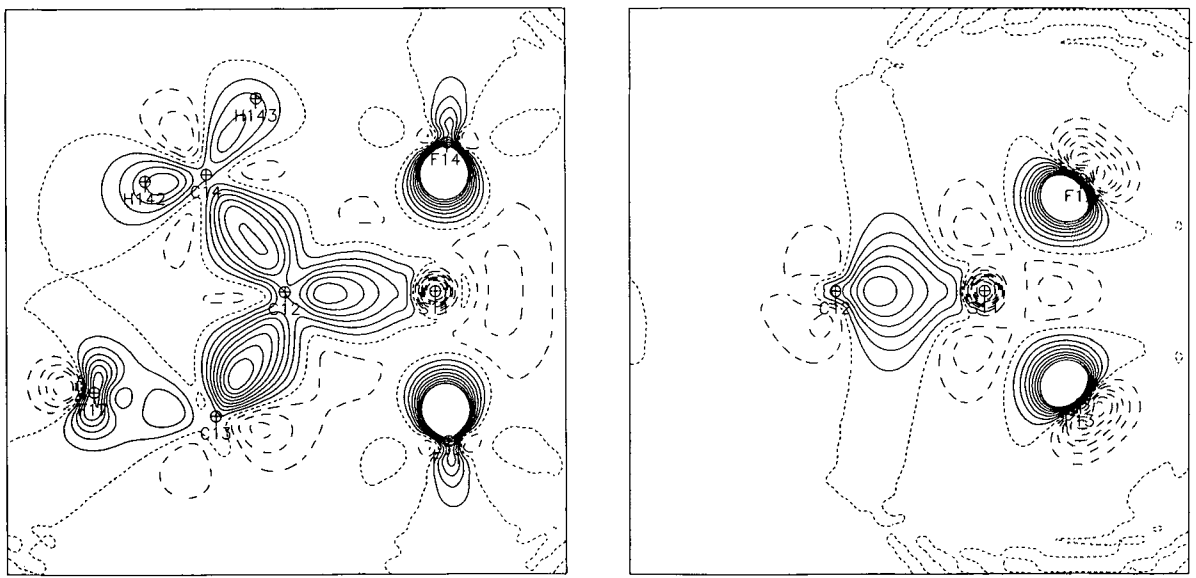

FIGURE 58. Electron deformation density maps of $CF_3(CH_3)C{=}SF_4$: axial plane (left) and equatorial plane (right). The maps represent a static deformation density, obtained by subtracting from the electron-density distribution the density of a spherical atomic model and by extrapolating to zero atomic vibration[341]. Reprint with permission from Buschmann *et al.*, *J. Am. Chem. Soc.*, **113**, 233–238. Copyright (1991) American Chemical Society

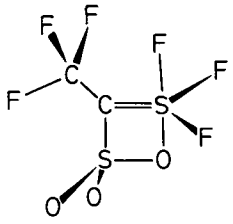

FIGURE 59. The structure of a 1,2,4-oxadithiete derivative with five-coordinated sulfur

TABLE 16. Structural parameters of SF_5X molecules[a]

X	S—F (mean) (Å)	Δ(SF)[b] (Å)	S—X (Å)	F_e—S—F_a (deg)	Reference
F	1.5623(4)	0	1.5623(4)	90	345
Cl[c]	1.570(1)	−0.001(8)	2.055(1)	89.6(1)	346
Br[d]	1.569(1)	0.011(8)	2.232(2)	89.3(1)	347
OF	1.555(3)	0[f]	1.671(7)	90.1(8)	348
—OCN	1.554(2)	0[f]	1.653(6)	90.4(6)	349
$OOSF_5$	1.561(3)	0[f]	1.660(6)	88.8(2)	350
SF_5	1.569(2)	0.027(6)	2.274(5)	89.8(1)	351
—NCO	1.567(2)	0[f]	1.668(6)	90[f]	352
$NHSF_5$	1.567(3)	−0.015[e]	1.679(7)	88.4(5)	353
$NFSF_5$	1.555(4)	−0.026[e]	1.685(5)	88.1(9)	353
CF_3	1.570(2)	0.010(7)	1.887(8)	89.5(2)	354
CF_2SF_5	1.562[e]	0.022(11)	1.908(7)	89.6(2)	355
—CN	1.564(6)	0.008[f]	1.765(5)	90.1(2)	356
$CH{=}CH_2$[d]	1.581(1)	0.020(16)	1.787(9)	88.4(3)	357
C≡CH[d]	1.574(1)	0.018(14)	1.736(6)	88.9(2)	357
C≡CH	1.574(2)	0.001(14)	1.728(5)	88.9(2)	358
$C{\equiv}SF_3$	1.559(2)[g]	0[f]	1.699(12)	88.6(3)	320

[a] From ED experimental data combined with rotational constants in some cases. r_a distances unless otherwise noted.
[b] $\Delta(SF) = r(S—F_e) - r(S—F_a)$.
[c] r_g distances.
[d] r_z distances.
[e] Calculated from the original data.
[f] Assumed.
[g] Mean of all S—F bond lengths.

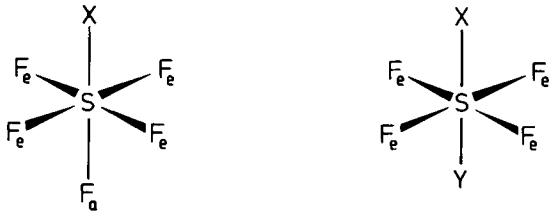

FIGURE 60. Equatorial and axial bonds in distorted octahedral SF_5X and SF_4XY molecules

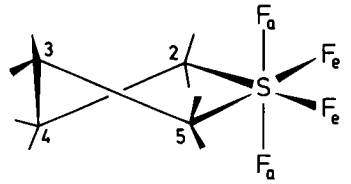

FIGURE 61. Puckered C_2 ring and the SF_4 group in octafluorotetrahydrothiophene tetrafluoride

The chemistry and structures of molecules with carbon–sulfur multiple bonds and the stabilizing effect of fluorine substituents are discussed in Reference 344.

Six-coordinated S(VI) compounds are regarded as substituted derivatives of SF_6. Table 16 lists important structural parameters for SF_5X molecules.

The VSEPR model[1] predicts that the equatorial S—F_e bonds are pushed away from a less electronegative substituent and are longer than the axial S—F_a bonds (Figure 60). The data in Table 16 follow these expectations in general, but deviations from the regular octahedral geometry in the SF_5 moiety are often within uncertainties. It is also expected that the mean S—F bond length, which is more accurately defined, exceeds that in SF_6. The C—S bond is long in SF_5CF_3 and $(SF_5)_2CF_2$. A very large S—C—S angle of 124.3(7)° has been found in the latter molecule[355].

Disubstituted derivatives of SF_6 have been studied by ED[359]. The *trans* isomers of $CF_3SF_4CF_3$, CF_3SF_4Cl and $CF_3SF_4CH_3$ are formed exclusively or predominantly from the corresponding sulfides with ClF[359]. Parameters r_a (see Figure 60) are the following:

X	Y	S—F_e(Å)	S—X(Å)	S—Y(Å)	F_e—S—X(deg)
CF_3	CF_3	1.592(2)	1.874(3)	1.874(3)	90
CF_3	Cl	1.583(2)	1.884(6)	2.050(6)	89.6(2)
CF_3	CH_3	1.606(3)	1.896(6)	1.787(10)	87.2(5)

Further lengthening of the S—F_e bonds occurs here relative to the mean S—F distances (Table 16) and even to the S—F_e bonds in the monosubstituted derivatives. The data above also demonstrate the remarkable lengthening of the C—S bond observed[12,359] upon substituting CH_3 by CF_3.

If sulfur is part of a small ring, *cis* disubstitution is enforced. The five-membered ring in $\overline{SF_4(CF_2)_3CF_2}$ (Figure 61) does not distort the octahedral sulfur bond angles beyond estimated errors[360], C—S—C 90.0(9), F_e—S—F_a 90.5(15), F_e—S—F_e 87.7(29)°. Here it is the axial bonds that are *cis* to both C—S bonds, and, as expected, they are longer, 1.594(6) Å, than the S—F_e bonds, 1.558(6) Å, giving (with the notation in Table 16) S—F (mean) 1.576(3) and Δ(SF) −0.036(9) Å. The C—S bond is again long, 1.896(7) Å. Similarly, the bonds in tetrafluoro-1,3-dithietane octafluoride[355], $(SF_4CF_2)_2$, are S—F_a 1.590(6), S—F_e 1.572(6), S—F (mean)[360] 1.581(3), Δ(SF) −0.018(9), C—S 1.886(4) Å, but the angles are distorted in the planar four-membered ring, C—S—C 83.8(3), F_e—S—F_a 90.1(8), F_e—S—F_e 88.6(10)°.

VII. CONCLUSION

The position of sulfur in the Periodic Table defines its role in organic chemistry and biology, the plethora of its organic compounds and reactions. The variety of bonding

situations and nonbonded interactions around sulfur comes from its different valence states and coordination, availability of d orbitals, presence of lone pairs, capability of catenation, of forming π bonds and participating in hydrogen bonding, etc.

The geometrical structures of sulfur-containing organic molecules have been reviewed in this chapter, arranged according to the coordination of sulfur and the functional groups it forms. The wealth of the material implies that even important classes of compounds have been left unmentioned.

Geometry is not separable from the motion of molecules, and this is especially true for molecules performing low-frequency large-amplitude motion. Elucidation of the geometrical structure gives some insight into the dynamics of molecules and crystals, gives information on vibrational amplitudes, conformational behavior, potential barriers, energy differences, etc. Experimental techniques yield parameters averaged over molecular motion, theoretical (quantum chemical, molecular mechanics) calculations provide the equilibrium structure. Structures from a parallel usage of different experimental and calculational techniques or even from a joint analysis of data are often reported. The different physical meanings of parameters have to be considered. Effects of the environment in solid and liquid phases may cause real structural differences.

Both the pursuits of structure determination and the needs it covers seem to take two divergent courses. Accurate molecular structures, small variations of parameters due to changes in intramolecular or intermolecular environment are important to the theoretical chemist, while often only the approximate shape of the molecule, its conformation, charge distribution, or packing in the crystal are needed for the interpretation of structures and processes in which the molecule participates. The two aspects complement each other. The detailed and accurate structure determinations form the basis of understanding the nature of interactions within and between molecules in general, and detect special effects in given structures.

The determination of crystal and molecular structure has become an integral part of studies in different fields of physics, chemistry and biology. One challenge to structural studies is to find relations between structure and properties of materials. Structural investigations of organic sulfur compounds are applied in or are paralleled with research in fields like astrophysics, solid state physics, electric and magnetic properties, synthetic chemistry, identifying reaction products, clarifying reaction paths, solid state and surface chemistry, electrochemistry, biochemistry, pharmacology or herbicide chemistry.

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CHAPTER 3

The conformational analysis of sulphur-containing rings

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I. INTRODUCTION

The general principles that underlie the theory of the conformational analysis of heterocyclic compounds are now well understood. The major differences between heterocyclic and carbocyclic rings arise from differences in mechanical properties of molecules introduced by heteroatoms such as non-bonded repulsions, bond torsions and bond angle deformations, and also from differences in atom size, polarity and polarizability. These effects have been discussed in quantitative terms[1,2] and, more recently, molecular mechanics programs that incorporate them and give good models for heterocyclic systems have become available. An early review of the conformational analysis of six-membered sulphur-containing rings was presented by Zefirov and Kazimirchik[3].

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There are three principal geometric effects that differentiate the conformational analysis of sulphur-containing rings from the more widely studied oxygen- and nitrogen-containing rings. First, the C—S bond (*ca* 181 pm) is longer than the C—C (*ca* 154 pm), C—O (*ca* 142 pm) and C—N (*ca* 148 pm) bonds. Second, since sulphur is a second-row element, its van der Waals radius is larger than that of oxygen or nitrogen, but probably smaller than that of a methylene group. Third, the C—S—C bond angle is generally smaller than tetrahedral (typically *ca* 100°). These geometric effects lead to rings that are more puckered than their alicyclic counterparts.

Torsional barriers about C—S bonds are slightly lower than about C—C bonds leading to somewhat easier deformation of S-containing rings in the region near to sulphur. In contrast the torsional potentials for S—S bonds are very different to those for C—C or C—S bonds, with preferred 90° dihedral angles and a larger barrier to rotation.

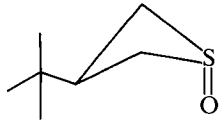
Anomeric effects are also very apparent when electronegative substituents are placed on the carbon atom adjacent to sulphur. Other interesting differences arise because of the ability of sulphur readily to expand its valence shell, and stable compounds with two, three or four ligands on sulphur are known. More 'conformational anomalies' are thrown up in the conformational analysis of sulphur-containing rings than in any other, and so the topic has stimulated a large amount of interest and is still being actively researched.

II. FOUR-MEMBERED RINGS

Four-membered rings have one degree of conformational freedom which can be represented as the movement of one of the atoms out of the plane of the other three. Nearly all four-membered saturated rings show evidence of such behaviour[1].

There is extensive evidence that four-membered sulphur-containing rings have non-planar conformations. Eectron diffraction[4,5], microwave spectra[6–11] and far-infrared spectra[12–15] on thietane (**1**) and substituted thietanes, thietane-1-oxide and 1,1-dioxide

(**1**)



(**2**)

show a puckered four-membered ring in the gas phase. The electron diffraction shows a dihedral angle for ring puckering of $26 \pm 20°$. In contrast to what is observed for oxetane the first four vibrationally allowed energy levels fall below the ring inversion barrier. An *ab initio* force field allows good fitting of the observed transition frequencies[15]. Analysis of the ^1H NMR spectra in oriented liquid-crystalline solvents agrees that the molecules are non-planar[16,17]. Examination of coupling constants and chemical shifts of 3-substituted thietane-1-oxides in both *cis* and *trans* isomers reveals a preference for both the *C*- and *S*-substituents to occupy an equatorial position[18,21]. For the *trans* 3-*t*-butyl-1-oxide (**2**) the *t*-butyl group is equatorial and the S=O group axial. Solid state NMR on thietane shows that the folded conformation also exists in the solid[22]. There is evidence of unusual chemical shift shielding effects in the ^{13}C and ^{17}O NMR spectra of four-membered ring sulphones compared to other-sized sulphone rings[23].

III. FIVE-MEMBERED RINGS

Whereas for four-membered rings only one coordinate is required to specify the ring puckering, two such coordinates are required for an adequate conformational description of five-membered rings[1].

If cyclopentane had a planar ring, the internal C—C—C angles would be those of a regular pentagon (108°) and they would differ so little from those of a regular tetrahedron that there would be no contribution to the strain energy of the molecule. The planar molecule would, however, have considerable strain arising from the five, perfectly eclipsed, C—C bonds. There are two ways that cyclopentane can deform in order to relieve this torsional strain whilst still retaining some of the original symmetry of the planar ring. Displacement of one carbon atom above or below the plane of the other four gives the envelope form which retains one of the original planes of symmetry. Alternatively, displacement of two adjacent carbon atoms equal distances on either side of the plane of the other three gives the half-chair form which retains one of the original two-fold axes of symmetry. Both modes of deformation reduce torsional interactions at the expense of a limited increase in bond-angle deformation energy.

Calculations indicate that, for cyclopentane, both the envelope and half-chair are of approximately equal energy and that there is a negligible energy of activation for passage between them[1]. In fact, the puckering of the cyclopentane ring is not of a definite, well defined type and the angle of maximum puckering rotates around the ring in a motion termed pseudorotation. The two terms required to define the conformation of a five-membered ring are, therefore, the amount of puckering and the position of maximum puckering in the ring. In a pseudorotation the atoms themselves do not rotate; it is the phase of the puckering that rotates around the ring. A general description of ring puckering coordinates that includes pseudorotation has been given by Cremer and Pople[24]. The challenge in the conformational analysis of five-membered ring systems is to describe the potential energy surface for the pseudorotation process.

The sulphur-containing rings thiophane (**3**) and 1,3-dithiolan (**4**) show evidence of much greater puckering and restriction of pseudorotation than do cyclopentane or

(3)

(4)

similar oxygen-containing rings. Thermodynamic studies on thiophane suggest a barrier to pseudorotation of *ca* 2.8 kcal mol^{-1}[1,25]. This picture of the molecule was later confirmed by spectroscopic data[26]. Electron diffraction and molecular mechanics studies by Seip's group showed that the half-chair form with C_2 symmetry was about 2–3 kcal mol^{-1} more stable than the envelope form[27]. This view was subsequently confirmed by a detailed study of the microwave, infrared and Raman spectra of the 2,2,5,5-tetradeuterio derivative, which showed the molecule to adopt a conformation of C_2 symmetry[28]. Detailed analyses of the ^{1}H NMR spectra of thiophane have been presented by Lambert's group[29] and by Esteban and Diez[30], who show that thiophane is probably the most puckered of all the simple saturated five-membered ring heterocycles. The most recent work arises from a molecular mechanics study of five-membered rings which confirms that thiophane prefers a half-chair conformation and has one of the highest barriers to pseudorotation of any of the five-membered rings[31].

The ^{13}C NMR spectra of all twelve mono- and dimethylated (except on sulphur) thiophanes have been reported. The results were interpreted in terms of an equilibrium

between half-chair conformations and the conformational preferences of the methyl groups were discussed[32].

Thiophane-*S*-oxide and some of its methyl derivatives have been subject to a multinuclear NMR study combined with force-field calculations. The conformation of the ring depends upon the number and position of the substituents[33].

1,3-Dithiolan derivatives have been studied by X-ray crystallography[34] and by vibrational spectroscopy[35]. Several commonly occurring bands were observed in the region 900–300 cm^{-1} from which it was postulated that the most stable conformation for the 2-substituted derivatives is the half-chair. Lambert's *R*-value expression (described in more detail in the section on six-membered rings) was used by Sternson and coworkers to examine the C—C torsion angle in 1,3-dithiolan derivatives[36]. The value obtained for 1,3-dithiolans (49°) was compared with that obtained for 1,3-dioxolans (42°). The *R*-value method does not work as well for five-membered as for six-membered, rings[37]. Nevertheless, it was suggested that the apparent increase found for the sulphur-containing ring compared to its oxygen-containing counterpart was significant and that, 1,3-dithiolan is more puckered than 1,3-dioxolan. This work did not distinguish between preferred half-chair or envelope conformations.

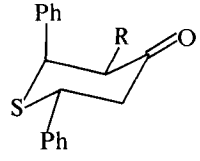
Pihlaja and coworkers have studied the conformational analysis of alkyl derivatives of 1,3-dithiolan using a combination of NMR and chemical equilibration techniques. 2-Alkyl-4-methyl and 2-alkyl-2,4-dimethyl derivatives show low energy differences between the *cis* and *trans* stereoisomers (< 0.24 kcal mol^{-1}). It appears that the ring is reasonably flexible with a possible minimum energy conformation being defined only if there is a bulky substituent in the 2- position[38]. Similar conclusions were reached in a study of derivatives with methyl groups in positions 2, 4 and 5[39]. In a related study using ^{13}C NMR it was concluded that the magnitude and variety of the substituent effects upon chemical shifts are best explained with the aid of a predominant half-chair conformation[40].

IV. SIX-MEMBERED RINGS

A. Thian

A fair number of single-crystal X-ray diffraction studies of thian rings are now available, although they are mainly concerned with *S*-substituted derivatives. They show that thian rings are more readily deformable around the sulphur atom than are cyclohexane rings, and that in general thian rings are more puckered than cyclohexane. The bond angle at sulphur is typically about 100° but the long C—S bond (typically *ca* 181 pm) compared with the C—C bond opens out the ring between atoms C(2) and C(6). Distances and geometries in the C(3,4,5) region are more nearly comparable with those in cyclohexane.

Studies on 3-methyl- (**5**, R = Me) and 3-ethyl-2,6-diphenylthian-4-one (**5**, R = Et) reveal chair conformations for the rings with average internal torsion angles in the ring of 55.0 – 55.5°, which are marginally smaller than in cyclohexane[41]. The C-S-C bond angles are around 99°. Where there is an axial phenyl at the 2-position in the ring, the C—S



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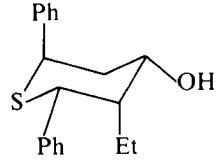

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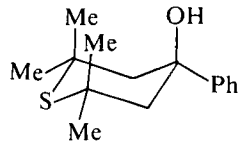
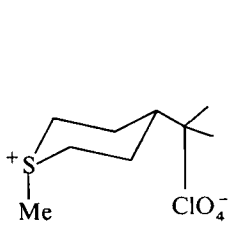


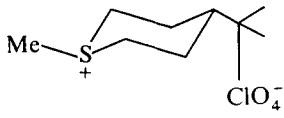
(7)

bond is longer (183.0/183.5 pm) than where the phenyl is equatorial (181.5/181.1 pm), possibly due to strain caused by the axial group. In a related alcohol (**6**) the average internal ring torsion angles are 4.5° greater than in the ketone, showing the thiane ring to be more puckered than cyclohexane. In the 2,2,6,6-tetramethyl derivative (**7**) the C—S—C bond angle is opened out to 105.6°, possibly to relieve strain between the axial methyls at positions 2 and 6[42].

Several X-ray diffraction studies of *S*-methylthianium salts have been reported. The early work reported by Gerdil[43] on *S*-methylthianium iodide has been reinterpreted using a different space group[44]. Nevertheless, this still shows a ring that is appreciably more puckered than cyclohexane. The structures of *cis*- and *trans*-1-methyl-4-*t*-butylthianium perchlorates (**8** and **9**) have been reported by Eliel and coworkers[45]. The *trans*-isomer has both alkyl groups equatorial. The *cis*-isomer has the *t*-butyl group equatorial and the *S*-methyl axial. There is considerable distortion around the sulphur atom in the *cis*-isomer. The C(2,6) bond angles expand from 107° in the equatorial isomer to 115°. The ring dihedral angles along the S—C(2) ane C(2)—C(3) bonds are 64° and



(**8**)



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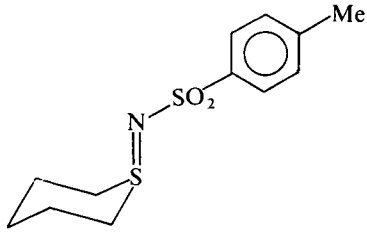


(**10**)

69°, respectively, with an equatorial methyl group, and decrease to 46° and 59° when the *S*-methyl is axial. The ring with the axial methyl is much flatter than its equatorial counterpart with the *S*-methyl group leaning out from the ring. The fact that such large changes in geometry are associated with the relatively small free-energy difference between the isomers (0.3 kcal mol^{-1}) shows that the ring is very readily deformed about the sulphur atom.

Both isomers of 3-acetoxy- and of 4-acetoxy-1-methylthianium perchlorates have been studied by Jensen[46,47]. In all cases the *S*-methyl group is observed to be axial and the acetoxy group is axial or equatorial according to whether it is *cis* or *trans* to the *S*-methyl.

X-ray diffraction studies on thian-1-tosylimide (**10**) and several *C*-substituted derivatives have been reported by a Hungarian group[48]. The tosylimino group is found to be axial in the parent compound and in derivatives with *cis*-substituents at C(2) and C(4). With *trans*-substituents at C(2) and C(4) the tosylimino group is observed to be equatorial.

Obtaining detailed structural information for molecules in solution is more difficult than in the solid state. In principle, vicinal coupling constants from ^{1}H NMR spectra give a direct measure of the dihedral angles by application of the Karplus equation. In practice, it is difficult to extract this information because of the dependence of the constants in the Karplus equation upon electronegativity, bond lengths and bond angles. The *R*-value method introduced by Lambert attempts to overcome these problems by measuring the ratio of the *cis* and *trans* vicinal couplings, hopefully cancelling the effects of the Karplus constants[49,50]. *R*-values of around 2 are indicative of a perfect chair conformation. Values less than 2 show a flattened chair or a twist conformation. Values greater than 2 show a ring that is more puckered than cyclohexane. In those derivatives of thian that have been examined by the *R*-value method, values greater than 2 (typically

2.5–2.7) are found, indicating that inclusion of sulphur in the ring leads to greater puckering[51,53].

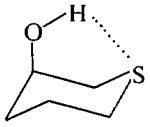
The conformational free-energy differences of methyl groups at the 2-, 3- and 4-positions of the thian ring have been determined by Willer and Eliel using low-temperature NMR methods[54]. They are C(2) 1.42, C(3) 1.40 and C(4) 1.80 kcal mol^{-1}. The observed free-energy difference at C(4) is similar to that in cyclohexane (1.7 kcal mol^{-1}) because of the similarity of the axial and equatorial environments in both systems. For the axial 3-methyl group, one *syn*-axial C—H bond in cyclohexane has been replaced by an electron pair on sulphur which causes lower non-bonded interactions. For the C(2) position, repulsions between the 2-axial methyl and the *syn*-axial hydrogen on C(6) are reduced relative to cyclohexane by the long C(2)–C(6) distance.

The anomeric effect, in which electronegative substituents at the 2-position in tetrahydropyran rings prefer the axial orientation, is also seen in thian rings. This effect has been demonstrated for Cl, OH, OR, SR, SAr and $P(S)(OR)_2$ substituents[55,56].

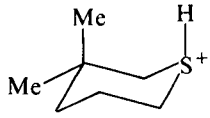
There is evidence that hydrogen bonding influences the conformational equilibrium in 3-hydroxythian in two ways [57]. The conformational equilibrium in chloroform solution is concentration-dependent, with the amounts of the axial 3-hydroxy conformation increasing as the concentration is lowered. At higher concentrations, intermolecular hydrogen bonding dominates and the hydroxyl is predominantly equatorial. As the concentration decreases, the extent of intermolecular hydrogen bonding decreases and intermolecular hydrogen bonding of the axial hydroxyl group to the sulphur atom becomes more important (cf. **11**). At very low concentrations (0.01–0.001 M) there are almost equal amounts of axial and equatorial conformations present.

The barrier to ring inversion of the thian ring has been measured to be 11.7 kcal mol^{-1} [51,58].

One most interesting conformational feature of the thian system is the preference of certain 1-substituents to occupy an axial position. Thus, in protonated thian, thian 1-oxide



(**11**)



(**12**)

and thian 1-(*N*-tosyl)imide the 1-axial conformation is preferred[59,60]. Coupling constant measurements on the S—H resonance indicate that *S*-protonated thian exists with the S—H axial and the axial preference is > 1.5 kcal $^{-1}$ mol^{-1}. This axial preference persists even when there is an axial 3-methyl present as in the 3,3-*gem*-dimethyl group of[12].

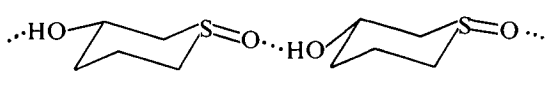
The axial preference of oxygen in thian-1-oxide has been known for many years[61] and is quantitatively measured to be 0.175 kcal mol^{-1} [62]. Unlike the situation in *S*-protonated thian, this axial preference is removed in the presence of an axial 3-methyl group[59]. The axial preference persists when the substituent is a 1-(*N*-tosyl) imide group (0.145 kcal mol^{-1})[63], but again this group is forced equatorial by an axial 3-methyl substituent[59].

It is generally accepted that attractive van der Waals interactions are operating between the axial 1-substituent and the *syn*-axial hydrogens on carbons 3 and 5 and are responsible for these axial preferences. The long C—S bond places the S-substituents and the *syn*-axial hydrogens in the feebly attractive portion of the interaction potential. However, when a 3-axial methyl is present, the interaction of the methyl with the larger oxygen

and nitrogen substituents turns the interactions from attractive to repulsive. The repulsion is not experienced by the axial 1-hydrogen, which remains axial irrespective of the 3-substituent.

The conformational analysis of *S*-alkylthianium salts has been studied in detail by Eliel and Willer[64]. *S*-alkylthianium salts undergo a thermally induced inversion at sulphur which is sufficiently rapid at 100 °C to allow chemical equalibrations between diastereoisomers to be investigated. Equilibration of 4-*t*-butyl-*S*-methylthianium perchlorate at 100 °C in chloroform shows that the equatorial *S*-methyl is more stable by 0.275 kcal mol^{-1}. With a 2-methyl group present, the free-energy difference increases to 0.59 kcal mol^{-1}. This probably arises because of a buttressing effect of the 2-methyl group on the axial *S*-methyl which has been shown to lean out of the ring (*vide supra*). With *cis*-2,6-dimethyl groups present, this buttressing effect is even more pronounced, making it harder for the axial *S*-methyl group to lean out from the axial position and the conformational free-energy difference is increased to 1.00 kcal mol^{-1}. Free energy differences for *S*-ethyl and *S*-benzyl groups were also determined. Carbon-13 NMR spectra of a substantial number of *S*-substituted thians are in agreement with the above observations[65].

Conformational equilibria on the ring carbons in thian-1-oxide have been examined by Eliel and coworkers[66,67]. *Cis*-3-hydroxythian-S-oxide shows a very marked dependence of the position of the equilibrium on concentration[66]. At higher concentrations, the equilibrium is strongly to the side of equatorial hydroxyl with intermolecular hydrogen bonding (shown in **13**) dominating. As the concentration is lowered the axial conformation, which contains a stabilizing intramolecular hydrogen bond between the hydroxyl group and the axial S=O, becomes more important until at 0.0023 M the energy difference in favour of the 3-axial conformation exceeds 1.3 kcal mol^{-1}.



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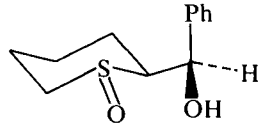

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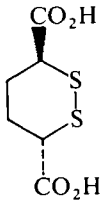
For *trans*-2-(1-hydroxybenzyl)thian-*S*-oxide (**14**) intermolecular hydrogen bonding is observed in the solid using X-ray diffraction, and intramolecular hydrogen bonding becomes observable using infrared spectroscopy is dilute solution[67]. In both the solid and the hydrogen-bonded conformation in solution the S=O and the 2-substituents are equatorial. A detailed molecular mechanics profile of the conformations involved in this molecule has been presented.

B. 1,2-Dithian

One of the most interesting aspects of 1,2-dithian conformational analysis is that the preferred dihedral angle in open chain disulphides of *ca* 90° has to be constrained by its presence inside a six-membered ring. Remembering that the cyclohexane internal torsion angle is *ca* 55°, this should cause some observable strain and distortion in this portion of the ring. Available crystal structure determinations illustrate this point. In racemic 1,2-dithian-3,6-dicarboxylic acid (**15**)[68] the C—S—S—C dihedral angle is 60° and in (4*R*, 6*R*)-1,2-dithian-4,5-diol[69] this angle is 58.8°. In both cases, the angle is greater than in cyclohexane to accommodate the desire of the S—S bond to open its dihedral

angle. There must be some strain in the molecule arising from its constraint on the C—S—S—C dihedral angle. The structure of 3,3,6,6-tetramethyl-1,2-dithian-4,5-dione is described as 'highly skewed' but details of the internal C—S—S—C dihedral angle are not given[70].

Ring inversion in 1,2-dithian derivatives has been studied and barriers to ring inversion in **16** and **17** are found to be 11.6 and 13.8 kcal mol^{-1}, respectively[71].



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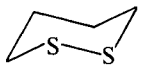

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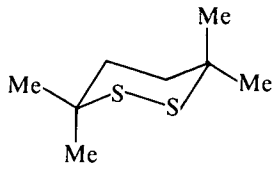

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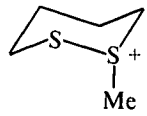

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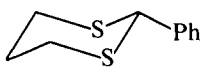
1,2-Dithian-1-oxide has been shown by several groups to prefer the S=O axial conformation[72–77] even in the presence of a 5,5-*gem*-dimethyl group and the axial preference has been estimated as >3.0 kcal mol^{-1} [77]. This almost certainly arises from a strong S—S=O anomeric interaction. The 1,1-dioxide exhibits a rapid ring inversion in its NMR spectra at temperatures as low as -90 °C.

Monomethylation of 1,2-dithians with $(CH_3)_3O^+BF_4^-$ in $CHCl_3/CH_3NO_2$ has been shown to be selective with the 1-methyl going into an axial position[78]. The axial preference of CH_3 in the parent compound (**18**) has been demonstrated by NMR techniques[78].

C. 1,3-Dithian

As with the 1,3-dioxans, the 1,3-dithian system has proved to be very popular with investigators of conformational effects. The reasons are similar: they are readily synthesized with a wide variety of substituents at all positions in the ring, they have readily interpretable ^{1}H and ^{13}C NMR spectra and they have a facile acid-catalysed ring opening closing reaction which allows ready equilibration of stereoisomers.

A large number of X-ray diffraction studies of 1,3-dithian derivatives have been reported. At the time of writing the Cambridge Structural Database had the structures of sixty-eight 1,3-dithians on record, too many to discuss in this chapter, so only the most significant will be mentioned. The basic structure of the 1,3-dithian ring is shown in the structural determination of 2-phenyl-1,3-dithian (**19**)[79]. The internal dihedral angles in the ring are similar to or slightly greater than those in cyclohexane, showing the ring to be slightly more puckered. *R*-value measurements give a similar result[80]. The puckering of the ring increases in the series **20–22** as the sulphurs are successively converted to sulphoxides[81]. For example, the internal dihedral angles about C(5) in the disulphoxide



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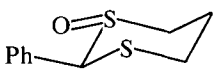

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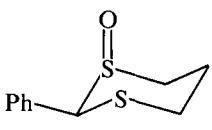

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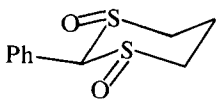

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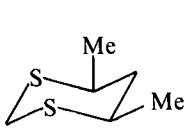
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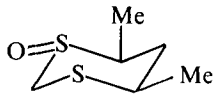
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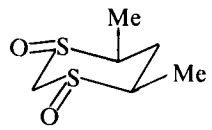
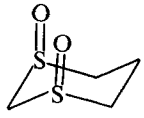

(25)

22 are found to be 72.5°, dramatically larger than in cyclohexane. A similar effect is seen in the series **23–25**[82].

In the parent disulphoxides **26** and **27** the *cis*-isomer is observed to exist in the diaxial conformation and to show '.. remarkable distortion in the dithian ring'[83]. The S–S distance across the ring is 314.0 pm in the *cis*-isomer compared to 300.5 pm in the *trans*-isomer. The S—C—S bond angle is considerably larger in the *cis* (120.2°) than in the *trans* (113.0°). The *cis*-isomer is flatter in the crowded region compared to the *trans*, but both isomers show large dihedral angles in the C(5) region of the ring (*ca* 70°). A similar diaxial conformation was observed earlier for 2,2-diphenyl-1,3-dithian-1,3-dioxide[84].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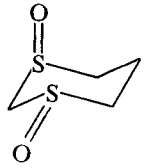
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Using acid-catalysed equilibration, Eliel and Hutchins measured the conformational free-energy differences of alkyl substituents at various positions in the 1,3-dithian ring[85]. Their observations are recorded in Table 1. A few years later Pihlaja pointed out that the chair-twist free-energy difference in 1,3-dithian was sufficiently low that twist conformations might contribute towards the conformational composition of the least stable isomers. Therefore, he revised Eliel's data slightly to take this into account[86].

Pihlaja and Nikander subsequently determined the thermodynamic parameters for the chair/twist equilibrium in 1,3-dithian by studying the acid-catalysed epimerization of 2-*t*-butyl-4,6-dimethyl-1,3-dithian[87]. They found $\Delta G_{ct} = 3.32\,\text{kcal mol}^{-1}$ at 342 K with $\Delta H_{ct} = 4.28 \pm 0.17\,\text{kcal mol}^{-1}$ and $\Delta S_{ct} = 4.7 \pm 0.5\,\text{cal mol}^{-1}\,\text{K}^{-1}$[87]. The chair/twist energy difference in 1,3-dithian is therefore smaller than in cyclohexane, which in turn is less than in 1,3-dioxan. It is believed that the relative lengths of the C—O, C—C and C—S bonds which make the dioxan ring more compact and the dithian ring less compact than cyclohexane are responsible for the relative magnitudes of these parameters[88].

^{13}C NMR spectra have been used for investigating conformational equilibria in 1,3-dithians starting with the derivation of ^{13}C substituent effects on chemical shifts by

TABLE 1. Conformational free-energy differences of alkyl substituents in the 1,3-dithian ring (kcal mol^{-1})[85]

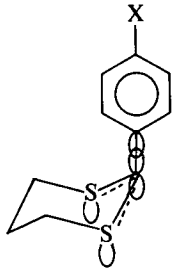
2-Me 1.77	2-Et 1.54	2-*i*-Pr 1.95	2-*t*-Bu > 2.7
4-Me 1.69	—	—	—
5-Me 1.05	5-Et 0.77	5-*i*-Pr 0.8	—

Eliel and coworkers[89]. Similar substituent effects were used by Pihlaja and Björkqvist to study conformational equilibria at the 5-position in the ring[90]. A value of 0.91 ± 0.07 kcal mol^{-1} was found, close to that determined by chemical equilibration. The same group used ^{1}H NMR spectra to study the equilibria in 2-ethyl-2-methyl- and 2-isopropyl-2-methyl-1,3-dithians. In these molecules the ethyl group marginally prefers to be axial whilst the isopropyl group prefers to be equatorial.

Two groups have shown that there is an axial preference for a 5-hydroxy group in 1,3-dithians with evidence of a stabilizing hydrogen bonding interaction between the hydroxyl group and the sulphur atoms, although their values for the magnitude of the conformational free-energy difference varied (0.8 kcal mol^{-1} and 0.5 kcal mol^{-1})[91,92]. By contrast, 5-methoxy and 5-methylthio groups prefer the equatorial position by 1.22 and 1.57 kcal mol^{-1}, respectively[93]. These latter equilibria are influenced by the 'gauche repulsive effect' first described by Zefirov and coworkers[94–98].

Anomeric interactions are particularly noticeable at the 2-position in the 1,3-dithian ring and have attracted a substantial amount of interest[99–109]. Thus, electron-withdrawing substituents at the 2-position display conformational equilibria that contain more of the 2-axial conformation than would normally be expected. This has been quantified by Juaristi and coworkers for the 2-diphenylphosphinoyl substituent by equilibration of the *cis*-4,6-dimethyl derivative in ethanolic NaOH[99,100]. The ΔG° value is found to be 1.0 kcal mol^{-1} in favour of the 2-axial isomer, indicating an anomeric effect of 3.7 kcal mol^{-1}[99].

The effect extends to 2-chloro[106], 2-seleno[107], 2-carboxy[108] and 2-aryl[109] substituents. In the latter case the axial/equatorial equilibrium has been shown to be remarkably sensitive to the nature of the *para* substituent on the phenyl ring and to depend on solvent. A careful study showed that ΔG° has a linear dependence on σ_p. In all of the cases studied the aryl substituent preferred the equatorial position. However, the amount of axial substitution at equilibrium increased with the increasing electron-withdrawing power of the *p*-substituent. This suggests that there is the stabilizing hyperconjugative interaction shown in **28** between the lone pairs on sulphur and the σ^* orbital of the axial aryl-C(2) bond. A similar interaction is not possible with an equatorial substituent. Similar electronic interactions are believed to be responsible for the axial preferences in the other systems described above with electronegative 2-substituents.



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When the group 14 elements are placed at the 2-position in a 1,3-dithian ring as in trimethylsilyl, stannyl and plumbyl groups, it is found that they have a much greater equatorial preference than in cyclohexane[110]. For example, the conformational free energy favouring the equatorial location for a trimethylplumbyl group is 0.7 kcal mol^{-1} in cyclohexane, but > 2 kcal mol^{-1} in 1,3-dithian. These results are in contrast to those obtained with electronegative substituents described above. They are reminiscent of the

6 kcal mol^{-1} preference for the equatorial position exhibited by a 2-lithio substituent[111-115] and of the calculations by Lehn and Wipff[116] showing that a carbanion between two sulphurs is 9 kcal mol^{-1} more stable when equatorial than when axial. Electropositive substituents such as the group 14 metals, it seems, have an enhanced equatorial preference at the 2-position in 1,3-dithian.

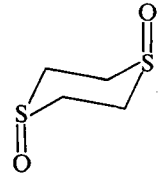
Low temperature ^{1}H NMR spectra on 1,3-dithian-1-oxide show two conformations in the ratio 84:16 at -81.5 °C ($\Delta G = 0.63$ kcal mol^{-1}) with the major conformation having the S=O equatorial[117]. This result confirms earlier reports[75] and is in contrast to the conformational preference of the S=O group in 1,2- and 1,4-dithians for the equatorial location[75]. Interestingly, it also appears to be opposite to the preference in 1,3-oxathian-3-oxide in which the axial S=O group is preferred by 0.57 kcal mol^{-1} [118].

For 1,3-dithian-*cis*-1,3-dioxide (**26**) the diaxial conformation is observed by X-ray diffraction techniques in the solid[83]. In solution its ^{1}H NMR spectrum displays an interesting coalescence phenomenon in which the AB quartet for the C(2) hydrogens at room temperature becomes a singlet as the temperature is lowered, the reverse of that normally expected for a dynamic phenomenon[117]. Lambert and coworkers suggested that this arose from a monomer/dimer equilibrium arising from the strong dipoles in the molecule; however, in the absence of contrary evidence they believed that the diequatorial conformation was probably involved. A monomer/dimer equilibrium is just as likely, if not more likely, in the diaxial conformation because the dipoles can more nearly exactly line up in opposition to each other in the dimer structure.

D. 1,4-Dithian

A large number of X-ray diffraction studies of 1,4-dithian derivatives have been reported largely due to the ability of the molecule to form adducts with a number of other species such as iodine, iodoform, antimony trioxide and diiodoacetylene. At the time of writing the Cambridge Structural Database has fifty structures recorded. The structure of the parent compound in the solid state has been reported and is unremarkable with standard bond lengths and angles[119]. The extra puckering found in sulphur-containing rings appears as a rather large S—C—C—S dihedral angle of 69°. The structure found was similar to that observed in a very early gas-phase electron diffraction study by Hassel and Viervoll[120].

The α- (or *trans*-) dioxide **29** crystallizes with both oxygens axial[121]. The β- (or *cis*-) isomer **30** has one oxygen axial and the other equatorial[122]. The preference for S=O to occupy an axial position is therefore carried over into the 1,4-dithian series. Both *trans*-2,3-dichloro- (**31**) and *trans*-2,5-dibromo-1,4-dithian (**32**) have both halogens axial[123,124]. Again, these axial preferences arise from the anomeric effect on the carbon next to sulphur seen earlier in this chapter. For the dichloro-derivative the two internal S—C—C—S dihedral angles on opposite sides of the ring are different. For the side carrying the two chlorines the dihedral angle is 59°, whilst the side with no chlorines is much more puckered with a dihedral angle of 71°. The chlorines, and to a lesser



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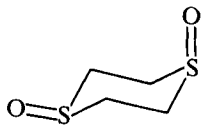

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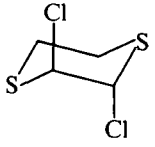

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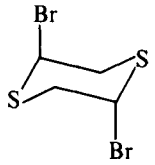
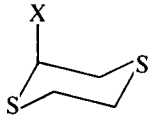


(32)

extent the bromines are observed to lean out of the ring somewhat, to relieve gauche repulsive interactions.

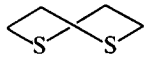
The puckering observed in the solid by X-ray diffraction methods is also seen in the solution phase by the use of *R*-value measurements[49], 1,4-Dithian and 1,4-diselenan give *R*-values of 3.38 and 3.49, respectively. Such values are considerably greater than expected for a normal chair ($R = 2$) and consistent with a considerable degree of puckering.

In contrast to the other rings discussed earlier in this chapter, little information is available concerning conformational equilibria for substituted 1,4-dithians[125,126]. Derivatives with electronegative substituents on C(2) such as R = Hal, OR or SR are found to prefer the axial conformation (**33**)[127]. However, when R = alkyl the equatorial conformation is preferred[128]. The conformational free-energy difference for a 2-methyl group is estimated to be -1.20 ± 0.14 kcal mol^{-1}. When the 2-substituent is of the type CH_2X where X is electronegative, such as acetoxy or halogen, the axial conformation is again preferred. Molecular mechanics calculations reported in the same paper suggest that the 1,4-twist (**34**) and 2,5-twist (**35**) conformations are respectively 4.2 and 3.1 kcal mol^{-1} less stable than the chair.



(**33**, X = halogen, OR, SR)

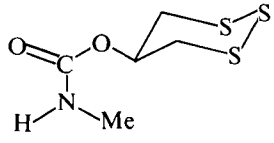
(**34**)



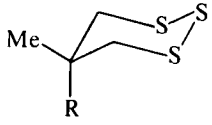
(**35**)

E. 1,2,3-Trithian

The structure of the *N*-methyl carbamate of 1,2,3-trithian-5-ol (**36**) is the only reported X-ray diffraction study of a 1,2,3-trithian derivative. The ring is in a chair conformation with the 5-sustituent equatorial[125]. Conformational equilibria and ring inversion barriers in some derivatives of 1,2,3-trithian have been reported based on ^{1}H NMR studies[130,131]. For the 5-methyl-5-alkyl series (**37**) the R group marginally prefers the axial position when it is ethyl, *n*-propyl, isopropyl or *s*-butyl but marginally prefers the equatorial position when it is isobutyl, neopentyl or phenyl.



(**36**)



(**37**)

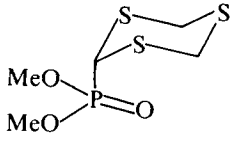
F. 1,3,5-Trithian

The structure of the parent compound, which is the condensation product from formaldehyde and hydrogen sulphide, has been investigated in the solid state by X-ray diffraction. The molecule is found to exist in the expected chair conformation[132,133]. The S—C—S bond angle is opened out with respect to a true tetrahedral angle (114.7°). The internal dihedral angles in the ring are all in the region 66°–67° showing the 1,3,5-trithian ring to be considerably more puckered than cyclohexane. Similar geometrical features are shown by other 1,3,5-trithian rings.

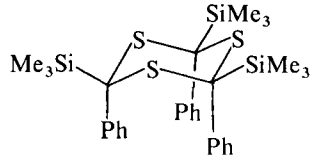
The condensation product between acetaldehyde and hydrogen sulphide has two

isomers. These were initially investigated in early gas-phase electron work by Hassel and Viervoll[134]. Subsequent X-ray diffraction work on the solids has confirmed that they exist in the chair conformation with all methyls equatorial (β)[135,136] and two equatorial and one axial (α)[137].

The axial preference of electronegative groups due to anomeric interactions is also found in equilibria in 1,3,5-trithian derivatives. Thus, the 2-dimethoxyphosphoryl group attached to a carbon in the 1,3,5-trithian ring is found to be axial (**38**) both in the solid by X-ray diffraction and in solution by NMR spectroscopy[104].



(**38**)



(**39**)

X-ray diffraction shows that β-2,4,6-triphenyl-2,4,6-tris(trimethylsilyl)-1,3,5-trithian (**39**) has a chair conformation with the three trimethylsilyl groups equatorial[138]. The three axial phenyl groups lean out from the true axial position somewhat and form a 'basket-shaped' cavity. It is possible that this is a further reflection of the reverse anomeric effect observed at the 2-position in 1,3-dithians with group 14 elements showing a marked equatorial preference[111].

Interestingly, a twist conformation is found by X-ray diffraction for *trans*-2,4,6-tris(trichloromethyl)-1,3,5-trithian in which CCl_3 groups occupy pseudoequatorial positions[139]. The reasons for this are not clear.

As with 1,3-dithian-*S*-oxide it is found that 1,3,5-trithian-*S*-oxide prefers the S=O equatorial conformation in solution[117]. This result is reinforced by the molecular mechanics calculations of Allinger and Kao[140]. However, in the solid state, X-ray diffraction shows that the S=O axial conformation is preferred[141].

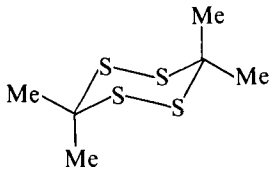
An infrared spectroscopic investigation of 1,3,5-trithian at high pressures shows that above 60 kbar the molecules are, in effect, flat[142]. Other six-membered rings should show the same effect at high enough pressures.

G. 1,2,4,5-Tetrathian

The 1,2,4,5-tetrathian ring contains two S—S bonds which prefer to have 90° dethedral angles and probably have a larger barrier to rotation than C—C bonds. This results in the twist conformation being the preferred form of the molecule and in a substantial barrier to ring inversion.

The tetramethyl derivative **40** which has been shown by X-ray diffraction to exist in a twist conformation in the solid state[143] was dissolved in carbon disulphide at −80 °C and gave a solution at that temperature whose ^{1}H NMR spectrum was only consistent with a conformationally homogeneous populations of twist conformations[144–146]. Allowing the solution to warm up slowly caused the conversion of the exclusive population of twist conformations to an equilibrium mixture of chair and twist forms. The chair:twist ratio at −15 °C is 1.0:2.6 ($\Delta G = 0.49$ kcal mol^{-1}). The barrier to the chair-to-twist interconversion was found to be 16 kcal mol^{-1}. This is consistent with a half-life of the chair or twist forms at −80 °C of *ca* 75 h. For the spiro derivative **41**, $n = 4$, the chair conformation is found to be the more stable species in solution; however for **41**, $n = 5$, the twist is again the more stable species. Solutions of the chair conformation at −80 °C may be obtained by crystallizing the compound as a guest in a lattice of

hexakis(*p*-*t*-butylphenylthiomethyl)benzene[147]. The crystal lattice constrains the molecule to a centrosymmetric (chair) conformation which is therefore observed on dissolution in a cold solvent.



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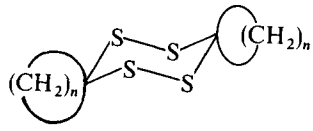
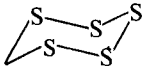


(41)

Theoretical calculations have been made of these conformational changes and the stability order of the conformations discussed[148].

H. Six-membered Rings with Five Sulphurs

Unlike the first-row elements, sulphur is capable of forming relatively stable chains of more than three atoms and this is evident in the variety of six-membered rings known that contain five sulphur atoms. 1,2,3,4,5-Pentathian (**42**) has been prepared and it shows an AB quartet for the ^{1}H NMR spectrum of its methylene group at ambient temperature[149]. This is consistent with a chair conformation undergoing slow ring inversion. The barrier to ring inversion was found to be $> ca 15$ kcal mol^{-1}. This result is consistent with our ideas of high barriers to rotation about heteroatom–heteroatom bonds. Subsequently, an X-ray diffraction study showed that both the parent ring and the 1,1-dibenzyl derivative have chair conformations in the solid state[150].



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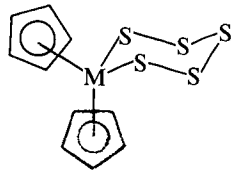

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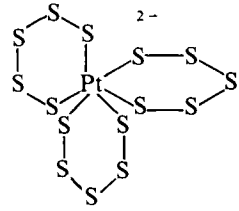


(44)

The metal-containing MS_5 ring is found in a variety of disguises. The cyclopentadienyl complexes (**43**, M = Ti, Zr, Hf) have been prepared and show barriers to ring inversion of 18.2, 11.7, 13.9 kcal mol^{-1}, respectively[151,152]. The fascinating platinum-containing ion (**44**) has been studied by ^{195}Pt NMR[153]. The spectra show a temperature dependence which probably comes from an equilibrium between the C_3 all-chair conformation and a conformation in which one of the MS_5 rings has inverted, lowering the symmetry of the molecule. Whilst it seems certain that the ring inversion barriers in these MS_5 rings derive in large part from the S—S torsion potential, the effects of M—S bond length and rotation barrier, S—M—S bond angle size and deformation, the formal oxidation state of the metal and the nature of the M—S bonding could all exert an influence.

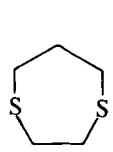
V. SEVEN-MEMBERED AND LARGER RINGS

As ring size increases, the degrees of freedom associated with bond rotations become greater and therefore the conformational complexity also increases. For this reason the

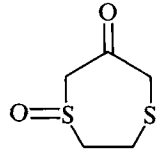
conformational analysis of seven-membered and larger rings has been much less studied than that of the smaller rings[1].

For cycloheptane, two families of conformations are important: the chair/twist-chair family and the boat/twist-boat family. The chair family is calculated to be of lower energy than the boat family. Each family interconverts amongst its own members by a low-energy pseudorotation process, but interconverts with the other family only via a high-energy ring inversion process. These ideas are also seen in sulphur-containing rings[1]. An early review of the conformational analysis of seven-membered rings has been given by Tochterman[154].

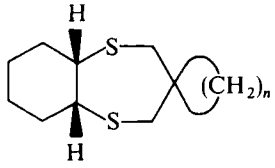
The structure of 1,4-dithiacycloheptane (**45**) in the solid state has been investigated by X-ray diffraction[155]. The molecules are seen to occupy a twist chair conformation of approximately C_2 symmetry. For this conformation the dihedral angles in the ring are different about different bonds. Interestingly, the sulphurs occupy sites in the ring where they are in bonds with the largest dihedral angles (73°–93°) and not at the sites where the smallest dihedral angle occurs. This is in keeping with the tendency of sulphur in five- and six-membered rings to open out the dihedral angles of its bonds. A similar conformation is found in solution for some 1,4-dithiepan-6-ones[156] and in the gas phase for 1,4-dithiepane[157]. The *S*-oxide of 1,4-dithiepane-6-one (**46**) has a twist chair conformation in the solid with the S=O pseudoaxial[156] in keeping with the axial preference of this group in smaller rings.



(**45**)

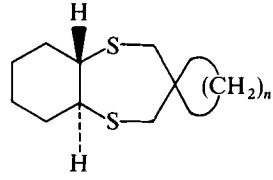


(**46**)



(**47**)

$n = 3, 4, 5$



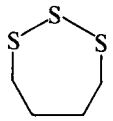
(**48**)

$n = 3, 4, 5$

The tricyclic compounds **47** and **48** have been investigated by high-field ^1H and ^{13}C NMR. The isomers with *cis* ring fusion show evidence of two conformational processes, the first being a ring inversion of the fused bicyclic portion of the molecule and the second being a restricted pseudorotation of the seven-membered ring[158]. For the *trans* fused isomers, no ring inversion is possible and only a pseudorotation process is observed[159].

Further effects of sulphur substitution affecting the conformational properties of seven-membered rings are seen in polythia-substituted cycloheptanes[160,161]. For 1,2,3-trithiepane (**49**) the very low barrier to pseudorotation in cycloheptane is raised to a *ca* 6—7 kcal mol^{-1}. The further substitution of two more sulphur atoms to give 1,2,3,5,6-pentathiepane (**50**) again increases the observed barrier. A coalescence in the

^{1}H NMR spectrum is observed at −60 °C, and at −90 °C the spectrum consists of two singlets. This is best explained on the basis of a freezing out of the chair–boat ring inversion. Rapid pseudorotation in the chair and boat families would average all ^{1}H sites in these two species and give rise to two singlets for the methylenes.



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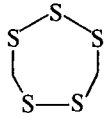

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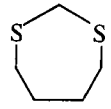

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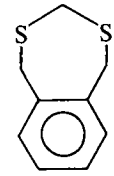
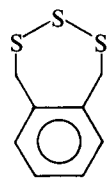


(52)

The conformational complexity of cycloheptene derivatives is less than that of cycloheptane due to the rigidity of the C=C double bond. If one regards the C=C unit as 'one atom', the conformational situation in cycloheptene derivatives is seen to be similar to that in cyclohexane. A study of 5,5-difluorocycloheptane gives as a reference compound an enthalpy of activation for ring inversion of 7.4 kcal mol^{-1}[162]. The dithia compound (**51**) shows similar activation parameters ($\Delta G_c^{\ddagger} = 8.5$ kcal mol^{-1}) and the benzo system (**52**) has a barrier that is 2.4 kcal mol^{-1} greater[163–165].

When the two sulphur atoms are placed alongside each other as in **53**, the ring inversion barrier increases to 13.5 kcal mol^{-1} and both the chair and twist-boat conformations give rise to separate signals[166]. At −60 °C the pseudorotation of the twist boat system is frozen out ($\Delta G_c^{\ddagger} = 10.4$ kcal mol^{-1}). For the trithiane system (**54**), the ring inversion barrier increases to 17.4 kcal mol^{-1} and the pseudorotation barrier remains about the same[166]. When two ortho methyls are added to the benzene ring (**55**) the ring inversion barrier increases further ($\Delta G_c^{\ddagger} = 19.8$ kcal mol^{-1}) and the pseudorotation barrier increases to 11.5 kcal mol^{-1}[166]. Comparison of compounds **52** to **55** dramatically illustrates the effects on ring inversion and pseudorotation processes of increasing catenation of sulphur atoms within rings.

(53)



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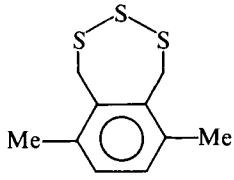


(55)

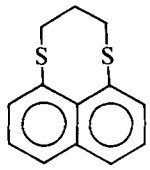
Other work on dithiabenzocycloheptanes has been reported by Klimovitskii and coworkers[167,168].

There are generally two conformations considered to be important for cyclooctane, the crown and the boat chair[1]. Molecular mechanics calculations reveal that there are many ring inversion and pseudorotation processes of low activation energy available to cyclooctane. X-ray diffraction studies reveal that sulphur-containing rings can exist in both types of conformation[169–173]. Gas-phase photoelectron spectroscopy combined with molecular mechanics calculations suggest that a boat conformation is most probable for 1,5-dithiacyclooctane[157].

An eight-membered ring with three atoms constrained to be coplanar exhibits, in principle, the same conformational complexity as a six-membered ring. Thus,

naphtho[1,8-*b*,*c*]-1,5-dithiocin (**56**) has been shown to exist in a chair conformation in solution that is 0.6 kcal mol^{-1} more stable than the boat. The chair-to-chair ring inversion barrier was found to be 8.9 kcal mol^{-1}. The monosulphone, disulphoxide and sulphoxide–sulphone were also studied and found to have a chair conformation in solution with S=O equatiorial whereas a boat is observed in the solid[174].

1,5-dithiacyclononane and 1,6-dithiacyclodecane have been studied by X-ray crystallography and gas-phase photoelectron spectroscopy[155,157]. The nine-membered ring exists in a twist boat chair (C_2) conformation and the ten-membered ring in a boat chair boat (C_{2h}) conformation.



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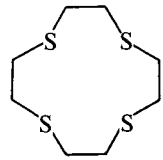

(57)

1,2-dithiacyclononane has a temperature-dependent Raman spectrum in the S—S stretch region which shows the existence of a conformational equilibrium with ΔH° 1.2 ± 0.2 kcal mol^{-1}[175]. The temperature dependence of the ^{1}H NMR spectrum is characteristic of a ring inversion process with $\Delta G^\ddagger = 11.7 \pm 0.3$ kcal mol^{-1}. These results are tied together by molecular mechanics calculations which predict that a lowest energy conformation of symmetry C_2 should be in equilibrium with another conformation[175].

Tetrathia crown 12 (**57**) has been shown by an X-ray diffraction study to have a square conformation with the sulphurs at the corners[176]. The structures of (1*RS*, 2*RS*, 7*RS*, 8*RS*)- and (1*R*, 2*S*, 7*R*, 8*S*)-tetrahydroxy-4,5,10,11-tetrathiacyclododecane have been reported[177,178].

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CHAPTER 4

Thermochemistry of organosulphur compounds

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I. INTRODUCTION

At an ever-accelerating pace, over the past two decades there have been eight volumes published in Patai's series, *The Chemistry of Functional Groups*, that explicitly discuss sulphur-containing species:

(1) The Chemistry of the Thiol Group (1974).
(2) The Chemistry of the Cyanates and Their Thio Derivatives (1977).
(3) Supplement E: The Chemistry of Ethers, Crown Ethers, Hydroxyl Groups and Their Sulphur Analogues (1980).
(4) The Chemistry of the Sulphonium Group (1981).
(5) The Chemistry of Sulphones and Sulphoxides (1988).
(6) The Chemistry of Sulphinic Acids, Esters and Their Derivatives (1990).
(7) The Chemistry of Sulphenic Acids and Their Derivatives (1990).
(8) The Chemistry of Sulphonic Acids, Esters and Their Derivatives (1991).

Some of these volumes contained chapters on the thermochemistry of the appropriate class of compounds. Some did not. By intent or by accident, these earlier chapters omitted some references that the current authors deem relevant, and of course there have been some new studies that appeared in the primary literature after a given chapter was completed. Some authors limited their definition of thermochemistry to include only heats of formation. Others included entropies, phase change enthalpies and heat capacities. Our goal is to provide some sense of coherence between the various classes of sulphur-containing species, e.g. we recognize that a compound formed from one sulphur and oxygen and two affixed organic groups can be either a sulphoxide or a sulphenate,

and is naturally related to species with more oxygens such as sulphones and sulphinates, as well as to those with fewer (i.e. no) sulphurs such as ethers and ketones. As such, we are using our current chapter in this supplemental volume to provide interrelationships between the heats of formation of the various classes of sulphur-containing groups, rather than aiming for completeness and a comprehensive update for the earlier chapters and other volumes[1]. The price of this, however, is that we limit our attention to heats of formation and, because they are so sparse and scattered over often unique structural types, we have not attempted to derive the now standard Benson increments to reflect this diversity[2].

In our attempt for conceptual coherence, we have made extensive use of various data archives which allow for comparatively uniform biases and assumptions. It also simplifies the writing and reading of the text by having fewer reference citations. This is particularly desirable for the discussion of those species for which we had to make thermochemical assumptions in order to derive the heat of formation of a compound of interest. Indeed, any unreferenced thermochemical quantity in our chapter implicitly comes from one of these sources. In particular, heat of formation, vaporization and sublimation data on organic compounds were usually taken from the compendium by Pedley, Naylor and Kirby[3]. We have occasionally needed the heat of fusion of a solid organic compound, or the data for some solid or liquid organic, and so used the compilation by Domalski and his coworkers[4], while for corresponding entropy data on gas-phase species, we chose the values given by Stull, Westrum and Sinke[5]. We have also occasionally needed thermochemical data of one variety or another on some inorganic compound and so used the archive by Wagman and his coworkers[6].

As part of our goal of obtaining conceptual coherence, our thermochemical predilection and prejudice is for gas-phase species because in that phase, ideally, there are no complicating intermolecular interactions. Should gas-phase numbers be absent, liquids are preferred over solids because the former are essentially isotropic, and indeed, we have even used aqueous solution phase data on ions despite the idiosyncracies of water and clearly strong solute–solvent interactions.

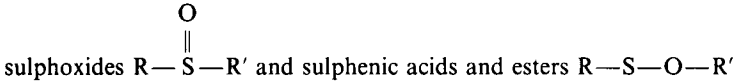
We now acknowledge that in one very important way our chapter lacks coherence and this betrays the very nature of data on the energetics of organic compounds. On the one hand, there is the strong desire to have high accuracy and precision. For many compounds there are measurements of heats of formation reported to the nearest tenth of a kilojoule. It is these numbers that characterize the thermochemical awareness for compounds discussed in Section II of this chapter. It is these species and the homologous series they engender that impel us to examine the consequences of molecular homology. On the other hand, there is the strong desire to understand unusual species, those that fail to belong to any homologous series and often seem to be singular examples of molecular structure and energetics. To understand these species it has often been necessary to use far coarser data and to make plausible, and hopefully precedented, assumptions. These species and the associated reasoning fill Section III of this chapter, where our derived heats of formation are often no better than tens of kilojoules.

We have two final choices of convention in our chapter. The first is that of units. The reader has already seen that we use kilojoules. Following 'orthodox' thermochemical practice, we use kJ instead of kcal where, by definition, 4.184 kJ ≡ 1 kcal. This choice of kJ was made because it means our analysis most closely corresponds to the majority of the primary or secondary data we have used. We acknowledge we have found most chemists are more comfortable in kcal but that comparatively few have an intuitive feel for the numbers at hand, at least for the majority of sulphur compounds of greatest interest and importance here. Perhaps the reader will join us in becoming 'bilingual'. The second reason acknowledges that there is considerable dispute as to the nature of

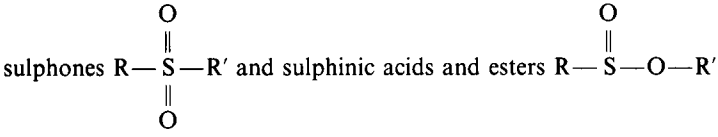
bonding in sulphoxides, sulphones and most other compounds with sulphur–oxygen bonds. Is it 'double', 'single', 'semipolar', 'dative', 'coordinate'? Should we write $>S{=}O$, $>S{-}O$, $>S^{+}{-}O^{-}$, $>S^{\delta+}{-}O^{\delta-}$, $>S\rightarrow O$? Should we invent our own symbol, such as $>S\sim O$? We have decided to write $>S{=}O$ because it is simple and conveys the fact that the isomeric sulphoxides and sulphenates are really quite differently bonded.

Indeed, because there is often bonding ambiguity and even more often linguistic ambiguity in the discussion of sulphur–oxygen compounds, we close the introduction with a brief glossary for the classes of sulphur-containing groups that will be presented in this chapter:

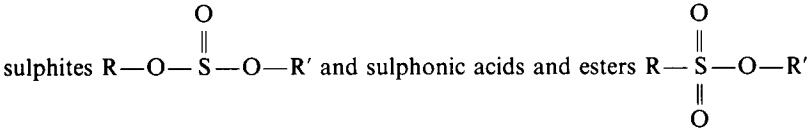
thiols (mercaptans) R—S—H
sulphides (thioethers) R—S—R′
disulphides R—S—S—R′



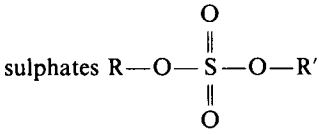
sulphoxides R—S(=O)—R′ and sulphenic acids and esters R—S—O—R′



sulphones R—S(=O)(=O)—R′ and sulphinic acids and esters R—S(=O)—O—R′



sulphites R—O—S(=O)—O—R′ and sulphonic acids and esters R—S(=O)(=O)—O—R′



sulphates R—O—S(=O)(=O)—O—R′

II. SYSTEMATICS OF THIOLS, SULPHIDES, DISULPHIDES, SULPHOXIDES, SULPHONES, SULPHITES AND SULPHATES

A. Linear Relationships of the Heats of Formation and Heats of Vaporization

Regularities in the thermochemical properties of a variety of homologous series have often been demonstrated by their linear dependence on the number of carbon atoms in the hydrocarbyl substituent[5,7]. Examination of experimental enthalpies from ten sulphur-containing families indicates that separate linear relationships exist for each of them also. Thus, we can write equation 1 which expresses the standard molar heats of formation of *n*-alkyl thiols, *t*-alkyl thiols, 1,ω-dithiols and the dialkyl derivatives of the sulphides, disulphides, sulphoxides, sulphones, sulphites and sulphates as a linear function of the number of carbon atoms in the compound, n_c. Similarly, the heats of vaporization for each series (and the heat of sublimation in the case of the di-*n*-alkyl sulphones) are also linear functions of the number of carbon atoms, according to equation 2. Application of a least-squares analysis to the measured enthalpy data produces the numerical values in Table 1.

TABLE 1. Constants from the least-squares analysis of the heats of formation and vaporization of sulphur-containing compounds[a] (kJ mol^{-1})

Series [n_c][b]	$\Delta H_f(l)$		$\Delta H_f(g)$		ΔH_v	
	m	b	m	b	m	b
n-Thiol [C_4-C_7, C_{10}]	−25.18	−24.56	−20.46	−7.03	4.73	17.51
t-Thiol [C_4-C_6]	−23.90	−44.44	−19.35	−31.67	4.55	12.77
1,ω-Dithiol [C_2-C_5][c]	−25.36	−3.61	−20.44	31.32	4.92	34.94
Sulphide Me-S-R-*n* [C_4-C_6]	−24.33	−21.19	−19.84	−2.95	4.50	18.20
(*n*-R)$_2$S [C_4, C_6, C_8]	−25.30	−18.16	−20.92	0.12	4.38	18.28
n-R-S-R′-*n* [C_4-C_6, C_8]	−25.37	−18.00	−20.95	0.13	4.40	18.17
Disulphide *n*-R-SS-R-*n* [C_4, C_6, C_8]	−25.70	−17.30	−21.10	9.57	4.63	26.76
Sulphoxide *n*-R$_2$SO [C_4, C_6]	−30.74	−145.2	−24.65	−107.0	6.05	38.20
Sulphone[d] *n*-R$_2$SO$_2$ [C_4, C_6, C_8]			−20.08	−348.6		
Sulphite (*n*-RO)$_2$SO [C_4, C_6, C_8]	−23.07	−508.4	−18.19	−479.4	4.92	28.88
Sulphate (*n*-RO)$_2$SO$_2$ [C_4, C_6, C_8]	−22.87	−721.7	−18.10	−683.8	4.79	37.89

[a] In the least-squares analyses of equations 1 and 2, the individual enthalpies were weighted inversely as the squares of the experimental uncertainty intervals. In all cases for equations 1 and 2, $r^2 \geqslant 0.998$.
[b] n_c = total number of carbons in the compound.
[c] The compound designated as 1,2-propanethiol in Reference 3 is actually 1,3-propanethiol.
[d] There are insufficient data to calculate the constants for ΔH_f and ΔH_v.

$$\Delta H_f(1, g) = m(n_c) + b \quad (1)$$

$$\Delta H_v = m(n_c) + b \quad (2)$$

Examination of easily generated graphical plots of the heats of formation in the gaseous or liquid phase versus the number of carbon atoms clearly shows that the heats of formation and vaporization of the methyl or dimethyl compounds in each homologous series deviate from the otherwise apparently linear relationships[8]. This 'methyl effect' is well-known, as is the associated observation that linear expressions such as equations 1 and 2 are better obeyed when $n_c \geqslant 4$[9]. We showed previously that the parameters for equations 1 and 2 are different for two categories of ethers, the methyl *n*-alkyl ethers and the di-*n*-alkyl ethers[10]. Therefore it is not surprising that the enthalpy data for methyl *n*-alkyl sulphides and di-*n*-alkyl sulphides are also better fitted independently of each other, although the difference is larger for the sulphides than for the ethers[11]. Nor do the heats-of-formation values for methyl ethyl sulphone and methyl ethyl sulphite (the only two compounds for which methyl *n*-alkyl SO_x data are available) fit the parameters for the corresponding di-*n*-alkyl SO_x series given in Table 1. Deviations may

be reckoned in two ways: from linearity established by the best fit of the experimental data and from the 'universal' slope[7]. By either method, the deviations of methyl thiol and the dimethyl derivatives of the sulphides and disulphides are all within a rather narrow range below *ca* 10 kJ mol^{-1} in the gaseous phase. However, dimethyl sulphone, dimethyl sulphite and dimethyl sulphate deviate by much larger values. The deviations of these dimethyl derivatives using the values in Table 1 are 16, 32 and 33 kJ mol^{-1} respectively, while deviations from the 'universal' slope are 14, 23 and 23 kJ mol^{-1}. Dimethyl sulphoxide, because the sulphoxide series slope is steeper than the universal slope, is an intermediate case; its deviation using Table 1 values is only 5 kJ mol^{-1} while the deviation from universality[12] is 17 kJ mol^{-1}.

The graph of the symmetrical di-*n*-alkyl sulphides also reveals that the heats of formation of liquid and gaseous di-*n*-pentyl sulphide deviate significantly [5.3 kJ mol^{-1} (l); 4.5 kJ mol^{-1} (g)] from the straight lines established by the diethyl, dipropyl and dibutyl sulphides[13]. That the measured 'pentyl' enthalpies are probably incorrect is also indicated by the anomalous heats of reaction for this compound which are discussed later in the text. Of the di-*n*-alkyl sulphides available for our thermochemical/numerical analysis, three are symmetrical and two are unsymmetrical. The least-squares fits for both the symmetrical sulphides and the combined symmetrical/unsymmetrical sulphides are shown in Table 1 to demonstrate the influence of small enthalpy differences on the *m* and *b* terms.

For the thiols, dithiols, sulphides, disulphides and sulphones, the methylene increment *m* for the gaseous phase is close to the 'universal' increment of 20.6 kJ mol^{-1} found for so many functionalized hydrocarbons[7]. Noteworthy is the somewhat smaller value for the sulphites and sulphates (*ca* 18 kJ mol^{-1}) and the larger value for the sulphoxides (24.65 kJ mol^{-1}). Along with the 1,ω-alkanediols[14], aldehydes and ketones[12], these methylene increments are among the most discrepant of any organic homologous series. The question arises as to which of two situations pertains: there exists a universal methylene increment for all *n*-alkyl functionalized series and for 'large enough' n_c the enthalpies may be expected to conform; or that each series has a unique methylene increment from which only the 'lower members' deviate. If the first is correct, then it would seem that for the SO_x series mentioned above, n_c is nowhere near 'large enough' and estimations made for some higher members using the values in Table 1 would be in error. If, on the basis of the data at hand, we assume the second situation, at least for a total $n_c < 8$, then it might be instructive to compare the various sulphur-containing series with each other and with other compounds which they structurally resemble. If nothing else, these comparisons may lend insight into short-range intramolecular interactions for these 'lower members' before the effects are eventually subsumed into the substituent constant *b*.

Comparisons among sulphur-, oxygen- and carbon-containing compounds seem to be natural choices. Sulphur and oxygen are members of the same group in the periodic chart but have substantially different electronegativities, bond lengths and bond angles; the hydrocarbon and oxygen analogues are both isoelectronic and isosteric; and although carbon and sulphur share neither periodic chart column nor row membership, they have comparable electronegativities.

B. Comparison of the Heats of Formation of Sulphur-, Oxygen- and Carbon-containing Compounds

We wish to compare the least-squares fits for the functional group constant *b* and the methylene increment *m* in equation 1 for the gaseous phase. For simple isomeric compounds within classes such as alkanes, alkenes, alcohols and thiols the more highly branched compound has a more negative heat of formation and is more stable[15]. This

difference in thermodynamic stability in most cases may be associated with the *b* values calculated from equation 1, since they are merely the extrapolations of the lines upon which the members of each homologous series fall[11]. For 'large enough', n_c, *m* is the ΔH_f of strainless —CH_2— (either unique or not) in a homologous series which is not affected by specific functional group interactions. For small n_c, *m* may be influenced by such factors as hydrogen-bonding, strain, electrostatic and other intramolecular interactions. If *m* for acyclic series is functional group dependent, this suggests that it is the electronic effects of the functional group which determine the magnitude of *m*. Consistent with Montgomery and Rossini's conclusion[12], we expect less negative *m* values to be associated with more electronegative functional groups[16].

The intercept for the *n*-thiols is higher than that for the *t*-thiols (−7.034 and −31.67 kJ mol^{-1}, respectively). If we calculate the terms in equation 1 for 2-propanethiol and 2-butanethiol, the two unbranched secondary thiols for which we have thermochemical data, then the *b* value is an intermediate −14.10 kJ mol^{-1}. The *b* values for the analogous isosteric alcohols and alkanes, ROH and RCH_3 (R = 1°, 2°, 3°), show the identical relative order. Comparing the *m* values in the same way, we find that while the alcohols and alkanes have the same relative order of primary > secondary > tertiary (least negative), the thiol order is secondary > primary > tertiary. But the differences between the primary and secondary categories are not large and the secondary thiol calculation included the 'less desirable' $n_c = 3$. Comparison of thiols, alcohols and alkanes within a primary, a secondary or a tertiary category shows that, in each case, the alcohol has the least negative *m*. However, the overall order within each category differs with respect to the relative positions of RCH_3 and RSH; in the secondary and tertiary categories the thiol has the most negative *m* and in the primary category the alkane has the most negative *m*. This is consistent with an electronegativity effect on the relative *m* values within a category—oxygen is significantly more electronegative than either carbon or sulphur, which have comparable electronegativities. Although we cannot directly compare the *b* values for the *n*-thiols and the 1,ω-dithiols, the methylene increments are virtually identical. But because the electronegativity of sulphur is less than that of oxygen and is comparable to that of carbon, we might not have expected the two sulphydryl groups to lower the *m* value to the same degree as do two hydroxyl groups (from *ca* −18 to −16 kJ mol^{-1}) for the 1,ω-alkanediols.

The *n*-thiol series has a more negative *b* value than the sulphide series. Inspection of sets of thiol/sulphide isomers shows that the thiol is indeed the most stable while methyl *n*-alkyl sulphides are less stable than di-*n*-alkyl sulphides[11]. This same stability order is observed for the alcohol/ether analogues and is paralleled by their *b*-value order. If we assume that the electron-attracting effect of an X—H group is greater than that of an X—R group, we can understand the less negative *m* values for the thiols and alcohols compared to, respectively, the di-*n*-alkyl sulphides and di-*n*-alkyl ethers. However, overall, the sulphur series *m* value order is RSR > RSH > MeSR while the oxygen series order is MeOR > ROR > ROH, differing in the position of MeXR. We can view this anomaly from a different perspective as we compare the isosteric analogues and their *m* values: RSR > RCH_2R > ROR and $MeCH_2R$ > MeOR > MeSR. Based on our earlier understanding, MeSR looks very much out of place.

For the disulphur compounds, 1,ω-dithiols are less stable and have a less negative *m* value than the isomeric disulphides (RSSR). In this behaviour they do not resemble the monosulphur compounds. However, the two sulphur atoms are bonded in the disulphides but separated in the dithiols so the comparison is not straightforward.

The negative numerical values of the methylene increments in the SO_x functional group series decrease with an increase in *x*, the number of electron-attracting oxygen atoms for $x = 1$–4. But it is not immediately obvious why the sulphone value should be only a little lower than a sulphide or why the sulphoxide methylene group contribution

should be so much higher. This result does not parallel intuition based on electronegativities, atomic charges on sulphur, or steric interactions in the SO_x group for the three cases of $x = 0, 1, 2$[17].

C. Comparison of the Heats of Vaporization of Sulphur-, Oxygen- and Carbon-containing Compounds

For sulphur-containing compounds, the order of heats of vaporization (kJ mol^{-1}) for the dipropyl substituted species (the only dialkyl substituents for which there is appropriate phase-change data for all functional groups) are sulphone (79.9) > sulphoxide (74.5) > sulphate (67.0) > sulphite (58.5) > disulphide (54.2) > sulphide (44.6). The preceding is identical to the order of b values from equation 2, and differs from the order of m values in the relative positions of the sulphites and sulphates.

Comparing the heats of vaporization of n-thiols, n-alkanols and n-alkanes, we find ROH > RSH > RCH_3 which parallels the strength of their respective intermolecular forces, including especially hydrogen-bonding. This is reminiscent of the boiling point order $H_2O > H_2S > CH_4$. The magnitude of these intermolecular forces is more apparent when compared to compounds in which they are absent—the sulphides and ethers. Ethers and alkanes have comparable heats of vaporization which are lower than those of the analogous sulphides. The near-equality of ΔH_v for ethers and alkanes is due to different degrees of contribution of dipolar effects and total polarizability to the attractive forces in these two classes of compounds. Dipolar interactions and the large polarizability of sulphur result in the higher sulphide heat of vaporization.

D. Difference Quantities Among the Thiols and Sulphides

Because of the regularities of the heats of formation of the thiols and the sulphides, we can derive meaningful reaction quantities which interrelate their enthalpies[18]. Consider the reactions in equations 3a–5a:

$$RSH + R'SH \longrightarrow R{-}S{-}R' + H_2S \tag{3a}$$

$$RSH + R'SH \longrightarrow R{-}SS{-}R' + H_2 \tag{4a}$$

$$R{-}S{-}R' + 1/8\,S_8 \longrightarrow R{-}SS{-}R' \tag{5a}$$

Although we can obtain enthalpy values for liquid phase H_2S, H_2 and S_8 by suitable corrections, we wish to write heat of reaction equations in such a way that species in these anomalous phases can be simply by-passed. Thus we will define (equations 3b–5b) the following reaction quantities:

$$\delta_3(*) \equiv \delta\Delta H_f(*,RSR',RSH,R'SH) = \Delta H_f(RSR')\text{-}[\Delta H_f(RSH) + \Delta H_f(R'SH)] \tag{3b}$$

$$\delta_4(*) \equiv \delta\Delta H_f(*,RSSR',RSH,R'SH) = \Delta H_f(RSSR')\text{-}[\Delta H_f(RSH) + \Delta H_f(R'SH)] \tag{4b}$$

$$\delta_5(*) \equiv \delta\Delta H_f(*,RSSR',RSR') = \Delta H_f(RSSR')\text{-}\Delta H_f(RSR') \tag{5b}$$

For sixteen pairs of alkyl groups, including dimethyl, $\delta_3(l) = 28.1 \pm 1.9$ kJ mol^{-1} and $\delta_3(g) = 8.81 \pm 1.6$ kJ mol^{-1}. The diversity of alkyl group pairs included in this calculation is remarkable, encompassing almost all ten combinations of methyl, primary, secondary and tertiary groups (we lack data only for a secondary/tertiary combination). The reaction to give di-t-butyl sulphide is abnormally high [48.4 kJ mol^{-1} (l); 30.3 kJ mol^{-1} (g)], presumably because of the steric strain in the resulting sulphide[19]. Two other combinations also have significantly higher heats of reaction, isobutyl/isobutyl [34.8 kJ mol^{-1} (l); 15.1 kJ mol^{-1} (g)] and n-pentyl/n-pentyl [36.2 kJ mol^{-1} (l); 15.3 kJ mol^{-1}(g)]. The deviation in the dipentyl case is clearly due to the discrepant values for dipentyl sulphide

mentioned earlier. The reason for the abnormal diisobutyl case is not known because there are no other branched primary thiols or sulphides with which to compare enthalpies.

The dehydrogenation reaction heats are also remarkably constant. For formation of four symmetrical disulphides, $\delta_4(l) = 26.9 \pm 1.1$ kJ mol^{-1} and $\delta_4(g) = 17.9 \pm 0.5$ kJ mol^{-1}. It is noteworthy that the $\delta_3(l)$ and $\delta_4(l)$ are very close while $\delta_4(g)$ is significantly more than $\delta_3(g)$ due to the difference in the heats of vaporization of the mono- and disulphides. Unlike the determination of the δ_3 mean reaction heats, calculation of the δ_4 mean heats excluded the dimethyl and included the di-*t*-butyl compounds. Evidently, the atypical dimethyl effect is again manifest and there is no unusual steric strain in di-*t*-butyl disulphide. The reaction involving isobutyl/isobutyl is once again significantly higher than the others, suggesting that if there is an error in the measured enthalpies, it is for the isobutyl thiol.

As we complete a simple Hess cycle, we find for equation 5b the heats $\delta_5(l) = -2.05 \pm 1.2$ kJ mol^{-1} and $\delta_5(g) = 8.6 \pm 0.4$ kJ mol^{-1}. Now the calculation of the means includes the isobutyl/isobutyl compounds (reinforcing our suspicion about isobutyl thiol) and excludes the di-*t*-butyl (steric effect) and dimethyl (inherently atypical) compounds.

E. Difference Quantities Among the Sulphur–Oxygen Compounds

Herron[20] showed that the S—O bond dissociation energies for the sulphoxides, sulphones and sulphates are remarkably consistent for a given hydrocarbyl-substituted series. By not including the heat of formation of atomic oxygen in the calculation we

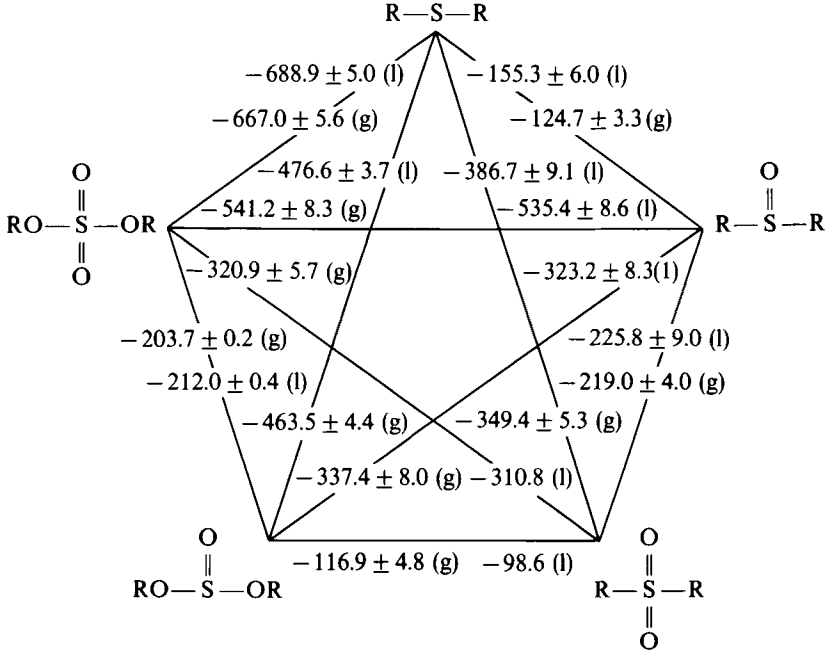


FIGURE 1. Difference quantities $\delta_6(*, x, y)$. Exothermic values (kJ mol^{-1}) are for $XO_y \rightarrow SO_x$ where $x > y$

can express more simply a heat-of-formation difference quantity, in either the gaseous or liquid phase, by δ_6 derived in equation 6:

$$\delta_6(*, x, y) \equiv \delta\Delta H_f(*, RSO_xR', RSO_yR') = \Delta H_f(*, RSO_xR') - \Delta H_f(*, RSO_yR') \quad (6)$$

The results are shown in Figure 1 where the difference quantities between any two species appear on the line which connects them. The uncertainty intervals are standard deviations from the mean. It is gratifying that such constancy of difference exists among all of these combinations of compounds.

For the sulphone/sulphoxide difference quantities, $\delta_6(*, 2, 1)$ (the only series for which there are data), the ethyl allyl and diphenyl difference quantities are essentially the same as for the saturated dialkyl derivatives. Unlike the difference quantities where x and $y \geqslant 1$, none of the $\delta_6(*, x, 0)$ values included the discrepant dimethyl derivatives.

F. Substituent Exchange Reactions

In order to extend the usefulness of the quantities δ_3–δ_6 described in the preceding sections, we next ask if we can confidently derive heats of formation for alkyl-substituted sulphides and sulphones by assuming thermoneutrality in the reactions of equations 7 and 8.

$$R{-}SO_2{-}R + R'{-}SO_2{-}R' \longrightarrow 2\,R{-}SO_2{-}R' \quad (7)$$

$$R{-}S{-}R + R'{-}S{-}R' \longrightarrow 2\,R{-}S{-}R' \quad (8)$$

Examining nine sulphone data sets in the gaseous phase with such substituents as methyl, alkyl, phenyl and benzyl we find that the range of absolute differences between the measured and derived values is 3.6 (ethyl *t*-butyl) to 18.2 kJ mol^{-1} (methyl butyl) and has an average of 10.2 ± 4.9. The result from fourteen data sets of sulphides is slightly more satisfactory having a range of absolute differences of 0.15 (methyl butyl) to 11.8 (ethyl *t*-butyl). The average of the values in the range is 2.7 ± 3.4 kJ mol^{-1}.

There are not enough data to test the sulphoxides, sulphites and sulphates, but given the regularity of behaviour observed previously for the several sulphur-containing series, we are encouraged to believe in the near-thermoneutrality of their reactions also[21].

G. Difference Quantities Between Sulphur-, Oxygen- and Carbon-containing Compounds

As before with alcohol and ether 'methylene exchanges'[10], we will deal now with thiols and sulphides by deriving the difference quantities defined by equations 9 and 10[18];

$$\delta_9(*, R) = \delta\Delta H_f(*, RCH_3, RSH) = \Delta H_f(*, RCH_3) - \Delta H_f(*, RSH) \quad (9)$$

$$\delta_{10}(*, R, R') = \delta\Delta H_f(*, RCH_2R', RSR') = \Delta H_f(*, RCH_2R') - \Delta H_f(*, RSR') \quad (10)$$

Additionally, we will compare these exchanges with those derived for alcohols and ethers (equations 11 and 12) and with those between sulphur and oxygen analogues (equations 13 and 14):

$$\delta_{11}(*, R) = \delta\Delta H_f(*, RCH_3, ROH) = \Delta H_f(*, RCH_3) - \Delta H_f(*, ROH) \quad (11)$$

$$\delta_{12}(*, R, R') = \delta\Delta H_f(*, RCH_2R', ROR') = \Delta H_f(*, RCH_2R') - \Delta H_f(*, ROR') \quad (12)$$

$$\delta_{13}(*, R) = \delta\Delta H_f(*, ROH, RSH) = \Delta H_f(*, ROH) - \Delta H_f(*, RSH) \quad (13)$$

$$\delta_{14}(*, R, R') = \delta\Delta H_f(*, ROR', RSR') = \Delta H_f(*, ROR') - \Delta H_f(*, RSR') \quad (14)$$

The results are summarized in Tables 2 and 3.

TABLE 2. Heats-of-formation differences between thiols, alcohols and corresponding hydrocarbons[a,b] (kJ mol^{-1})

R =	Methyl	Primary	Secondary	Tertiary
δ_9(l, R)		$-48.5 \pm 1.4, n = 10$	$-48.3 \pm 0.8, n = 5$	$-50.0 \pm 0.7, n = 4$
δ_9(g, R)	−60.9	$-58.0 \pm 1.1, n = 11$	$-57.7 \pm 0.8, n = 5$	$-57.9 \pm 1.1, n = 4$
δ_{11}(l, R)		$153.1 \pm 1.8, n = 12$	$162.7 \pm 1.6, n = 5$	$170.0 \pm 3.7, n = 4$
δ_{11}(g, R)	117.7	$127.8 \pm 1.6, n = 10$	$138.6 \pm 0.7, n = 5$	$147.2 \pm 3.8, n = 4$
δ_{13}(l, R)	−192.4	$-202.3 \pm 1.0, n = 10$	$-209.9 \pm 2.2, n = 5$	$-219.7 \pm 3.7, n = 3$
δ_{13}(g, R)	−178.6	$-186.6 \pm 1.3, n = 10$	$-194.2 \pm 2.6, n = 5$	$-205.2 \pm 3.4, n = 3$

[a]Mean values calculated from equations 9, 11 and 13. Uncertainty intervals are standard deviations from the mean.
[b]Thiol and hydrocarbon heats of formation are from Reference 3. Alcohol heats of formation are from Reference 10.

TABLE 3. Heats-of-formation differences between gaseous sulphides, ethers and corresponding hydrocarbons[a,b] (kJ mol^{-1})

	Methyl	Primary	Secondary	Tertiary
δ_{10}(g, R, R′)				
Methyl	−67.2	$-65.3 \pm 0.7, n = 4$	$-62.7 \pm 0.7, n = 2$	−64.8
Primary		$-61.9 \pm 1.2, n = 5$	−57.6	−57.9
Secondary			−59.7	?
Tertiary				−52.7
δ_{12}(g, R, R′)				
Methyl	79.4	$91.1 \pm 0.3, n = 4$	98.3	$100.8 \pm 4.8, n = 2$
Primary		$105.2 \pm 0.1, n = 4$	?	114.7
Secondary			117.5	133.6
Tertiary				120.4
δ_{14}(g, R, R′)				
Methyl	−146.6	$-156.2 \pm 0.5, n = 3$	−161.5	−162.2
Primary		$-167.4 \pm 1.0, n = 4$	?	?
Secondary			−177.2	?
Tertiary				−173.1

[a]Mean values calculated from equations 10, 12 and 14. Uncertainty intervals are standard deviations from the mean.
[b]Sulphide and hydrocarbon heats of formation are from Reference 3. Ether heats of formation are from Reference 10.

Wiberg and his coworkers[22] noted that the CH_3/OH endothermic exchange energies, δ_{11}, fell into distinct groups and attributed some of the difference in the heats of formation between primary, secondary and tertiary alcohols and their corresponding hydrocarbon analogues to the differential stabilization of the electron-deficient α-carbon by the alkyl groups. The CH_3/SH exchange energies, δ_9, show no such behaviour; all primary, secondary and tertiary exothermic enthalpy differences (but not the methyl derivative) fall within a narrow range. The relatively large exothermic thiol/alcohol exchange energies, δ_{13}, are again distinct with respect to functional group classification. We can conclude that, compared to a C—O bond, the C—S bond is not very polar.

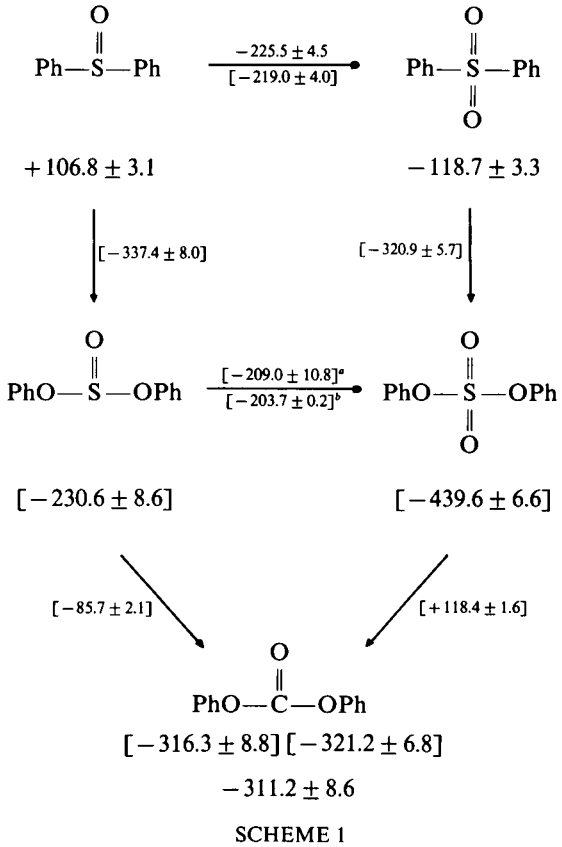
There is only slightly more discrimination by R group classification for δ_{10} and δ_{14}, similar to that found[10] for δ_{12} when R and R′ are variously methyl, primary, secondary or tertiary. However, the paucity of data makes any conclusions based on these differences rather tenuous.

H. Difference Quantities Between Alicyclic Sulphur–Oxygen and Carbon–Oxygen Compounds

The 'exchange' of a sulphinyl or a sulphonyl group for a carbonyl group is neither isoelectronic nor isosteric. Nonetheless, after defining the difference quantity, δ_{15}, for identically substituted pairs we find the derived results quite useful:

$$\delta_{15}(*, x, y) = \delta_{15}(*, \mathrm{RCO}_x\mathrm{R}', \mathrm{RSO}_y\mathrm{R}')$$
$$= \Delta H_f(*, \mathrm{RCO}_x\mathrm{R}') - \Delta H_f(*, \mathrm{RSO}_y\mathrm{R}') \quad (15)$$

Extending Shaw's[23] preliminary conclusion, we find for the sulphones and corresponding ketones that there are twelve pairs whose average $\delta_{15}(g, 1, 2)$ is $+172.5 \pm 6.2\,\mathrm{kJ\,mol^{-1}}$ and three pairs whose average $\delta_{15}(1, 1, 2)$ is $+211.8 \pm 6.1\,\mathrm{kJ\,mol^{-1}}$. The data for the dimethyl and di-*t*-butyl compounds, for which the differences are at opposite extremes of the range, are excluded[24]. It is remarkable that the data seem to have no other regularity with respect to structural similarities. Such structurally and electronically disparate examples as the diethyl and the diphenyl derivatives are near the middle of the gaseous range.



SCHEME 1

[a]From the heat of reaction for the equations as written.
[b]From Figure 1.

For the sulphoxide/ketone pairs there are only four difference quantities and here also the gas and liquid values for the dimethyl substituted pair are at the lower extremes of the ranges. The δ_{15}(g, 1, 1) for the remaining three pairs is -47.9 ± 7.2. The diphenyl and diethyl values are nearly equal, -51.9 and -52.3 kJ mol^{-1} respectively. Because of the paucity of data, undue weight is given to the value for the ethyl *t*-butyl difference quantity (-39.6) and it might be reasonable to assume that with more values, the average difference would approach -52 kJ mol^{-1}. We are reluctant to average the difference quantities for the remaining two liquid pairs, diethyl (-28.5 kJ mol^{-1}) and ethyl *t*-butyl (-7.6 kJ mol^{-1}).

Unfortunately, there is only one carbonate, diethyl carbonate, for which there is an archival heat of formation to compare with the corresponding sulphite and sulphate. The difference quantity δ_{15}(g, 3, *y*) is -85.7 ± 2.1 kJ mol^{-1} using the sulphite and $+118.4$ kJ mol^{-1} using the sulphate.

If these δ_{15}(*, 3, *y*) values for the diethyl pairs are typical for sulphites and sulphates, as they seem to be for the sulphones and presumably the sulphoxides, then we are justified in using them to derive heats of formation of carbonates from sulphur-containing compounds. As a test of this assumption, beginning with diphenyl sulphoxide and diphenyl sulphone, we will estimate values for the heat of formation of diphenyl carbonate and compare them to the archival value of -311.2 ± 8.6 kJ mol^{-1} (g). In Scheme 1, the SO*y*→SO*x* difference quantities are from Figure 1, derived values are shown within brackets while archival experimental values are shown without brackets. Uncertainty intervals are calculated as the square root of the sum of the squares of the experimental uncertainties.

I. Alicyclic Sulphur-containing Compounds

In principle, our analysis can be extended to cyclic species, but what data are there? Experimental thermochemical characterization of most cyclic analogues of sulphur-containing species has not been reported. However, we can explore the simplest comparison, that of thiacycloalkanes and cycloalkanes, where we might expect the least steric perturbation and the most electronic similarity. However, there is no reason to expect no strain energy difference between cycloalkanes and their sulphur analogues because the C—C bond length is shorter than the C—S bond length and the C—C—C bond angle is larger than the C—S—C bond angle. In fact, unlike the exchange of —O— in cyclic monoethers for —CH_2— which was 'rather constant'[10], here change of $-CH_2$— to —S— has major consequences on heats of formation. We find for 3- through 7- membered rings the following differences in the heat of formation of the gaseous compounds: 28.9, 32.2, 42.3, 59.9 and 52.3 kJ mol^{-1}. The exchange in a ring of 'infinite' members would be similar to that of the strainless di-*n*-butyl sulphide/*n*-nonane exchange of 60.8 kJ mol^{-1}.

There has been no direct calorimetric measurement of the heats of formation of the cyclic sulphoxides, sulphones, sulphites and sulphates. To do more than assume constant increments requires approximations and assumptions which we would rather conduct for more exotic classes of compounds that we discuss in the subsequent sections.

III. DIVERSITY AND UNITY OF ORGANOSULPHUR CHEMICAL ENERGETICS

A. Some Interrelations of the Energetics of Sulphinic and Sulphonic Acids

We start the discussion of the heats of formation of sulphinic acids by acknowledging that we do not know of any directly measured quantity, and so in this regard, we are not any more definitively knowledgeable than had been Bujnicki, Mikołajczyk and

Omelanczuk[25], the thermochemistry chapter authors of the earlier Patai sulphinic acid volume. We also acknowledge that we know of only one new heat of formation[26] of a sulphonic acid published subsequent to publication of the corresponding thermochemistry chapter[27] of the appropriate Patai book. This measurement is for solid 3-carboxy-4-hydroxybenzenesulphonic acid ('sulphosalicylic acid') dihydrate, and is one of the very few direct calorimetric measurements of this class of compounds. The reported value is -1982 ± 3 kJ mol^{-1}. Is this value consistent with our previous knowledge of the energetics of sulphonic acids[27]? To make comparisons it will be necessary to mentally dehydrate the compound. The heat of formation of liquid water is -285.830 kJ mol^{-1}, and assuming an interaction energy of precisely 0.0 kJ mol^{-1} between the sulphonic acid and water, we conclude that the heat of formation of solid 3-carboxy-4-hydroxybenzenesulphonic acid is -1411 kJ mol^{-1}. Whether hydrogen bonding or proton transfer (hydronium salt formation) results, this sulphonic acid/water interaction energy is clearly nonzero. We recall the suggested[27] -527 kJ mol^{-1} for the difference of the heats of formation of solid sulphonic acids and the corresponding sulphur-free compound. The heat of formation of the relevant solid desulphonated species, 2-hydroxybenzoic acid[28], is -589 kJ mol^{-1}. From these numbers we would derive an interaction energy of $-1411 - [-589 + (-527)]$ or nearly 300 kJ mol^{-1}. This value is excessively high, at least by comparison with the hydration energy of any oxyacid known to the current authors[29].

It is not obvious where the discrepancy lies: we note that this *ca* 300 kJ mol^{-1} value is nearly equal to the heat of formation of liquid water. We wonder if the literature compound is not some higher hydrate? We know of one relatively small component of the error. The reader may recall from Reference 27 two approximation rules, one just cited which asserted that the difference of heats of formation of solid RH and RSO_3H is *ca* 527 kJ mol^{-1}, and another which asserted that the difference for their aqueous solutions is 611 kJ mol^{-1}. It was also argued that the difference of these two values, 84 kJ mol^{-1}, is a reasonable difference for the heats of solution of a solid hydrocarbon and its sulphonic acid. Reasonable it may be by comparison with other strong acids[29], yet it is nonetheless apparently wrong. Recent studies show that the heat of solution of liquid benzene in water[30] is nearly thermoneutral, 2.1 ± 1.9 kJ mol^{-1}, and so the heat of solution of solid benzene[31] is a likewise endothermic 12 kJ mol^{-1}. The heat of solution of solid benzenesulphonic acid[32] is 'merely' -32.0 ± 0.5 kJ mol^{-1}, and so the difference is only 44 kJ mol^{-1}, and not 84 kJ mol^{-1}. Relatedly, the heat of solution of liquid methane sulphonic acid[32] in water is -48.3 ± 0.3 kJ mol^{-1} while for liquid methane[33] it is *ca* -5 kJ mol^{-1}. The difference here is *ca* 43 kJ mol^{-1}, and not 84 kJ mol^{-1}. From the heat of formation of an aqueous solution of methane of -89 kJ mol^{-1}, we conclude that the heat of formation of aqueous methanesulphonic acid is $-89 - 611 = -700$ kJ mol^{-1}. Since the heat of formation of liquid benzene is 49 kJ mol^{-1}, the heat of formation of aqueous benzenesulphonic acid is thus deduced to be $49 + 2 - 611 = -560$ kJ mol^{-1}. We are more confident of these and any other estimations for heats-of-formation differences for sulphonic acids and their desulphonated derivatives in aqueous media than in the differences for the condensed phase[34], and for the resulting heats of formation of the sulphonic acids. However, we still know of no way we can arrive at an interaction energy of sulphosalicylic acid and two waters of 300 kJ mol^{-1} and so remain suspicious of the literature measurement of the heat of combustion of sulphosalicylic acid dihydrate.

To compensate in large part for our ignorance of the energetics of sulphinic and sulphonic acids, it is necessary to make estimates so as to calibrate the sparse energetics data we do have for these species. Let us commence with sulphinic acids; in particular, let us consider benzenesulphinic acid. Indeed, rather than discussing the acid *per se*, let us consider now aqueous solutions of its sodium salt. After all, few sulphinic acids are isolable and sulphinate salts are considerably more stable than the parent acids[35]. Our goal is to derive the heat of formation of aqueous sodium benzenesulphinate.

Some fifteen years ago Kice and his coworkers reported[36] the heat of solution of solid benzenesulphinic acid, the thermochemistry of the alkaline hydrolysis of the sulphinyl sulphone, diphenyl disulphide *S,S,S'*-trioxide[37], and the disulphone, diphenyl disulphide tetroxide. These reactions formed sodium benzenesulphinate, and a 1:1 mixture of the sodium salts of benzenesulphinic and benzenesulphonic acids, via equations 16 and 17, respectively.

$$PhSOSO_2Ph + 2Na^+ OH^- \longrightarrow 2(Na^+ PhSO_2^-) + H_2O \quad (16)$$

$$PhSO_2SO_2Ph + 2Na^+ OH^- \longrightarrow Na^+ PhSO_2^- + Na^+ PhSO_3^- + H_2O \quad (17)$$

Starting with solid disulphide polyoxide and finishing with dissolved salts, these authors determined that the first reaction was some 97 ± 9 kJ mol^{-1} less exothermic than the latter. Using some plausible assumptions we equate the heats of sublimation of the two polyoxides[38] and so can directly use the heats of formation of gaseous trioxide and tetraoxide from Benson's organosulphur thermochemical review[39]. From use of Hess cycle reasoning, we deduce equation 18.

$$[\Delta H_r(16) - \Delta H_r(17)] - [\Delta H_f(g, PhSOSO_2Ph) - \Delta H_f(g, PhSO_2SO_2Ph]$$
$$= [\Delta H_f(aq, PhSO_2^-) - \Delta H_f(aq, PhSO_3^-)] \quad (18)$$

From the difference of the heats of formation of the polyoxides, -263 ± 18 kJ mol^{-1}, we find that the difference of the heats of formation of solvated sulphinate and sulphonate salt is 360 ± 25 kJ mol^{-1}. Is this difference plausible, or at least consistent with what else we know? It behooves us to answer this before we derive a heat of formation of aqueous sodium benzenesulphinate using this relation and our earlier heat of formation of aqueous benzenesulphonate. We do not think this 360 kJ mol^{-1} heat-of-formation difference is likely if we are willing to extrapolate from our understanding of the energetics of inorganic sulphinates and sulphonates. We find the heats of formation of aqueous sodium bisulphite and bisulphate to be 259 kJ mol^{-1} and of sodium sulphite and sulphate to be 274 kJ mol^{-1}. The heats of formation of another set of aqueous sodium sulphur oxyanion salts, namely $Na_2S_2O_4$, $Na_2S_2O_5$ and $Na_2S_2O_6$ at '1:∞' (i.e. infinite), 1:700 and 1:400 dilution, are -1233.9, -1469.6 and -1667.7 kJ mol^{-1}, respectively. This corresponds to sequential heat-of-formation differences of 236 and 198 kJ mol^{-1}. Yet, what other information do we have?

Recall the earlier suggested[27] difference of heats of formation of sulphonates and hydrocarbons, $\delta\Delta H_f$ (aq, RSO_3Na, RH) $= -849$ kJ mol^{-1}. From the heat of formation of liquid benzene and its heat of solution in water[32] we conclude that the heat of formation of aqueous sodium benzenesulphonate is *ca* -800 kJ mol^{-1}. If we assume an average value of *ca* 230 ± 40 kJ mol^{-1} as the energy difference of 'arbitrary' sulphonates and sulphinates[40], we conclude that the heat of formation of aqueous sodium benzenesulphinate is *ca* -570 ± 40 kJ mol^{-1}.

Ashworth[41] has described some analytically important redox chemistry that interrelates sulphinic and sulphonic acids. In particular, we find that aqueous $HOCH_2SO_2^-$ is oxidized to aqueous $HOCH_2SO_3^-$ by $HgCl_2$ and I_2. The heat of formation of aqueous $HOCH_2SO_3^-$ may be derived to be -852 kJ mol^{-1} by taking the difference of the heats of formation suggested[27] for aqueous $HOCH_2SO_3Na$, -1092.0 kJ mol^{-1}, and the -240.1 kJ mol^{-1} of aqueous Na^+ ion. From the heats of formation of the oxidized and reduced forms of the additional inorganic species for these redox reactions, we conclude that the heat of formation of aqueous $HOCH_2SO_2^-$ must be more positive than -733 and -707 kJ mol^{-1}. We have also been told[42] that the oxidation electrode potential of reaction 19 is 0.935 V, which by use of the Nernst equation corresponds to a free energy change of -180 kJ mol^{-1}. But we want ΔH, not ΔG. We lack the relevant entropy data from which to make this correction from free energy to enthalpy directly.

However, we find for other singly charged oxyanion redox reactions 20 with X = N, $n = 2$; X = Cl, $n = 2$ and 3; X = Br, $n = 3$; X = I, $n = 3$ and X = 'HS'[43], $n = 3$ that ΔH is *ca* 80 ± 20 kJ mol^{-1} more positive than ΔG. Accepting this generality, we conclude that reaction 4 is $180 - 80 = 100$ kJ mol^{-1} exothermic and so ΔH_f(aq, $HOCH_2SO_2^-$) = -580 ± 20 kJ mol^{-1}. Mentally reforming the aqueous solution of the sodium sulphinate salt by adding Na^+ (aq) results in a predicted heat of formation of ΔH_f(aq, $HOCH_2SO_2Na$) = -821 ± 20 kJ mol^{-1}. This gives us a 270 kJ mol^{-1} difference between a sulphinate and corresponding sulphonate, a rather plausible number. This gives us a heat of formation of aqueous sodium benzenesulphinate of $-800 - (-270) = -530$ kJ mol^{-1}. Accepting the heat-of-formation value of aqueous $HOCH_2SO_2Na$ and aqueous CH_3OH and generalizing, we derive a tentative $\delta\Delta H_f$(aq, RSO_2Na, RH) = -575 ± 20 kJ mol^{-1}. In summary, using a composite of electrochemical and thermochemical measurements and assumptions, we conclude here that the desired heat of formation of aqueous sodium benzenesulphinate is -525 ± 20 kJ mol^{-1}.

$$HOCH_2SO_2^- + 2OH^- \longrightarrow HOCH_2SO_3^- + H_2O + 2e^- \quad (19)$$

$$XO_n^- + 2OH^- \longrightarrow XO_{n+1}^- + H_2O + 2e^- \quad (20)$$

Zoller[44] tells us that the reaction of alkenes with SO_2 (equation 21) to form allylic sulphinic acids lies mostly on the left while the corresponding reaction of cumulenes to form the conjugated alkadienylsulphinic acids (equation 22) lies mostly on the right. Previous experience with reactions that interconvert 'two things and one' suggests that the formation of the sulphinic acids should be accompanied by a decrease of entropy-derived free energy of *ca* 42 kJ mol^{-1}. That reaction 21 prefers the left side suggests that sulphinic acids are no more than *ca* 42 kJ mol^{-1} more stable than the corresponding hydrocarbon $+ SO_2$, yet the facility of reaction 21 in both directions suggests that its free energy change cannot be too large. This suggests that 1,3-butadiene-2-sulphinic acid, the archetypical member of the class of species on the right side of the equation, is no more (but not much less) than 42 kJ mol^{-1} more stable[45] than 1,3-butadiene $+ SO_2$, but unlike allylic sulphinic acids it fails to decompose into these products for want of a suitable cyclic transition state[46]. From the archival heats of formation of 1,3-butadiene and sulphur dioxide, we conclude that the heat of formation of gaseous 1,3-butadiene-2-sulphinic acid cannot be any lower than $(110 - 297 - 42) = -229$ kJ mol^{-1}, but cannot be any higher than $(162 - 297 - 42) = -177$ kJ mol^{-1} because it would not form from the 1,2-butadiene and SO_2. Let us thus choose for now an average heat of formation value of -203 ± 26 kJ mol^{-1}.

$$H—C—C=C + SO_2 \rightleftharpoons C=C—C—S(O)—OH \quad (21)$$

$$H—C—C=C=C < + SO_2 \rightleftharpoons C=C—C(=C <)—S(O)—OH \quad (22)$$

How can one estimate heats of formation of gaseous benzenesulphinic acid from that of 1,3-butadiene-2-sulphinic acids? Intuitively, substituent effects on benzene and butadiene should be comparable. It is well-established that substituent effects on benzene and ethylene parallel[47] and those on ethylene and butadiene are presumably not 'that different'[48]. Equivalently, the difference in the heats of formation of benzenesulphinic acid and benzene should be nearly equal to 1,3-butadiene-2-sulphinic acid and 1,3-butadiene. We hereby generalize this near-equality to be a constant. From the experimental heat of formation of 1,3-butadiene of 110 kJ mol^{-1}, we take this constant to be -313 kJ mol^{-1}, where we admit that this difference, δ_{23} (equation 23), is accurate only to some ± 26 kJ mol^{-1}. Combining this relation with the heat of formation of gaseous benzene of 83 kJ mol^{-1}, we conclude that the heat of formation of gaseous benzenesulphinic acid is -230 kJ mol^{-1}. We do not have the heat of sublimation of

benzenesulphinic acid, nor any other sulphinic acid. However, since the heats of sublimation of diphenyl sulphoxide and benzophenone (diphenyl ketone) are nearly identical, we set the desired quantity equal to the heat of sublimation of benzoic acid. From this value of 91 kJ mol^{-1}, we deduce the heat of formation of solid benzenesulphinic acid to be -321 ± 30 kJ mol^{-1}. Kice and his coworkers[36] also tell us that the heat of neutralization of benzenesulphinic acid in 60% dioxane is 68 kJ mol^{-1}: let us assume that the same value is found in water[49]. From the archival heats of formation of aqueous NaOH and water, we derive a heat of formation of aqueous sodium benzenesulphinate equal to -573 ± 30 kJ mol^{-1}.

$$\delta_{23}(\text{g, } RSO_2H\text{, RH}) \equiv \Delta H_f(\text{g, } RSO_2H) - \Delta H_f(\text{g, RH}) = -312 \text{ kJ mol}^{-1} \quad (23)$$

We now have four values for the heat of formation of aqueous sodium benzenesulphinate: -440 ± 25, -570 ± 40, -525 ± 20 and -573 ± 30 kJ mol^{-1}. We opt for the value -540 ± 20 kJ mol^{-1} which overlaps the last three results within their error bars, and ignores (for no reason except consensus) the first result. Generalizing, $\delta\Delta H_f$(aq, RSO_2Na, RH) equals *ca* -590 kJ mol^{-1}. We remind the reader of our earlier suggested generalization: $\delta\Delta H_f$(aq, RSO_3Na, RH) $= -849$ kJ mol^{-1}. We welcome definitive experimental measurements to test this, but then again, as the reader has seen, we recall that such studies are absent for the energetics of many classes of sulphur-containing species. We welcome their inclusion in the next sulphur supplement of the Patai series.

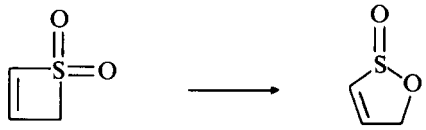
B. Ring Size Considerations of the Energetics of Sulphinic Acids, Their Esters and Sulphones

A casual observation of the thermochemistry of organic sulphur/oxygen compounds shows sulphones with their single sulphur, two oxygens and two affixed groups to be comparatively well-understood. In a recent volume of the Patai series, Herron[20] gives the reader relevant Benson group increments[2] and simple rules of thumb for deriving the heats of formation and bond energies of sulphones. By contrast, the situation of our knowledge of the energetics of the isomeric sulphinic acids and sulphinate esters is rather bleak, even though they are also composed of a single sulphur, two oxygens and two affixed groups. Our literature searching has shown that no directly measured heats of formation have been reported for either sulphinic acids or sulphinates. Perhaps we should thus not be surprised that the appropriate volume on sulphinic acids[50] in the Patai series has but a brief energetics chapter in which Bujnicki, Mikołajczyk and Omelanczuk[25] deal mostly with the thermolyses of these species, such as rearrangements of allyl sulphinates to form (transposed) sulphones, rather than the thermochemistry of sulphinates, *per se*[51]. In particular, we will cross-reference various chapters in the sulphinic acid[50] and sulphone/sulphoxide[52] volumes as secondary sources of both qualitative and quantitative information about the energetics of sulphinic acids and their esters.

As inferred above, the sulphinate–sulphone rearrangement figures prominently in the study of sulphinates. For example, it is discussed in Patai volume chapters on the rearrangement of sulphinates[53] and of sulphones[54,55] by Braverman and by Schank, and on the role of sulphinates *in* synthesis[56] and *of* sulphones[57] by Drabowicz, Kiełasiński and Mikołajczyk, and by Dittmer and Hoey, respectively. Disappointingly, we lack information as to the heat of this rearrangement—the thermochemistry of sulphones is well-established enough to provide us with either an experimental or highly accurate derived heat of formation of almost any sulphone we care about, and thereby we would achieve a highly accurate derived heat of formation of the sulphinate ester of interest. A somewhat more conceptually useful input for the derivation of bounds for the difference of energy of sulphones and their isomeric sulphinates is the rearrangement of propargyl

sulphinates to allenyl sulphones—alkynes are somewhat more stable than the isomeric allenes[58] and, as we discuss in greater length later in this chapter, allenyl sulphones, like other unsaturated sulphones, are slightly destabilized when compared to their saturated counterparts.

We find considerably more evocative the rearrangements involving cyclic sulphones and sulphinates chronicled in the just-cited Patai chapters. Care must be taken in the choice of examples. Photochemical rearrangements do not qualify because one generally does not learn the relative energies of the starting material and product. There is the ambiguity of how much the light transforms a symmetry-forbidden reaction into an allowed one, and how much it provides a source of energy to drive an endothermic reaction. Likewise, there are many base-assisted reactions but, since they convert a relatively strong base into a relatively weak one, e.g. when an alkyl lithium or other organometallic is used to transform a sulphone into a sulphinate salt, it is not obvious how much the energy of effectively neutralizing the strong base 'drives' the reaction. We conclude that the conceptually most useful reactions are thus thermal rearrangements. Those that do not change the number of rings have the additional virtue that the entropy of reaction is expected to be small. The first qualifying example that we will discuss is the sulphone-to-sulphinate rearrangement of thiete sulphone (**1**) into the unsaturated γ-sultine, 5*H*-1,2-oxathiol-3-ene sulphoxide (**2**) (equation 24). If we neglect all conjugative

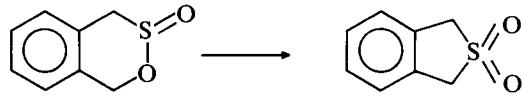


(**1**) (**2**) (24)

interactions of the double bonds with either the SO_2 of the cyclic sulphone or with the SO of the cyclic sulphinate, we conclude that the difference in heats of formation of sulphones and sulphinates is less than the strain energy difference of thiete and 5*H*-1,2-oxathiol-3-ene. Equivalently, there is the decrease of strain energy accompanying the transformation of a 'special' four-membered ring into a 'special' five-membered ring that compensates for the rearrangement of a sulphone into the less stable sulphinate isomer. But we don't know the strain energy of either sulphur-containing heterocycle[59]. Either by enlightened inspection or by use of a more formal/mathematical understanding of strain energies[60], we deduce that the strain energy difference of a four-membered ring (4MR) and the identically 'decorated' five-membered ring (5MR) equals the difference between $[\Delta H_f(4MR) + \Delta H_f(—CH_2—)]$ and $\Delta H_f(5MR)$, wherein $—CH_2—$ is the universal 'strainless' methylene increment[61] and its accompanying heat of formation is *ca* -20.6 kJ mol^{-1}. For the simplest and undecorated four- and five-membered rings, cyclobutane and cyclopentane respectively, the strain energy difference is thus $[28.4 + (-20.6)] - (-76.4) = 84.2 \pm 1.0$ kJ mol^{-1}, nearly identical to the value of 84.1 kJ mol^{-1} set equal to the difference of the individual strain energies recommended in Reference 59. What 'decorations' should we use for the thiete and oxathiolene? One choice is to use their least decorated unsaturated analogues, the carbocyclic cyclobutene and cyclopentene, with the strain energy difference[62] of 102.2 ± 2.1 kJ mol^{-1}. Another choice is to use their saturated, sulphur-containing analogues, thietane and thiolane, with a difference in strain energies of 74.1 ± 1.9 kJ mol^{-1}, while a difference of 116.8 ± 4.1 kJ mol^{-1} is found for the sulphones of thiete and 2,3-dihydrothiophene. The spread of these strain energy differences, some 95 ± 25 kJ mol^{-1}, is large. However, from this analysis, we can be convinced that sulphinates are no more than 95 ± 25 kJ mol^{-1} higher

in energy than the isomeric sulphone. Though this difference is only a bound and has large error bars, it is nonetheless useful information that was derived without recourse to the need of performing any new additional experimental measurements.

The second sulphinate-to-sulphone rearrangement that qualifies is the transformation of the benzoannelated δ-sultine, 1,4-dihydrobenzo[*c*]-1,2-oxathiene sulphoxide (**3**), into 1,3-dihydrobenzo[*c*]thiophene sulphone (**4**) (equation 25). If we neglect all allylic/benzylic



(3) (4) (25)

interactions of the double bonds with either the $>SO_2$ of the cyclic sulphone or with the $>SO$ of the cyclic sulphinate, we conclude that the difference in heats of formation of sulphones and sulphinates is less than the strain energy difference of 1,4-dihydrobenzo[*d*]-1,2-oxathiene and 1,3-dihydrobenzo[*c*]thiophene. Equivalently, the increase of strain energy accompanying the conversion of a 'special' six-membered ring into a 'special' five-membered ring is inadequate to prevent the formation of a sulphone by the rearrangement of the less stable sulphinate isomer. But we don't know the strain energy of either heterocycle. Mimicking this difference through the use of the carbocyclic 2-ring species indane and tetralin, we find a difference of 14.1 ± 2.6 kJ mol^{-1}. Relatedly, making use of the heats of formation of the 1-ring carbocyclic cyclopentane and cyclohexane results in a strain energy difference of 26.4 ± 1.1 kJ mol^{-1}, while the use of the 1-ring sulphur species thiolane and tetrahydrothiopyran gives a value of 8.8 ± 1.7 kJ mol^{-1}. Again, there is a comparatively large spread of values of strain energy differences, some 15 ± 10 kJ mol^{-1}, that is deemed inadequate to allow thermal transformation of a sulphone into the isomeric sulphinate. Summarizing the above, we conclude that sulphinates lie between 15 and 95 kJ mol^{-1} higher in energy than their isomeric sulphones.

Dittmer and Hoey[57] provide us with another conceptually useful comparison. Substituted 1,2-oxathietane sulphoxides (**5**), i.e. β-sultines, undergo a facile thermal decomposition into olefins + SO_2 via reaction 26 proceeding to the left. In contradistinction, reaction 27 of cyclopropanes with SO_2 to form 1,2-oxathiolane sulphoxides **6**, i.e. γ-sultines, proceeds to the right. For our discussion, we will consider only unsubstituted species, i.e. equations 26 and 27 as written, and assume that our error due to omission of substituents will be rather small. The number of rings change in these thermal reactions. Entropy is thus expected to be important, but the entropy changes are not unpredictable. We find that there is a surprising near-constancy associated with entropy changes of unimolecular decomposition reactions[63]. As such, we conclude that the entropy change associated with equations 26 and 27 proceeding in their preferred direction are *ca* 140 and -140 J mol^{-1} K^{-1}, respectively. Equivalently, the free energy change is *ca* 42 and -42 kJ mol^{-1} at the 'typical temperature' of 300 K. Without loss of either qualitative or quantitative understanding, we equate the ethylene in equation 26 with 'cycloethane'[64] and so conclude the strain energy difference of a two-membered ring (2MR) and the identically 'decorated' four-membered ring is the difference of $[\Delta H_f(2MR) + 2\Delta H_f(\text{—}CH_2\text{—})]$ and $\Delta H_f(4MR)$. The strain energy difference associated with the ring expansion from cycloethane to cyclobutane, the undecorated two- to four-membered rings, equals 39.7 ± 0.7 kJ mol^{-1} and so equation 28 for formal synthesis of strainless sulphinates would have had to be exergonic by at least $40 + 42 \approx 82$ kJ mol^{-1} for reaction 26 to have proceeded to the right, as opposed to the left which is the observed reaction direction.

$$C_2H_4 + SO_2 \rightleftharpoons \underset{(5)}{\text{O=S(O)-O cyclic}} \quad (26)$$

$$c\text{-}C_3H_6 + SO_2 \rightleftharpoons \underset{(6)}{\text{O=S(O)-O cyclic}} \quad (27)$$

$$R—R' + SO_2 \longrightarrow R—S(O)—O—R' \quad (28)$$

Relatedly, we conclude that the strain energy difference of a three-membered ring and the identically 'decorated' five-membered ring is the difference between $[\Delta H_f(3MR) + 2\Delta H_f(—CH_2—)]$ and $\Delta H_f(5MR)$. This strain energy difference associated with the ring expansion from cyclopropane to cyclopentane, the undecorated three- to five-membered rings, equals 88.5 ± 1.0 kJ mol^{-1} and so reaction 28 for the formal synthesis of strainless sulphinates would have had to be endothermic by at least $89 - 42 \approx 47$ kJ mol^{-1} for reaction 28 not to have proceeded to the right as is observed.

We find that the average difference between the heats of formation of gaseous dialkyl sulphone RSO_2R' and the related hydrocarbon RR' is *ca* 300 kJ mol^{-1}. From the well-established heat of formation of gaseous SO_2 of -296.830 kJ mol^{-1}, we conclude that reaction 29, the formal synthesis of strainless sulphones, is exothermic by some 3 kJ mol^{-1}, i.e. essentially thermoneutral. Combining the energetics of reactions 28 and 29 results in the conclusion that the isomerization of sulphinates to sulphones (equation 30) is exothermic by less than 47 kJ mol^{-1}, a result consistent with our other inequalities in this section.

$$R—R' + SO_2 \longrightarrow R—S(O)_2—R' \quad (29)$$

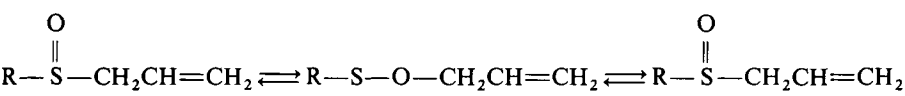
$$R—S(O)—O—R' \longrightarrow R—S(O)_2—R' \quad (30)$$

Let us use in concert the earlier enunciated heat-of-formation regularity that asserted that the heat of formation of an arbitrary gaseous sulphinic acid RSOOH is 313 ± 26 kJ mol^{-1} more negative than the corresponding hydrocarbon, RH, and the additional one[65] that asserts methyl esterification of an arbitrary gaseous oxyacid, XOH, to form XOMe is accompanied by a 20 ± 15 kJ mol^{-1} increase in heat of formation. Admittedly with some trepidation let us also use the 'universal' methylene increment to transform RH into RMe and thereby assert that there is an accompanying -20.6 kJ mol^{-1} change of heat of formation[66]. Equivalently, we conclude that the heat of formation of an arbitrary R—S(O)—OMe is $-313 + 20 - (-20.6) = -272 \pm 30$ kJ mol^{-1} more negative than for RMe. Finally, at the risk of equating the heat-of-formation effects associated with Me with those of other hydrocarbon groups, we conclude that sulphones are more stable than the isomeric sulphinate esters by 28 ± 30 kJ mol^{-1}. That is, while it is numerically consistent with our last finding that sulphinates are more stable than sulphones, it is much more plausible that they are less stable by some 30–60 kJ mol^{-1}. All of our results on the stability of sulphinate esters and the parent sulphinic acids are consistent. While we are confident of our results, we acknowledge chemistry is still an experimental science. Will someone please measure the heat of formation of at least one such species?

C. Some Interrelations of the Energetics of Sulphenic Acids, Their Esters and Sulphoxides

A casual observation of the thermochemistry of organic sulphur/oxygen compounds shows sulphoxides with their single sulphur and oxygen, and two affixed groups, to be comparatively well-understood. In two different volumes of the Patai series, Herron[20] and Shaw[23] give the reader relevant Benson group increments[2] and simple rules of thumb for deriving the heats of formation and bond energies of sulphoxides. By contrast, the situation of our knowledge of the energetics of the isomeric sulphenic acids and sulphenate esters is rather bleak, even though they, too, are composed of a single sulphur and oxygen, and two affixed groups. Our literature searching has shown that only four indirectly measured heats of formation have been reported for sulphenic acids[67], and none at all for sulphenate esters. Perhaps we should thus not be surprised that the appropriate volume on sulphenic acids in the Patai series[68] lacks a thermochemistry chapter. Indeed, the heats of formation of sulphenic acids have only been mentioned rather tangentially in the thermochemistry chapter[27] of the corresponding volume on sulphonic acids. Parallelling our success at using information on sulphones to aid us in the understanding of the energetics of sulphinic acids and their derivatives, the current section makes use of available information on sulphoxides in the understanding of the energetics of sulphenic acids and sulphenate esters. In particular, we will cross-reference various chapters in the sulphoxide/sulphone[52] and sulphenic acid[68] volumes as secondary sources of both qualitative and quantitative information about the energetics of sulphenic acids and their esters.

As part of thorough reviews on sulphoxide[69] and sulphenic acid/ester[70] rearrangements, Braverman has discussed the interconversion and accompanying stereochemical consequences of allyl sulphoxides and (transposed) sulphenates (equation 31). From the energy of activation for the racemization of the sulphoxide ($\Delta H^{\ddagger} = ca$ 90 kJ mol^{-1}), we



(R) (S) (31)

immediately deduce that the heats of formation of sulphenate esters lie no higher than 90 kJ mol^{-1} above the isomeric sulphoxides. This is useful as an upper bound to derive the heats of formation of general sulphenate esters should we know the heats of formation of the precursor sulphoxides[71]. Using available experimental techniques, we think that better than an upper bound can be achieved. A direct measurement of the energy of activation for the rearrangement of a sulphenate ester to the sulphoxide will allow us to establish the absolute heat of formation difference of sulphoxides and sulphenate esters as the difference of $\Delta H^{\ddagger}\rightarrow$ and $\Delta H^{\ddagger}\leftarrow$. Alternatively, a combination of T-jump and reaction calorimetry techniques on sulphenate esters (i.e. rapidly heat the sample, and measure the additional temperature rise due to the sulphenate/sulphoxide rearrangement) should also provide the desired quantity. We hope to find the results from these or related experiments chronicled in the next 'Sulphur Supplement' volume in the Patai series. But lacking this information, we now proceed to discuss estimation approaches and *already reported* measurements from which one can derive (at least) upper or lower bounds for the heats of formation of sulphenic acids and esters.

Before presenting the analysis of the literature and using assorted estimation assumptions and techniques, it seems desirable to discuss the reliability of the few reported measurements[67] for sulphenic acid heats of formation. The four sulphenic acids,

R—S—O—H, for which there are experimentally derived data for their gas-phase heats of formation have R = Me, −190; CH_2=CH, < −16; HC≡C, 102 and Ph, −34 kJ mol^{-1}. If the steric and electronic effects of a substituent depended only on the substituent, and not what it is affixed to, then the heat-of-formation difference quantity δ_{32}(g, Ph, Me, X) in equation 32 would be independent of X. We would also conclude that equation 33 would be an identity for all substituents X and Y:

$$\delta_{32}(\text{g, Ph, Me, X}) \equiv \Delta H_f(\text{g, PhX}) - \Delta H_f(\text{g, MeX}) \tag{32}$$

$$\delta(\text{g, Ph, Me, X}) = \delta(\text{g, Ph, Me, Y}) \tag{33}$$

We know that this optimism is obviously unrealized. Yet, experience[27] has shown that, at least for a set of π-withdrawing electronegative substituents, the identity is valid within a range of 20 kJ mol^{-1}. For the case of interest, we set X = —SOH and now ask what Y best 'mimics' this X. That is, for what group Y is the putative equality of equation 34 most accurately obeyed. Using the literature values[67] of the heats of formation of sulphenic acids, we find the left-hand side equals 156 kJ mol^{-1}. One might have simply thought that of all the π-withdrawing groups, sulphoxide > SO would have been similar to —SOH since —S(H)O and —S—O—H are isomeric. But the value for > SO is 129 kJ mol^{-1}. We find for this π-withdrawing class of substituents a 'normalized' (i.e. per phenyl/methyl) range resulting from *ca* 124 (—COOMe) to *ca* 142 (—NO_2) kJ mol^{-1}. We find the 156 kJ mol^{-1} difference between the heats of formation of MeSOH and PhSOH unintelligible, even if we consider π-electron-donating substituents as well[72].

$$\delta(\text{g, Ph, Me, SOH}) = \delta(\text{g, Ph, Me, Y}) \tag{34}$$

Before proceeding further, let us now discuss what is the relative energy of the R—S—O—H and R—S(O)—H tautomers of sulphenic acids? After all, Barrett[73], among others, has noted that while most sulphenic acids 'preferred' the hydroxylic R—S—O—H tautomer, there was occasional evidence for the sulphoxide R—S(O)—H form as well[74]. What can be said about this alternative form? Perhaps more precisely, what is the difference between the heats of formation of the two tautomers, δ_{35} (g, R, H, SO)?

$$\delta_{35}(\text{g, R, H, SO}) \equiv \Delta H_f(\text{g, R—S—O—H}) - \Delta H_f(\text{g, R—S(O)—H}) \tag{35}$$

We consider here only MeSOH and PhSOH because the reported heat of formation of CH_2=CHSOH is 'merely' an upper bound, and that for HC≡CSOH arises from some 'plausible' assumptions about thermochemically uncharacterized acetylenic sulphoxides.

From our earlier analysis we conclude that the heat of formation of a gaseous sulphoxide $R^1S(O)R^2$ is *ca* 125 kJ mol^{-1} more negative than the corresponding sulphide. We note that a *ca* 10 kJ mol^{-1} smaller difference, −113 kJ mol^{-1}, arises when both R^1 and R^2 are Me than for when either or both R^1 and R^2 are larger alkyl groups. Let us apply this difference analysis to the cases when one group is Me or Ph, and the other is hydrogen where even a smaller difference might be expected than when it is methyl. From the archival heats of formation of gas-phase MeSH and PhSH of −22.9 and 112.4 kJ mol^{-1}, we thus conclude that the heats of formation of MeS(O)H and PhS(O)H exceed $-22.9 - 113 \cong -136$ and $112.4 - 113 \cong -1$ kJ mol^{-1}, values some 55 and 35 kJ mol^{-1} higher than those reported for MeSOH[75] and PhSOH. Relatedly, there is a nearly 50 kJ mol^{-1} difference between the heats of formation of an arbitrary sulphoxide and the corresponding carbonyl compound, a difference increased to 66 kJ mol^{-1} when $R^1 = R^2$-Me, and expected to be even larger when one group is hydrogen than when it had been methyl. Using the well-established heats of formation of MeCHO and PhCHO of −166.1 and −36.7 kJ mol^{-1} we conclude that the heats of formation of gas-phase MeS(O)H and PhS(O)H exceed $-166.1 + 66 \simeq 100$ and $-36.7 + 66 \simeq 29$ kJ mol^{-1}, some

90 and 60 kJ mol^{-1} higher than those reported for MeSOH[75] and PhSOH.

Summarizing, if either of the two predictions of the heats of formation of both MeS(O)H and PhS(O)H is used, it is safe to say that the sulphenic acid tautomer is considerably more stable than the sulphoxide[76]. We may even conclude that any reported presence of the sulphoxide tautomer is not due to a gas-phase equilibrium and thus is due to an alternative, but intramolecularly non-equilibrating, synthetic pathway[77].

Drabowicz, Lyżwa and Mikołajczyk[78] and Hogg[79] provide convincing evidence that the sulphoxide/(sulphenic acid + olefin) reaction (equation 36) must have an equilibrium constant near unity because simple variation in temperature can shift the side of the reaction which dominates. One can use knowledge of this reaction to estimate the heat of formation of sulphenic acids since we know, or can readily derive, the heat of formation of both the sulphoxide and the olefin. For example, let R = Me and the olefin be equal to isobutene. The heat of formation of the desired methyl *t*-butyl sulphoxide can be obtained from that of the sulphide (-121 kJ mol^{-1}), and so equals *ca* -245 kJ mol^{-1}. Alternatively, it can be obtained from methyl *t*-butyl ketone (-291) and so equals *ca* -236 kJ mol^{-1}. A value -240 kJ mol^{-1} is quite convincing. However, one cannot merely set the difference of the heats of formation of the reactants and products in equation 37 equal to zero and then solve for the heat of formation of MeSOH. After all, there are two 'things' on the right and only one on the left, and so the decomposition of sulphoxides is entropically favoured. Recall that we earlier argued that processes such as these have an entropy change of *ca* 140 J mol^{-1} K^{-1}. We know temperatures for which the reaction proceeds to the right and temperatures for which the reaction proceeds to the left. Interpolating, we conclude an equilibrium constant of unity is found for reaction conditions of *ca* 180 °C or *ca* 450 K. Correcting the heat of reaction by $T\Delta S$ with T and ΔS set equal to the above, admittedly approximate, values[80], we find an 'entropy' effect of some 63 kJ mol^{-1}. From the archival value of ΔH_f(g, $Me_2C{=}CH_2$), -16.9 ± 0.9 kJ mol^{-1}, and our estimated value for ΔH_f(g, *t*-BuS(O)Me), -245 ± 2 kJ mol^{-1}, we may immediately conclude that the heat of formation of gaseous CH_3SOH must be more negative than *ca* $-240 - (-17 + (-63)) = -160$ kJ mol^{-1}.

$$RS(O)—C—C—H \rightleftharpoons RSOH + >C{=}C< \tag{36}$$

$$MeS(O)Bu\text{-}t \rightleftharpoons MeSOH + Me_2C{=}CH_2 \tag{37}$$

Braverman[68], Drabowicz, Lyżwa and Mikołajczyk[78] and Hogg[79] also chronicle reversible intramolecular ring openings of sulphoxides to form unsaturated sulphenic acids. These are mostly associated with bicyclic penicillin–cephalosporin rearrangements[81]. Let us remove most of the interesting 'decorations' and consider the intramolecular rearrangement of thiolane sulphoxide to 1-butene-4-sulphenic acid. We know of no experimental heat of formation of the former. However, it may be estimated in several different ways. The first is to modify the heat of formation of the parent sulphide, tetrahydrothiophene, and derive a value of -159 kJ mol^{-1}. Alternatively, we transform the related ketone, cyclopentanone, and derive a value of -148 kJ mol^{-1}. Since it is well established that strain energy of sulphur-containing rings is significantly less than for their all-carbon analogues[82], no doubt the latter heat of formation of thiolane sulphoxide is too positive. We will accept the value of -159 kJ mol^{-1} as more plausible. No entropy data are available from experiment for any of our species. However, we mimic the entropy change by that of the reaction methylcyclopentane to form 1-hexene, i.e. *ca* 45 J mol^{-1} K^{-1} or a free-energy change of *ca* 13 kJ mol^{-1} at 298 K. We thus deduce a value of -146 kJ mol^{-1} for the heat of formation of gaseous 1-butene-4-sulphenic acid. If we assume that the reaction in equation 38 is thermoneutral[83], then, using the literature heats of formation of ethane and 1-pentene, we obtain a value of -209 kJ mol^{-1} for the heat of formation of methanesulphenic acid. Agreement of this value with those obtained before is generally called 'relatively poor'. Yet, given the

crudeness of all the above enthalpy and entropy assumptions and equating penicillins with cyclopentanes, the agreement is highly encouraging.

$$CH_2{=}CHCH_2CH_2SOH + CH_3CH_3 \longrightarrow CH_2{=}CHCH_2CH_2CH_3 + CH_3SOH \quad (38)$$

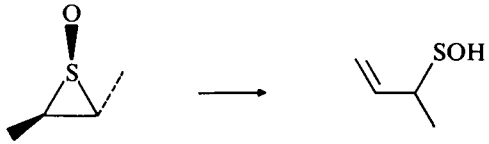
We are also told[69,78,79] that the thermolysis of β-cyano- and β-acylsulphoxides is more facile than that of other sulphoxides which lack the β-electron-withdrawing groups. How much is that due to destabilization of the sulphoxide? We have no heat-of-formation data for any such β-substituted sulphoxide with which comparison of an unsubstituted sulphoxide can be made. However, there are heat-of-formation data for $NC(CH_2)_2CN$ and $PhCO(CH_2)_2CN$ from which one can derive such quantities for β-substituted nitriles. By comparing the heat of formation of these two $X(CH_2)_2CN$ species with singly substituted species, stabilization or destabilization energies may be obtained. Consider the following formal gas-phase processes (equation 39) for our two choices of X:

$$X(CH_2)_2CN + Me(CH_2)_2Me \longrightarrow Me(CH_2)_2X + Me(CH_2)_2CN \quad (39)$$

For X = CN the reaction is nearly 17 kJ mol^{-1} exothermic, while for X = COPh the reaction is nearly thermoneutral. Equivalently, a β-cyano group destabilizes a nitrile by 17 kJ mol^{-1} and a β-benzoyl group destabilizes a nitrile essentially not at all. Some destabilization of the substituted sulphoxide is thus suggested. Relatedly, we expect conjugation in the resulting cyano and acylalkene to provide some stabilization of the product. This may be estimated by looking at the gas-phase 'desaturation' energy of the cyano and acylalk*a*nes as opposed to the 'methylalkane'. For the formal dehydrogenation process (equation 40) we find exothermicities increasing in the order X = CHO, 100.5; CN, 106.3; Me, 113.6 kJ mol^{-1}. This corresponds to some 13 and 8 kJ mol^{-1} of stabilization for cyano and acylalk*e*nes[84]. It is thus most likely that the β-cyano and acylsulphoxides are destabilized and that the resulting cyano and acylalk*e*nes enjoy some resonance stabilization. However, it is highly unlikely that the elimination of sulphenic acid from either of these sulphoxides, or any other, is exothermic as opposed to just possibly exergonic. Indeed, that sulphenic acids can be trapped by acrylonitrile and acrylate esters at ambient temperatures tells us that the reaction is essentially reversible with a rather small free-energy change.

$$Me(CH_2)_2X \longrightarrow (E)\text{-}MeCH{=}CHX + H_2 \quad (40)$$

We are told[69,78,79] that at slightly higher than ambient temperature, *trans*-2,3-



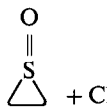
(7) (41)

dimethylthiirane sulphoxide (7) spontaneously rearranges to 1-butene-3-sulphenic acid (equation 41). Interestingly, the corresponding *cis*-isomer does not rearrange under these conditions. However, since we can think of no reason why this *trans* vs *cis* isomeric difference can be due to the intrinsic heat or free energy of the reaction as opposed to ease of concertedness of the necessary hydrogen transfer, we will be rather indifferent to the stereochemistry of the sulphoxide. Estimation of the heat and entropy of this rearrangement along with estimation of the heat of formation of the sulphoxide will give us a lower bound on the heat of formation of the sulphenic acid. The first step of our analysis might be assumed to consist of estimating the heat of formation of the

dimethylthiirane sulphoxide. We choose, instead, to study the rearrangement of 2-methylthiirane sulphoxide to propene-3-sulphenic acid. This is because we are 'spooked' by the literature values of the heats of formation of the precursor 2,3-dimethylthiirane. From our primary organic thermochemistry archive, we find that the heat of formation of 2,2- and *cis*-2,3-dimethylthiirane are identical in both the liquid and gaseous state to within ± 0.2 kJ purported precision. This is also true as found in the primary sources cited by this source. Our intuition is strongly violated by this—we do not expect isomers to be *that* close in energy[85]. We can only deduce that some error occurred, either of transcription of the data or in the identification of the compound, and we would rather not try to disentangle this here. We accept the suggested heat of formation of thiirane sulphoxide from Herron's review[20] and suggest that the heat-of-formation difference between the sulphoxides of monomethylthiirane and thiirane is nearly the same as the unoxygenated sulphides. The heat of formation of methylthiirane is thus *ca* -78 kJ mol^{-1}. As with the penicillin sulphoxide story, it is necessary to estimate entropies. We simulate the $>SO$ group of sulphoxides by $>CHCH_3$ and the —S—OH group of sulphenic acids by $—CH_2CH_3$. The entropy of methylthiirane sulphoxide is thus estimated as that of 1,2-dimethylcyclopropane[86], *ca* 309 J mol^{-1} K^{-1}, and that of propene-3-sulphenic acid taken as that of 1-pentene, 345.6 J mol^{-1} K^{-1}. The rearrangement of interest is exergonic if the heat of formation of propene-3-sulphenic acid is less than *ca* -67 kJ mol^{-1}. By analogy to the 1-butene-4-sulphenic acid story above, we assume that the reaction given in equation 42 is also essentially thermoneutral. We conclude[87] that the heat of formation of methanesulphenic acid is no higher than -151 kJ mol^{-1}.

$$CH_2{=}CHCH_2SOH + CH_3CH_3 \longrightarrow CH_2{=}CHCH_2CH_3 + CH_3SOH \qquad (42)$$

Another interesting reaction[69,78,79] interrelating thiirane sulphoxides and sulphenic acid derivatives is that of the parent thiirane sulphoxide and chloromethyl methyl ether:



$$+ ClCH_2OMe \longrightarrow Cl(CH_2)_2—S—O—CH_2—OMe \qquad (43)$$

Let us set the free energy of reaction equal to 0, and thus obtain a lower bound for the stability of the resulting sulphenate ester. To a first approximation, we are releasing the strain energy of the three-membered ring (from Herron[20], a suggested 'ring correction' of 83 kJ mol^{-1}) and exchanging the anomeric stabilization of $Cl—CH_2—O—$ and $—O—CH_2—O—$ (taken as 24 and 73 kJ mol^{-1}, respectively[88]). We are also trading a sulphoxide for a sulphenate (the quantity we wish to estimate). There is also an entropy correction; we are going from two molecules to one, although the thiirane sulphoxide is quite inflexible and thus of relatively low entropy. A convenient model for the entropy of reaction 43 is given in equation 44. In this equation there is an entropy change[89] of only 82 J mol^{-1} K^{-1}, and a free energy change of *ca* 25 kJ mol^{-1}. We conclude that sulphenate esters cannot lie higher than their isomeric sulphoxides by more than 106 kJ mol^{-1}.

$$+ MeCH_2CH_2Me \longrightarrow Me(CH_2)_2—CH_2—CH_2—CH_2—CH_2Me \qquad (44)$$

$$2RSOH \longrightarrow RS(O)SR + H_2O \qquad (45)$$

One of the most interesting reactions[90] of sulphenic acids is their spontaneous dehydration to form their anhydrides, species alternately known as thiolsulphinates or

disulphide sulphoxides (equation 45). Few other hydroxylic species dehydrate so easily and, indeed, we have no data as to whether or not dehydration of sulphenic acids to form their 'classical' anhydrides, i.e. R—S—O—S—R, is energetically favoured as well. We do note, however, that the corresponding dehydration of HOCl and unstrained alcohols ROH is also energetically favoured[91]. We accept Bujnicki, Mikołajczyk and Omelanczuk's assumption[25] that the S=O bond in any RS(O)SR is of equal strength to that found in PhS(O)SPh, and likewise their acceptance of Benson's value cited in Reference 39 for the gas-phase heat of formation of the latter species (244 kJ mol^{-1}). From these numbers [in particular, ΔH_f(g, MeS(O)SMe) = − 126 kJ mol^{-1}] and the well-established heat of formation of gaseous H_2O, we conclude that ΔH_f(g, MeSOH) is no less than − 183 kJ mol^{-1}. This result is 'more or less' compatible with the value deduced by Tureček and his coworkers[67]. By contrast, we deduce ΔH_f(g, PhSOH) is no less than 1 kJ mol^{-1}, very different from that of Tureček and his coworkers. No explanation for the discrepancy is apparent.

The second conceptual interrelation of sulphenic acids and disulphide sulphoxides relates to the thermal decomposition[69,78,79] of the latter into the former and thiocarbonyl compounds. In particular, we will discuss reaction 46 as an archetype of this process.

$$\text{MeS(O)SMe} \longrightarrow \text{MeSOH} + \text{CH}_2\text{S} \tag{46}$$

Again, we will accept Bujnicki, Mikołajczyk and Omelanczuk's analysis[25] and suggested value of ΔH_f(g, MeS(O)SMe). The entropy change is taken as the value we suggested earlier, namely 140 J mol^{-1} K^{-1}, corresponding to a change of free energy of some 55 kJ mol^{-1} at the recorded temperature of 96 °C. Finally, using one of the very few reported heats of formation of any thiocarbonyl compound, namely ΔH_f(g, CH_2S) = 105 kJ mol^{-1} from the ion–molecule reaction energetics measurements of Roy and McMahon[92], we conclude that ΔH_f(g, MeSOH) cannot exceed − 176 kJ mol^{-1}.

D. Thermochemical Considerations of Sulphenyl Halides and Sulphenamides

A quick examination of the Patai series volume[68] on sulphenic acids and their derivatives shows the synthesis and reaction chemistry of sulphenyl halides (RSF, RSCl, RSBr and RSI) and sulphenamides ($R^1SNR^2R^3$) to be of respectable interest and importance. However, their thermochemistry has been almost totally ignored by theorists and experimentalists alike. What follows is our attempt to make meaningful statements about the heats of formation of sulphenyl halides and sulphenamides using largely a composite of indirect experimental measurements and assumption-laden theoretical reasoning.

1. Sulphenyl fluorides

To the best of our knowledge, there are no experimental measurements of the heat of formation of any member of this class of compounds. We note that the heats of formation of SF_2 and the two isomers of S_2F_2 (i.e. F—S—S—F and F_2S=S) have been comprehensively discussed[93], while there are suggestive data[94] as to the heats of formation of the mixed sulphuranyl sulphenyl fluorides, SF_3SF and SF_3SSF. One can crudely approximate[95] the heat of formation of an arbitrary RSF species by taking the average of R_2S and SF_2. However, *ab initio* quantum chemical calculations[96] show the relevant exchange or disproportionation reaction for R = H (equation 47) is endothermic by 68 kJ mol^{-1} and represents an example of the anomeric effect on a central element other than carbon[97]. We also note that a far less electronically extreme reaction (equation 48) can be shown to be endothermic from experimental heats of formation by 12.3 kJ mol^{-1}. Finally, we recall interrelations[98] between the heats of formation of XF

and XOH species that suggest they should be comparable[99] for condensed phase species and that the former should be *ca* 25 kJ mol^{-1} more negative than the latter in the gas phase. However, as discussed earlier, the thermochemical data on the relevant XOH species, i.e. the sulphenic acids, are sufficiently problematic to make this additional interrelationship far less useful here than it may initially appear.

$$H_2S + SF_2 \longrightarrow 2HSF \tag{47}$$

$$H_2S + Me_2S \longrightarrow 2MeSH \tag{48}$$

2. Sulphenyl chlorides

Turning now to sulphenyl chlorides, we find that they are likewise poorly thermochemically characterized. Benson (cf Reference 39) gives us four estimated values, all for gas-phase species. These are: MeSCl, -28 ± 6; PhSCl, 106 ± 6; MeSSCl, -21 ± 6; PhSSCl, 113 ± 6 kJ mol^{-1}. He derived these numbers using the experimentally measured heats of formation of SCl_2 and S_2Cl_2 and some plausible assumptions associated with bond additivity. As such, it is no surprise that the exchange or disproportionation reaction 49 is essentially thermoneutral for both R = Me and Ph and, solely from archival data, so is reaction 50 for both R's as well. Although the currently available editions of what had been Benson's sources of information[100] give values for the heats of formation of SCl_2 and S_2Cl_2 that have shifted by *ca* 1 kJ mol^{-1} from his original choices, we have not deemed it either necessary or desirable to readjust his suggested values here. We are convinced that the data and all of the analysis are too imprecise to warrant this additional effort.

$$R_2S + SCl_2 \longrightarrow 2RSCl \tag{49}$$

$$R_2S + Et_2S \longrightarrow 2RSEt \tag{50}$$

We may ask, however: are these estimated sulphenyl chloride heat-of-formation values plausible? The first observation is that the differences for the two pairs of methyl and phenyl compounds (MeSCl and PhSCl, MeSSCl and PhSSCl) are 134 kJ mol^{-1} in both cases. This value is nearly identical to those found for the difference of heats of formation of MeSH and PhSH, MeSMe and PhSMe, $\frac{1}{2}$[MeSMe and PhSPh] and $\frac{1}{2}$[MeSSMe and PhSSPh]. It differs very significantly from the values earlier mentioned for MeSOH and PhSOH. However, as we had enunciated that sulphenic acids seem out of line and that Benson's values arise from group-increment and bond-additivity reasoning, the general near-equality of the difference of interest with that of other MeS— and PhS— compounds is not surprising. We now ask: what independent results for heats of formation of sulphenyl chlorides, preferably those of MeSCl and PhSCl, can be gleaned?

Drabowicz, Lyżwa and Mikołajczyk[78] tell us that sulphenyl chlorides can be synthesized by the chlorination of disulphides (equation 51). As such, we can be optimistic that this reaction is exothermic, regardless of the choice of R[101]. From the archival heats of formation of gas-phase Me_2S_2 and Ph_2S_2 of -24.2 ± 1.0 and 243.5 ± 4.1 kJ mol^{-1}, respectively, and the definitional value of 0 for Cl_2(g), we conclude ΔH_f(g, MeSCl) and ΔH_f(g, PhSCl) are smaller than -12 and 122 kJ mol^{-1}, respectively, results consistent with Benson's numbers. But the analyses of other reactions are not so useful. For example, we are also told that cyclic sulphides are chlorinated with concomitant ring opening, i.e. for $n = 2, 3$ and 4, reaction 52 is observed. From the experimentally measured heats of formation of the cyclic thioethers ($n = 2$, 82.0 ± 1.3; $n = 3$, 60.6 ± 1.4; $n = 4$, -34.1 ± 1.3 kJ mol^{-1}), we thus conclude that ΔH_f(g, Cl(CH$_2$)$_n$SCl) cannot exceed 82, 61 and -34 kJ mol^{-1}, respectively. We should think that $n = 4$ is large enough to minimize interactions between the Cl and SCl group. If so, we may assume that equation 53 is thermoneutral for any affixed group R. As is so often the case, we lack information for

most compounds of interest, in this case for those containing truly relevant R groups. Using $\Delta H_f(g, Cl(CH_2)_4SCl) = -34$ kJ mol^{-1} and letting R = Me, *n*-Bu, and Cl[102], we deduce that ΔH_f(g, MeSCl) cannot exceed *ca* 55 ± 2 kJ mol^{-1}. While this is mathematically compatible with the earlier enunciated upper bound of -12 kJ mol^{-1}, as chemists we are not particularly benefited by the new finding. However, since two species are converted to one species with a 25 kJ mol^{-1} entropy-derived free-energy correction[103], we derive an upper bound for ΔH_f(g, MeSCl) of 30 kJ mol^{-1}. This is still rather far from Benson's sugested value for this quantity.

$$RSSR + Cl_2 \longrightarrow 2RSCl \tag{51}$$

$$(CH_2)_nS + Cl_2 \longrightarrow Cl(CH_2)_nSCl \tag{52}$$

$$MeR + Cl(CH_2)_4SCl \longrightarrow MeSCl + R(CH_2)_4Cl \tag{53}$$

Relatedly, the chlorination of acetyl sulphide (equation 54) is interesting because of the acetylsulphenyl chloride formed. From the archival heats of formation of Ac_2S, Cl_2 and AcCl, we deduce ΔH_f(g, AcSCl) cannot exceed -74 kJ mol^{-1}. Should we make the not-too-unreasonable assumption that equation 55 is nearly thermoneutral, we conclude that ΔH_f(g, MeSCl) cannot exceed 97 kJ mol^{-1}, an even less useful result. As such, we have neither a mechanistic nor a quantitative thermochemical understanding as to why the chlorination of acetyl disulphide does not result in acetylsulphenyl chloride (equation 56), but rather asymmetrically cleaves as shown in equation 57. Indeed, we note that trusting Benson's values for the various RSCl and RSSCl shows that the asymmetric chlorination of R_2S_2 is energetically preferred by 19 kJ mol^{-1} for R = Me and 57 kJ mol^{-1} for R = Ph. Perhaps we were inappropriately surprised that AcSSCl is the preferred product in the chlorination of Ac_2S_2 as opposed to AcSCl.

$$Ac_2S + Cl_2 \longrightarrow AcCl + AcSCl \tag{54}$$

$$AcSCl + MeSH \longrightarrow AcSH + MeSCl \tag{55}$$

$$Ac_2S_2 + Cl_2 \longrightarrow 2AcSCl \tag{56}$$

$$Ac_2S_2 + Cl_2 \longrightarrow AcSSCl + AcCl \tag{57}$$

It has recently been shown that the thermochemistry of chloro and cyano species are both conceptually and numerically interrelated[104]. Let us assume that reactions 58 and 59 are thermoneutral, even though we acknowledge that reaction 60 is not thermoneutral, but instead is *ca* 17 kJ mol^{-1} exothermic. From the heats of formation of MeSCN[105] and MeCN[106] we deduce ΔH_f(g, MeSCl) equals respectively -42 and -23 kJ mol^{-1}, in good agreement with what Benson told us.

$$MeSCN + \tfrac{1}{2}(Cl_2) \longrightarrow MeSCl + \tfrac{1}{2}[(SCN)_2 \tag{58}$$

$$MeSCN + MeCl \longrightarrow MeSCl + MeCN \tag{59}$$

$$\tfrac{1}{2}Cl_2 + \tfrac{1}{2}C_2N_2 \longrightarrow ClCN \tag{60}$$

3. *Sulphenyl bromides and iodides*

Let us now consider the energetics of sulphenyl bromides and iodides. While Drabowicz, Lyżwa and Mikołajczyk[78] tell us that sulphenyl bromides can be synthesized by the bromination of thiols or disulphides, they also assert that stable sulphenyl iodides only rarely arise from iodinating thiols and seemingly never from disulphides. That is, as noted by Capozzi, Modena and Pasquato[107], reaction 61 proceeds to the left for X = Cl and Br, but to the right with X = I. For X = Br, no thermochemical quantitation is seemingly available except for reaction 62, which is favoured on the left side by

13 kJ mol^{-1} when the elements are in their standard state, and by 16 kJ mol^{-1} whether all of the species are taken as liquids or as gases[108]. For X = I, we know of no heat-of-formation data on S_2I_2 in any phase.

$$2RSX \rightleftharpoons (RSS(X)R)^+ X^- \rightleftharpoons RSSR + X_2 \quad (61)$$

$$BrSSBr \rightleftharpoons \tfrac{1}{4}S_8 + Br_2 \quad (62)$$

Furthermore, as one proceeds from X = Cl to Br to I, the charge on the X in the intermediate sulphonium ion becomes increasingly positive. As such, eventually attack on X by X^- becomes more likely than attack on sulphur[109], i.e. reaction 61 is more likely to proceed to the right. In addition, Benson (cf Reference 39) had also noted that a driving force for reaction 61 to proceed to the right for X = I is the *ca* 60 kJ mol^{-1} heat of solidification[110] of I_2(g). Indeed, Benson and his coworkers proceeded to synthesize HSI[111] and MeSI[112] in the gas phase by reaction of H_2S and Me_2S respectively with I_2 and concomitantly they derived heats of formation of these sulphur–iodine compounds as 42.2 ± 2.8 and 30.0 ± 3.1 kJ mol^{-1}, respectively. It would appear that in the gas phase, the iodination of disulphides, reaction 61 with X = I, is approximately thermoneutral. We find it intriguing that the sole sulphenyl halides for which there is definitive thermochemical information are those that are seemingly the least thermodynamically stable and most incompletely experimentally investigated.

4. *Sulphenamides*

Let us turn now to sulphenamides. If knowledge of synthesis of sulphenyl chlorides was relatively useless for deriving thermochemical information, the situation for sulphenamides is seemingly worse. Consider the generic synthesis of sulphenamides (equation 63) from sulphenate esters as discussed by Drabowicz, Lyżwa and Mikołajczyk[78]. As chronicled earlier, we have inadequate knowledge of the heat of formation of any sulphenate ester to derive a meaningful heat of formation of any sulphenamide. On the other hand, with their better leaving groups, sulphenyl halides readily react with amines to form sulphenamides—accompanied by the appropriate ammonium salts (equation 64). However, the reaction step that forms the ammonium salt, i.e. that of HX and the amine, is exothermic enough to eradicate any meaningful information about the sulphenamide if all we know is that reaction 63 proceeds. For example, the reaction of gaseous HCl, HBr and HI with dimethylamine is between 160 and 180 kJ mol^{-1} exothermic. Other reactions involve reagents and/or products for which thermochemical data are absent, e.g. silver(I) and mercury(II) mercaptides formed by addition of metal ion to disulphide/amine mixtures. Yet we are highly optimistic that meaningful thermochemistry on sulphenamides should be achievable noting that heats of formation of the sulphinamide and sulphonamide $Et_2NS(O)NEt_2$ and $Et_2NSO_2NEt_2$, and the 'disulphenamide' $Et_2NSSNEt_2$ are all adequately well established. For now, it is not obvious whether the formal and experimental generic deoxygenation reactions of sulphoxides and sulphones (equations 65 and 66) and the generic desulphidation reaction of disulphides (equation 67) result in a consistent heat of formation of Et_2NSNEt_2, i.e. in the current and admittedly special case for which $R^1 = R^2 = Et_2N$. We should not be optimistic because of the diverse

$$R^1SOR^2 + R^3R^4NH \longrightarrow R^1SNR^3R^4 + R^2OH \quad (63)$$

$$R^1SX + 2R^2R^3NH \longrightarrow R^1SNR^2R^3 + R^2R^3NH_2{}^+ X^- \quad (64)$$

$$R^1S(O)R^2 \longrightarrow R^1SR^2 \quad (65)$$

$$R^1SO_2R^2 \longrightarrow R^1SR^2 \quad (66)$$

$$R^1SSR^2 \longrightarrow R^1SR^2 \quad (67)$$

dipolar resonance structures and varying lone pair–lone pair interactions that characterize the sulphen-, sulphin- and sulphonamides and the disulphandiamides of interest and relevance here.

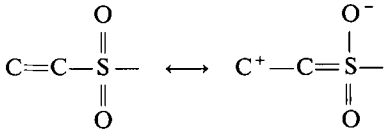
E. Conjugation and Aromaticity in Unsaturated Sulphur-containing Species

In the pedagogical literature, it is not uncommon to see the chemistry of unsaturated sulphur-containing species explained in terms of ionic resonance structures. For example, the facile carbon-protonation, and thus hydrolysis, of vinyl sulphides has often been understood in terms of a resonance contributor that results in partially positive sulphur and partially negative β-carbon:

$$C{=}C{-}S{-} \longleftrightarrow C^{-}{-}C{=}S^{+}{-} \tag{68}$$

Bridge two vinyl groups by a sulphide, and tie their β-carbons together to form a ring, and one conceptually synthesizes thiophene. The aromaticity[113] and ease of electrophilic substitution of thiophenes is a natural extension of the resonance structure analysis of acyclic vinyl sulphides.

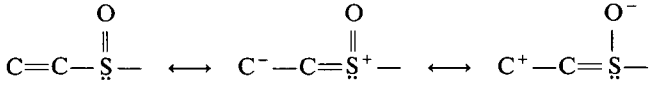
Relatedly, the pedagogical literature often understands the Michael reaction acceptor behaviour of vinyl sulphones in terms of a resonance contributor that results in partially negative oxygen and partially positive β-carbon:



(69)

Relatedly, tie two vinyl groups with a sulphone and cyclize the product via its two β-carbons results in thiophene sulphone. While application of simple resonance structure reasoning might have suggested thiophene and its dioxide should both be stabilized, only the former is. We recall Hückel's rule and note that there are 6 π-electrons in thiophene as opposed to 4 π-electrons in the sulphone. This is reminiscent of the relative stabilities of the 6π aromatic cyclopentadienide anion and 4π antiaromatic cyclopentadienyl cation.

Resonance structures with positive sulphur and negative carbon, and also with negative oxygen and positive carbon, can be drawn for vinyl sulphoxides:



(70)

This does not mean that no stabilization results because there are opposite polarities in different resonance structures. It is, however, unclear whether to expect thiophene sulphoxide to be more like the sulphone or like the parent heterocycle[115].

In this section we will discuss resonance stabilization in sulphides, sulphoxides and sulphones, whether they be found attached to vinyl or to other conjugating hydrocarbyl groups, and whether they be found in acyclic or in cyclic environments. No effort will be made to address the relative importance of the various resonance structures cited above. All we will do is chronicle the net stabilization, where we will limit our attention to those species for which heat-of-formation data are directly available from experiment. In all cases we will discuss only gas-phase species, unless data for the condensed phase are the only ones available.

Our intuition suggests that thiophene represents sulphur conjugation 'at its best'. Yet, regardless of our findings, we will only briefly discuss thiophene because it is 'so' aromatic that discussion is almost irrelevant. Because of the significant additional stabilization, it is not obvious if thiophene belongs in the same chapter as the other sulphur-containing species discussed here—after all, would one think that an extensive discussion of benzene or pyridine derivatives belongs in a chapter on olefins or imines, respectively?

1. Stabilization of thiophene and the isomeric dithiins

Thiophene has a π-electron sextet which is expected to show concomitant Hückel aromaticity for which stabilization is expected to be strongest. A simple probe of this extra stability is the comparison of the relative heats of hydrogenation of thiophene and cyclopentadiene[114]; due to the comparable electronegativities of carbon and sulphur, σ-effects are expected to be relatively small[115]. We will also contrast these findings with those of furan, since oxygen and sulphur are in the same column of the periodic table and so they and their corresponding compounds are recognized as valence isoelectronic.

From the heats of formation of thiophene, furan and cyclopentadiene, and their tetrahydro derivatives thiolane, tetrahydrofuran and cyclopentane, we find the hydrogenation energies to be -149.0 ± 1.7, -149.3 ± 1.1 and -210.7 ± 1.7 kJ mol^{-1}, respectively. From this analysis, we would thus conclude that thiophene and furan are almost identically aromatic with a net stabilization of *ca* 60 kJ mol^{-1}. It is usually suggested[116] that thiophene is more aromatic than furan, and so this hydrogenation-derived conclusion may be somewhat disconcerting. Indeed, our prior expectations are confirmed when we use a recent thermochemical definition[117] for aromaticity for thiophene, furan and cyclopentadiene, in which the greater the difference of the heats of formation of Ph_2X[118] and the cyclic $(CH{=}CH)_2X$, the greater the aromaticity of the latter. We find aromaticity decreases in the expected order: thiophene > furan > cyclopentadiene.

If thiophene is understood to be aromatic because of its 6 π-electrons, then the isomeric dithiins with their 8 π-electrons may be expected to be antiaromatic. Let us compare them to each other and to thiophene. The sole 1,2-dithiin (**8**) for which there is a known heat of formation is its 3,6-diphenyl derivative, 422.4 ± 3.6 kJ mol^{-1}. We know of no corresponding data on 2,5-diphenylthiophene or on any other arylated thiophene. From our archives, we find demethylation of toluene is accompanied by an increase in the heat of formation of 32.2 ± 0.9 kJ mol^{-1}, while the same process for 2- and

(**8**)

3-methylthiophene results in essentially the same number, 31.4 ± 1.4 and 32.0 ± 1.4 kJ mol^{-1}, respectively. Let us assume that the heat of dephenylation of biphenyl and either 2- or 3-phenylthiophene results in the same change in heats of formation, namely a decrease of 98.8 ± 2.1 kJ mol^{-1}, and this is true regardless of substitution. Applying this correction twice to the diphenyldithiin results in a predicted heat of formation for the parent 1,2-dithiin of 225 kJ mol^{-1}. This value is *ca* 110 kJ mol^{-1} higher than that of thiophene, in contrast to the *ca* 10 kJ mol^{-1} higher heat of formation of di-*n*-alkyl disulphides than of monosulphides. We do not know how to apportion this $110 - 10 = 100$ kJ mol^{-1} difference, whether to the aromaticity of thiophene, the antiaromaticity of 1,2-dithiin, or even to the *cis* (*vs gauche*) —S—S— geometry of the latter. However, it

is unequivocal that 1,2-dithiins lack the pronounced and therefore aromatic stabilization of thiophenes[119].

The sole 1,4-dithiin for which we have thermochemical data is the dibenzo-analogue, thianthrene, with its heat of formation[120] of 282 ± 8 kJ mol^{-1}. Assignment of the heat of 'debenzo-ation', applied twice of course, to 1,4-dithiin is non-trivial. Debenzo-ation to form the archetypical aromatic species benzene, i.e. its transformation from naphthalene, is accompanied by a decrease in the heat of formation by 68 kJ mol^{-1}, while for the less aromatic thiophene the transformation results in a decrease in the heat of formation of only 51 kJ mol^{-1}. For non-aromatic species such as cyclohexene, cyclopentene and cyclopentadiene, derived from tetralin, indane and indene, respectively, the reactions are favoured by 31, 27 and 29 kJ mol^{-1}. These values of *ca* 29 kJ mol^{-1} are almost identical to that of the antiaromatic maleic anhydride[121] relative to phthalic anhydride. Although some care must be taken in comparing species with 'unsaturated' carbon–carbon bonds flanked by elements with lone pairs[91], nearly the same value, 25 ± 9 kJ mol^{-1}, is found for the difference of the heats of formation of *o*-dichlorobenzene and (*Z*)-1,2-dichloroethylene. Since the presence of seeming aromaticity makes a difference in the debenzo-ation energy but non- *vs* antiaromaticity seemingly does not, we may bypass the question of the non- *vs* antiaromaticity question of 1,4-dithiin. We safely conclude that the heat of formation of 1,4-dithiin is *ca* 225 kJ mol^{-1}. This value is 110 kJ mol^{-1} higher than that of thiophene, and again it is not immediately obvious how to disentangle the destabilization and antiaromaticity of the two-sulphur species and the stabilization and aromaticity of the one-sulphur species.

It is noteworthy that the heats of formation of 1,2- and 1,4-dithiin are essentially identical. Is that reasonable? A suitable (but acyclic and saturated) mimic for isomeric species with two sulphurs adjacent and 1,4-relative to each other would seem to be that of the isomeric pair, dipropyl disulphide and 1,2-bis(ethylthio)ethane. Their gas-phase heats of formation differ by 34 kJ mol^{-1}, resulting from individual heats of formation of -117.3 ± 1.1 and -83.0 ± 1.5 kJ mol^{-1}, respectively[122]. Yet, of course, there is no reason why the dithiin and acyclic pair should have the same heat-of-formation differences, if for no other reason than the different number and type of conjugating groups in the dithiins: in the 1,2 there are two vinyl sulphide units, one formally conjugated diene and a disulphide, while in the 1,4 there are four vinyl sulphide units.

2. *What is the resonance stabilization energy in simple vinyl sulphides?*

The answer to this question, like any and all others involving resonance energy, ultimately returns us to the question of the choice of reference states. In our archive, if we ignore thiophenes, dithiins and any of their annelated or substituted derivatives, we find the heat of formation of one species containing the C=C—S—$R_{saturated}$ substructure. This is 2,3-dihydrothiophene[123] with its gas-phase heat of formation of 90.7 ± 1.3 kJ mol^{-1}. It seems logical that its extra stabilization (resonance) energy can be obtained by comparing its hydrogenation energy with that of a comparable olefin lacking the sulphur, say cyclopentene. From heats of formation of cyclopentene and cyclopentane we derive the heat of hydrogenation of cyclopentene, -110.3 kJ mol^{-1}. Relatedly, from the heats of formation of 2,3-dihydrothiophene and tetrahydrothiophene, we find the heat of hydrogenation of 2,3-dihydrothiophene, -124.8 kJ mol^{-1}! This suggests that the resonance energy associated with vinyl sulphides is nearly -15 kJ mol^{-1}, i.e. there is destabilization associated with having C=C and —S— adjacent to each other[124]. This conclusion is corroborated by the fact that the non-conjugated 2,5-dihydrothiophene is more stable than the conjugated 2,3-isomer by nearly 4 kJ mol^{-1}.

These last findings run counter to our intuition about conjugative stabilization in vinyl sulphides. For the heats of hydrogenation of gaseous divinyl sulphide and its

corresponding hydrocarbon analogue, 1,4-pentadiene, we derive the values[125] (for $2H_2$ addition[126]) of -189.6 ± 4.1 and -218.0 ± 1.7 kJ mol^{-1}, respectively, a seemingly much more sensible set of numbers since there is stabilization associated with the vinyl sulphide link[124]. However, problems remain. We recall the earlier conclusion[47] that the difference between the heats of formation of corresponding gas-phase phenyl and vinyl derivatives has been shown to be quite constant, namely *ca* 30 kJ mol^{-1} per phenyl/vinyl group. We find a total heat-of-formation difference for diphenyl and divinyl sulphides somewhat over 115 kJ mol^{-1}, or nearly twice as much after correcting for the two phenyl or vinyl groups. And lest one argue that steric repulsion between the two phenyls in diphenyl sulphide strongly destabilizes this compound relative to its divinyl analogue, we note that the total heat-of-formation difference for gaseous divinyl and diphenyl ether is 58.6 kJ mol^{-1}, or the essentially normal 29 kJ mol^{-1} per phenyl/vinyl group. We wonder if the divinyl sulphide was contaminated by the presence of some undetected polymer. It would thus seem that we are currently thwarted from giving a meaningful value for the resonance energy of vinyl sulphides.

3. What is the resonance stabilization energy of vinyl sulphoxides?

The one appropriate gaseous vinyl sulphoxide for which we have an experimentally determined gas-phase heat of formation is divinyl sulphoxide[127]: 25.0 ± 3.0 kJ mol^{-1}. Analogous to the above discussion on divinyl sulphide, we deduce a heat of hydrogenation of divinyl sulphoxide of -230.6 kJ mol^{-1}, more exothermic than that of 1,4-pentadiene and suggestive of some vinyl–sulphoxide destabilizing interaction. The total heat-of-formation difference of the divinyl and diphenyl sulphoxides is 81.8 ± 4.3 kJ mol^{-1} and the nearly 42 kJ mol^{-1} per phenyl/vinyl group exchanged is still meaningfully larger than what we would have expected based on earlier experience[47] of the energetics of this group exchange.

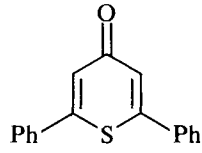
4. What is the resonance stabilization energy of acyclic vinyl sulphones?

Unlike the situation of vinyl sulphides and vinyl sulphoxides, there are considerable heat-of-formation data which we can use for the sulphones. Parallelling the earlier sections in which the divinyl derivative figured prominently, we commence with divinyl sulphone[128] itself with its gas-phase heat of formation of -156.6 ± 5.0 kJ mol^{-1}. We derive a gas-phase heat of hydrogenation of -272.7 kJ mol^{-1}, higher than for either divinyl sulphide or sulphoxide, and suggestive of even greater destabilizing interactions with vinyl sulphones than with vinyl sulphoxides or sulphides. While this is perhaps resonable (cf Reference 115), the degree of destabilization is surprisingly high. To calibrate our thinking, let us consider the energetics of other sulphones. To begin with, the phenyl/vinyl comparison shows sequential heat-of-formation increases from divinyl sulphone to phenyl vinyl sulphone to diphenyl sulphone of 26.4 and 10.3 kJ mol^{-1}. Only the former seems at all normal, but then again, the series of divinyl sulphide, sulphoxide and sulphone has already demonstrated unusual behaviour. If we conclude that conjugative vinyl–sulphone interactions are inherently destabilizing, we are not surprised that the three isomeric 1-methyl-4-(X-butenylsulphonyl)benzenes increase in stability X = 2- (i.e. allylic) < 1- (i.e. conjugated) < 3-(i.e. homoallylic)[129]. Relatedly, the conjugated (1-propynylsulphonyl)benzene is less stable than its 2-propynyl isomer, and both are less stable than their conjugated allenyl phenyl sulphone isomer. Admittedly, prejudices as to stability of substituted propynes and allenes are no doubt derived from considerations of hydrocarbons. For example, the replacement of SO_2Ph by Me results in the 20 kJ mol^{-1} spread and normal order of gas-phase stability: 1-butyne $\approx$ 1,2-butadiene < 2-butyne. That the order is reversed and that this spread is dwarfed

by the 40 kJ mol^{-1} for the sulphones remains a surprise. Regrettably, we lack the corresponding heat-of-formation data for the analogous sulphide and sulphoxide series.

5. What are the resonance stabilization energies of thiapyrone derivatives

Before attempting to answer this question, it is imperative to ask 'which derivatives'? Thiapyrones may be expected to show aromatic character like thiophenes, unless one is talking about their sulphone derivatives and then they are expected to show some antiaromatic character. Interestingly, there is one study[130] that discusses the 2,6-diphenyl derivatives of both 1-thia-4-pyrone (**9**) and its sulphone, and both of their tetrahydro



(**9**)

derivatives. There are two hitches though: heats of combustion, but not heats of formation, were reported and the data are solely for the species as solids. As discussed elsewhere, it is quite precarious to derive heats of formation of sulphur compounds from heat-of-combustion measurements without accompanying details as to products and calorimetric reaction conditions. Nonetheless, we will proceed. We note that our archive gives us the heat of formation of the saturated 2,6-diphenyltetrahydro-1-thia-4-pyrone, -60.0 ± 6.7 kJ mol^{-1}, derived from an alternative set of heat-of-combustion measurements[131]. These resulted in a value -9518.6 ± 6.7 kJ mol^{-1} which is 'not-too-far'[132] from the earlier one[130] of -9491.8 ± 9.7 kJ mol^{-1}. We accept the newer heat of combustion and of formation, and then correct the others from Reference 130 by the same difference of 27 kJ mol^{-1}. Reference 130 tells us that the difference between the heat of combustion of saturated 2,6-diphenyltetrahydro-1-thia-4-pyrone and its sulphone is 334 kJ mol^{-1}. Since the formulas of these two substances differ by 1 molecule of O_2 which has heats of combustion and formation of precisely 0, the heat of formation of the parent sulphide and derived sulphone is 334 kJ mol^{-1}. The heat of formation of solid 2,6-diphenyltetrahydro-1-thia-4-pyrone sulphone is thus $-334 - 60 = -394$ kJ mol^{-1}. Now, 2,6-diphenyltetrahydro-1-thia-4-pyrone sulphone and 2,6-diphenyl-1-thia-4-pyrone differ in their molecular formulas and in their heat of combustion products, by two molecules of water. The difference between the heats of combustion[130] of these two substances is -98 kJ mol^{-1}. From the experimentlly measured heat of formation of liquid H_2O of -286 kJ mol^{-1}, we conclude that the heat of formation of solid unsaturated 2,6-diphenyl-1-thia-4-pyrone is $-394 - 2(-286) - 98 = 80$ kJ mol^{-1}. As with the tetrahydro derivative we may make an immediate comparison of heats of combustion and of formation of the corresponding sulphone, and since the heat of formation of solid unsaturated 2,6-diphenyl-1-thia-4-pyrone sulphone is 198 kJ mol^{-1} smaller, it equals $80 - (198) = -118$ kJ mol^{-1}. There are many numbers here. Perhaps the most useful comparison is that the difference in the heats of formation[130] of the saturated sulphone and sulphide is 334 kJ mol^{-1} while it is only 198 kJ mol^{-1} for the unsaturated species. There is regretably not enough information on how to ascribe the $334-198 = 136$ kJ mol^{-1} effect of unsaturation as to the aromaticity of the thiapyrone and the antiaromaticity of its dioxide.

It is not obvious how much effort should be made. Remember that all of the these numbers are for the species of interest as solids. What data do we have for the difference

between the heats of formation of solid sulphones and sulphides? Our archives document considerable heat-of-formation data for solid sulphones, but seemingly not for the related sulphides. However, we may derive an approximate heat of formation of the solid sulphides via equation 71 wherein ΔH_{fus} is the heat of fusion and T_M is the melting point[133]. Using heats of melting from archival compendia by Domalski and his coworkers[4], we find that the difference between the heats of formation of solid R_2SO_2 and R_2S is *ca* 384 kJ mol^{-1} for R = Et and *ca* 370 kJ mol^{-1} for R = *n*-Bu. While both values are disturbingly distant from the 334 kJ mol^{-1} found for the above saturated pyran case, that the differences for the ethyl and *n*-butyl cases themselves are so disparate is likewise distressing. We leave it to the reader to decide the validity of the data accompanying analysis in this section.

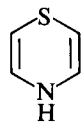
$$\Delta H_f(s) \approx \Delta H_f(l) - \Delta H_{fus}\,(T_M) \tag{71}$$

6. Thiophene sulphone and its derivatives

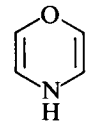
Of all the reported thiophene sulphones or their benzoannelated analogues, there have seemingly been calorimetric measurements[134] for the heats of formation of only four solid-phase alkylated derivatives of benzothiophene sulphone: 3-methyl, 214.0; 3,5-dimethyl, 10.5; 3,7-dimethyl, 52.5; 2-ethyl-3,5,7-trimethyl, 108.3 kJ mol^{-1}. Are these numbers plausible? Let us make comparisons among these species and between them and other alkylated ring systems. The monomethyl and dimethylbenzothiophene sulphones have heats of formation that differ by between 160 and 200 kJ mol^{-1}. By contrast, the heats of formation of solid monomethyl and dimethylnaphthalenes differ by between 20–50 kJ mol^{-1}, a much smaller and more plausible difference[135]. Furthermore, we can think of no reason why dimethyl benzothiophene sulphone should have a lower heat of formation than the ethyl, trimethyl species unless it alone did not oligomerize or otherwise decompose on standing. Admitting these complications in understanding the substituent effects on benzothiophene sulphones, nonetheless, we may still ask what we would have predicted their heats of formation to be. We will estimate the heat of formation of solid 3-methylbenzothiophene sulphone. We had earlier noted that the difference in the heat of formation of a solid saturated sulphide and its corresponding sulphone is *ca* 370 kJ mol^{-1}. Assuming no aromaticity effects in the benzothiophene nor antiaromaticity effects in its sulphone, we would thus predict a heat of formation of the solid parent benzothiophene sulphone of *ca* −270 kJ mol^{-1}. Accepting the monomethylation energy from the difference between the heats of formation of naphthalene and its 2-methylated derivative of 33 kJ mol^{-1}, we conclude that the heat of formation of solid 3-methylbenzothiophene sulphone is *ca* −300 kJ mol^{-1}. The difference of *ca* 520 kJ mol^{-1} is inexplicable, no matter what assumptions are made about aromaticity and antiaromaticity. Something is seriously wrong with the suggested heats of formation in this section. While we cannot definitively ascertain the source of error, we note it appears plausible that the product analysis of the combustion processes is problematic: especially since we are told that the final sulphur-containing species for all four compounds is SO_2, and not sulphuric acid at some concentration. We would not have expected extrusion of SO_2 without any subsequent oxidation[136]. We consider thiophene sulphones to be interesting species. To disentangle the complications of sample identity and combustion product gas analysis, and of the wiles of both aromaticity and the organic solid state, we recommend a calorimetric study of dibenzothiophene sulphone.

7. Dibenzoannelation of 8π heterocycles

We conclude this chapter with a brief discussion of the energetics of some other dibenzo (DB)-heterocycles. Returning to the dibenzo-analogue of of 1,4-dithiin, we



(10)



(11)

explicitly consider those of 4*H*-1,4-thiazine (**10**) and 4*H*-1,4-oxazine (**11**) (i.e. thianthrene, 10*H*-phenothiazine and 10*H*-phenoxazine). An interesting comparison consists of contrasting these three-ring species 'DB-1,4-X,Y' and the 'open' two-ring diphenylsulphide, ether and amine. That is, we define (equation 72) the difference quantity, $\delta_{72}(X, Y)$.

$$\delta_{72}(X, Y) = \Delta H_f(g, \text{"DB-1,4-X,Y"}) - [\Delta H_f(g, Ph_2X) + \Delta H_f(g, Ph_2Y)] \quad (72)$$

For the three cases itemized above, gaseous (S, S), (S, N) and (O, N), the differences[137] $\delta_{72}(X,Y)$ are 180 ± 9, 172 ± 5 and 167 ± 4 kJ mol^{-1}, respectively, and making use of an estimated heat of formation of the (O, O) species[138], a value of 167 kJ mol^{-1} is found. What does this tell us about the antiaromaticity of these heterocycles? Perhaps because we have become almost so expecting of multi-kJ mol^{-1} discrepancies in the latter part of our chapter, we may tranquilly conclude that all of these three-ring heterocycles are of comparable antiaromaticity[139]. Alternatively, we note the decreasing order of aromaticity of the 1-ring, single heteroatom-containing 6-π, 5-atom thiophene, pyrrole and furan, i.e. S > NH > O > CH_2 = 'zero'. There is much the same (but now) decreasing order of antiaromaticity in the 3-ring, two heteroatom-containing 8-π, 6-atom (S + S) > (S + NH) > (O + NH) $\simeq$ (O + O) $\gg$ (CH_2 + CH_2) = 'zero'. Aromaticity and antiaromaticity continue to be antiparallel[140]. As for now, we have insufficient experimental information and conceptual understanding to answer our final question of aromaticity and antiaromaticity—our ignorance and interest balance as we wait.

IV. ACKNOWLEDGEMENTS

The authors would like to thank the following individuals for discussions about the structure and energetics of organosulphur compounds: Robert L. Benoit, Donald C. Dittmer, John T. Herron, Carl F. Melius, Raphaël Sabbah, Leif J. Sæthre and José Artur Martinho Simões. JFL also thanks the Chemical Science and Technology Laboratory, National Institute of Standards and Technology, for partial support of his research. We also wish to thank Connie K. Lê for her assistance with the statistical analyses.

V. REFERENCES AND NOTES

1. We do not intend any earlier chapter author to be mortified by citing any omission, commission or even diverse sense of mission on his/her part. Rather, we wish to provide the mortar to allow even further uniting of earlier chapters in other, more specialized, volumes. Indeed, the philosophy in our chapter is related to the word 'Mosaic', both in the noun-sense of a picture that is a composite of small pieces, and in the adjective-sense derived from Moses and his attempts to transform a cacophonous assemblage of tribes into the multivoiced chorus of a coherent nation. We thus recognize the volume *Patai's 1992 Guide to the Chemistry of Functional Groups* by Saul Patai (Wiley, Chichester, 1992) as a premier example of a chemical research monograph with the mosaic sense of which we speak.
2. We find the most useful exposition of Benson's group increments and their use to be his own book, S. W. Benson, *Thermochemical Kinetics*, 2nd edition, Wiley, New York, 1976. It will be noted that Benson offered a plethora of groups and introduced correction terms derived from

individual molecules when the assumption of group additivity was violated. Perhaps because we admit some of our assumptions are extreme, we are reticent to devise increments or correction terms for new functional groups concomitant with our estimating heats of formation.

3. J. B. Pedley, R. D. Naylor and S. P. Kirby. *Thermochemical Data on Organic Compounds*, 2nd ed., Chapman & Hall, London and New York, 1986.
4. E. S. Domalski, W. H. Evans and E. D. Hearing, Heat Capacities and Entropies of Organic Compounds in the Condensed Phase, *J. Phys. Chem. Ref. Data*, **13** (1984), Suppl. 1, and the supplement by E. S. Domalski and E. D. Hearing, *J. Phys. Chem. Ref. Data*, **19**, 881 (1990).
5. D. R. Stull, E. F. Westrum, Jr. and G. C. Sinke, *The Chemical Thermodynamics of Organic Compounds*, Wiley, New York, 1969.
6. D. D. Wagman, W. H. Evans, V. B. Parker, R. H. Schumm, I. Halow, S. M. Bailey, K. L. Churney and R. L. Nuttall, The NBS Tables of Chemical Thermodynamic Properties: Selected Values for Inorganic and C_1 and C_2 Organic Substances in SI Units, *J. Phys. Chem. Ref. Data*, **11** (1982), Suppl. 2.
7. J. D. Cox and G. Pilcher, *Thermochemistry of Organic and Organometallic Compounds*. Academic Press, New York, 1970.
8. A recent exploration of 'statistical pitfalls' attending the analysis of thermochemical data is found in J. A. Martinho Simões, C. Teixeira, C. Airoldi and A. P. Chages, *J. Chem. Educ.*, **69**, 475 (1992) in which they point out the danger of assessing goodness of fit from correlation constants (r) only. Our attempts at correlation are less precarious in that there is experimental uncertainty in only one variable (usually less than 3 kJ mol^{-1}) and the variable is weighted in the analysis. Nonetheless, as a precaution against over-confidence in 'good' correlation coefficients obtained from regressions which include 'bad' data, we routinely plot the data and inspect for obvious outliers.
9. Equation 1 is a modified form of the more general relation, $\Delta H_f[Y—(CH_2)_m—H] = A + Bm + \delta$, first proposed for homologous hydrocarbon series by E. J. Prosen, W. H. Johnson and F. D. Rossini, *J. Res. Natl. Bur. Stand.*, **37**, 51 (1946); A is a constant associated with a specific end group Y, B is a constant for all normal alkyl series independent of the end group (-20.6 kJ mol^{-1}) and δ is the deviation from linearity for a given member of the series. In Reference 7, Cox and Pilcher discuss the applicability of the equation to homologous series other than hydrocarbons. They conclude from the three series they analysed that in the C_4–C_{16} range the n-alkyl bromides and n-alkyl thiols behave normally and the n-alkyl alcohols behave slightly abnormally. Using our archival values for the n-alkyl thiols, none of which show more than 0.51 kJ mol^{-1} difference from those in Reference 7, we find a slight difference in the constant terms (-20.46 vs -20.64 kJ mol^{-1} for the slope). Thus, we emphasize the sensitivity of the numerical analysis to the experimental data and associated uncertainty intervals.

   The question arises as to whether the diethyl-substituted compounds should be counted as $n_c = 4$ because earlier observations of deviation were based upon homologous series of the type $Y—(CH_2)_{n_c}—H$. For the cases in which the functional group is bonded to only the methylene group, specific intramolecular effects between non-bonded atoms are greatest for the lower members and deviations from linearity become increasingly insignificant for higher members. This suggests that better data for the $H—(CH_2)_{n_c}—Y—(CH_2)_{n_{c'}}—H$ compounds is associated with both n_c and $n_{c'} \geqslant 4$, as opposed to merely total $n_c \geqslant 8$. However, because of the lack of data, we have no choice but to use whatever is available.

   An alternative presentation of the data for these linear relationships is to assume the existence of a 'universal' methylene heat-of-formation increment, established for the n-alkanes, and to calculate the deviations of each member from the 'universal' slope. We have chosen to present the best linear fits of the experimental data in order to give the reader a more immediate, and perhaps ultimately intuitive, cognizance of the overall magnitude of deviation from ideality.
10. S. W. Slayden and J. F. Liebman, in *Supplement E: The Chemistry of Hydroxyl, Ether and Peroxide Groups*. Vol. 2 (Ed. S. Patai), Wiley, Chichester, 1993. The Me—X—R cases may be considered examples of the 'methyl effect' deviation from R—X—R linearity. Me—X—Me deviates from R—X—R as well as from Me—X—R.
11. It can be shown using the parameters in Table 1 that the two series of gas-phase sulphides have identical numerical heats of formation at hypothetical $n_c = 2.8$, i.e. the lines cross. The consequence is that the extrapolated ΔH_f values have an inverted order relative to those of sulphide isomers with $n_c > 3$.

12. R. L. Montgomery and F. D. Rossini, *J. Chem. Thermodyn.*, **10**, 471 (1978) evaluated the deviation from linearity of several Me—X compounds using the 'universal' methylene increment and experimental heats of formation for gaseous members of each series. They found, within the uncertainties, that the order of increasing values of $\delta(n_c = 1)$ corresponds to the order of increasing electronegativity of the atom X. The order of deviation from the 'best data fit' slope, $MeSH < Me_2SO < Me_2SO_2 < Me_2SO_3 < Me_2SO_4$, is in accord with our intuition regarding the electronegativity of the functional groups. However, the opposite order of deviation from the universal slope with respect to the sulphoxide and the sulphone is consonant with the relative electronegativities of these groups as calculated by Boyd and Boyd [R. J. Boyd and S. L. Boyd, *J. Am. Chem. Soc.*, **114**, 1652 (1992)].
13. It could be asked if this is an example for which n_c and $n_{c'} \geqslant 4$ and if the linear relationship should be established by the dibutyl and dipentyl sulphide enthalpies. However, this is not the only evidence we will adduce for the unreliability of these enthalpies. We note now that for the difference quantities to be discussed, the intramolecular effects of lower members largely cancel.
14. P. Knauth and R. Sabbah, *Can. J. Chem.*, **68**, 731 (1990).
15. This relationship has been dubbed the 'Rossini effect' in G. J. Janz, *Thermodynamic Properties of Organic Compounds*, Physical Chemistry Vol. VI (Eds. E. Hutchinson and P. V. Rysselberghe), Academic Press, New York and London, 1967. The fully enunciated principle balances steric effects and carbon branching, so we do not define as 'simple' those compounds such as di-*t*-butyl ether where the two large tertiary groups are brought into close proximity.
16. Montgomery and Rossini[12] showed that the correlation of $\delta(n_c = 1)$ with electronegativity varies broadly in that they combined the deviations of different classes of compounds containing the same heteroatom, e.g. mercaptans, sulphides and disulphides were compared with alcohols and ethers. Here, we are assessing the usefulness of m for $n_c > 1$ in gauging relative electronic effects of individual series in their deviation from the 'universal' m of 20.6 kJ mol^{-1}. Knauth and Sabbah[14], in their study of the 1,ω-alkanediols, concluded that the low —CH_2— group contribution to the heat of formation is due to the electron-attracting effect of the hydroxyl groups which lowers the mean C—C bond enthalpy compared to other aliphatic compounds.
17. Using m as an indicator of group electronegativity gives the following order: $R_2SO_4 > R_2SO_3 > R_2SO_2 > RSH > R_2S > RSSR > R_2SO$. The two groups which seem out of place, the disulphide and sulphoxide, are also the two series which have m values more negative than the universal m, implying that these groups are less electronegative than a hydrocarbon.
18. This derivation and the ultimate constancy of the quantities presupposes the universality of the universal methylene increment. Will this in fact be confirmed from measurements of the heats of formation of members of our various classes of sulphur compounds with more carbons, or will it be shown that 'some increments are more equal than others'?
19. In Reference 10 we observed a descrepant heat quantity for the formation of di-*t*-butyl ether from *t*-butyl alcohol and attributed it to steric strain in the ether.
20. J. T. Herron, in *The Chemistry of Sulphones and Sulphoxides* (Eds. S. Patai, Z. Rappoport and C. Stirling), Wiley, Chichester, 1988.
21. The one combination we can examine is methyl ethyl sulphite. Using ΔH_f(l) values for dimethyl sulphite (-523.6 ± 1.1 kJ mol^{-1}) and diethyl sulphite (-600.7 ± 0.9 kJ mol^{-1}), we calculate the ΔH_f(l) of methyl ethyl sulphite as -562 ± 1.4 kJ mol^{-1}. This is quite close to the measured value of -567.5 ± 1.2 kJ mol^{-1}. Herron[20], using the method of group additivity, has demonstrated that a reported heat of formation for $C_3H_8O_4S$ of -898.1 ± 1.5 kJ mol^{-1} (l) is incompatible with the compound being either methyl ethyl sulphate or isopropyl hydrogen sulphate. We concur after deriving a value of -774.4 kJ mol^{-1} for the appropriate sulphate substituent exchange reaction, or a value of -779.5 kJ mol^{-1} using the difference quantity $\delta_6(1, 73, 4)$ in Figure 1 and the measured value of methyl ethyl sulphite.
22. K. B. Wiberg, D. J. Wasserman, E. J. Martin, and M. A. Murcko, *J. Am. Chem. Soc.*, **107**, 6019 (1985); K. B. Wiberg and S. Hao, *J. Org. Chem.*, **56**, 5108 (1991).
23. R. Shaw, in *The Chemistry of the Sulphonium Group* (Eds. C. J. M. Stirling and S. Patai), Wiley, Chichester, 1981.
24. We note again the oft- but not universally-observed anomalous effect of methyl substitution on difference quantities. The larger endothermicity of the di-*t*-butyl sulphone/ketone exchange is due to a suggested steric effect in the ketone which is evidently not present in the sulphone.

Sellers attributes 15–20 kJ mol^{-1} steric energy to di-*t*-butyl ketone on the basis of enthalpy differences upon additional α-methyl substitution. [P. Sellers, *J. Chem. Thermodyn.*, **2**, 211 (1970)]. We find also from a perusal of the ketone isomers in our archival source that the heats of formation of the di-*t*-butyl and di-*n*-butyl ketones are identical within uncertainty intervals while di-isobutyl ketone is about 12 kJ mol^{-1} more stable than either. Contrast this with the sulphones; di-*t*-butyl is more stable than di-isobutyl (by 10.7 kJ mol^{-1}) which in turn is more stable than di-*n*-butyl (by 25.8 kJ mol^{-1}). The smaller C—S(O_2)—C bond angle compared to a C—C(O)—C angle would imply a larger steric effect which is partially compensated for by the longer C—S bond length.

25. B. Bujnicki, M. Mikołajczyk and J. Omelanczuk, in *The Chemistry of Sulphinic Acids, Esters and Their Derivatives* (Ed. S. Patai), Wiley, Chichester, 1990.
26. K. V. Rajagopalan, R. Kalyanaraman and M. Sundaresan, *J. Indian Inst. Sci.*, **70**, 409 (1990). These authors also reported the heats of formation of its hydrated 1:1 'AlOH^{+2}' and Ca^{+2}, Mg^{+2}, and Zn^{+2} salts. These last ionic/chelated species cannot be compared with any other sulphur-containing species we know about, and thus no further mention will be made of them save for chronicling here their heats of formation, 'AlOH'·$4H_2O$, -2487 ± 4; Ca·$2H_2O$, -2068 ± 4; Mg·$4H_2O$, -2500 ± 2; Zn·$4H_2O$, -2310 ± 2 kJ mol^{-1}.
27. J. F. Liebman, in *The Chemistry of Sulphonic Acids, Esters and Their Derivatives.* (Eds. S. Patai and Z. Rappoport), Wiley, Chichester, 1991.
28. M. Colomina, P. Jimenez, M. V. Roux and C. Turrion, *An. Quim. Ser. A*, **77**, 114 (1981).
29. By taking the difference of the heats of formation on pure acid and its aqueous, ionized solution we derive the interaction energies of liquid H_2SO_4 and FSO_3H with water to be nearly 96 and 77 kJ mol^{-1}, respectively, while for H_2SO_3 (cf gaseous SO_2) it is but 26 kJ mol^{-1}.
30. W. E. May, S. P. Wasik, M. M. Miller, Y. B. Tewari, J. M. Brown-Thomas and R. N. Goldberg, *J. Chem. Eng. Data*, **28**, 197 (1983).
31. We ascertained the heat of solution of solid benzene by explicitly summing the 2 kJ mol^{-1} heat of solution of liquid benzene suggested by May and his coworkers[30], and the 10 kJ mol^{-1} heat of solidification of benzene, as found in the evaluated compendia Reference 4. (For any compound, its heats of fusion and solidification are equal except for the sign of the numbers.)
32. R. L. Benoit, M. Fréchette and D. Boulet, *Can. J. Chem.*, **67**, 2148 (1989).
33. We determined the heat of solution of liquid methane by explicitly summing the heat of solution of gaseous methane (from Wagman and his coworkers[6]) and an estimated heat of condensation of methane of *ca* -8 kJ mol^{-1}. This last quantity was obtained by averaging the -7.7 kJ mol^{-1} derived from equation 2 of J. S. Chickos, A. S. Hyman, L. H. Ladon and J. F. Liebman, *J. Org. Chem.*, **46**, 4294 (1981) for hydrocarbon heats of vaporization (heats of vaporization and condensation are equal but of opposite sign) and the -8.5 kJ mol^{-1} value found in the compendia by Domalski and his coworkers[4]. Though the agreement of these two independent sources is good, the value should only be considered approximate because the former value is derived from equations not designed for such few carbon species, and the latter is for a measurement at 99 K, which is not the 298 K we wish to use, need for proper thermochemical comparisons and implicitly employ in our reasoning.
34. This is because we are comparatively suspicious of corrections to standard temperature conditions of the high temperature sulphonation reactions of the various aromatic compounds. Indeed, we may even inquire as to their phase under the relevant reaction conditions.
35. This is documented by the rich nucleophilic chemistry of sulphinate anions, cf the chapter by T. Okuyama, and of the stability of the representative and transition metal ion salts and complexes of sulphinic acids, cf the chapter by H. Fujihara and N. Furukawa, both in *The Chemistry of Sulphinic Acids, Esters and Their Derivatives* (Ed. S. Patai), Wiley, Chichester, 1990.
36. J. L. Kice, H. C. Margolis, W. S. Johnson and C. A. Wulff. *J. Org. Chem.*, **42**, 2933 (1977).
37. The '*S,S,S*' is unnecessary since there is no other possible way of putting three oxygens on a disulphide. However, for the first time we mention this compound we append these letters to remind the reader that we are not talking about PhS(O)—O—S(O)Ph, the 'classical' but still unisolated, anhydride of benzenesulphinic acid.
38. Kice and coworkers observed[36] that a peri (1,8)-bridged naphthalene cyclic sulphinyl sulphone had nearly the same heat of solution as the corresponding disulphone and so suggested that diphenyl disulphide trioxide has nearly the same heat of solution as its corresponding

disulphone, namely 162 kJ mol^{-1}. We find that the heats of sublimation of diphenyl sulphoxide and diphenyl sulphone differ by but 7 kJ mol^{-1} Finally, adding the archival heats of vaporization (at 298 K) and fusion (at the melting point) of dimethyl sulphoxide to derive the heat of sublimation of dimethyl sulphoxide is within 1 kJ mol^{-1} of the recommended value for dimethyl sulphone.

39. We opted for the heat of formation suggested by Benson in his specialized thermochemistry review [S. W. Benson, *Chem. Rev.*, **78**, 23 (1978)] although this value and our archival value from Pedley and his coworkers[3] are nearly indistinguishable. Benson alone gives us the heat of formation of diphenyl disulphide trioxide—and those of the other lower disulphide oxides—that he obtained by thermochemical kinetic analysis of sulphinyl and sulphonyl free radical reactions such as (self and mixed) dimerization. There is some dispute about these radical energetics (cf Benson's review) and those by C. Chatgilialoglu, in *The Chemistry of Sulphones and Sulphoxides* (Eds. S. Patai, Z. Rappoport and C. Stirling), Wiley, Chichester, 1988, and D. Griller, J. A. Martinho Simões and D. D. M. Wayner, in *Sulfur-Centered Intermediates in Chemistry and Biology* [Eds. C. Chatgilialoglu and K.-D. Asmus), Plenum Press, New York, 1991.
40. We understand the possible resistance of the reader to consider this analogy. Yet, how much is it due to the classical inorganic/organic dichotomy and that the $S_2O_x^{-2}$ anions are customarily called dithionite, pyrosulphite and dithionate for $x = 4$, 5 and 6? We also admit that there is a rather common anion with $x = 3$, but this has the altogether different structure of SSO_3^{-2} and the common name of thiosulphate.
41. We find it surprising, given the rich redox chemistry of sulphinic acids, that so little quantitative data has been reported. Besides that of Ashworth[42], chapters in *The Chemistry of Sulphinic Acids, Esters and Their Derivatives* (Ed. S. Patai), Wiley, Chichester, 1990, that address generally qualitative features of this redox chemistry, especially disproportionation reactions, include those by C. J. M. Stirling, J. Hoyle, S. Oae and H. Togo, and T. Takata and T. Endo.
42. M. R. F. Ashworth, in *The Chemistry of Sulphinic Acids. Esters and Their Derivatives* (Ed. S. Patai), Wiley, Chichester, 1990.
43. This is for bisulphite and bisulphate—we also note that a comparable difference is found for the corresponding sulphite/sulphate pair, as well as the non-oxyanion pairs of cyanide and cyanate, and formate and bicarbonate.
44. U. Zoller, in *The Chemistry of Sulphinic Acids, Esters and Their Derivatives* (Ed. S. Patai), Wiley, Chichester, 1990.
45. Equivalently, the right side is expected to be no more than 94 kJ mol^{-1} more stable than its precursors 1,2-butadiene + SO_2. This 94 kJ mol^{-1} is expected to be rather general because the *ca* 52 ± 2 kJ mol^{-1} difference in the heats of formation of the isomeric 1,2- and 1,3-butadienes is shared by the difference of 61 ± 3 and 54 ± 3 kJ mol^{-1} for gaseous 1,2- and 2,3-pentadienes vs an averaged value for (*Z*)- and (*E*)-1,3-pentadiene, and 54 ± 2 kJ mol^{-1} for 3-methyl-1,2-butadiene and 2-methyl-1,3-butadiene. [The necessary heat of formation of gaseous 3-methyl-1,2-butadiene is taken from W. V. Steele, R. D. Chirico, A. Nguyen, I. A. Hossenlopp and N. K. Smith. *AIChE Symp.*, **279**, 138 (1991).]
46. We recall warnings given by C. J. M. Stirling, in *The Chemistry of Sulphinic Acids, Esters and Their Derivatives* (Ed. S. Patai), Wiley, Chichester, 1990, about the numerous chemical differences of carboxylic and sulphinic acids although they are both 'RXOOH' species. Nonetheless, we recognize the formal similarity of the facile loss of SO_2 from allylic sulphinic acids (as opposed to other types of sulphinic acids from which this decomposition mode is seemingly rare) and the relative ease of decarboxylation of β-ketocarboxylic acids that form energetically 'expensive' enols (in contrast to 'normal' carboxylic acids).
47. (a) J. F. Liebman, in *Molecular Structure and Energetics: Studies of Organic Molecules*, Vol. 3 (Eds. J. F. Liebman and A. Greenberg), VCH, Deerfield Beach, 1986.
(b) P. George, C. W. Bock and M. Trachtman, in *Molecular Structure and Energetics: Biophysical Aspects*, Vol. 4 (Eds. J. F. Liebman and A. Greenberg), VCH, New York, 1987.
48. There is, in fact, very little experimental data to support this plausible assumption. It is based on the optimistic interpolation between the nonconjugated ethylene and aromatic benzene and noting that both of them have symmetric backbones composed of essentially neutral and equally charged, trigonal and sp^2 carbons.
49. While we know of no heat-of-solution data for H_2SO_4 in aqueous dioxane at any concentration,

we find that the heat of solution of H_2SO_4 in water exceeds that in diethyl ether by only 10–15 kJ mol^{-1} at the reported 1:5, 1:10, 1:15, 1:20 and 1:25 pure acid/pure solvent mixtures.

50. S. Patai (Ed.), *The Chemistry of Sulphinic Acids, Esters and Their Derivatives*, Wiley, Chichester, 1990.
51. B. Bujnicki, M. Mikołajczyk and J. Omelanczuk[25] cite one sulphinic acid derivative, the sulphinyl sulphide (thiolsulphinate) PhS(O)SPh. In Benson's specialized organosulphur thermochemistry review[39] he also cites the related di- and trioxides, PhS(O)S(O)Ph and $PhS(O)SO_2Ph$. We consider these latter diphenyl disulphide oxides also to be sulphinic acid derivatives, since we define members of this class of compound to be any species with the RS(O)X substructure where R is some hydrocarbyl group and X is a group attached by some 'hetero' atom (i.e. neither carbon nor hydrogen). However, since we do not know how to proceed from knowledge of the heats of formation of these species with the heteroatom equalling sulphur to any compound with the hetero-atom equalling oxygen, we do not discuss these species further.
52. S. Patai, Z. Rappoport and C. Stirling (Eds.), *The Chemistry of Sulphones and Sulphoxides*, Wiley, Chichester, 1988.
53. S. Braverman, in *The Chemistry of Sulphinic Acids, Esters and Their Derivatives* (Ed. S. Patai), Wiley, Chichester, 1990.
54. S. Braverman, in *The Chemistry of Sulphones and Sulphoxides* (Eds. S. Patai, Z. Rappoport and C. Stirling), Wiley, Chichester, 1988. Braverman has written two chapters in this volume, one on sulphones and the other on sulphoxides. This citation refers to the former.
55. K. Schank, in *The Chemistry of Sulphones and Sulphoxides* (Eds. S. Patai, Z. Rappoport and C. Stirling), Wiley, Chichester, 1988.
56. J. Drabowicz, P. Kiełbasiński and M. Mikołajczyk, in *The Chemistry of Sulphinic Acids, Esters and Their Derivatives* (Ed. S. Patai), Wiley, Chichester, 1990.
57. D. C. Dittmer and M. D. Hoey, in *The Chemistry of Sulphinic Acids, Esters and Their Derivatives* (Ed. S. Patai), Wiley, Chichester, 1990.
58. For example, we find propyne is nearly 6 kJ mol^{-1} more stable than allene, and while 1-butyne is only some 3 kJ mol^{-1} more stable than 1,2-butadiene, the 'internal alkyne' 2-butyne is nearly 20 kJ mol^{-1} more stable than 1,2-butadiene. To calibrate our thinking, we note that 1,3-butadiene is some 50 kJ mol^{-1} more stable than 1,2-butadiene, documenting that conjugation has a larger stabilizing effect than hyperconjugation.
59. A. Greenberg and J. F. Liebman, *Strained Organic Molecules*, Academic Press, New York, 1978.
60. J. F. Liebman and D. Van Vechten, in *Molecular Structure and Energetics: Physical Measurements*, Vol. 2 (Eds. J. F. Liebman and A. Greenberg), VCH, Deerfield Beach, FL, 1987.
61. The reader is reminded of our earlier questions and caveats as to the true universality of the universal methylene increment. If this increment is universal, then it is not particularly surprising that this value designed for the understanding of *n*-alkyl derivatives is nearly identical to the heat of formation of the 'diagonal' strainless $—CH_2—$ increment, defined as precisely 1/6 of the heat of formation of cyclohexane for the study of cycloalkanes and other alicyclic hydrocarbons, by D. Van Vechten and J. F. Liebman, *Isr. J. Chem.*, **21**, 105 (1981). If the increment is not universal, then its application to alicyclic rings requires perhaps even more scrutiny for its immediate application to a new series of alkyl derivatives, although the derived value of -20.6 kJ mol^{-1} remains numerically precise in the current case.
62. It should be noted that A. Greenberg and J. F. Liebman[59] cite two literature values for the strain energy of cyclobutene that differ by a *ca* 15 kJ mol^{-1}.
63. More precisely, we limit our attention to those unimolecular decomposition reactions wherein there are two 'things' on the right and only one on the left, and so the decomposition of either of the sultines is entropically favoured. A perusal of Benson and O'Neal's compendium [S. W. Benson and H. E. O'Neal, *Kinetic Data on Gas Phase Chemical Reactions*, Natl. Stand. Ref. Data Ser., Natl. Bur. Stand., 66 (1970)] shows numerous elimination reactions to have an entropy change of *ca* 140 J mol^{-1} K^{-1}. For example, for the thermolysis of the *n*-butyl, isobutyl, *s*-butyl and *t*-butyl acetates the entropies are 135, 136, 147 and 158 J mol^{-1} K^{-1} while for the related bromides they are 139, 136, 143 and 156 J mol^{-1} K^{-1}. Admittedly, there is a 'mass effect' associated with changes in translational entropy. However, for the thermolysis of the acetate esters of ethanol and its 1-phenyl derivative the entropies are 126 and 141 J mol^{-1} K^{-1}.
64. A. Greenberg and J. F. Liebman, in Reference 59, p. 66, (we normally would not single out one

page in a publication, except that we have found numerous individuals who are bothered by the name 'cycloethane' and the pictorial description it conveys, and have found numerous others who immediately acknowledge the structural and electronic tautology inherent in the two names.)

65. For the one (strong) sulphur oxyacid for which there are data, sulphuric acid, the difference between gas-phase heats of formation is 24 kJ mol^{-1} per methyl group; for the very weak, weak and strong nitrogen oxyacids NH_2OH, HNO_2 and HNO_3, the differences are 16, 14 and 13 kJ mol^{-1} and for the weak carbon oxyacids, ROH with R = Et, Ac and Ph, the differences are 19, 22 and 28 kJ mol^{-1}, respectively. [All data come from Reference 3 except for H_2SO_4, from M. W. Chase, Jr., C. A. Davies, J. R. Downey, Jr., D. J. Fruip, R. A. McDonald and A. N. Syverud, *JANAF Thermochemical Tables*, 3rd ed., *J. Phys. Chem. Ref. Data*, **14** (1985), Supplement 1; NH_2OH and NH_2OMe, from S. W. Benson, F. R. Cruickshank, D. M. Golden, G. R. Haugen, H. E. O'Neal, A. S. Rogers, R. Shaw and R. Walsh, *Chem. Rev.*, **69**, 279 (1969); and HNO_2 and HNO_3, from Reference 4.]
66. The assignment of the value of -20.6 kJ mol^{-1} follows from recognizing that the homologous series of n-alkanes can be mentally generated by sequentially inserting methylenes into C—C bonds starting with ethane or into primary C—H bonds starting with methane. We acknowledge Benson's lecture[39] that the difference between the heats of formation of the compounds formed by attaching a group to H and to Me depends very strongly on the electronegativity of the group.
67. F. Tureček, L. Brabec, T. Vondrak, V. Hanus, J. Hajicek and Z. Havlas, *Coll. Czech. Chem. Commun.*, **53**, 2140 (1988).
68. S. Patai (Ed.), *The Chemistry of Sulphenic Acids and Their Derivatives*, Wiley, Chichester, 1990.
69. S. Braverman, in *The Chemistry of Sulphones and Sulphoxides* (Eds. S. Patai, Z. Rappoport and C. Stirling), Wiley, Chichester, 1988. This citation referes to the chapter on sulphoxides.
70. S. Braverman, in *The Chemistry of Sulphenic Acids and Their Derivatives* (Ed. S. Patai), Wiley, Chichester, 1990.
71. There is also the difference between the heats of solution of the sulphoxide and sulphenate ester. However, we expect this difference to be quite small in non-polar, non-hydrogen bonding solvents such as hydrocarbons and ethers.
72. We do note that δ(g, Ph, Me, SOH) = δ(g, Ph, Me, Y) is numerically fulfilled exactly by Y = H, although H is not normally viewed as a substituent. Alternatively, one might have thought that —SH should be similar to —SOH since both involve divalent sulphur, which is comparatively π-electron donating. The relevant difference between heats of formation is 135 kJ mol^{-1}. Relatedly, the values for the likewise electron-donating —SMe, >S and —S—S— are 125, 134 and 126 kJ mol^{-1}, while for the $-SO_2Me$ and $>SO_2$ which are even more electron withdrawing than is >SO, the values are 127 and 120 kJ mol^{-1}. In terms of both measured and estimated substituent constants for —SOH and the other sulphur groups presented [see M. Charton, in *The Chemistry of Sulphenic Acids and Their Derivatives* (Ed. S. Patai), Wiley, Chichester, 1990], it seems surprising how similar these sulphur-containing substituents are with regard to differences of heats of formation of Me- and Ph-containing compounds. (More precisely, Charton gives us values for three sigma substituent parameters for—SSMe and for—SSPh and shows that these two sulphur-containing substituents are nearly identical to each other and to —SOH.) One might also have recognized that sulphenic acids are α-nucleophiles and so an anomalous difference for δ_{31} might have been expected. However, δ_{31}(g, Ph, Me, NH_2) equals 110 kJ mol^{-1} and the related α-nucleophile difference δ_{31}(g, Ph, Me, $NHNH_2$) equals 118 kJ mol^{-1}.
73. G. C. Barrett, in *The Chemistry of Sulphenic Acids and Their Derivatives* (Ed. S. Patai), Wiley, Chichester, 1990.
74. Neutralization–Reionization Mass Spectrometry has unequivocally shown that neutral and radical cationic MeSOH and yet another tautomer $CH_2S(H)O$ have indpendent existence: F. Tureček, D. E. Drinkwater and F. W. Lafferty, *J. Am. Chem. Soc.*, **111**, 7696 (1989). Neutral and radical cationic CH_2=CHSOH have been related to the corresponding forms of MeCH=S=O; F. Tureček, F. W. McLafferty, B. J. Smith and L. Radom, *Int. J. Mass Spectrom. Ion Proc.*, **101**, 283 (1990).
75. These values are consonant with the MP4/6-31G* isomerization heat of 92 kJ mol^{-1} for MeSOH and MeS(O)H reported by S. Wolfe and H. B. Schlegel, *Gazz. Chim. Ital.*, **120**, 285

(1990). (Relatedly, at the same quantum chemical level, these authors found HSOH to be more stable than H_2SO by 113.4 kJ mol^{-1} and at the MP4/6-31G** level the difference is 116.9 kJ mol^{-1}. These last results are corroborated by the BAC-MP4 HF/6-31G** quantum chemically calculated heats of formation of H_2SO, -28.6 ± 5.4 kJ mol^{-1}, and HO(S)H, -128.1 ± 6.0 kJ mol^{-1} (C. F. Melius, personal communication). For description of this method, see P. Ho and C. F. Melius, *J. Phys. Chem.*, **94**, 5120 (1990). Heats of formation so calculated are generally reliable, e.g. theory and experiment for H_2S and CH_2O agree to better than a few kJ mol^{-1}. That CH_2O has a more negative heat of formation than H_2SO by 80 ± 7 kJ mol^{-1} is consistent with our expectations, though we must admit that the corollary finding, that the heat of formation of H_2SO is only 8 ± 7 kJ mol^{-1} more negative than that of H_2S, is disconcerting.

76. We may generalize these results to sulphenate esters. From the literature heat of formation of MeSOH[67] and the suggested[65] 20 ± 15 kJ mol^{-1} increased heat of formation upon O-methylation, we find gaseous methyl methanesulphenate is -170 ± 15 kJ mol^{-1}, *ca* 20 ± 15 kJ mol^{-1} more negative than DMSO [$\Delta H_f(g) = -151.3 \pm 0.8$ kJ mol^{-1}]! This disconcerting conclusion was reached earlier by Wolfe and Schlegel[75], who proposed a difference of *ca* 25–35 kJ mol^{-1}. They also suggested that the customary isomer sulphoxide/sulphenate stability order arises from condensed-phase intermolecular forces. Indeed, from the logic used by J. F. Liebman and J. B. Chickos [*Struct. Chem.*, **1**, 501 (1990)] for estimating heats of vaporization of acyl derivatives, we derive the heat of vaporization of a sulphenate ester to be *ca* 30 kJ mol^{-1} lower than that of its isomeric sulphoxide.
77. Equilibrium truly means ΔG. However, we can be confident that the sulphenic acid has a higher entropy than the suphoxide if for no other reason than that the rotational barrier of sulphenic acids is considerably less than the inversion barrier of sulphoxides. The S → O proton transfer interconverting RS(O)H and RSOH is isoelectronic to a 1,2-H shift in a carbanion, and so it is a Woodward–Hoffmann forbidden reaction. (Wolfe and Schlegel[75] calculate barrier heights of *ca* 100 kJ mol^{-1} between the more stable sulphenic acid and the less stable thiol sulphoxide.)
78. J. Drabowicz, P. Lyżwa and M. Mikołajczyk, in *The Chemistry of Sulphenic Acids and Their Derivatives* (Ed. S. Patai), Wiley, Chichester, 1990.
79. D. R. Hogg, in *The Chemistry of Sulphenic Acids and Their Derivatives* (Ed. S. Patai), Wiley, Chichester, 1990.
80. We find in Benson and O'Neal[63] that heat capacity changes accompanying most thermolysis reactions are relatively small, and so little error is introduced by ignoring temperature dependences of reaction heats and entropies.
81. We know of heat of combustion data for condensed-phase methyl penicillin (R.B. Woodward, A. Neuberger and N. T. Trenner, in *The Chemistry of Penicillin* (Eds. H. T. Clarke, J. R. Johnson and R. Robinson), Princeton University Press. Princeton, 1949) but not of the rearrangement of its sulphoxide to any cephalosporin derivative. We note, however, the calorimetric and calculational study [D. D. Wilson and J. B. Deeter, *J. Org. Chem.*, **56**, 447 (1991)] that provided heats of isomerization for the S- (i.e. vinyl sulphide) and N- (i.e. enamide) conjugated Δ^2- and Δ^3-cephalosporins, with the unconjugated 3-exo-methylene species.
82. See Greenberg and Liebman[59] and the commentary in Reference 61. Alternatively, consider the formal gas-phase reaction:

$$EtSEt + (CH_2)_5 \longrightarrow EtCH_2Et + (CH_2)_4S$$

This reaction is 11 kJ mol^{-1} exothermic. Equivalently, the strain energy of thiolane is less than cyclopentane by 11 kJ mol^{-1}. By contrast, the corresponding enthalpy difference for diethyl ether and tetrahydrofuran is less than 4 kJ mol^{-1}.
83. We note that the following related reaction deviates from thermoneutrality by less than 2 kJ mol^{-1}:

$$CH_3CH_2CH_2CH_2SMe + CH_3CH_3 \longrightarrow CH_3CH_2CH_2CH_2CH_3 + CH_3SMe$$

84. We have opted to contrast $Me(CH_2)_2X$ and (*E*)-MeCH=CHX because we are less confident of the thermochemical data for CH_2=CHCHO than for MeCH=CHCHO, and because we know of no experimental value for the heat of formation of any acetylethylene. [For a recent review of enone and enal thermochemistry, see J. F. Liebman and R. M. Pollack, in *The Chemistry of Enones* (Eds. S. Patai and Z. Rappoport), Wiley, Chichester, New York, 1989.]

85. For example, we find (*Z*)-, (*E*)- and *gem*-substituted olefins spread over a several $kJ\,mol^{-1}$ range; e.g. for the butenes, the heats of formation of the isomeric (*Z*)-MeCH=CHMe, (*E*)-MeCH=CHMe and $Me_2C{=}CH_2$ are -7.1 ± 1.0, -11.4 ± 1.0 and $16.9 \pm 0.9\,kJ\,mol^{-1}$ (gases) and -29.7 ± 1.0, -33.0 ± 1.0 and $-37.5 \pm 0.9\,kJ\,mol^{-1}$ (liquids). For cyclopropanes, there is an analogous spread of heats of formation: for *cis*-1,2-, *trans*-1,2- and 1,1-dimethylcyclopropanes, we find -26.3 ± 0.7, -30.7 ± 0.8 and $-33.3 \pm 0.8\,kJ\,mol^{-1}$ (liquids). (We know of no experimental gas-phase values for either 1,2-species.)
86. We use the average of the entropy values for gaseous *cis*- and *trans*-1,2-dimethylcyclopropane as given in Reference 63.
87. In the case of 1-butene-4-sulphenic acid we know the heat of formation of no 4-substituted 1-butene other than 1-pentene. We know the desired value for several other 3-substituted propenes, in particular, the ethylthio and ethylsulphonyl derivatives. These result in upper bounds of -145 and $-154\,kJ\,mol^{-1}$. The upper bound suggested in this section, $-151\,kJ\,mol^{-1}$, remains reasonable.
88. We assumed that the sulphur did not affect the interaction energy of the adjoining oxygen, and accepted the *ab initio* quantum chemical results of P. v. R. Schleyer, E. D. Jemmis and G. W. Spitznagel, *J. Am. Chem. Soc.*, **107**, 6393 (1985) on $ClCH_2OH$ and $HOCH_2OH$.
89. The value for the entropy of gaseous methylcyclopropane was taken from Reference 63, and those of the gaseous butane and octane were taken from Reference 5. We earlier asserted that the transformation of 'two things' into one is accompanied by a decrease of some $140\,J\,mol^{-1}\,K^{-1}$. Some of the seeming discrepancy of $140-85 = 55\,J\,mol^{-1}K^{-1}$ disappears when one recognizes that our previous examples involved only acyclic species. Cyclic species have lower entropies than their acyclic analogues, e.g. from Reference 5 we find that the entropy of propylene oxide is some $25\,J\,mol^{-1}K^{-1}$ lower than for ethyl methyl ether.
90. See, for example, the chapter by P. de Maria, in *The Chemistry of Sulphenic Acids and Their Derivatives* (Ed. S. Patai), Wiley, Chichester, 1990, who included discussion of this phenomena and how it makes the study of the acidity of sulphenic acids both interesting and problematic.
91. For HOCl, the requisite data are found in Reference 6, while for alcohols, a brief discussion of the consequence of this for alcohol and ether thermochemistry can be found in Reference 10.
92. M. Roy and T. B. McMahon, *Org. Mass Spectrom.*, **17**, 392 (1982).
93. J. T. Herron, *J. Phys. Chem. Ref. Data*, **16**, 1 (1987).
94. O. Lösking, H. Willner, H. Baumgärtel, H. W. Jochims and E. Rühl, *Z. Anorg. Allg. Chem.*, **530**, 169 (1985).
95. For example, this was done in J. F. Liebman, *J. Fluorine Chem.*, **25**, 481 (1984) in an attempt to mechanistically rationalize some anomalous fluorinated thiolate reaction chemistry.
96. This value is for the 3-21G basis set results, as found in R. A. Whiteside, M. J. Frisch and J. A. Pople (Eds.), *The Carnegie-Mellon Quantum Chemistry Archive*, 3rd edn., Carnegie-Mellon University, Pittsburgh, 1983. See also A. Schmiedekamp, D. W. J. Cruickshank, S. Skaarup, P. Pulay, I. Hargittai and J. E. Boggs, *J. Am. Chem. Soc.*, **101**, 2002 (1979).
97. P. v. R. Schleyer and A. Reed, *J. Am. Chem. Soc.*, **109**, 7302 (1987).
98. (a) S. W. Benson, Reference 39.
    (b) See, for example, the following studies by A. A. Woolf, *Adv. Inorg. Chem. Radiochem*, **24**, 1 (1981); *J. Fluorine Chem.*, **11**, 307 (1978); **20**, 627 (1982); **32**, 433 (1986).
    (c) J. F. Liebman, in *Fluorine-Containing Molecules: Structure, Reactivity, Synthesis and Applications* (Eds. J. F. Liebman, A. Greenberg and W. R. Dolbier, Jr.), VCH, New York, 1988.
99. In fact, these results are 'fortuitously' valid for X bonded to F or OH by either C or S, in that the X—F, X—OH exchange energy is electronegativity-dependent (D. L. Kunkel and J. F. Liebman, unpublished results based on a composite of semiempirical quantum chemical calculations and experimentally measured heats of formation).
100. See the compendia in References 6 and 65, respectively. These compendia are complementary in that (i) the former has data for compounds of all the elements, the latter is more selective; (ii) the data in the former are unreferenced, that in the latter often have numerous literature citations; (iii) the data in the former are the experimental values, modified minimally except to gain self-consistency by 'chemical thermodynamic networks'; those in the latter have a philosophy reminiscent of our mosaic orientation.
101. Our optimism is perhaps even more easily shown by noting the gas-phase heats of formation of SCl_2 and S_2Cl_2. That is, if they are exothermically formed by the reaction of Cl_2 with solid

sulphur with its eight S—S bonds per molecular unit, unequivocally S—S bond cleavage in the gas is even more energetically favoured.

102. The requisite heat of formation of $Cl(CH_2)_4Cl$ was derived by summing the heat of formation of $Cl(CH_2)_3Cl$ and the 'universal' methylene increment.
103. It is incumbent on us to try to estimate the entropy change associated with equation 52, at least for the $n = 4$ case. We have no data on the 4-chlorobutanesulphenyl chloride, nor on any other sulphenyl chloride. How can we mimic sulphenyl chlorides? From Reference 6, we find $S°$ for Cl_2 is 226.6 J mol^{-1} K^{-1}, while Reference 5 tells us $S°$ for MeCl and C_2H_6 equal to 234.6 and 229.5 J mol^{-1} K^{-1}. From Reference 6, we find $S°$ for S_2Cl_2 is 331.5 J mol^{-1} K^{-1}, and from Reference 5 $S°$ for MeSSMe is 336.6 J mol^{-1} K^{-1}. This casually tells us that $S°$ for Cl bonded to 'something' is comparable to that of Me so-bonded. Likewise, from Reference 6 we find 270.2, 275.9 and 269.9 J mol^{-1} K^{-1} for CH_2Cl_2, $MeCH_2Cl$ and CH_2Me_2 documenting our intuition. This analysis suggests that $S°(Cl(CH_2)_4SCl)$ should approximately equal $S°(Me(CH_2)_4SMe)$. From Reference 5 we find this value equal to 451 J mol^{-1} K^{-1}, which is the value we will use for 4-chlorobutanesulphenyl chloride. The entropy value for $(CH_2)_4S$ is 309.4 J mol^{-1} K^{-1} and so there is an entropy decrease of some 85 J mol^{-1} K^{-1} and thus some 25 J mol^{-1} K^{-1} in free energy. Recall our earlier assertion that the transformation of 'two things' into one is accompanied by a decrease of some 140 J mol^{-1} K^{-1}. The seeming discrepancy of 140–85 = 55 J mol^{-1} K^{-1} disappears when one recognizes that our previous examples involved only acyclic species. Cyclic species have lower entropies than their acyclic analogues, e.g. from Reference 5 we find that the entropy of cyclopentene is some 50–60 J mol^{-1} K^{-1} lower than that of the three acyclic *n*-pentenes.
104. M. Meot-Ner (Mautner), S. M. Cybulski, S. Scheiner and J. F. Liebman, *J. Phys. Chem.* **92**, 2738 (1988).
105. R. Shaw, in *The Chemistry of Cyanates and Their Thio Derivatives* (Ed. S. Patai), Wiley, Chichester, 1977.
106. X.-W. An and M. Mansson, *J. Chem. Thermodyn.*, **15**, 287 (1983).
107. G. Capozzi, G. Modena and L. Pasquato, in *The Chemistry of Sulphenic Acids and Their Derivatives* (Ed. S. Patai), Wiley, Chichester, 1990.
108. We have taken the heat of formation of the (hypothetical) liquid S_8 at 298.15 K from Reference 65 to derive the given value for the liquid. We know of no experimental measurement for the heat of vaporization of S_2Br_2. However, throwing all caution to the wind, we may estimate it using the —Br and —SS— heat-of-vaporization parameters for substituted hydrocarbons from J. S. Chickos, D. G. Hesse, J. F. Liebman and S. Y. Panshin, *J. Org. Chem.*, **53**, 3424 (1988). This is clearly absurd because there are neither hydrogens nor carbons in the species of interest. Yet, since the heats of vaporization of S_8, Br_2 and S_2Cl_2 are reproduced by this additivity approach to within 6 kJ mol^{-1}, our new results gain credibility.
109. This point was made explicitly in Reference 107, although neither the authors nor anyone else to our knowledge has investigated the reaction of disulphides with the interhalogens ICl or IBr. We also recall that some interesting interactions found in sulphur–iodine cations such as S_7I^+ have been documented [cf. N. Burford, J. Passmore and J. C. P. Sanders, in *From Atoms to Polymers: Isoelectronic Reasoning* (Eds. J. F. Liebman and A. Greenberg), VCH, New York, 1989]. The only reactions of disulphides with ClF we know of are for some perfluorinated species R_fSSR_f' that result in the S—S cleaved products, R_fSF_4Cl and R_fSF_5 [T. Abe and J. M. Shreeve, *J. Fluorine Chem.*, **3**, 187 (1973)].
110. This energy term is normally referred to as the heat of sublimation of (definitionally) solid I_2 which is numerically equal to the quantity quoted within a sign. This number was taken from the data compendium of Reference 2.
111. R. J. Hwang and S. W. Benson, *J. Am. Chem. Soc.*, **101**, 2615 (1979).
112. L. G. S. Shum and S. W. Benson, *Int. J. Chem. Kinet.*, **15**, 433 (1983).
113. (a) For a review of the aromaticity of chalcogen-containing heterocycles, see D. C. Dittmer, *Rev. Heteroatom Chem.*, **2**, 185 (1989).
(b) For a novel approach to both aromaticity and electrophilic substitution, see L. J. Sæthare and T. D. Thomas, *J. Org. Chem.*, **56**, 3935 (1991).
(c) The most recent conclusion, derived from varying analyses of differing theoretical rigour is that thiophenes are aromatic while their sulphoxides 'are better described as ylides', I. Rojas, *J. Phys. Org. Chem.*, **5**, 74 (1992).

114. This heat of hydrogenation will be ascertained by taking the difference between the heats of formation of the unsaturated and saturated species, rather than from the heat of a direct measurement. A quick perusal of the hydrogenation literature [e.g. the review by J. L. Jensen, *Prog. Phys. Org. Chem.*, **12**, 189 (1977)] is notable for the absence of sulphur-containing species. This, however, is no surprise since the sulphur deactivates ('poisons') most catalysts used for hydrogenation.
115. An example of the conflicts of σ- and π-effects is seen in the smaller resonance energy found for conjugated enones than for the corresponding conjugated dienes; cf J. F. Liebman and R. M. Pollack, in *The Chemistry of Enones* (Eds. S. Patai and Z. Rappoport), Wiley, Chichester, 1989.
116. For example, see the results of most of the aromaticity criteria discussed by A. R. Katritzky, M. Karelson and N. Malhotra, *Heterocycles*, **32**, 127 (1992).
117. See R. S. Hosmane and J. F. Liebman, *Tetrahedron Lett.*, **32**, 3949 (1991), for applications to furan and pyrrole, wherein thiophene was ignored in that study because of different σ-effects such as the different size, and thus steric effects, associated with dicoordinated O (and also NH) and S. Nonetheless, that conceptual consistency was achieved in understanding the aromaticity of the five-membered and six-membered ring heterocycles should encourage us in the application of this reasoning to thiophene.
118. We remind the reader that Hosmane and Liebman[117] did not use archival heat of formation of gaseous diphenylmethane from Reference 3 but instead made use of the new phase-change data reported by J. S. Chickos, R. Annunziata, L. H. Ladon, A. S. Hyman and J. F. Liebman, *J. Org. Chem.*, **51**, 4311 (1986).
119. Using the criterion for aromaticity suggested in Reference 117, we find that stabilization decreases in the order: benzene (153.5 kJ mol^{-1}) > thiophene (116.3) > 1,3-cyclohexadiene (36.7) > 1,2-dithiin (18.2). From the reasonable assignment that 1,3-cyclohexadiene is taken to be non-aromatic, we hereby conclude that 1,2-dithiin is antiaromatic.
120. We chose the relatively recent measurement of the heat of formation of solid thianthrene, W. H. Johnson, *J. Res. Natl. Bur. Stand.*, **79A**, 561 (1975), 184.2 ± 1.5 kJ mol^{-1}, which Pedley and his coworkers seemingly ignored in Reference 3, rather than their choice, namely 182.0 ± 1.8 kJ mol^{-1} derived from a composite of values measured some 10–20 years earlier. In fact, the precise choice is almost irrelevant because of uncertainty in the temperature-corrected heat of sublimation of 97.5 ± 6.3 kJ mol^{-1} [D. J. Sandman, A. J. Epstein, J. S. Chickos, J. Ketchum, J. S. Fu and H. A. Scheraga, *J. Chem. Phys.*, **50**, 305 (1979)]. [For a review of heat-of-sublimation values, techniques, correction and estimations, see J. S. Chickos, in *Molecular Structure and Energetics: Physical Measurements*, Vol. 2 (Eds., J. F. Liebman and A. Greenberg), VCH, New York, 1987.]
121. R. S. Hosmane and J. F. Liebman, *Tetrahedron Lett.*, **33**, 2303 (1992).
122. The heat of formation of the disulphide is from the archive in Reference 3, but the dithioether is enigmatically absent and had to be taken from the primary reference, M. Mansson, *J. Chem. Thermodyn.*, **6**, 1153 (1974). For completeness, we additionally note that Mansson's paper also discusses the energetics of bis(ethylthio)methane, for which the heat of formation is (l), -116.0 ± 1.5; (g), -65.2 ± 1.5 kJ mol^{-1}.
123. We exclude here the (*Z*)- and (*E*)-isomers of 1,2-bis(benzylthio)ethylene for two reasons. First, they contain the R—S—C=C—S—R substructure as well and it is unclear how much additional stabilization (or destabilization) arises from there being two sulphurs. Second, the available data are only for the solid state and so comparison with any gas-phase species is suspect.
124. This is in marked contrast to vinyl ethers for which there is significant resonance stabilization[10]. This conclusion in especially bewildering because furan has less resonance stabilization than thiophene.
125. The requisite heat of formation of gaseous divinyl sulphide is 106.0 ± 4.0 kJ mol^{-1}, obtained from M. G. Voronkov, V. A. Klyuchnikov, S. N. Kolabin, G. N. Shvets, P. I. Varushkin, E. N. Deryagina, N. A. Korchevin and S. I. Tsvebtnitskaya, *Dokl. Phys. Chem.* (*Dokl. Akad. Nauk SSSR, Engl. Transl.*), **307**, 650 (1989). For completeness, the heat of formation of the corresponding liquid is 67.7 ± 3.0 kJ mol^{-1}.
126. Disconcertingly, we know of no heat-of-formation data for the intermediate (i.e. single H_2 addition) product, ethyl vinyl sulphide.

127. We obtained the heat of formation of gaseous divinyl sulphoxide from Reference 125 and note that the heat of formation of the corresponding liquid from that source is -26.2 ± 2.5 kJ mol^{-1}.
128. We obtained the heat of formation of gaseous divinyl sulphone from Reference 125 and note that the heat of formation of the corresponding liquid from that source is -213.0 ± 4.5 kJ mol^{-1}.
129. The 3-isomer is also recognized as an 'external' olefin while its 1- and 2-isomers are 'internal'. If this is corrected for, by say the nearly 11 kJ mol^{-1} difference in heats of formation of 1- and 2-pentene, we find the non-conjugated 'homoallylic' isomer to be more stable than its conjugated isomer by nearly 7 kJ mol^{-1} and to be nearly identical to the other non-conjugated isomer.
130. Heat-of-combustion results are reported in F. Arndt, G. T. O. Martin and J. R. Parrington, *J. Chem. Soc.*, 602 (1935) quoting the study of L. Lorenz-Oppau and H. Sternitzke, *Z. Elektrochem.*, **40**, 501 (1934). There are no primary data and while 'details of these experiments are to be published elsewhere', our search of *Chemical Abstracts* has not turned up the new study. For completeness, we now give the raw heat-of-combustion data for the solids of interest: 2,6-diphenyltetrahydro-1-thia-4-pyrone, -9491.8 ± 9.7 kJ mol^{-1}; 2,6-diphenyltetrahydro-1-thia-4-pyrone sulphone, -9157.1 ± 11.9 kJ mol^{-1}; 2,6-diphenyl-1-thia-4-pyrone, -9060.5 ± 11.6 kJ mol^{-1}; 2,6-diphenyl-1-thia-4-pyrone sulphone, -8862.6 ± 9.8 kJ mol^{-1}.
131. G. Geiseler and J. Sawistowsky, *Z. Phys. Chem.* (*Leipzig*), **250**, 43 (1972), who cited neither study in Reference 130.
132. Normally, we would disparage a 30 kJ mol^{-1} discrepancy between two measurements but we suspect that much of the difference is that of differing degrees of dilution of the resulting H_2SO_4 solution. We also do not know if the two studies made use of the same *cis/trans* isomeric compositions of the saturated thiopyrans.
133. This equation is only exact at the melting point, since it assumes no heat-capacity differences for solid and liquid compound and that no correction of the results to 298 K is needed. While these assumptions are untrue, the errors are small compared to those introduced by many of the other assumptions made in this chapter.
134. S. Nuritdinov, I. U. Numanov and I. M. Nasvrov, *Dokl. Akad. Nauk Tadzh. SSR*, **72**, 34 (1973); *Chem. Abstr.*, **79**, 77571a (1973).
135. The isomeric 3,5- and 3,7-dimethylbenzothiophene sulphones may seem to have surprisingly disparate heats of formation, but the 42 kJ mol^{-1} difference is mimicked by the observation that solid 2,3-, 2,6- and 2,7-dimethylnaphthalene have the same heat of formation to within 4 kJ mol^{-1}, while their 1,8-isomer is less stable by *ca* 30 kJ mol^{-1}. More precisely, we recognize considerable 'peri'–repulsive interactions between the 1,8-methyls in the disubstituted naphthalene and the 7-methyl and sulphur-bound oxygens in the disubstituted benzothiophene sulphone.
136. We note that complete oxidation from gaseous SO_2 to aqueous H_2SO_4 (at infinite dilution) is exothermic by *only* 326 kJ mol^{-1}, significantly less than the disparity we cite.
137. For this analysis, we made use of the earlier enunciated heat of formation of dibenzo-1,4-dithiin[120], and those of gas-phase dibenzo-1,4-4H-thiazine (278.2 ± 1.9 kJ mol^{-1}) and dibenzo-1,4-4H-oxazine (94.1 ± 2.8 kJ mol^{-1}) of R. Sabbah and L. El Watik, *Thermochim. Acta*, **197**, 381 (1992). For completeness, the heats of formation of the two solid 4*H*-azines are 166.7 ± 1.9 and -2.1 ± 2.8 kJ mol^{-1}, respectively.
138. W. M. Shaub, *Thermochim. Acta*, **55**, 59 (1982), with a suggested heat of formation of -63 kJ mol^{-1}.
139. Using the heat of formation of gaseous diphenylmethane as done earlier[117], we find the related difference $\delta_{72}(CH_2, CH_2)$ for the presumably non-aromatic 9,10-dihydroanthracene to be *ca* 146 kJ mol^{-1}.
140. An example of this is the amelioration of both aromaticity and antiaromaticity of 1-ring conjugated species with increasing ring size, as seen by the reactivity and seeming stability of cyclobutadiene, benzene and cyclooctatetraene and of the related sulphur-containing π-isoelectronic thiirene, thiophene and thiepin.

CHAPTER 5

NMR and ESR of organosulphur compounds

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ABBREVIATIONS

CP-MAS	cross polarization–magic angle spinning
DMPO	5,5-dimethyl-1-pyrroline-*N*-oxide
DSP	dual substituent parameters
fod	6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionato
LIRAS	a computer program for analysis of lanthanide shifts
LIS	lanthanide induced shift
LROCSM	a 2D NMR sequence for long range shift correlation
MNP	2-methyl-2-nitrosopropane
QCC	quadrupolar coupling constant
SCS	substituent-induced chemical shift
SOMO	singly occupied molecular orbital
SROCSM	a 2D NMR sequence for short range shift correlation

I. THE NMR SPECTRA OF ORGANOSULPHUR COMPOUNDS

A. Introduction

There are numerous sulphur-containing organic compounds of which many have been the subject of previous volumes in this series[1-3]. The aim of this part of the review is to report recent studies of the NMR of derivatives of the sulphur acids, sulphenic, sulphinic and sulphonic acids and the sulphides, sulphoxides and sulphones, together with a few assorted aliphatic compounds such as thioesters. Aromatic sulphur compounds in which sulphur is part of the aromatic ring system are not within the scope of this review. For this chapter the literature has been reviewed from 1989 to mid-1992 and material covered in earlier volumes[1-3] has not been duplicated here. The aim is to present an account of contemporary NMR studies of organosulphur compounds with the emphasis being on the variety of problems that NMR can tackle, and the use of modern techniques, such as 2-D NMR and CP-MAS NMR, in addition to the usual compilations of chemical shift data. Proton and carbon-13 NMR chemical shift data and substituent-induced chemical shift effects (SCS) are to be found in the standard compendia such as *The Aldrich Library of N.M.R. Spectra*[4] for ^{1}H NMR spectra and the books by Levy, Lichter and Nelson[5] and Breitmair and Voelter[6] for ^{13}C NMR. Sulphur-33 NMR has been thoroughly reviewed up to 1987[7].

The study of organosulphur compounds by NMR spectroscopy is of interest for a number of reasons, in addition to the intrinsic interest of NMR parameters, since such compounds have interesting conformational properties, find wide use in organic synthesis and some have beneficial medicinal properties. A substituted sulphur atom can also be the source of asymmetry in molecules and the study of diastereotopic oxygen nuclei in sulphones has been the subject of much recent activity as described in Section I.C.2. The variety of compounds, the large number of nuclei available for study and the different reasons for carrying out the research in the NMR properties of organosulphur compounds makes the organization of this chapter rather difficult. The format that has been adopted is to describe the NMR of these compounds classified by nucleus rather

TABLE 1. The NMR properties of some nuclei[a]

Nucleus	Mass number	Spin QN	Abundance	Receptivity rel to carbon	γ (10^7 rad $s^{-1}T^{-1}$)	Q[b] ($10^{-28}m^2$)
Hydrogen	1	1/2	99.985	5.67×10^3	26.7522	—
Carbon	13	1/2	1.108	1.00	6.7283	—
Nitrogen	14	1	99.63	5.70	1.9338	1.67×10^{-2}
	15	1/2	0.37	2.19×10^{-2}	−2.7126	—
Oxygen	17	5/2	0.037	6.11×10^{-2}	−3.6280	-2.6×10^{-2}
Sulphur	33	3/2	0.76	9.78×10^{-2}	2.0557	-6.4×10^{-2}

[a] From Reference 8.
[b] Nuclear electronic qudrupolar moment.

than by class of compound. In this way the common features of the rather closely-related sulphur compounds can be emphasized. One particular problem that arises due to the organization by nucleus format is that there are some comparative studies between the two quadrupolar nuclei ^{17}O and ^{33}S. The occurrence of these papers is noted in the text and, where the comparisons are particularly important or revealing, they are discussed along with the ^{33}S NMR.

The nuclei that are covered are ^{1}H, ^{13}C, ^{17}O, ^{14}N and ^{15}N, and ^{33}S. The NMR properties of these nuclei are compared in Table 1. The labelling of atoms or groups within an organosulphur compound follows the usual protocol.

$$\underset{\delta}{C}—\underset{\gamma}{C}—\underset{\beta}{C}—\underset{\alpha}{C}—S(O)_n—X—\underset{\alpha'}{C}—\underset{\beta'}{C}—\underset{\gamma'}{C}—\underset{\delta'}{C}—\underset{\varepsilon'}{C}$$

Where the central sulphur atom is attached to a heteroatom X (where X = S, O, NR) the substituents on that hetereoatom are always labelled α', β' etc.

B. Proton and Carbon-13 NMR

1. Chemical shift studies and substituent-induced chemical shift effect (SCS) determinations

As there have been extensive studies in the past on these subjects and values for most classes of interest are available, activity has declined somewhat, but surprisingly it appears that SCS effects for the ^{13}C NMR spectra of sulphides, sulphonium salts, sulphoxides and sulphones had not been systematized until a recent report by Dyer and Evans[9]. As with the sulphur acid derivatives[1-3] the electron-withdrawing properties of the sulphur groups are a major contributor to the ^{13}C NMR shieldings of the α-carbon in particular. Typical values of some substituent constant for selected sulphur-containing groups are given in Table 2.

The ^{13}C NMR chemical shifts of some related sulphides, sulphonium salts, sulphoxides and sulphones are given in Table 3. The data in Table 3 were used to calculate SCS values for the SO, SO_2 and SCH_3^+ groups relative to the parent sulphide; these data are given in Table 4. A very small difference between the chemical shifts for alkanes RCH_2R and the corresponding sulphide RSR wal also noted, with the very small α-SCS of +2–3 ppm being ascribed to the slightly larger Allred 'average' electronegativity[11] of sulphur (2.58) compared with that of carbon (2.55). A rather surprising observation from the SCS values of Table 4 is that the α-deshielding is very similar at about +20 ppm

TABLE 2. Some substituent constants for selected sulphur-containing groups[a]

Group	σ_m	σ_p	σ_I	σ_R
SO_2Me	0.64	0.73	0.59	0.16
SO_2O^-	0.31	0.37	0.23	0.07
SO_2NH_2	0.53	0.6	0.44	0.12
$^+SMe_2$	1.00	0.90	0.89	0.17
SO·Me	0.52	0.49	0.5	0.0
SO·NMe_2	0.29	0.27	0.30	0.03
SO_2^-	0.22	0.31	—	0.0
SMe	0.14	0.06	0.13	−0.16

[a] Taken from Reference 10.

TABLE 3. ^{13}C NMR chemical shifts of some organosulphur compounds and reference hydrocarbons[a]

No.	Compound	δ (ppm) C-α	C-β	C-γ	C-δ	Reference
1	$(CH_3CH_2)_2CH_2$	22.6	13.7			14
2	$(CH_3CH_2)_2S$	25.52	14.84			9
3	$(CH_3CH_2)_2SO$	44.85	6.72			9
4	$(CH_3CH_2)_2SO_2$	46.21	6.58			9
5	$(CH_3CH_2CH_2)_2CH_2$	32.4	23.0	13.9		9
6	$(CH_3CH_2CH_2)_2S$	34.3	23.3	13.7		15
7	$(CH_3CH_2CH_2)_2SO$	54.4	16.3	13.4		15
8	$(CH_3CH_2CH_2)_2SO_2$	54.5	15.5	13.2		15
9	$(CH_3CH_2CH_2)_2S^+CH_3I^-$	43.5	17.9	12.9		15
10	$(CH_3CH_2CH_2CH_2)_2CH_2$	29.7	32.3	22.9	13.9	6
11	$(CH_3CH_2CH_2CH_2)_2S$	31.94	31.94	22.12	13.73	9
12	$(CH_3CH_2CH_2CH_2)_2SO$	52.18	22.11	24.66	13.70	9
13	$(CH_3CH_2CH_2CH_2)_2SO_2$	52.15	21.28	23.97	13.54	6
14	$(CH_3CH_2CH_2CH_2)_2S^+CH_3BF_4^-$	41.33	21.60	22.15	13.32	9
15	$(CH_3CH_2CH_2CH_2CH_2CH_2)_2S$	32.27	28.78	31.54	29.79	9
16	$(CH_3CH_2CH_2CH_2CH_2CH_2)_2SO$	52.50	22.39	31.40	28.54	9
17	$(CH_3CH_2CH_2CH_2CH_2CH_2CH_2)_2SO_2$	52.77	21.96	31.24	28.22	9
18	$C_6H_5CH_2SC_6H_5$	39.09				9
19	$C_6H_5CH_2SOC_6H_5$	63.82				9
20	$C_6H_5CH_2SO_2C_6H_5$	62.68				9

[a] Data refer to 5–10% solutions in $CDCl_3$ solutions, referenced to internal TMS.

for both SO and SO_2, despite the greater inductive effect of the SO_2 group. This effect is different from that in the thiosulphinates and thiosulphonates where the α-SCS is about 6 ppm greater for the more oxidized thiosulphonate than for the thiosulphinate[12,13]. There are, however, examples of series of sulphinates and sulphonates where there is no obvious trend in α-chemical shifts that can be related to simple arguments based on electron-withdrawing abilities[2,3]. The data in Table 4 support the view that ^{13}C nuclei that are β to sterically proximal substituents experience a low-frequency shift relative to the unsubstituted analogue[12,16,17]. The variation in β-SCS in the sulphones and

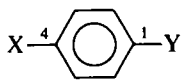
TABLE 4. SCS values for the SO, SO_2 and SCH_3^+ groups relative to the parent sulphide

	Compound (As Table 3)	SCS (ppm)[a] α-C	β-C	γ-C
δ_{SO}-δ_S	**3**	19.33	−8.12	
	7	20.1	−6.9	−0.3
	12	20.24	−9.83	2.52
	16	20.23	−6.39	−0.14
	19	24.73		
δ_{SO_2}-δ_S	**4**	20.69	−8.26	
	8	20.2	−7.7	−0.5
	13	20.21	−10.66	+1.85
	17	20.5	−6.82	−0.3
	20	23.59		
$\delta_{(SCH_3^+)}$-δ_S	**9**	9.2	−5.3	−0.8
	14	9.39	−10.34	0.03

[a] Data from Reference 9; δ and ε effects are less than 0.5 ppm for relevant compounds.

sulphoxides (−6.39 to −10.66) was related to differing degrees of steric hindrance[9]. The γ-SCS and more remote effects in the sulphones and sulphoxides are generally very small. The deshielding effect of the full positive charge in the sulphonium derivatives is less at the α-carbon than the effect of an oxygen atom, but the β-effect is similar, despite the considerably greater electron-withdrawing ability suggested by the σ values (Table 2).

NMR is a well-established method for the study of the transmission of substituent effects in disubstituted aromatic compounds of the type **21**.



(21)

The methods used now are based on the interpretation of SCS effects in terms of dual substituent parameters (DSP) in which inductive and resonance contributions are deconvoluted[18–22]. The correlation of the ^{13}C NMR chemical shifts of **21** with the SCS values for the monosubstituted benzenes (**21**, Y = H) has been discussed by Lynch[22] and Craik[18] and is widely interpreted in terms of the Lynch equation[22].

$$^{13}C \text{ NMR chemical shift } C_x(Y) = a + bSCSC_x(H) \quad (1)$$

where, in **21**, Y is the fixed substituent (the one containing sulphur for the purposes of this review) and X is variable. The slope *b* and intercept *a* are usually determined graphically, with *a* being the value of the chemical shift of the appropriate carbon nucleus in **21**, Y = H, and *b* being an indication of the effect on the chemical shift of the substituent Y. The value of *b* for the carbon nuclei *ipso* and *ortho* (C-4 and C-3,5) to the variable substituent, X, is usually close to unity, as the fixed substituent, Y, has little effect on these carbon nuclei. However, the substituent Y can have a markedly enhanced effect on its *ipso*-carbon (C-1) and discussion here is limited to those carbon nuclei. There is no

generally accepted explanation for this enhancement of the SCS but Taft and coworkers[19] have discussed the effect in terms of a 'shift to charge ratio' that is approximately expressed as $\rho_R^Y/\rho_R^H \times 189$ ppm per electron, where ρ_R^Y and ρ_R^H are the resonance transmission coefficients obtained from DSP correlations for C-1 in YC_6H_4X and the *para* carbon in C_6H_5X, respectively. The DSP equation relating these parameters is

$$^{13}C\ SCS = \rho_I\sigma_I + \rho_R\sigma_R^\circ \tag{2}$$

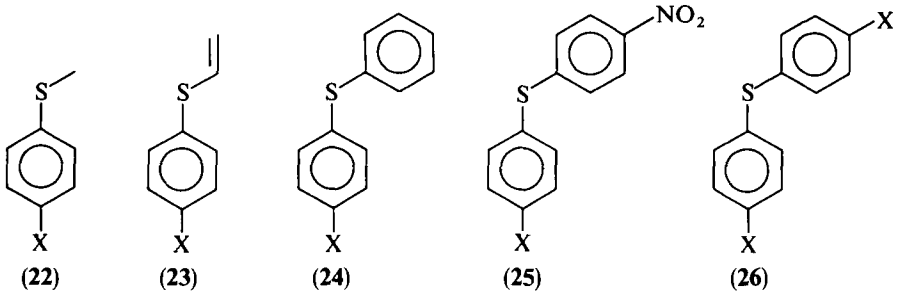
By using standard values for σ_I and σ_R°, values for ρ_I and ρ_R are obtained. The ratio ρ_I/ρ_R is often quoted as λ, and when λ is greater than 2 a strong dependence on π-delocalization is evident[20]. The Lynch analysis and the Taft analysis of the enhancement of SCS effects in **21** have been compared[23,24]. The ratio ρ_R^Y/ρ_R^H is approximately equal to the Lynch slope b in most cases. It can be shown that ρ_R^Y/ρ_R^H will be equal to b when ρ_I^Y can be neglected relative to ρ_R^Y in the DSP relationship

$$\delta C_x(Y) - \delta C_H(Y) = \rho_I^Y\sigma_I + \rho_R^Y\sigma_R^\circ \tag{3}$$

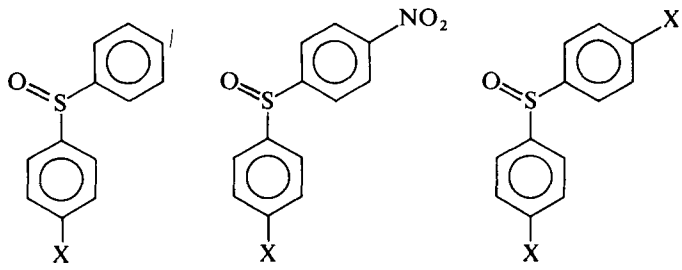
A correlation using 24 available literature values showed that the approximate identity relationship may be used to estimate ρ_R^Y from b without having to carry out a full DSP analysis by applying

$$\rho_R = 20.32b + 1.18 \tag{4}$$

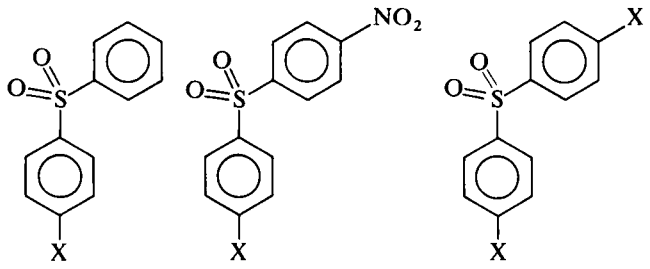
The terms b and ρ_R^Y/ρ_R^H have no anambiguous, independent meaning and it is generally accepted that they are connected with the polarizability of Y and the extent to which Y engages in resonance interactions with the aromatic ring. The sulphides **22–26**, the sulphoxides **27–29** and sulphones **30–32** have been studied by the methods described above, and the values for b and λ are given in Table 5.



(22) **(23)** **(24)** **(25)** **(26)**



(27) **(28)** **(29)**

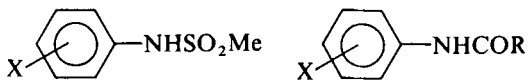


(30) (31) (32)

Reynolds and McClelland[26] studied series **23** and the oxygen analogues and found the order of transmission of substituent effects from the ring to the vinyl group to be S > O.

Perumal and coworkers[23] examined the series **24–26** and the data in Table 5, together with an analysis of much other chemical shift data, led them to conclude that there is transmission of inductive (field) and resonance effects from one of the aryl rings to the other except when both rings bear the same substituents, and there was some evidence to support the suggestion that there is some π-polarization in the unsubstituted phenyl ring in **24**. In a more extensive second study the same authors[24] reported results for the series **27–32**. The values for ρ_I and ρ_R show a large decrease for the structural change —S—Ar to —SO—Ar, but only a very small change for —SO—Ar to —SO_2—Ar. The Taft non-linear resonance variation to the DSP analysis was also applied to these series and, for the substituents PhS, PhSO and $PhSO_2$, it was concluded that there was a slight electron donation with PhS and an increasing electron acceptance for PhSO and $PhSO_2$.

A similar analysis was applied by Wazeer and Ali[27] to the methane sulphonamides **33**.



(33) (34)

TABLE 5. DSP correlations, Lynch slopes and resonance transmission ratios for the carbons *para* to X in the series **22–32**[a]

Series	b	ρ_R^Y/ρ_R^H	ρ_I	ρ_R	λ	n[b]	Reference
22	1.143	1.13	5.7	24.3	4.9	7	25[c]
23	1.536	1.38	10.9	29.6	2.7	9	26
24	1.64	1.68	10.5	36.2	3.5	9	24
25	1.53	1.47	9.5	31.5	3.3	7	24
26	1.04	1.09	4.7	23.4	5.0	8	24
27	1.12	1.12	6.0	24.2	4.0	9	23
28	1.09	1.14	4.0	24.0	6.0	7	23
29	0.99	1.01	4.2	21.7	5.2	8	23
30	0.97	0.98	4.9	21.1	4.3	8	23
31	1.01	1.03	4.9	21.6	4.4	7	23
32	0.82	0.84	3.3	18.1	5.6	8	23

[a] See text for explanation of symbols.
[b] n = number of compounds in the series.
[c] Data calculation from Reference 23.

TABLE 6. The ^{13}C NMR chemical shifts of some sulphur amides in solution and in the solid state

Compound	Solvent/ solid	δ(ppm) S—CH_3	C—CH_3	C-1	C-2	C-3	C-4	C-5	C-6	N—CH_3 ($\Delta\nu_{1/2}$)	Reference
$CH_3SO_2NMe_2$	$CDCl_3$	36.7								32	32
	Solid	39.3								31.9 (90)	32
p-$ClC_6H_4SO_2NMe_2$	Acetone			139.1	129.9	130.3	134.8	130.3	129.9	37.9	32
	Solid			141.2	127.3	127.3	130.7	127.3	127.3	34.0 (100)	32
p-$CH_3C_6H_4SO_2NH_2$	Acetone			143.1	126.7	129.9	141.8	129.9	126.7		33
	Solid			145.5	126.5	130.3	138.3	130.3	126.5		30
p-$CH_3C_6H_4SO_2NHMe$	Acetone			137.1	127.5	130.0	143.4	130.0	127.5	29.3	32
	Solid			133.7	128.2	128.2	143.8	128.2	128.2	31.3; 30.2 (150)	32
p-$CH_3C_6H_4SO_2NMe_2$	Acetone			133.4	128.4	130.2	144.0	130.2	128.4	38	32
	Solid			133.6	129.6	130.6	145.9	130.6	129.6	39.5; 38.1 36.4; 34.9 (290)	32
o-$NO_2C_6H_4SO_2NH_2$	Acetone			137.1	148.7	125.6	133.8	134.5	130.1		33
	Solid			138.0	149.2	129.1	135.6	135.6	130.7		31
o-$NO_2C_6H_4SO_2NMe_2$	Acetone			130.5	149.4	124.7	132.6	134.9	131.1	37.8	31
	Solid			131.6	146.9	124.9	133.5	134.5	131.6	38.8, 36.8 34.3	31
$C_6H_5SO_2NMe_2$	Acetone			135.1	127.5	129.0	132.7	129.0	127.5	37.7	33
	Solid			133.8	129.4		133.8		129.4	40.3; 38.9	31
p-$BrC_6H_4SONMe_2$	Acetone			139.8	130.9	132.7	131.6	132.7	130.9	31.5	32
	Solid									34.6; 31.6 (430)	32
CH_3SNMe_2	Acetone		32.9							44.0	32
	Solid		32.7							44.6 (120)	32
o-$NO_2C_6H_4SNMe_2$	Acetone			142.7	145.7	125.4	126.4	134.8	125.5	47.2	31
	Solid			137.7	143.0	123.0	124.6	133.0	124.6	46.7; 44.9	31
o-$NO_2C_6H_4SO_2NH_2$	Acetone			143.6	148.9	125.4	126.7	135.4	125.8		31
	Solid			142.2	145.5	124.4	126.0	136.5	126.7		31

The series **33** were compared with **34** and it was concluded that there is a greater resonance interaction of the nitrogen lone pair and the X substituent for $NHSO_2Me$ than for the NHCOR group[28] and that the inductive effect of the $NHSO_2Me$ group is much greater than that for the NHCOR group.

The sulphonamides are also the subject of several other recent reports. According to *Chemical Abstracts*[29], Kiyoko observed spin–spin coupling between the NH proton and the benzylic protons in a series of compounds $RC_6H_4SO_2NHCH_2C_6H_4R'$ and related sulphinates, where the benzylic protons were diastereotopic. Ruostesuo and Häkkinen have extended their multinuclear investigations on sulphonamides and related compounds to include ^{13}C CP-MAS spectra in recent papers[30–33]. Solution ^{13}C NMR measurements on some disubstituted sulphur amides revealed the expected non-additivity of SCS effects, but Lynch and DSP analyses were not carried out on the data. The CP-MAS spectra of

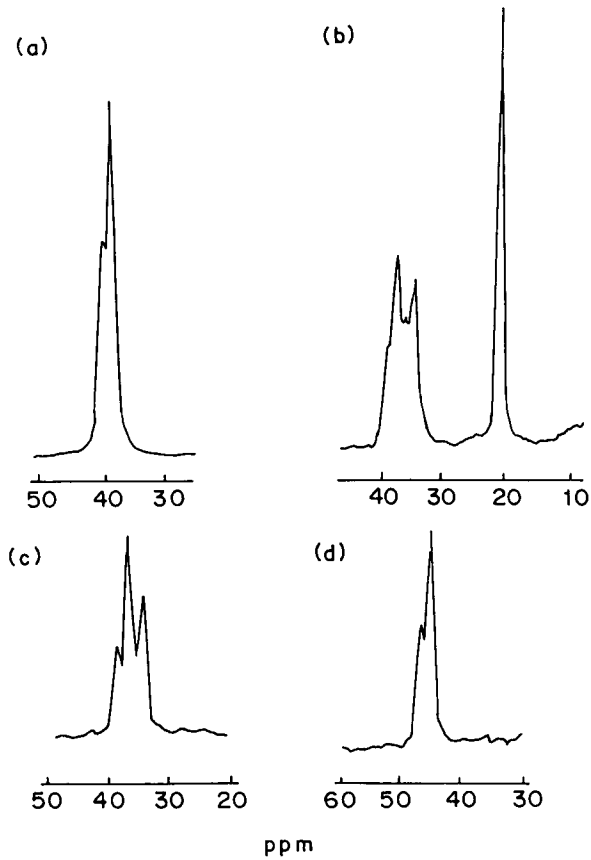
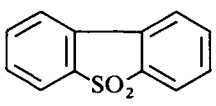


FIGURE 1. Methyl carbon signals (δ/ppm) in the ^{13}C CP-MAS spectra of some sulphur amides: (a) *N,N*-dimethylbenzenesulphonamide; (b) *N,N*-dimethyltoluene-*p*-sulphonamide; (c) *N,N*-dimethyl-*o*-nitrobenzenesulphonamide; (d) *N,N*-dimethyl-*o*-nitrobenzenesulphenamide. Reproduced by permission of the Royal Society of Chemistry from Reference 31

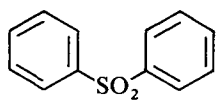
a large selection of sulphur amides is given in Table 6 together with the corresponding solution data for comparison. The most characteristic feature of the CP-MAS spectra was the appearance of a doublet pattern in the N—CH_3 carbons in the aromatic amides resulting from the quadrupolar interaction of the ^{14}N nucleus with the attached carbon nuclei. Some examples are illustrated in Figure 1. It frequently occurs that one part of the doublet is half the height of the other part and this appears to be characteristic of the ^{13}C CP-MAS NMR spectra of many nitrogen-containing compounds[34,35]. The solid state spectra of *N,N*-dimethyltoluene-*p*-sulphonamide, **35**, and *N,N*-dimethyl-*o*-nitrobenzenesulphonamide, **36**, showed extra splitting in the N—CH_3 signals[31] and an X-ray crystallographic study showed that in **35** there are two short intramolecular distances between an N—CH_3 hydrogen and SO_2 oxygen atoms. This suggested some interaction between the methyl groups and the oxygen atoms of the SO_2 group. An alternative explanation for the extra splitting in terms of anisochronous methyl groups (consistent with the X-ray structures) was also considered. The chemical shift differences between the solution and solid spectra were noted, but not analysed other than to suggest that they may reflect differences in conformation between the solid and liquid states.

2. *Proton and carbon-13 NMR as a conformational and configurational probe*

In a detailed investigation Abraham and Hawarth[36] obtained conformational information on some diaryl sulphones using the lanthanide-induced shift methodology with $La(fod)_3$ and $Yb(fod)_3$. Dibenzothiophene sulphone, **38**, is conformationally rigid and was used as a model for the complexation of the lanthanide in a study of the conformationally mobile diaryl sulphones, **38** and **39**. The LIS data revealed that the literature assignments of both ^1H NMR[37] and ^{13}C NMR[38] chemical shifts were in error and the corrected assignments are reported. A variety of complexation models were investigated, including mono and bidentate, and one, two or three-site coordination of the lanthanide to the sulphone. The three-site and two-site monodentate models were considered the best following analysis by LIRAS[39].



(37)



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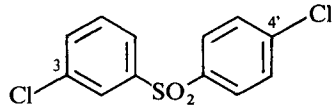
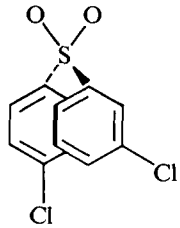


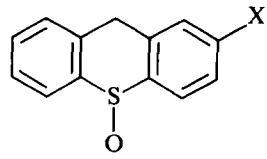
(39)

Following a detailed analysis it was concluded that the preferred conformation of **39** was that shown below, in which the two aromatic rings are facing one-another, rather than a conformation relating to that of **37** in which the rings are co-planar.

In view of the smaller number of chemical shifts to examine in the more symmetrical **38** there was insufficient data for a full analysis, but the data pointed towards a similar preferred conformation as for **39**.

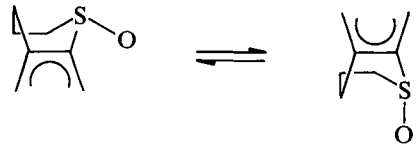


A 2-D ^{1}H and ^{13}C NMR study has been carried out on a series of 2-substituted thioxanthene sulphoxides, **40**. Long- and short-range chemical shift correlations LROCSM and SROCSM[40] were used.



(40)

In addition to a complete chemical shift assignment it was suggested that the data were consistent with the ring undergoing rapid inversion in the equilibrium shown below, with the preferred conformation being that with the sulphoxide oxygen equatorial, eq, for **40** that have no peri-substituents. A thesis has also been published, from the same group, on the NMR of conformationally mobile 4,4′-diaryl suphides, sulphoxides and sulphones[41].



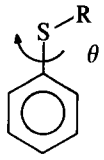
e a

It has been claimed[42] that there is an interaction in the ground state of the *gauche* conformer in some alkyltio-substituted propanones $MeCOCH_2S(O)_nEt$. For $n = 0$, 1 and 2 respectively the α-carbon chemical shifts are reported as 42.5, 62.2 and 62.9 ppm. The SCS values of 20.7 for SO and 21.4 for SO_2 are therefore entirely consistent with those reported by Dyer and Evans[9]. The arguments supporting the orbital interactions are based on infrared, ultraviolet and NMR spectroscopy. The NMR analysis is based on a discrepancy between the observed ^{13}C chemical shifts and the calculated chemical shifts, but as the parameters used in the calculation are not given it is difficult to evaluate this evidence.

Proton NMR has been used to determine the enantiomeric purity and correlate the absolute configuration of aryl sulphoxides by running the spectra in the presence of enantiomerically pure 2,2′-dihydroxy-1,1′-binaphthyl[43].

The favoured rotamers of sulphonamido ketones are reported[44] to be those in which the SO bonds overlap the alkyl groups R, R′ in a series of compounds $RR'C(NHSO_2C_6H_4Me\text{-}p)COMe$. The preferred orientation was inferred from infrared spectra and confirmed by proton NMR measurements on the diastereotopic methylene protons where R = Et. The magnetic anisotropy of the SO bond was calculated as $12.9 \pm 0.8 \times 10^{-6}\,cm^3\,mol^{-1}$, and that of the SO_2 bond was twice that value.

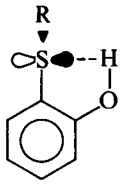
Schaeffer and coworkers have published a series of thorough and careful studies of thiophenols and thioanisoles **41**, R = H, Me. The twofold barrier to internal rotation about the Ar-S bond can be determined by measurement of appropriate long-range coupling constants and the method has been reviewed[45]. Briefly, it depends on the $\sin^2\theta$ dependence of the spin–spin coupling over six bonds between *alpha* and *para* nuclei. The *alpha* nuclei are protons for the thiophenols and ^{13}C nuclei (in enriched samples) for the thioanisoles. From the $^{6}J^{HH}$ or $^{6}J^{CH}$ values the out-of-plane angle θ may be



$\theta = 0°$

(41)

obtained, and from this the rotational barrier V_2 may be calculated by application of a hindered rotor model. Using this approach a value for the rotational barrier in thiophenol of 3.4 kJ mol^{-1} was obtained[46] and this was in good agreement with the barrier obtained from microwave and far-infrared spectroscopy[47]. The barrier increases to 9 kJ mol^{-1} in *p*-nitrothiophenol, attributed to a larger mobile C—S bond order[47]. The conformation with $\theta = 0°$ is, in the absence of specific effects, of lower energy than when $\theta = 90°$, which is the maximum energy conformation for thiophenols and anisoles with no *ortho* or strongly interacting substituents. There is a stereospecific intramolecular hydrogen bond in 2-hydroxythiophenol, **42**, which forces the S—H bond into a plane perpendicular to the ring plane, and this is reflected in the long-range coupling constants[48].



$\theta = 90°$

(42)

The rotational angle dependence of $^5J_m^{H,SH}$ in benzenethiol has also been investigated and related to the π- and σ-electron contributions to the coupling constant[49]. It was also found that *meta* substituents in a series of 3,5-disubstituted thiophenols increased the twofold rotational barrier[50]. The barriers varied between 3.5 kJ mol^{-1} for the 3,4-dichlorothiophenol and 7.0 kJ mol^{-1} for the 3,5-difluorothiophenol. The barrier for 3,5-dichloro-4-hydroxythiophenol was determined as -0.8 kJ mol^{-1}, where the negative value indicates that the preferred conformation is the one with the SH bond perpendicular to the ring plane ($\theta° = 90°$). The long-range ^{13}C-^{13}C coupling constants for twenty-three thioanisoles have been measured and correlated with rotational barriers[51]. The magnitude of the $^5J^{HH}$ coupling was shown to be a good conformational indicator. It was also shown that 2-hydroxythioanisole has the same conformation as **42**, but in 2-aminothioanisole the thiomethyl group twists out of plane by 60° to optimize the N—H 3p interaction.

C. Oxygen-17 NMR

1. Chemical shift and quadrupolar coupling constant (QCC) determinations

Despite its low natural abundance (0.037%), low receptivity (0.061 compared to carbon) and being quadrupolar (spin 5/2) ^{17}O is a very common nucleus for the study of sulphonic and sulphinic acids and their derivatives, sulphones and sulphoxides, and

thioesters. There have been a number of recent reviews of the use of ^{17}O NMR in organosulfur chemistry, in particular by Evans who has made a major contribution in this field[52,53].

The usual standard is H_2O and shifts in this chapter are all referenced to water. The ^{17}O chemical shifts of a number of a compounds that have been reported recently are given in Table 7. The linewidths have only been reported in a few cases despite the fact

TABLE 7. Oxygen-17 data for some sulphur-containing compounds

Compound	$\delta^{17}O$ (ppm)[a]	$\Delta\nu_{1/2}$ (Hz)	q_O^b	Reference
(1) sulphoxides				
CH_3SOCH_3	15		−335	55
$(CH_2)_3SO$	64		−333	55
$(CH_2)_4SO$	11		−342	55
$(CH_2)_5SO$	−4		−339	55
$(CH_2)_6SO$	11			55
$(CH_3CH_2)_2SO$	−6			53
$((CH_3)_2CH)_2SO$	−20			53
(2) Sulphones				
$CH_3SO_2CH_3$	164		−281	55
$(CH_2)_3SO_2$	183		−270	55
$(CH_2)_4SO_2$	164		−284	55
$(CH_2)_5SO_2$	144		−286	55
$(CH_2)_6SO_2$	153		−270	55
(3) Sulphonic acid derivatives				
CH_3SO_2I	282	100–200		56
CH_3SO_2Br	259	100–200		56
$CH_3SO_2SeC_6H_5$	216	100–200		56
p-$CH_3C_6H_4SO_2I$	264	100–200		56
p-$CH_3C_6H_4SO_2Br$	241	100–200		56
p-$CH_3C_6H_4SO_2Cl$	222	100–200		56
p-$CH_3C_6H_4SO_2F$	171	100–200		56
p-$CH_3C_6H_4SO_2NH_2$	159	100–200		57
p-$CH_3C_6H_4SO_2CH_3$	157	100–200		56
p-$CH_3C_6H_4SO_2SeC_6H_5$	201	100–200		54
$ClCH_2SO_2Cl$	223	100–200		54
m-$ClO_2SC_6H_4SO_2Cl$	223	100–200		54
m-$NO_2C_6H_4SO_2Cl$	225	100–200		54
(4) Sulphinic acid derivatives				
CH_3SOCl	192			54
CH_3SONMe_2	72			54
CH_3SOOCH_3	142			54
$(CH_3)_2NSOCl$	226			54
CH_3SOSCH_3	73			53
$CH_3SOSCH_2CH_3$	64			53
p-$CH_3C_6H_4SOCl$	174			54
p-$CH_3C_6H_4SONMe_2$	61			54
p-$CH_3C_6H_4SOOCH_3$	109			54

[a] Reference H_2O.

[b] Calculated atomic charge on oxygen (*ab initio* STO-3G*), in milli-electrons.

that they can give useful information. It would be desirable for all future reports of ^{17}O chemical shifts to be accompanied by the linewidths.

Barbarella[54], in an article that includes sulphur-33, has discussed ^{17}O shieldings in terms of the familiar Pople MO approximation[58–60], where, for an atom A,

$$\sigma_p^A = -(\mu e^2 h/8m^2)\langle r^{-3}\rangle_{2p}(\Delta E^{-1})\sum_B Q_{AB} \quad (5)$$

σ_p is the paramagnetic contribution to the shielding constant, $\langle r^{-3}\rangle_{2p}$ is the mean inverse cube of the distance between the nucleus and its valence electrons, ΔE^{-1} is the average excitation energy and $\sum_B Q_{AB}$ is a bond order term.

The variation of ^{17}O chemical shift between sulphoxides and sulphones was analysed[54] and an explanation was sought for the large deshielding for the sulphonyl oxygen atoms relative to the sulphoxides. The suggestion was rejected that the sulphone deshielding could be due only to an increase in the $\sum Q$ contribution to the paramagnetic component of the nuclear shielding resulting from the greater sulphur–oxygen double-bond character in these compounds. It was pointed out that there is also a significant decrease in the negative charge at oxygen in the conversion SO to SO_2 which causes a decrease in the oxygen 2p orbital radius and hence the observed deshielding through the increase in the $\langle r^{-3}\rangle_{2p}$ term. It was concluded that the ΔE term, which would suggest a shielding in the conversion SO to SO_2, is less important in this case than the combined effects of the $\sum Q$ and $\langle r^{-3}\rangle$ contributions. The ^{17}O chemical shift of compounds containing either SO or SO_2 functional groups are sensitive to the ligands attached to those groups. The particular sensitivity of these shifts to substituent effects was attributed to the availability of the SO lone pair of electrons on sulphur for delocalization across the molecule on the one hand, and the interactions of the SO_2 oxygen lone pairs with the rest of the molecule on the other. The rationalization of ^{17}O chemical shifts in terms of orbital interactions has been explored in more detail by Barbarella, Chatgilialoglu and coworkers[56,61,62]. The same group[63] had previously observed that the SO_2 group, when bound to a chlorine atom, shows a notable deshielding of the oxygen atoms. The sulphonyl oxygen reasonances in CH_3SO_2Cl (δ 238 ppm) appear 68 ppm to high frequency of those in $CH_3SO_2OCH_3$ (δ 170 ppm), despite the similar electron-withdrawing properties of the chlorine and methoxy groups. It was suggested that this so-called 'chlorine effect' was due to an interaction of the oxygen lone-pair molecular orbitals with the low-lying σ^* (SCl) MO. This explanation was expanded and generalized[56] by examining the ^{17}O chemical shifts of two series of compounds, CH_3SO_2X and p-$C_6H_4SO_2X$, where X = I, Br, Cl, F, CH_3, $N(CH_3)_2$ and OCH_3. When the atom adjacent to sulphur varies down the same group of the periodic table, as in the halogens, the effects of electronegativity and conjugation on $\delta^{17}O$ operate in opposite directions. A plot of the electronegativity of X against $\delta^{17}O$ gave a reasonable straight line, and for both series the iodine nucleus was more deshielding [$\delta^{17}O$ (CH_3SO_2I) = 282 ppm] than the more electronegative fluorine [$\delta^{17}O$ (CH_3SO_2F) = 186 ppm]. This was taken as evidence that the ^{17}O variations in these examples are dominated by $n \rightarrow \sigma^*$ conjugative interactions. Conversely, for the first-row elements where such conjugative interactions are small, the chemical shifts in both series were dominated by the substituent electronegativities, and the ^{17}O chemical shifts increased in the order X = CH_3, $N(CH_3)_2$, OCH_3, F. In the series XSOY the $n \rightarrow \sigma^*$ conjugative interactions still contribute to the ^{17}O chemical shifts, but electronegativity effects are more important[61].

The ^{17}O chemical shifts of the carbonyl carbon atoms of thiol esters RCOSR′ has been compared[64] with the ^{17}O chemical shifts of the carbonyl carbon atoms of the corresponding esters RCOOR′, and some data are given in Table 8.

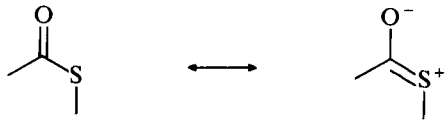
The spectroscopic properties of thiol esters resemble those of ketones rather than oxygen esters; for example, the ^{13}C chemical shifts are closer to the ketone values than the ester values[65]. Boykin[64] found that the carbonyl oxygen chemical shifts of the thiol esters

TABLE 8. Oxygen-17 chemical shifts for the carbonyl oxygen atoms in esters and thiol esters[64]

Compound	$\delta^{17}O$ (ppm)[a]
CH_3COOCH_3	361
CH_3COSCH_3	511
$CH_3COOCH_2CH_3$	363
$CH_3COSCH_2CH_3$	511
$CF_3COOCH_2CH_3$	352
$CF_3COSCH_2CH_3$	509
$CH_3CH_2COOCH_2CH_3$	353
$CH_3CH_2COSCH_2CH_3$	502
$CH_3CH_2CH_2COOCH_3$	356
$CH_3CH_2CH_2COSCH_3$	505
$CH_3COOC_6H_5$	370
$CH_3COSC_6H_5$	514
$CH_3COOC_6H_4CH_3$-*p*	369
$CH_3COOSC_6H_4CH_3$-*p*	514

[a] In acetonitrile at 75 °C, natural abundance in 0.5 M solutions.

were in the region δ500 ppm, which is about 150 ppm to higher frequency than the esters which have typical ^{17}O chemical shifts of about 350 ppm. The ketones have ^{17}O chemical shifts of about 550 ppm. The ^{17}O chemical shift of the thiol esters was discussed in terms of a relatively small contribution of the form **43b** compared with **43a** resulting in a greater carbonyl character in the CO bond compared with esters.



43a **43b**

The factors influencing changes in ^{17}O chemical shift of the carbonyl carbon were shown to be similar in thiol esters and esters by the linearity of the plot of $\delta^{17}O$ thiol esters ($r = 0.99$).

Lowenstein and Igner[66] carried out an interesting ^{17}O and ^{33}S NMR study of dimethyl sulphone and a ^{33}S NMR study of carbon disulphide in four liquid-crystal solvents. In liquid-crystal solvents the solute molecules are partially orientated and therefore their NMR spectra exhibit dipolar or quadrupolar splittings that cannot be observed in isotropic media because of complete motional averaging. The quadrupolar splittings are related to elements of the qudrupole coupling and to order matrix tensors. In this study, by consideration of three possible conformations for dimethyl sulphone, and by comparison with relaxation studies in chloroform and *ab initio* calculations, the QCC of ^{17}O in dimethyl sulphone was found to be of the order of 8.5 MHz.

2. Oxygen-17 NMR as a configurational probe

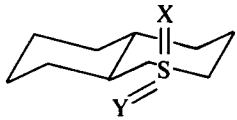
It is well-established that the diastereotopic oxygen atoms in both cyclic[53,55,67,68] and acyclic[69,70] sulphones may be differentiated by ^{17}O NMR spectroscopy. The chemical shift non-equivalence ($\Delta\delta = \delta_1 - \delta_2$) may be as large as 16 ppm.

TABLE 9. Oxygen-17 NMR chemical shift data for *S*-oxides and *S,S*-dioxides[a]

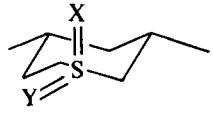
Compound	Solvent	Temp (°C)	$\delta^{17}O$(ppm) ±2 ppm	$\Delta\delta$	$\Delta\nu_{1/2}$ (Hz)	SO/SO_2 orientation
44	$CDCl_3$	30	123.9	15	139	ax
			138.9			eq
45α	CH_2Cl_2	amb	5.6			eq
45β	CH_2Cl_2	amb	−11.4			ax
46	$CHCl_3$	35	139	10		ax
			149			eq
47α	CH_2Cl_2	35	7			eq
47β	CH_2Cl_2	35	−14			ax
48	toluene	100	141		100–200	
49	toluene	100	140.3	5.1	100–200	
			145.4		100–200	
50	toluene	100	172.3	1.3	163	*trans*
			171.0		163	*cis*
51	CH_2Cl_2	30	134.78		430	
52	CH_2Cl_2	30	122.1	13.6	285	ax
			135.7		430	eq
53	CH_2Cl_2	30	140.6	14.5	320	ax
			155.1		400	eq
54	CH_2Cl_2	30	135.9	14.4	320	ax
			150.3		480	eq
55	CH_2Cl_2	30	143.4	10.7	480	ax
			154.1		480	eq
56	CH_2Cl_2	30	126.2	16.4	162	ax
			142.6		147	eq
57	CH_2Cl_2	30	133.3	12.6	251	ax
			145.9		255	eq
58	CH_2Cl_2	30	149.0	8.2	160	ax
			157.1		170	eq

[a] From Reference 71: ax = axial oxygen; eq = equatorial oxygen; *trans* = oxygen *trans* to the 3-isopropoxy group; *cis* = oxygen *cis* to the 3-isopropoxy group.

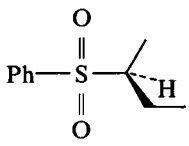
Table 9 gives data for the sulphones **44–58** as collated by Evans and coworkers[71]. Some of the assignments are based on the observation[72] that γ-gauche relationships between aryl substituents and sulphonyl oxygens result in an enhanced shielding effect on the ^{17}O nuclei.



(44) X = Y = O
(45α) X = 2e; Y = O
(45β) X = O; Y = 2e



(46) X = Y = O
(47α) X = 2e; Y = O
(47β) X = O; Y = 2e



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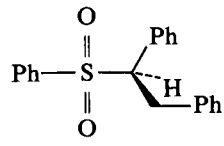

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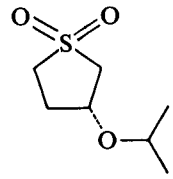

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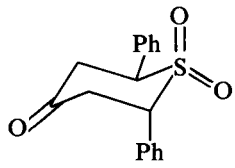

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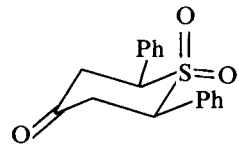

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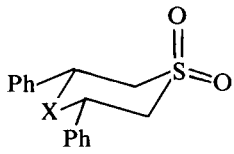
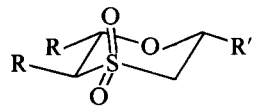


(53) X = NH
(54) X = NCH_3
(55) X = S



(56) R, R = $(CH_2)_4$; R′ = H
(57) R, R = $(CH_2)_4$; R′ = OEt
(58) R = H; R′ = OEt

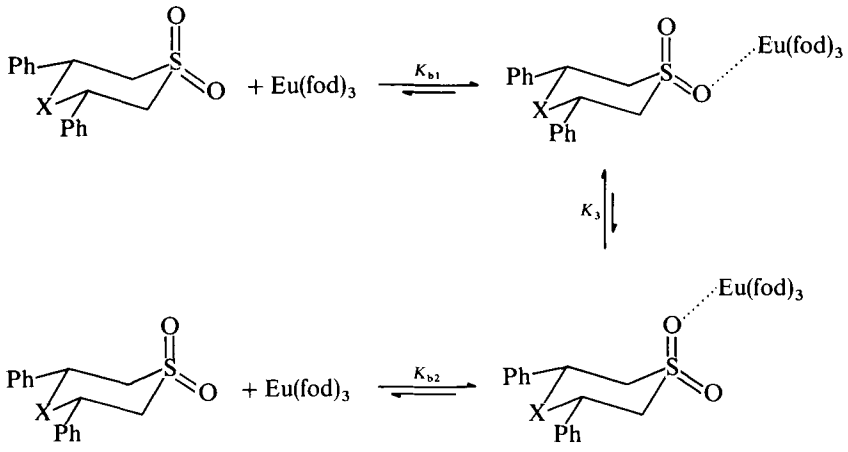
TABLE 10. Oxygen-17 NMR shifts, Ln.S equilibrium constants and binding sensitivity slopes[71]

Sulphone	Sulphonyl oxygen	α(eq ax)[a]	K_3 (M^{-1})	$\delta^{17}O$[b]
53	eq	−459.0 ± 18	2.20 ± 0.12	155.0
	ax	−209.3 ± 8		142.1
54	eq	−534.6 ± 11	4.02 ± 0.11	149.8
	ax	−132.9 ± 3		136.4
55	eq	−452.3 ± 11	2.89 ± 0.17	153.4
	ax	−156.5 ± 9		144.1
58	eq	−119.7 ± 7	0.57 ± 0.04	157.8
	ax	−210.2 ± 7		150.0

[a] Induced shift extrapolated to [Eu(fod)$_3$] = [substrate].
[b] Extrapolated to [Eu(fod)$_3$] = 0.

Evans and coworkers[71] made a detailed study of the interaction of sulphones **53–55** and **58** with Eu(fod)$_3$ and the equilibrium constant K_3 was measured (Table 10), where K_3 can be related to the free-energy difference between the two complexes by

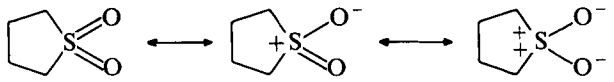
$$K_3 = e^{-\Delta G^\circ/RT} \tag{6}$$



It was assumed that the contact shift contribution dominates the observed ^{17}O shift increments so that increasing the Eu^{3+} concentration would result in increasing low-frequency shifts of the coordinated oxygen nuclei, and therefore serve as a probe to assess the steric inhibition to oxygen-to-metal binding. The equatorial oxygen nuclei show significantly greater shifts on addition of $Eu(fod)_3$ than the axial oxygen, in accord with the well-established observation that bulky groups favour equatorial positions. In this work a single-site coordination model was quite acceptable. These studies have been extended recently, accompanied by *ab initio* calculations.[73].

3. *Oxygen-17 NMR in equilibrium investigations*

Harris and coworkers[74] used a combination of ^{17}O and ^{33}S NMR to examine sulpholane in acetic acid and related solvents. The multinuclear NMR studies were used to probe specific interactions between the solvents and solute, such as hydrogen bonding and proton donation. The ^{17}O NMR linewidths and chemical shifts for both solvent and solute were measured for varying amounts of sulpholane in acetic acid, trifluoroacetic acid, methyl acetate and methyl trifluoroacetate. The solvent ^{17}O linewidths increased, for all solutions, with increasing sulpholane concentration as would be expected from viscosity considerations. The ^{17}O line-widths for sulpholane were, however, more revealing. There was a relatively small change for acetic acid (δ 100 $\pm$ 10 ppm at all concentrations), and with methyl esters as solvent the linewidths increased from about 50 Hz to 129 Hz as the concentration of sulpholane increased from 20 to 100% by volume. For sulpholane in trifluoroacetic acid there was a more dramatic change in the opposite direction as the ^{17}O linewidth was over 200 Hz for a 20% solution and which decreased to the value of 129 Hz for pure sulpholane. (The ^{33}S linewidths were even more diagnostic for specific interactions than the ^{17}O linewidths described in Section I.E.2). The ^{17}O NMR chemical shift titrations confirmed that there is a difference in the nature of the interaction between sulpholane and trifluoroacetic and the interaction between sulpholane and acetic acid. The ^{17}O NMR chemical shift of sulpholane increased from 158 ppm at 20% to the value of 167 ppm for pure sulpholane. For acetic acid as solvent there was only a small increase of about 2 ppm for the some concentration range. The results of these and other measurements including ^{33}S NMR was interpreted as being evidence for protonation, but only in the more strongly acidic trifluoroacetic acid. Protonation was said, in effect, to drive the structure of sulpholane towards the forms



(59a) (59b) (59c)

59b and **59c**, thereby removing charge from sulphur and transferring it to oxygen, in accord with the opposite signs of the slopes in the ^{17}O and ^{33}S titrations (see later). In a more general study Ilczyszyn[75] used ^{17}O NMR to investigate the nature of the interactions between *p*-toluenesulphonic acid and trifluoromethanesulphonic acid. For hydrogen-bonded systems AH---B the ^{17}O chemical shift induced by 1:1 complexation ($\Delta_{AHB} = \delta^{o}_{AHB} - \delta^{o}_{B}$) correlated with the H-bond chemical shift in a linear manner[76]. Δ_{AHB} decreased from -90 to -160 ppm when the interaction strength increased. For complete proton transfer in the presence of excess B to give BHB^+ species Δ_{BHB} was about -140 ppm.

Crumrine and Murray[77] used ^{17}O and ^{33}S to examine the aqueous solutions of methanesulphonic and trifluoromethane sulphonic acid and this is discussed in Section I.E.3.

D. Nitrogen NMR

The ^{14}N and ^{15}N NMR spectra of a number of sulphur amides has been reported in previous volumes[1-3]. Ruostesuo and coworkers carried out much of the original work and have recently extended the range of compounds studied[31] to include some *ortho*-nitro substituted aromatic sulphur amides. It was noted that the effect of an *ortho*-nitro substituent on the shielding of a ^{15}N nucleus was negligible in *N,N*-dimethyl substituted benzenesulphonamide and slight in *N*-unsubstituted benzenesulphonamide. The conclusion was reached that an *ortho*-nitro substituent therefore has almost no effect on the electron density of the nitrogen atom attached to the sulphur in a sulphonamide group.

E. Sulfur-33 NMR

1. Introduction

Despite the considerable disadvantages of ^{33}S as a nucleus for NMR investigations there is now a large body of information on the ^{33}S NMR of organosulphur compounds. For a review of the principles and practice of ^{33}S NMR the interested reader is referred to the comprehensive chapter by Hinton[7] in *Annual Reports on NMR Spectroscopy* where the literature is reviewed up to early 1987 and some 120 ^{33}S chemical shifts are tabulated (with some rather unusual features such as separate entries for sulphuryl chloride and SO_2Cl_2). For the purposes of this chapter some familiarity with ^{33}S NMR is assumed, and only recent papers are reviewed. Chemical shifts are given relative to SO_4^{2-}. Some authors use CS_2 as reference and these have been converted to the sulphate reference using δ -333 ppm as the chemical shift[78] for CS_2.

The remainder of this section is divided into two parts. The first part is concerned with chemical shift and quadrupolar coupling data and the second with sulphonic acids and related compounds as studied by ^{33}S NMR spectroscopy. These have been separated from the rest of the ^{33}S NMR discussion because they seem to form a self-contained set of investigations in which different aspects of ^{33}S NMR and sulphonic acid chemistry are brought together.

2. Chemical shift and quadrupolar coupling constant (QCC) determinations

The ^{17}O studies by Barbarella and coworkers[54,61] concerning substituent effects were accompanied by ^{33}S investigations. The ^{33}S chemical shifts and calculated atomic charges for some sulphones and sulphoxides are given in Table 11. The data in Tables 11 and 12 reveal that the ^{33}S chemical shifts are very sensitive to the substituent. The chemical shift difference between the sulphones and sulphoxides in Table 11 is remarkably small, considering the difference in oxidation states at the sulphur. Conversely, the difference between the ^{33}S chemical shifts of sulphinates and sulphonates as shown in Table 12 amounts to more than 200 ppm. It was said[54] that these differences were consistent with changes in nuclear screening being dominated by variations in the average excitation energy ΔE. For the compounds CH_3SO_2Y and $p\text{-}XC_6H_4SO_2Y$, contrary to that found for ^{17}O chemical shifts (See Section I.C.1), no real trends were found from a plot of $\delta^{33}S$ versus group electronegativity. All $\delta^{33}S$ were found in the region $\delta - 10 \pm 13$ ppm except for the iodides, which appear some 60 ppm to high frequency. It was suggested that this

TABLE 11. Sulphur-33 data for some sulphones and sulphoxides

compound	$\delta^{33}S$ (ppm)[a]	q_S[b]
(1) Sulphoxides		
CH_3SOCH_3	−8	307
$(CH_2)_3SO$	32	295
$(CH_2)_4SO$	27	291
$(CH_2)_5SO$	—	286
$(CH_2)_6SO$	—	
(2) Sulphones		
$CH_3SO_2CH_3$	−18	389
$(CH_2)_3SO_2$	−2	370
$(CH_2)_4SO_2$	35	376
$(CH_2)_5SO_2$	−12	374
$(CH_2)_6SO_2$	6	

[a] From Reference 62; Reference SO_4^{2-}; the original values are quoted relative to CS_2.
[b] Calculated atomic charge on sulphur (*ab initio* STO-3G*), in milli-electrons.

TABLE 12. Sulphur-33 data for some sulphinates and sulphonates

Compound	$\delta^{33}S$ (ppm)[a]	$\Delta\nu_{1/2}$ (Hz)
(1) Sulphinates		
$CH_3O—SO—Cl$	267	6500
$CH_3O—SO—OCH_3$	177	4000
$Cl—SO—Cl$	237	3500
$Br—SO—Br$	307	
(2) Sulphonates		
$CH_3O—SO_2—Cl$	−22	
$CH_3O—SO_2—OCH_3$	−14	
$Cl—SO_2—Cl$	−46	3500

[a] From Reference 54.

was not simply a 'heavy atom effect' as there was a linear relationship between the ^{33}S chemical shifts and electronegativity for Y = I, Br and Cl. The fluoro compound did not follow this relationship and a lack of conjugative ability was suggested, assuming that $n \rightarrow \sigma^*$ interactions dominate for Y = I, Br and Cl.

The ^{33}S chemical shift for the organic sulphate, dimethyl sulphate, has been reported[79] as being about −6 ppm.

Harris and coworkers[74] in the study of sulpholane in acetic and trifluoroacetic acids found that the linewidth of the ^{33}S resonance of sulpholane varied between about 200 Hz at a concentration of 20% by volume in trifluoroacetic acid to 21 Hz as a neat liquid at 40 °C. The linewidth of the ^{33}S resonance of sulpholane varied by only about 20 Hz in acetic acid, methyl acetate and methyl trifluoroacetate across the whole concentration range at 40 °C. The ^{33}S linewidth is a much more sensitive probe of the molecular structure than the ^{17}O linewidth in this particular example. The ^{17}O and ^{33}S linewidths for sulpholane were shown to be related at 40 °C by

$$\Delta\nu_{1/2}(^{17}O) = 105 + 0.64\Delta\nu_{1/2}(^{33}S) \quad (7)$$

As the sulpholane was diluted in trifluoroacetic acid, the ^{33}S nucleus was deshielded while the oxygen nucleus was shielded. This is consistent with the protonation of sulpholane removing electron density from the sulphur, with consequent electron transfer towards the oxygen nuclei.

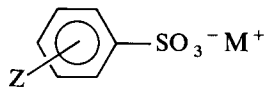
There have been two reports of the use of ^{33}S NMR in analytical chemistry, for which we have only had access to the abstracts: one is concerned with the ^{33}S NMR of petroleum sulphones[80] and the other appears to be a review[81].

The quadrupolar coupling constant (QCC) for the ^{33}S nucleus in dimethyl sulphone was measured as 8.5 MHz[66] and in the same study the QCC for the ^{33}S nucleus in carbon disulphide was found to be about 13.8 MHz. A value of 14.9 MHz has previously been reported[82].

3. *Sulphur-33 NMR of sulphonic acids*

The use of ^{33}S NMR to illuminate aspects of the chemistry of sulphonic acids has been the area of greatest activity since Hinton's review[7] was published. Of all the organosulphur compounds the sulphonic acids are perhaps the most suitable for ^{33}S NMR, since they are very strong acids that ionize fully in aqueous solutions (or their sodium, pottassium or ammonium salts are easily made) to give pyramidal ions with an approximately spherical electron distribution about the sulphur. This results in narrow linewidths which allow the ready determination of chemical shifts and linewidths.

In 1984 Hinton and Buster[83] reported that there was a linear relationship between the ^{33}S chemical shifts of some sulphonic acids anions **60** (Z = H, *p*-CH_3, *p*-Cl, *p*-NO_2) and the Hammett σ constants for the substituents. Crumrine and coworkers[84] in 1986 reported that there was a linear correlation between the ^{33}S chemical shifts of some sulphonic acid anions **60** (Z = H, *m*-CH_3, m-CF_3, *m*-NO_2, *p*-CH_3, *p*-NO_2) and their pK_a values. These were the starting points for the more recent investigations.



(60)

Crumrine and French[85] improved the correlation between ^{33}S chemical shifts and pK_a values in an extended study in which fifteen sulphonic acid anions were measured.

The pK_a values of some sulphonic acids that had been previously determined by UV techniques[86] were used as the basis for the calculations[85] and a linear regression analysis yielded the relationships.

$$pK_a = 0.130\delta^{33}S - 5.19 \quad \text{at } 20\,^\circ C \quad (r = 0.982) \tag{8}$$

$$pK_a = 0.130\delta^{33}S - 5.03 \quad \text{at } 39\,^\circ C \quad (r = 0.988) \tag{9}$$

These give the values for pK_a given in Table 13.

The Taft DSP plots (see Section I.B.1) for the fifteen compounds **60** using σ_I and σ_R gave excellent correlations ($r = 0.990$–0.994) with $\delta^{33}S$, as follows:

$$\delta^{33}S = -6.38\sigma_I - 6.69\sigma_R - 11.69 \quad \textit{meta} \text{ at } 20\,^\circ C \tag{10}$$

$$\delta^{33}S = -6.57\sigma_I - 5.32\sigma_R - 11.42 \quad \textit{para} \text{ at } 20\,^\circ C \tag{11}$$

$$\delta^{33}S = -6.31\sigma_I - 6.40\sigma_R - 11.99 \quad \textit{meta} \text{ at } 39\,^\circ C \tag{12}$$

$$\delta^{33}S = -6.10\sigma_I - 5.47\sigma_R - 11.81 \quad \textit{para} \text{ at } 39\,^\circ C \tag{13}$$

Sciacovelli and Musio[87] also examined a series **60** by ^{33}S NMR, and carried out a Taft[19] DSP analysis and obtained the relationship,

$$\delta^{33}S = -5.8\sigma_I - 3.19\sigma_R - 11.4 \quad \textit{para} \text{ at } 22\,^\circ C \tag{14}$$

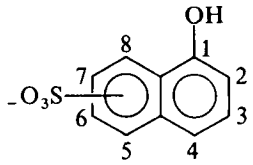
The chemical shifts and linewidths in the two studies showed very good agreement, and the correlation shown in equation 14 was said to be in reasonable agreement with those of Crumrine[85]. The ratio ρ_R/ρ_I of 0.55 supported the view that the inductive effect is more effective in transmitting substituent effects. Sciacovelli and Musio[87] also concluded on the basis of various correlations and calculations of the QCC values [0.4 for Cl to 1.6 for $N(CH_3)_2$] that resonance effects operate without direct conjugation between the aromatic ring and the sulphone group and that variations in the ^{33}S chemical shifts may be attributable to SO_3^- d–p π-polarization. Kosugi[88], on the other hand, attributed line broadening in some phenolate derivatives of sulphonic acid salts to a distortion of

TABLE 13. Sulphur-33 chemical shifts and linewidths for some sulphonic acid anions **60** and calculated pK_a values for the corresponding acids at 20 °C[a]

Z	$\delta^{33}S$ (ppm)	$\Delta\nu_{1/2}$ (Hz)	pK_a(UV)[b]	$pK_a(\delta^{33}S)$[c]
H	−11.3	8.8	−6.65 ± .05	−6.66
m-CH_3	−10.9	18.8	−6.56 ± .05	−6.61
m-SO_3^-	−13.9	21.5		−7.00
m-CF_3	−14.2	19.5		−7.04
m-NO_2	−15.9	49.0		−7.25
p-$N(CH_3)_2$	9.6	75.6		−6.43
p-NH_2	−9.8	51.5		−6.47
p-CH_3	−10.6	21.2	−6.62 ± .05	−6.57
p-NH_3^+	−14.2	18.1	−7.04 ± 0.5	−7.03
p-Br	−12.8	9.0	−6.86 ± .05	−6.86
p-Cl	−13.0	9.0		−6.88
p-$COCH_3$	−13.6	13.8		−6.96
p-SO_3^-	−13.8	18.8		−6.99
p-$NH(CH_3)_2^+$	−15.3	55.0		−7.18
p-NO_2	−15.7	58.8		−7.23

[a] From Reference 85; values at 39 °C are also given in paper.
[b] From Reference 86.
[c] ±0.04.

the sulphonate electron distribution by quinonoid structures. No signal could be observed for $p\text{-}^{-}OC_6H_4SO_3^{-}$ after accumulation for three days. A similar excessive line broadening was observed[89] in a series of naphthalenesulphonates, **61** and **62**.



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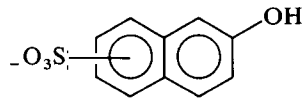


(62)

The ^{33}S NMR chemical shifts are given in Table 14 for some hydroxy compounds **61** and **62** together with their oxyanions. These figures seem to support Kosugi's[88] hypothesis as the most dramatic line broadenings occur when resonance interactions between the substituents are possible. Kosugi[90] has also examined some naphthalenesulphonic acids and claimed the first compression shift for ^{33}S NMR by measuring the chemical shift of the 1-substituted naphthalenesulphonic acid as $\delta - 15.21$ ppm, the 2-substituted analogue as $\delta - 11.65$ ppm and the 1,5-disubstituted as $\delta - 16.15$ ppm. *Peri* interactions between the 1-sulphonate group and 8-hydrogen atom were held responsible for the low-frequency shifts.

Crumrine and coworkers have used linewidth information to obtain relaxation parameters for sulphonic acid anions[91,92]. The first ^{33}S NMR relaxation study of an organic anion in aqueous and non-aqueous solutions was reported[91]. The data indicated

TABLE 14. ^{33}S NMR chemical shifts and linewidths of some hydroxy naphthalenes **61** and **62** together with the anions, measured at pH 12

Compound	Position of SO_3^-	$\delta^{33}S$ (ppm)[a]	$\Delta\nu_{1/2}$ (Hz)
61	2	−9.3	32
61	4	−13.5	65
		(−11.4)	(380)
61	5	−14	34
		(−12.7)	(33)
61	8	−10.4	30
		(−8.2)	(115)
61	3,6	−11.1	200
		(−11.4)	(200)
61	3,8	−13.1; −12.0	42; −100
		(−9.3; −9.3)	(250)
61	4,8	−14.2; −12.0	25; 150
		(−8.9; −6.2)	(170; 400)
62	1	−10.6	280
62	6	−11.5	7
		(−10.0)	(36)
62	7	−10.4	120
		(−8.0)	(v. broad)
62	6,8	−12.8; −16.5	26;40
		(−11.7; −15.3)	(6, 11 at 360 K)

[a] From Reference 89. At 298 K in 20% D_2O; values in parentheses refer to the oxy-anions.

that solvation of benzenesulphonate is similar in water and formamide, but different in *N*-methylformamide.

II. ELECTRON SPIN RESONANCE STUDIES

A. Introduction

Radicals derived from sulphur compounds have been extensively reviewed in recent years[93–95]. Among the radicals so reviewed are: $RSS^{\bullet}$[94], $RSO^{\bullet}$[94] and $RSO_2^{\bullet}$[93]; $[R^1SNR^{2\bullet}]$[94], $[R^1SONR^{2\bullet}]$[93] and $[R^1SO_2NR^{2\bullet}]$[95]; $[R^1SNR^2R^{3+\bullet}]$[93], $[R^1SO_2NR^{2\bullet}R^{3+\bullet}]$[95] and $[R^1SSR^{2+\bullet}]$[94]; and $[R^1SSR^{2-\bullet}]$[94], $[RSO_3H^{-\bullet}]$[95], $[R^1SO_2R^{2-\bullet}]$[95] and $[ArSO_2NMe_2^{-\bullet}]$[95]. Here, therefore, we set out to discuss the radicals not covered by the previous reviews, concentrating mainly on thiyl radicals and sulphide radical cations.

B. The Thiyl Radical, $RS^{\bullet}$

Thiyl radicals are formed by a variety of processes. Hydrogen atom abstraction from the parent thiol is the most direct method, and can be achieved by $HO^{\bullet}$ or $NH_3^{+\bullet}$ (equation 15). An important biological reaction related to this process is the formation of thiyl radicals from thiols by peroxidase enzymes. Alternatively, γ-radiolysis of the thiol will produce the thiyl radical. Photolysis or thermolysis of thioesters, such as thiocarboxylates, thiosulphinates, thionitrites or disulphides, results in the formation of a thiyl radical via homolytic cleavage of the S—X bond (equation 16).

$$R{-}SH \xrightarrow{OH^{\bullet}\text{ or }NH_3^{+\bullet}} R{-}S^{\bullet} \qquad (15)$$

$$RS{-}X \longrightarrow R{-}S^{\bullet} + X^{\bullet} \qquad (16)$$

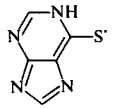
$$X = RCO,\ RSO,\ RS,\ NO$$

There have been many reported observations of the ESR spectra of thiyl radicals. Unfortunately, most of these have been incorrectly assigned[96]. Since the electron resides in a degenerate p_π orbital, the angular momentum must be quenched for an ESR spectrum to be observed. Such a situation may be obtained in the solid state, where hydrogen bonding can provide the required asymmetric environment. In solution, thiyl radicals have only been detected by the spin-trapping technique (see later).

Table 15 contains ESR data for selected thiyl radicals. The salient feature of these data is that thiyl radicals display an anisotropic **g**-tensor, the $g_\parallel$ component of which is large and consistent with the unpaired electron residing in a π orbital associated with the sulphur atom. The direction of this $g_\parallel$ component is along the C—S bond and its magnitude is very dependent upon the molecular environment, even varying within the same crystal. The isotropic g-value appears to lie within the range 2.05–2.09. Hyperfine coupling to the methylene protons is observed, and the occurrence of two separate couplings suggests that the radical adopts a preferred conformation. In the absence of an observable coupling in $CH_3S^{\bullet}$, the conformation remains unknown.

A radical with $g_1 = 2.214$, $g_2 = 2.0006$ and $g_3 = 1.990$ has been detected from the irradiation of *N*-acetylcysteine[101]. This was assigned to either $RCH_2SH^{-\bullet}$ or $RCH_2SH_2^{\bullet}$. The values are remarkably similar to those assigned to thiyl radicals, however, and are probably those of $(CH_3CONH)(HOOC)CHCH_2S^{\bullet}$. The interest in this species lies in the observation of nearly axially symmetric ^{33}S hyperfine coupling. The principal values of the ^{33}S coupling are 71G, 13.6G and 11.4G, which give rise to $a_{iso}(^{33}S) = 32G$ and $a_{aniso}(^{33}S) = 19.5$ G. These can be related to the values expected for coupling to an electron in sulphur 3s and 3p orbitals, which are 975G and 28G, respectively[102]. Thus, the

TABLE 15. ESR spectral data of selected thiyl radicals, RS·

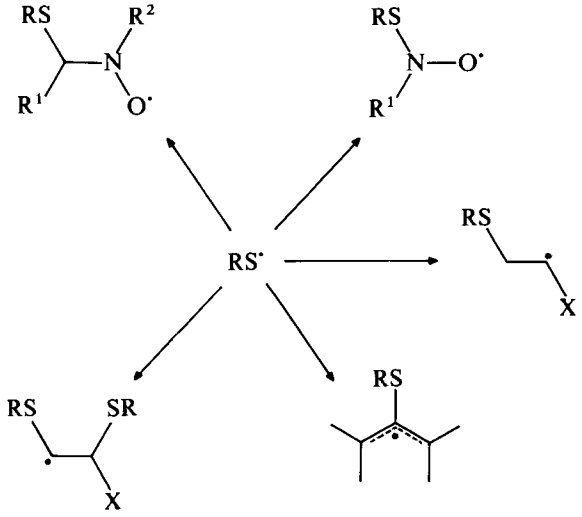
Radical	*g* value(s)	Hyperfine coupling constant (G) *a*(H)	Reference
$HO_2C(\overset{+}{N}H_3)CHCH_2S^{\cdot}$	2.29[a], 1.99[a], 1.99[a]	38(1H), 14(1H)	97
$HO_2C(\overset{+}{N}H_3)CHCMe_2S^{\cdot}$	2.297[a], 2.037[a], 1.921[a]		98
	2.158[b]		99
$H_2NCH_2CH_2S^{\cdot}$	2.23[a]	28(1H), 15(1H)	99
	2.158[b]		
$MeS^{\cdot}$	2.158[b]		99
$EtS^{\cdot}$	2.158[b]		99
$HO_2CCH_2S^{\cdot}$	2.158[b]		99
	2.173[a], 2.002[a], 1.989[a]	3.8(1H)	100

[a] Crystal.
[b] CD_3OD glass.

unpaired electron resides in a sulphur orbital that has a 3% contribution from the 3s orbital and 70% contribution from a 3p orbital. That is, the orbital containing the unpaired electron is essentially a p_π orbital.

In solution, thiyl radicals have been characterized by the spin-trapping method. Among the spin traps that have been used are nitrones[103–109], nitrosoarenes and 2-methyl-2-nitrosopropane[110–115], alkenes[116,117], alkynes[117,118], allenes[119] and thioketones[120] (Scheme 1). A report that *N*-nitrosamines are able to trap thiyl radicals[121] has been subsequently shown to be incorrect[122].

Table 16 contains selected spin-trapping data for a limited range of thiyl radicals. Of particular note is the magnitude of the nitrogen hyperfine coupling in nitroxyl radicals



SCHEME 1. Spin trapping of thiyl radicals

TABLE 16. ESR spectral parameters for some spin-trapped thiyl radicals

Radical	Spin trap[a]	g value	Hyperfine coupling (G) a(N)	a(H)	Reference
EtS$^{\bullet}$	DMPO	2.0066	15.3	17.1, 0.8(2H)	107, 109
	MNP		17.9		109
	MA	2.0032		19.9(1H), 8.2(1H)	117
	AA	2.0031		19.6(1H), 11.7(2H)	117
	PA	2.0048		16.6(1H), 8.4(1H)	117
	TBP	2.00321		2.86(2H, *ortho*), 1.20(2H, *meta*), 3.17(1H, *para*), 0.89(2H), 0.16(3H)	120
MeS$^{\bullet}$	TMA	2.0029		13.02(12H)	119
t-BuS$^{\bullet}$	DMPO		13.5	11.2	109
	MA	2.0032		19.9(1H), 7.2(1H)	117
	PA	2.0046		16.4(1H), 9.4(1H)	117
PhS$^{\bullet}$	PBN	2.0068	14.0	1.6(1H)	113
	MNP	2.0068	16.6		110, 111, 113, 114
	TBP	2.00304		2.81(2H, *ortho*), 1.17(2H, *meta*), 3.16(1H, *para*), 0.09(2H), 0.15(3H)	120
$H_2N(HO_2C)CHCH_2S^{\bullet}$	DMPO	2.0066	15.6	17.7	104, 107, 109
	BDA	2.0034		20.0(1H), 8.4(1H), 1.1(2H)	116
$CH_3CONH(HO_2C)CHCH_2S^{\bullet}$	DMPO		13.7	14.3	109

[a] DMPO = 5,5-dimethyl-1-pyrroline-*N*-oxide; MNP = 2-methyl-2-nitrosopropane: PBN = α-phenyl-*N*-*tert*-butylnitrone; MA = maleic acid; AA = acrylic acid; PA = propargyl alcohol; TMA = tetramethylallene; TBP = thiobenzophenone; BDA = 1,4-butenedioic diacid.

formed from 2-methyl-2-nitrosopropane (MNP). Such coupling is *ca* 17 G, whereas the corresponding coupling in analogous sulphonyl ($RSO_2^{\bullet}$) trapped radicals is *ca* 13G[93]. Sulphinyl radicals ($RSO^{\bullet}$) are not trapped by MNP. Thus MNP is able to distinguish between these three related radicals.

Both MNP and DMPO react with thiyl radicals with second-order rate constants in the region of $10^8\,dm^3\,mol^{-1}\,s^{-1}$ [107,110]. However, DMPO has been reported to give radicals whose signals are some one-hundred times more intense than those from MNP[110]. This is mostly due to the relative stabilities of the nitroxyl radicals so formed.

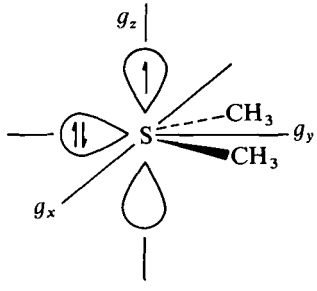
C. The Sulfide Radical Cation, $R^1R^2S^{+\bullet}$, and Sulphide Dimer Radical Cation, $[R^1R^2SSR^1R^2]^{+\bullet}$

Sulphide radical cations are formed most satisfactorily by γ- or X-irradiation of frozen solutions in freon solvents. Under most other conditions, e.g. the oxidation of the sulphides by $OH^{\bullet}$ or $NH_4^{+\bullet}$ or by $S_2O_8^{2-}/h\nu$ in solution, the radical cations so formed dimerise by reacting with a neutral substrate molecule (equation 17). Even in the solid state, irradiation of a sulphide leads to the formation of a sulphide dimer radical cation[129].

$$R_2S^{+\bullet} + R_2S \longrightarrow R_2SSR_2^{+\bullet} \tag{17}$$

Exceptions to this general observation are the electrochemical generation of the radical cation of di-*t*-butyl sulphide[126], the oxidation of vinyl sulphides by $OH^{\bullet}$ or $Cl^{-\bullet}$ [131] and the oxidation of certain cyclic dithianes using $AlCl_3$ in CH_2Cl_2 [133]. More recently, sulphide radical cations have been observed in aromatic solvents[135]. It is believed that the sulphide radical cations are stabilized by formation of a complex with the solvent in which the solvent behaves as a π-electron donor.

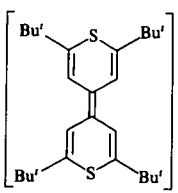
Table 17 contains the ESR spectral data for selected sulphide and sulphide dimer radical cations. Whereas the **g** tensor of the dimethyl sulphide cation radical is strongly anisotropic, that of the corresponding dimer cation radical is isotropic[136]. The two types of radical cation can further be distinguished by the differing magnitudes of the proton hyperfine couplings; coupling to the α-CH protons in the sulphide radical cations lies in the range 20–40 G, whereas coupling to these protons in the sulphide dimer radical cations is < 10 G (Table 17). The components of the **g** tensor for $Me_2S^{+\bullet}$ can be calculated from those of the corresponding $Me_2O^{+\bullet}$ [137] using equation 18, where g_S and g_O are the g values for the sulphur- and oxygen-derived radicals, respectively, g_e is the g value for the electron, and λ_S and λ_O are the spin–orbit couplings for sulphur and oxygen[138]. Table 18 compares the calculated and experimental values, and the remarkable agreement between the two is powerful evidence that the sulphide and ether radical cations have the same structure. This structure is a heteroatom centred radical, **63**, in which the



(63)

TABLE 17. ESR spectral data for selected sulphide and sulphide dimer radical cations

Sulphide radical cation	g value(s)[a]	Hyperfine coupling (G) a(H)	a(other)	Reference	Sulphide dimer radical cation	g values	Hyperfine coupling (G) a(H)	a(other)	Reference
$Me_2S^{+\cdot}$	2.032, 2.017, 2.002 (g_{iso} = 2.017)	20.4(6H)		123	$Me_2SSMe_2^{+\cdot}$	2.0103	6.8(12H)		124
$\overline{CH_2(CH_2)_3S^{+\cdot}}$	2.027, 2.014, 2.002 (g_{iso} = 2.014)	40(2H), 20(H)		125	$\overline{CH_2(CH_2)_3SS(CH_2)_3CH_2}^{+\cdot}$	2.0102	9.3(8H)		124
$Bu^t_2S^{+\cdot}$	2.032, 2.015, 2.005 (g_{iso} = 2.016)		32.5 (^{33}S)	125, 126	$Bu^tPr^iSSPr^iBu^{t+\cdot}$	2.0122	6.0(2H)	31.2(^{33}S)	126
$\overline{CH_2CH_2S^{+\cdot}}$	2.024, 2.024, 2.002 (g_{iso} = 2.017)	31(4H)		125					
$(4\text{-}HOC_6H_4)_2S^{+\cdot}$	2.00687	1.61(4H, *ortho*) 0.12(4H, *meta*) 1.02(2H, O*H*)		127					

$\overline{CH_2SCH_2SCH_2}^{+\cdot}$	2.0080	ca 6(4 or 6H)	125
$Me(Me_3SiCH_2)S^{+\cdot}$	2.0145	15(3H), 12.5(2H)	130
$(CH_2{=}CH)EtS^{+\cdot}$	2.0026	20.5(1H), 32.75(1H) 39.75(1H)	131 131
	2.009	0.532(4H)	134
$\overline{CH_2SCH_2CH_2SCH_2}^{+\cdot}$	2.019, 2.002	*ca* 4.4	125
$\overline{CH{=}CHSCH{=}CHS}^{+\cdot}$	2.0089	2.84(4H)	132
$\overline{CH_2SCH{=}CHSCH_2}^{+\cdot}$	2.0092	8.15(2H), 3.4(2H), 2.7(2H)	133
$\overline{CH_2CH_2SCH_2CH_2CH_2SCH_2}^{+\cdot}$	2.012	15.2(2H), 10.4(2H)	128
$\{[CH_3CONHCH(CO_2H)CH_2CH_2]MeS\}_2^{+\cdot}$	2.023, 2.013, 2.004	*ca* 6.5	129

[a] $g_{iso} = (g_1 + g_2 + g_3)/3$.

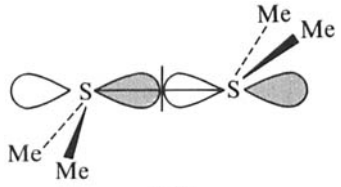
TABLE 18. Comparison of the experimental and calculated g values for $Me_2S^{+\cdot}$

Radical	g_x	g_y	g_z	g_{iso}
$Me_2O^{+\cdot}$	2.0138	2.0072	2.0045	2.0085
$Me_2S^{+\cdot}$ (calc)	2.031	2.015	2.008	2.018
$Me_2S^{+\cdot}$ (expt)	2.033	2.016	2.001	2.017

unpaired electron resides in a p_π orbital that is orthogonal to the C—S—C plane. Consistent with this formulation is the $a(^{33}S)$ hyperfine coupling for $Bu^t{}_2S^{+\cdot}$, 32.5 G, which corresponds to only a 3% population of the sulphur 3s orbital[126].

$$g_S = g_e + (g_O - g_e)\,\lambda_S/\lambda_O \tag{18}$$

Ab initio molecular orbital calculations using STO 3G[138] and 3-21G*[136] basis sets predict the structure of the radical cation to be almost identical with that of the neutral sulphide, except that the C—S—C bond angle in the radical cation is somewhat larger (102–103°) than in the sulphide (99.5°). The spin density at the sulphur atom is calculated to be 0.944, but the proton hyperfine coupling is a factor of 3 smaller than the experimentally observed value[136]. Nonetheless, the MO calculations correctly predict the relative magnitudes of the proton hyperfine couplings for the sulphide radical cation and sulphide dimer radical cation; experimentally the ratio is *ca* 3, computationally the ratio is 2.5[136]. The smaller hyperfine coupling in the sulphide dimer radical cations is attributed to the interaction of the methyl group orbitals with a molecular orbital that is σ^* antibonding[139]. The dimethyl sulphide dimer radical cation has been calculated to have the structure **64**.



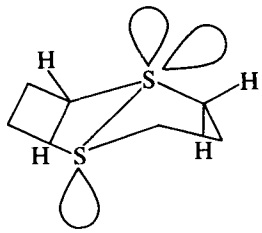
(64)

The direction of the SOMO is aligned with the S—S bond (which has a distance of 279.1 pm[136]) and inclined at an angle of *ca* 100° to the C—S—C, which compares to a value of 90° for the p_π orbital in the sulphide radical cation.

Radical cations of cyclic monosulphides have spectral characteristics similar to their acyclic counterparts. Cyclic disulphides, however, may be expected to display transannular interactions. The radical cation of 1,4-dithiacyclohexane exhibits small proton hyperfine coupling (Table 17), consistent with the structure **65** (an analogous structure has been proposed for dioxan[137]). In contrast, the radical cation of 1,5-dithiacyclooctane is believed to have structure **66** on the basis that there are only two triplet proton hyperfine couplings[128]. In structure **66** the two sulphur atoms are non-equivalent, the unpaired electron being associated with a trigonal bipyramidal sulphur atom. Unsaturated cyclic disulphide radical cations, such as those derived from 1,4-dithiin and 2,3-dihydro-1,4-dithiin, behave as π-delocalized systems.

Cyclic 1,3-disulphides (cyclic thioacetals) generate radical cations that are consistent with a transannular interaction, such as that shown in **65**, to form σ^* species. This is in contradistinction to the oxygen analogues, which form a radical cation that has a delocalized π structure[137].

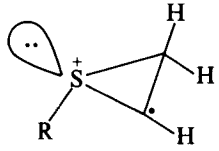
(65)



(66)

Radical cations of diaryl sulphides exhibit lower g values than their dialkyl counterparts, as expected if spin density is transferred onto the aryl ring. Hyperfine coupling to the ring protons is observed, and the magnitude follows the order *ortho*-H > *meta*-H, which is that for a π-radical. Hückel MO calculations satisfactorily reproduce the observed hyperfine couplings and identify each aryl ring as having *ca* 0.3 of the unpaired spin density, the remainder, *ca* 0.37, being associated with the sulphur atom[140]. Conducting solutions of poly(*para*-phenylene sulphide) exhibit a quintet in their ESR spectra with a hyperfine coupling, a(H), of 1.2 G[141]. This is quite consistent with a radical cation in which there is coupling to the four *ortho* protons of the aryl rings. However, on the basis of INDO calculations, the authors favour a radical in which the spin density at sulphur is 0.74 (being shared equally between the $3p_y$ and $3p_z$ orbitals) and in which the largest hyperfine coupling is to the *meta* protons of the ring[141]. These two descriptions of diaryl sulphide radical cations are mutually incompatible and should be resolved.

The radical cation of alkyl vinyl sulphides appears to have the cyclic structure **67** rather than the open-chain form **68**[131]. The evidence for this lies with the magnitude of the g-value, which is that expected for a carbon-centred radical, and the observation of three separate proton hyperfine couplings. Such a structure is in marked contrast to the oxygen analogues[137], which exist in the open-chain form. Presumably, the greater nucleophilicity of sulphur and its ability to stabilize a positive charge enables it to exert a powerful neighbouring group effect in such radical cations.



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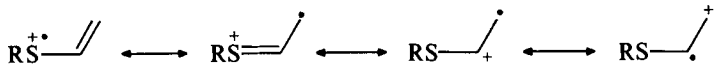


(68)

D. The Sulphide Radical Anion, $R_2S^{-\cdot}$

The radical anion of simple sulphides is unknown. Unlike disulphides, which have low-lying σ^* orbitals that can accept the extra electron, sulphides do not have readily

TABLE 19. ESR spectral for some nitro substituted sulphide radical anions

Radical	g value	Hyperfine coupling constant (G) a(N)	a(H)	Reference
$(2\text{-}NO_2C_6H_4)_2S^{-\cdot}$		5.8(2N)	1.74(4H; *H3*, *H5*), *H*$_3'$, *H5'*)	142
$(4\text{-}NO_2C_6H_4)_2S^{-\cdot}$		8.8(1N)	3.32(2H; *H3*, *H5*) 0.99(2H; *H2*, *H6*)	143
$(PhCH_2)(4\text{-}NO_2C_6H_4)S^{-\cdot}$	2.00487	9.06	3.50(2H; *H2*, *H6*) 1.06(2H; *H3*, *H5*)	144
$(Ph)(4\text{-}NO_2C_6H_4CH_2)S^{-\cdot}$		12.6	3.48(2*H*; *H3*, *H5*) 2.25(2H; *H2*, *H4*) 0.9(2H)	145
$(Me)(4\text{-}NO_2C_6H_4CH_2)S^{-\cdot}$		12.5	3.5(2H; *H3*, *H5*) 2.2(2H; *H2*, *H4*) 1.0(2H)	145
$(2\text{-}C_4H_3N_2)(Me_2NO_2C)S^{-\cdot}$		25.2 ($A_{\parallel}$43.5 $A_{\perp}$16.0)		146

available empty orbitals. However, sulphides that contain nitro groups do form radical anions, and ESR spectroscopic data for some of these is contained in Table 19. For nitroaryl sulphides the unpaired spin density is clearly associated with the nitroaryl ring, and the isotropic nitrogen hyperfine coupling implies that the nitrogen 2s orbital contributes only *ca* 2% to the molecular orbital containing the electron. Thus, the electron resides in a π^* molecular orbital in which the nitro group is essentially planar. Interestingly, the ESR spectrum of the radical anion of di(2-nitrophenyl) sulphide demonstrates that the unpaired spin density is delocalized over both aryl rings, whereas that of di(4-nitrophenyl) sulphide shows the unpaired spin density to be localized in one ring only. It is thought that delocalization occurs *via* electron transfer between the nitro groups, rather than through the sulphur atom, and that the difference in the behaviour of these two sulphides is determined by the different distances between the two nitro groups[142].

E. The Sulphinyl, RSO$^{\cdot}$, Sulphonyl, $RSO_2^{\cdot}$, Thiolperoxyl, RSOO$^{\cdot}$, Sulphinylperoxyl, RSOOO$^{\cdot}$, and Sulphonylperoxyl, $RSO_2OO^{\cdot}$, Radicals

Due to their ability to readily donate a hydrogen atom, thiols possess an important radioprotective property (equation 19).

$$R^{\cdot} + RSH \longrightarrow RH + RS^{\cdot} \qquad (19)$$

However, the thiyl radicals so produced may react with oxygen to generate a variety of sulphoxyl radicals*. In recent years Sevilla and coworkers, using the ^{17}O labelling technique, have identified many of the radicals involved[147,149–152]. Reaction of cysteine or glutathione thiyl radicals with oxygen yields the thiol peroxyl radical **69** (equation 20), which absorbs in the visible spectrum at λ_{max} 540 nm. Upon exposure to visible light the thiol peroxyl radical rearranges to the isomeric sulphonyl radical **70** (equation 21).

* Sulphoxyl is the name used here for radicals derived from functional groups containing sulphur and oxygen.

Further reaction of the sulphonyl radical with oxygen produces the sulphonyl peroxyl radical **71** (equation 22), which ultimately forms the sulphinyl radical **72** upon reaction with the parent thiol (equation 23).

$$RS^{\bullet} + O_2 \longrightarrow \underset{\textbf{(69)}}{RS{-}O{-}O^{\bullet}} \tag{20}$$

$$RS{-}O{-}O^{\bullet} \longrightarrow \underset{\textbf{(70)}}{RS(=O)(=O)^{\bullet}} \tag{21}$$

$$RS(=O)(=O)^{\bullet} + O_2 \longrightarrow \underset{\textbf{(71)}}{RS(=O)_2{-}O{-}O^{\bullet}} \tag{22}$$

$$RS(=O)_2{-}O{-}O^{\bullet} \xrightarrow{RSH} RS^{\bullet} \xrightarrow{O_2} RS{-}O{-}O^{\bullet} \xrightarrow{RSH} \underset{\textbf{(72)}}{RSO^{\bullet}} \tag{23}$$

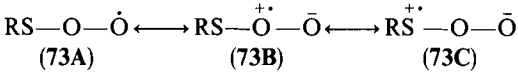
ESR spectral data for the radicals **69**–**72** are contained in Table 20. The sulphinyl (**72**) and sulphonyl (**70**) radicals are well known and have been documented in more detail elsewhere[93,94], whereas the thiyl peroxyl and sulphonyl peroxyl radicals have not been previously recorded. All four radicals can be readily distinguished and identified: the sulphinyl and sulphonyl radicals have different g_{iso} values; the thiol peroxyl and sulphonyl peroxyl radicals both exhibit two hyperfine couplings to oxygen atoms in the ^{17}O-labelled

TABLE 20. ESR spectral data for RSO$^{\bullet}$, RSOO$^{\bullet}$, $RSO_2^{\bullet}$ and $RSO_2OO^{\bullet}$ radicals

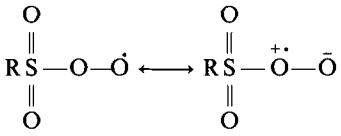
Radicals	g values				Hyperfine coupling/G		Reference
	g_x	g_y	g_z	g_{iso}	$a(^{17}O)^b$	a(H)	
Cys SO$^{\bullet}$	2.021	2.0094	2.0025	2.0109	56	16(1H)	148, 94
GSO$^{\bullet}$	2.021	2.0096	2.0025	2.0110	58	15(1H)	147, 94
Cys SOO$^{\bullet}$	2.035	2.008	2.002	2.015	81[c], 64[d]		147, 148
GSOO$^{\bullet}$	2.035	2.009	2.002	2.015	78[c], 63[d]		147
Cys $SO_2^{\bullet}$				2.0055	58	2.1(1H)	147, 93
$GSO_2^{\bullet}$				2.0056	58		147
Cys $SO_2OO^{\bullet}$	2.038	2.008	2.002	2.016	106[c], 44.6[d]		147
$GSO_2OO^{\bullet}$	2.039	2.007	2.002	2.016	105[c], 46[d]		147

[a] Cys = $HO_2CCH(NH_2)CH_2$—, G = $(HO_2C(NH_2)CHCH_2CONH)(HO_2CCH_2NHCO)CHCH_2$—.
[b] Parallel components only.
[c] Terminal oxygen atom.
[d] Inner oxygen atom.

species and the magnitudes of these hyperfine couplings are markedly different for the two radicals. The g values and $a(^{17}O)$ hyperfine coupling constants for the two peroxyl radicals are similar to those observed for analogous alkyl peroxyl radicals[137]. Indeed, for alkyl peroxyl radicals the sum of the parallel components of the ^{17}O hyperfine couplings to the two oxygen atoms lies in the range 152–156 G[137]; the corresponding values for thiol peroxyls and sulphonyl peroxyls are 141–145 G and 151 G, respectively. The sulphonyl peroxyl thus behaves like a normal peroxyl radical, whereas the thiol peroxyl appears to have a reduced spin density associated with the two oxygen atoms. An estimate for the extent of this reduction can be obtained if it is assumed that a sum total of 155 G for the hyperfine coupling of the two oxygen atoms in peroxyls is associated with unit spin density[137]. For thiol peroxyls, therefore, 92% of the spin density is associated with the two oxygen atoms, which would imply that the remaining 8% is associated with the sulphur atom. If this were so, however, thiol peroxyls would be expected to have a larger g value than sulphonyl peroxyls; Table 20 shows that they don't. The differences between the two types of peroxyls radical can be readily understood by considering the structure of the contributing resonance canonicals **73 A–C** and **74 A,B**.



(73A) **(73B)** **(73C)**



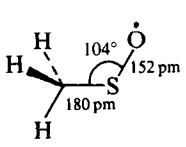
(74A) **(74B)**

For peroxyls in general the major contributors to the structure are **73A/74A** and **73B/74B**, the exact contribution of each depending mainly upon the electron-withdrawing ability of the group attached to the inner oxygen atom. For the sulphonyl peroxyl radical it is clear that the powerful electron-withdrawing effect of the sulphonyl group reduces the contribution of structure **74B** (of course, for this radical no structure corresponding to **73C** is possible) which results in the majority, *ca* 70%, of the spin density residing on the terminal oxygen atom, as seen experimentally (Table 20). Indeed, the ^{17}O hyperfine coupling for the terminal oxygen atom in the sulphonyl peroxyl radical is precisely that expected from the correlation expressed by equation 24[237] if one uses the value of 3.68 for the Taft σ^* parameter for the $MeSO_2$ group[153].

$$a_{\|}(^{17}O_{term}) = 94.1 + 3.3\sigma^* \tag{24}$$

For the thiol peroxyl radicals, the RS group is much less electron-withdrawing than the RSO_2 group and resonance structure **73B** would be expected to make a much greater contribution to the overall structure. This will result in an increase of the ^{17}O hyperfine coupling for the inner oxygen atom, and a corresponding reduction for the terminal oxygen atom. Experimentally, the spin density at the terminal oxygen atom is *ca* 51% and at the inner oxygen atom *ca* 41%. However, even if the small amount of spin density at the sulphur atom is taken into account, the ^{17}O hyperfine coupling for the terminal oxygen atom is much smaller than that expected, 99 G, from equation 24 using a σ^* value of 1.56 for the MeS group[153]. Clearly, transfer of spin density from the terminal oxygen atom in thiol peroxyl radicals depends on factors other than the electron-withdrawing ability of the group bonded to the inner oxygen atom.

Ab initio calculations have been performed for $MeSO^{\cdot}$, $MeSO_2^{\cdot}$, $MeSOO^{\cdot}$ and $MeSO_2OO^{\cdot}$[147,152]. The optimized structures of the four radicals are **75–78**.



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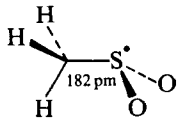

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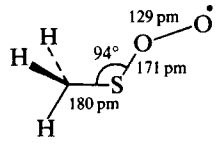

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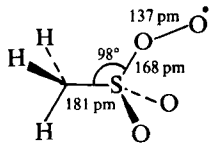
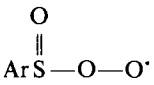


(78)

The hyperfine coupling constants obtained from these calculations are compared with the experimental values in Table 21. For $MeSO^{\cdot}$ the *ab initio* results correctly predict a π radical, although they underestimate the coupling to ^{33}S and overestimate the coupling to ^{17}O. This is a function of the calculated spin densities at oxygen and sulphur (Table 22). Significantly, using new values for the anisotropic coupling to sulphur ($2B = 71.74$ G) and oxygen ($2B = 120.2$ G), as well as allowing for nuclear screening, the total spin density at the sulphur and oxygen atoms determined from the experimental hyperfine couplings is 1.00[152]. This is a marked improvement on previous values[94], which for $MeSO^{\cdot}$ had 92% of the spin density at sulphur and for $SO_2^{-\cdot}$ had a total spin density of 1.16. For $MeSOO^{\cdot}$ the calculations predict a very small spin density on sulphur (much less than the 8% estimated above). The calculated oxygen hyperfine couplings appear also to underestimate the coupling to the inner oxygen atom. The calculations for $MeSO_2^{\cdot}$ correctly predict *ca* 10% of the spin density in the sulphur 3s orbital, as has been determined experimentally[93], but still underestimate the total spin density associated with the sulphur atom. For $MeSO_2OO^{\cdot}$ the calculations imply that the spin is entirely localized on the terminal oxygen atom, which is clearly not the case experimentally.

As well as being observed directly, the sulphonyl peroxyl radical has been investigated using spin-trapping techniques. Reaction of superoxide ion with a sulphonyl cloride generates the sulphonyl peroxyl radical (equation 25) that can be spin-trapped using DMPO[154]. The spectral characteristics of the spin-trapped radical, a(N) 12.8 G and a(H) 10.1 G, are consistent with the trapping of a peroxyl radical[137]. Similar reaction of superoxide ion with a sulphinyl radical generates the sulphinyl peroxyl radical, $RSOO^{\cdot}$ (**79**), which can also be spin-trapped with DMPO to give an adduct that has a(N) 12.8 G and a(H) 10.1 G.

$$ArSO_2{-}Cl + O_2^{-\cdot} \longrightarrow ArSO_2 - O{-}O^{\cdot} \qquad (25)$$



(79)

F. The Thioaminyl Radical, $[R^1SNR^2]^{\cdot}$

Thioaminyl radicals have been discussed in detail elesewhere[94]. Two recent reports have described the formation and ESR spectra of some exceptionally long-lived thioaminyl radicals[155,156], interest in these materials being derived from the search for organic ferromagnets. Oxidation, using PbO_2, of *N*-(2,4,6-triphenyl)phenyl-*S*-

TABLE 21. Comparison of calculated and experimental hyperfine coupling constants for MeSO$^{\cdot}$, MeSOO$^{\cdot}$, $MeSO_2^{\cdot}$ and $MeSO_2OO^{\cdot}$

Radical		Hyperfine coupling (G)					
		$a(^{33}S)$	$a(^{17}O)$			$a(^{13}C)$	$a(^{1}H)$
MeSO$^{\cdot}$[a]	$a_{\parallel}$	29.7(59)	−66.1(56)			0.13	2.0 2.0 1.98
	a_{iso}	12.0(8)	−36.3(−16)			−6.8	10.7(17), 10.7(17), −0.8(0)
	$2B$	17.7(51)	33.1(40)				
MeSOO$^{\cdot}$[b]	$a_{\parallel}$	−1.9	−89.9(81)[e],	−26(64)[f]			
	a_{iso}	−1.2	−41.5,	−19.2		−0.7	−0.2, −0.2, −1.2
	$2B$	1.0	−45	13			
$MeSO_2^{\cdot}$[c]	$a_{\parallel}$	89.5(90.1)	−50(−58),	−50(−58)		40	10.5, −2.5, −2.5
	a_{iso}	59.5(71.5)	−15,	−15		32.5	8.1, −3.0, −3.0
	$2B$	15(9.3)	−17.5	−17.5		3.75	1.2, 1.75, 1.75
$MeSO_2OO^{\cdot}$[d]	$a_{\parallel}$	−0.2	0.1[g], −0.2[g],				
	a_{iso}	−0.5	0.3, 0.3	−27(−45)[f],	−119(−105)[f]	0.1	0.4, 1.5, 2.8
	$2B$	0.35		−11.2	−35.9	−0.3	−0.5, 0, 0
				−7.8	−83.5	0.4	0.45, 0.75, 1.4

[a] Calculations at 6-31HG(3d) level, from Reference 152. Experimental values from References 152 and 94.
[b] Calculations at 6-31G(d) level, from Reference 152. Experimental values from Reference 147.
[c] Calculations at 6-31G* level, from Reference 147, Experimental values from References 147 and 93.
[d] Calculations at 3-21G* level, from Reference 146 Experimental values from reference 147.
[e] Terminal oxygen atom.
[f] Inner oxygen atom.
[g] Sulphonyl oxygen atoms.

TABLE 22. Spin densities in $MeSO^{\bullet}$, $MeSO_2^{\bullet}$, $MeSOO^{\bullet}$ and $MeSO_2OO^{\bullet}$

Radical	Spin density		Reference
	S	O	
$MeSO^{\bullet}$ (expt.)	0.59	0.41	152
(calc.)	0.44	0.58	152
$MeSO_2^{\bullet}$ (expt.)	0.07[a], 0.55[b]		93
(calc.)	0.15[a], 0.17[b]	0.27, 0.27	147
$MeSOO^{\bullet}$ (calc.)	0.01	0.15[c], 0.84[d]	152
$MeSO_2OO^{\bullet}$ (calc.)	0.005	0.005, 0.01, 0.02[c], 1.01[d]	147

[a] Spin density in sulphur 3s orbital.
[b] Spin density in sulphur 3p orbital.
[c] Inner oxygen atom.
[d] Terminal oxygen atom.

TABLE 23. ESR Spectral data for some thioaminyl radicals[155]

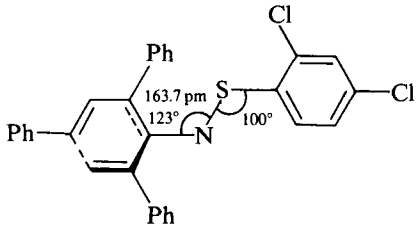
Radical	g value	Hyperfine coupling (G)			
		a(N)	$a(^{33}S)$	$a(^{13}C)$	a(H)
4-MeC_6H_4SN(2,4,6-$Ph_3C_6H_2$)$^{\bullet}$	2.0058	8.90	8.90	8.90	8.90
4-ClC_6H_4SN(2,4,6-$Ph_3C_6H_2$)$^{\bullet}$	2.0057	8.95			
4-BrC_6H_4SN(2,4,6-$Ph_3C_6H_2$)$^{\bullet}$	2.0059	8.94			
4-BrC_6H_4SN(2,4,6-d_{15}-$Ph_3C_6H_2$)$^{\bullet}$	2.0059	8.94			1.33(2H)[a], 0.88(2H)[b]
4-BrC_6D_4SN(2,4,6-$Ph_3C_6H_2$)$^{\bullet}$	2.0059	8.90			
4-BrC_6D_4SN(2,4,6-d_{15}-$Ph_3C_6H_2$)$^{\bullet}$	2.0059	8.94	5.1	10.2	1.34(2H)[a]
2,4-$Cl_2C_6H_3SN$(2,4,6-$Ph_3C_6H_2$)$^{\bullet}$	2.0055	8.95			
3,5-$Cl_2C_6H_3SN$(2,4,6-$Ph_3C_6H_2$)$^{\bullet}$	2.0054	8.91			
3-$NO_2C_6H_4SN$(2,4,6-$Ph_3C_6H_2$)$^{\bullet}$	2.0055	8.96			
4-$NO_2C_6H_4SN$(2,4,6-$Ph_3C_6H_2$)$^{\bullet}$	2.0054	8.90			

[a] *meta* protons of N-aryl group.
[b] *ortho* protons of S-aryl group.

arenesulphenamides **80** generates the corresponding thioaminyl radical **81** (equation 26), the ESR spectral characteristics of which are contained in Table 23.

$$\underset{\textbf{(80)}}{ArS{-}NHAr} \xrightarrow{PbO_2/K_2CO_3} \underset{\textbf{(81)}}{ArS{-}\dot{N}Ar} \qquad (26)$$

These data are entirely consistent with those previously reported[94], and are associated with a π radical in which the majority of the spin density resides on the sulphur and nitrogen atoms (0.22 and 0.44, respectively) but which is also delocalized over the S and N rings. The isolation of the radical **82** allows comparison of the structure deduced by ESR spectroscopy with that determined by X-ray crystallography. The S-aryl ring and the S and N atoms are coplanar, and the N-aryl ring is twisted some 18° out of this plane. This twist angle is much less than the 90° found for an *N*-(2,4,6-tri-*t*-butyl) analogue[94]. The three substituent phenyl groups are all twisted out of the N-aryl ring plane, the two *ortho* rings by 49° and 87° and the *para* ring by 27°. Thus, it is to be expected from



(82)

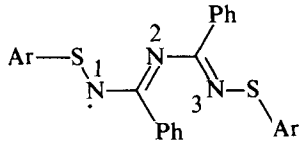
such a structure that spin density will be delocalized over the S and N atoms as well as the S-aryl and N-aryl rings.

The radical **83**, obtained by the photolysis or the PbO_2 oxidation of the parent *N*—H compound, displays ESR spectral characteristics that are consistent with the spin density being delocalized over the whole system (except the C-aryl groups)[156]. Thus, the *g* value is 2.0075, and hyperfine coupling to N^1 and N^3 is 4 G whereas coupling to N^2 is 2.8 G. Moreover, hyperfine coupling to both sulphur atoms (4.8 G) and coupling to the *ortho* and *meta* protons of the S-aryl ring (0.73 G and 0.22 G, respectively) are observed. Using equations 27 and 28 the spin densities at the nitrogen and sulphur atoms can be determined from the experimental hyperfine coupling constants.

$$a(^{33}S) = 23\rho_S^{\pi} \tag{27}$$

$$a(^{14}N) = 22\rho_N^{\pi} \tag{28}$$

These reveal that there is 0.186 spin density at each of the N^1 and N^3 atoms, 0.13 at the N^2 atom and 0.21 at each of the S atoms. Most of the spin density therefore resides on these five atoms.



(83)

The radical **83** dimerises at low temperatures *via* coupling between the two N^1 atoms.

G. Radical Cations and Anions of Sulphoxides, Sulphones and Related Compounds

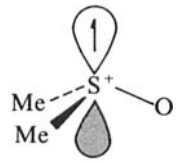
The radical cation of dimethyl sulphoxide, $Me_2SO^{+\cdot}$, generated by irradiating the parent compound in $CFCl_3$, displays a small hyperfine coupling to the six methyl protons and a large hyperfine coupling to ^{33}S[157] (Table 24). The coupling to the ^{33}S nucleus exhibits an isotropic value of 62 G and an anisotropic value for *2B* of 24 G. These correspond to 6.4% of the spin density residing in the sulphur 3s orbital, and 33.5% residing in a sulphur 3p orbital. Thus, 40% of the unpaired spin density resides at the sulphur atom, the remainder being associated with the oxygen atom. The sulphur orbital containing the unpaired electron has considerable s character, and the radical is pyramidal at sulphur (**84**).

The radical cation of $(MeO)_2SO$ also would be expected, like the parent $SO_3^{-\cdot}$ to be pyramidal. In the absence of observable coupling to ^{33}S, the structure of $(MeO)_2SO^{+\cdot}$

TABLE 24. ESR spectral parameters for radical cations and anions of sulphoxides, sulphones and related compounds

Radical	g value	Hyperfine coupling (G)			Reference
		a(H)	$a(^{33}S)$	$a(^{14}N)$	
$Me_2SO^{+\cdot}$	2.0122 2.0079 2.0020	5(6H)			157, 158
$(CD_3)_2SO^{+\cdot}$	*ca* 2.007	*ca* 2.0	50, 50 86		157, 159
$(CD_3)_2SO^{-\cdot}$[a]		2.97	*ca* 13		159
$Me_2SO_2^{-\cdot}$[a]	2.016 2.011 2.003	*ca* 3	143 122 122		159
$(CD_3)_2SO_2^{-\cdot}$		20.8(D)	*ca* 22		159
$CH_2CH_2CH_2CH_2SO^{+\cdot}$	2.010	23(2H)			157
$4\text{-}NO_2C_6H_4SO_2Me^{-\cdot}$		3.13(2H, *3* and 5*H*), 0.77(2H, *2* and 6*H*) 0.77(3H)		7.04	160
$4\text{-}NO_2C_6H_4SO_2CF_3^{-\cdot}$		2.53(2H, *3* and 5*H* or *2* and 6*H*) 3.06(3F)		4.58	160

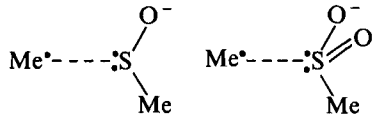
[a] See text for a description of this radical.



(84)

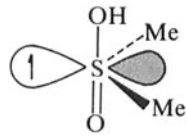
remains unknown. The radical cation of dimethyl sulphone, $Me_2SO_2^{+\bullet}$, has not been definitively observed, but the radical cation of tetrahydrothiophene-1,1-dioxide displays coupling to only two protons. Unfortunately, it is not known whether this coupling is to the α- or β-protons, and this will only be resolved by selective deuterium labelling experiments.

The anion radical of dimethyl sulphoxide has not been observed[159]. Instead, electron capture results in a species that is best described as an adduct (**85**) between a methyl radical and the methylsulphenate anion.



(85) (86)

Hyperfine coupling, $a(^2H)$, in the deuterated species is smaller than for the $CD_3^{\bullet}$ radical in the solid state, and $a(^{33}S)$ appears to be isotropic. Dimethyl sulphone behaves similarly, and forms an adduct that is best represented by structre **86**, for which $a(^{33}S)$ is essentially isotropic. The radical adducts are believed to be formed as a result of electron capture, which results in bond stretching that is halted by repulsive environmental forces. For the radical anion of dimethyl sulphoxide, no evidence for the formation of the expected stable trigonal bipyramidal structure has been found. In contrast, dimethyl sulphone in sulphuric acid solutions forms a radical that gives rise to $g_{iso} = 2.010$, and $a_{\|}(^{33}S) = 143$ G and $a_{\perp}(^{33}S) = 122$G. These sulphur hyperfine couplings yield values for a_{iso} and a_{aniso} of 129 G and 14 G, respectively. In turn, these represent unpaired spin densities of 0.13 and 0.25 in the sulphur 3s and 3p orbitals, consistent with the trigonal bipyramidal structure **87** for the protonated radical anion.



(87)

4-Nitrophenyl sulphone radical anions have much of the unpaired spin density associated with the nitrophenyl ring, as demonstrated by the ring proton and nitrogen hyperfine coupling constants (Table 24). However, comparison of the nitrogen hyperfine coupling (7 G) with those (9–12 G) for radical anions of other 4-nitrophenyl systems (e.g.

ethers, amines)[160] indicates that a significant proportion of the unpaired spin density resides in the sulphonyl group. This is also apparent if one compares the a(H) values for the CH_3 protons in the radical anions of $(4\text{-}NO_2C_6H_4)SMe$ and $(4\text{-}NO_2C_6H_4)SO_2Me$; in the former there is no observable coupling, in the latter the coupling is 0.77 G[160].

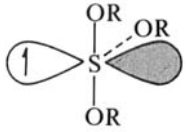
H. Sulphuranyl Radicals

Sulphuranyl radicals can be formed by the reaction of an alkoxyl radical with a disulphide, sulphenate or sulphide (equation 29), or by the addition of an alkoxyl or alkylthiyl with a sulphide (equation 30).

$$R^1S{-}SR^1 \xrightarrow{R^2O^\bullet} R^1S{-}OR^2 \xrightarrow{R^2O^\bullet} R^1S(OR^2)_2^\bullet \tag{29}$$

$$R_2{}^1S \xrightarrow{R^2O^\bullet} R_2{}^1SOR^{2\bullet} \tag{30}$$

ESR spectral data for some sulphuranyl radicals are contained in Table 25. Trialkoxysulphuranyl radicals, such as $(MeO)_3S^\bullet$, exhibit coupling to only two of the three sets of methyl proton. This has been interpreted in terms of a radical that has a T-shaped geometry which arises from a trigonal bipyramidal sulphur atom. However, the isotropic $a(^{33}S)$ hyperfine coupling of *ca* 50 G implies that the sulphur orbital containing the unpaired spin density only has about 5% 3s character. Thus, the unpaired spin essentially resides in a sulphur 3p orbital and the radical is 'quasi-trigonal bipyramidal' at sulphur, e.g. **88**. Unfortunately, the consequence of such a description



(88)

is that the non-bonding electron pair occupies an sp orbital, which means that the quasi-trigonal bipyramidal structure is effectively square-planar. The problem of why the two *trans* alkoxy groups couple to the unpaired electron whereas the *cis* alkoxy group doesn't then arises. Clearly, further work is needed to establish the structure of these radicals.

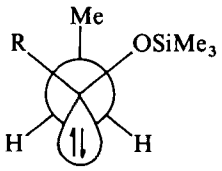
One interesting observation relating to the formation of the trialkoxy sulphuranyl radicals from $RO^\bullet$ and $(RO)_2S$ is that, by the use of deuterium labelling experiments, it has been established that the incoming alkoxyl radical takes up an apical position at sulphur[164].

Dialkoxysulphuranyl radicals are thought to have a structure similar to **88**, in which the alkoxy groups are apically positioned. In these radicals, coupling to the protons of the 'equatorial' alkyl or aryl group is observed. Indeed, coupling to the *ortho* and *para*, but not the *meta*, aryl ring protons in $Ph(OBu^t)_2S^\bullet$ is indicative of a π-type radical such as **88**.

In contrast to trialkoxy- and dialkoxysulphuranyls, the monoalkoxysulphuranyl radical, as exemplified by $Et_2(Me_3SiO)S^\bullet$ (**89**) appears to have a pyramidal structure at sulphur. This follows from the proton hyperfine coupling in radicals such as $Et_2(Me_3SiO)S^\bullet$, where coupling to two pairs of equivalent protons is evident. This arises

TABLE 25. ESR spectral data for some sulphuranyl radicals

Radical	g value	Hyper fine coupling (G)		Reference
		a(H)	a(other)	
$Me_2(CF_3S)S^{\bullet}$	2.0133	4.1(6H)	9.2(3F)	161
$(CD_3)_2(CF_3S)S^{\bullet}$	2.0133		9.2(3F)	161
$Et_2(CF_3S)S^{\bullet}$	2.0131	5.75(2H), 4.05(2H)	9.2(3F)	161
$(CF_3S)\dot{C}H_2CH_2CH_2CH_2S^{\bullet}$	2.0128	6.3(4H)	9.3(3F)	161
$(Bu^tCOS)Me_2S^{\bullet}$	2.0140	3.6(6H)		161
$Me_2(MeCOS)S^{\bullet}$	2.0127	3.7(6H), 1.8(3H)		161
$Me(OBu^t)_2S^{\bullet}$	2.0096	6.5(3H)		161
$Et(OBu^t)_2S^{\bullet}$	2.0095	2.9(2H)		162
$CF_3(OBu^t)_2S^{\bullet}$	2.0079		15.9(2F), 4.0(1F)	162
$Ph(OBu^t)_2S^{\bullet}$	2.0091	0.8(3H)		162
$Me_2(Me_3SiO)S^{\bullet}$	2.0076	7.7(6H)		126
$(CD_3)_2(Me_3SiO)S^{\bullet}$	2.0076	1.15(6D)		126
$Et_2(Me_3SiO)S^{\bullet}$	2.0074	10.0(2H), 7.2(2H)		126
$(MeO)_3S^{\bullet}$	2.0067	1.7(6H)	1.2 ($2 \times {}^{13}C$ apical)	163
			5.8 ($1 \times {}^{13}C$ equatorial)	164
$(CD_3O)_3S^{\bullet}$		0.3(6D)		164
$(Bu^tO)OMe_2CCH_2CMe_2OS^{\bullet}$	2.0069		47(15)	163



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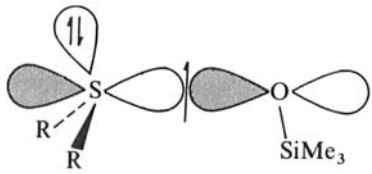

(90)

from the diastereotopic nature of the methylene protons in a structure such as **89**. For sulphuranyl radicals which are pyramidal at sulphur, the unpaired electron resides in a S—O σ^* orbital, as in **90**[126].

Similarly, the alkylthiol- and acylthiolsulphuranyl radicals, $(CF_3S)R_2^2S^{\cdot}$ and $(R^1COS)R_2^2S^{\cdot}$, adopt a similar structure to **90**, the σ^* orbital in this case being comprised mainly of $S^1(3p_x)$ and $S^2(3p_x)$ atomic orbitals[161]. The spin density at the three-coordinate sulphur may be estimated from a comparison of the coupling to the protons of the methyl groups in radicals derived from Me_2S (Table 25) with the corresponding coupling in the related radical $Me_2SSMe_2^{+\cdot}$ (Table 17), for which the spin density on each sulphur atom is 0.5. Such coupling arises through a hyperconjugative mechanism and obeys equation **31**, where ρ is the spin density at the sulphur atom.

$$a(\mathrm{H}) = \rho B\cos^2\theta \tag{31}$$

Using the average value for $\cos^2\theta$ of 0.5, a ρ value of 0.5 and $a(H) = 6.8$ G, a value for B of 27.2 G may be calculated. If one uses this value for sulphuranyl radicals, then the spin density at the three-coordinate sulphur atom is 0.57 for $Me_2(Me_3SiO)S^{\cdot}$, 0.3 for $Me_2(CF_3S)S^{\cdot}$ and 0.27 for $Me_2(CH_3COS)S^{\cdot}$. The larger spin density at sulphur in the oxygen substituted radical derives from the greater electron-withdrawing power of the oxygen atom which enables a greater contribution from the resonance form **91**.

$$R_2\dot{S}—OR \longleftrightarrow R_2S^{+\cdot}\ {}^{-}OR$$

(91)

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CHAPTER 6

Mass spectra of organosulfur compounds

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I. INTRODUCTION

The field of mass spectrometry continues to expand and new instrumental techniques are being developed for the purpose of improving the analytical capabilities of the method and its versatility for studying the chemistry of ions in the gas phase. The wide variety of ionization techniques available[1] and the general use of tandem mass spectrometric (MS/MS)[2] techniques have broadened the term mass spectrum to mean anything from a conventional 70 eV electron impact (EI) spectrum to a Collision-Induced Dissociation (CID) spectrum of a multiply charged biomolecule brought into the gas phase by electrospray[3]. Nevertheless, standard EI is still an unique ionization method in the sense that it is capable of providing structural information on numerous organic compounds and offers an experimental entry into the generation of ionic species, whose properties in the gas phase may be of general interest. In the present chapter the mass spectrometric properties of organosulfur compounds is treated from a mechanistic point of view with attention being paid to the uni- and bimolecular chemistry of positive as well as negative ions of these compounds together with the reactions of ions with sulfur containing species in the gas phase.

The selection of organosulfur compounds includes what can be considered to be the basic sulfur containing functional groups: (i) the thiol group, (ii) the sulfide and disulfide linkages, (iii) the C=S group, (iv) the oxidized forms of sulfides, i.e. sulfoxides and sulfones, and (v) the sulfenic, sulfinic and sulfonic acids. The coverage of the literature and in part also the selection of the topics are based on earlier reviews concerned with the mass spectra of thiols[4], sulfides[5], sulfoxides[6–8], sulfones[6–8] and the sulfinic[9] and sulfonic[10] acids together with their derivatives. The section of thiocarbonyl compounds is focussed on thioketones with some mentioning of thioesters and the treatment of derivatives of the sulfinic and sulfonic acids is restricted to their esters. The mass spectra of nitrogen containing derivatives of these compounds, for example, sulfin- and sulfonamides have been described previously[9,10] and are omitted from the present review. A further restriction concerns the mass spectrometric properties of heterocyclic aromatic compounds containing sulfur, which have been described elsewhere[8].

The main emphasis in the present chapter is put on the reactions of the ionized parent compounds and, in the instances where it proved possible, the decompositions of the protonated as well as the deprotonated species are described. The reactions of anions with sulfur containing compounds have been reviewed recently[11], but are summarized here together with the reactions of cations with sulfur containing compounds and the ion/molecule reactions of sulfur containing positive ions in order to provide a balanced treatment of the gas phase bimolecular chemistry of simple sulfur containing species.

II. THIOLS

A. Unimolecular Reactions

1. General characteristics

The main fragmentation reactions of the molecular ions of aliphatic thiols are[4,12]: (i) α-cleavage, (ii) β-cleavage, (iii) heterolytic cleavage of the C—S bond leading to a carbenium ion and (iv) elimination of H_2S. These processes are shown in equations 1–4 for the molecular ion of *n*-propanethiol together with the relative peak intensities in the 70 eV mass spectrum of this compound and the associated reaction enthalphies as estimated from data given in Reference 13.

$$^{\gamma}CH_3{}^{\beta}CH_2{}^{\alpha}CH_2SH^{+\cdot}\ (m/z\ 76) \longrightarrow$$

100% → $CH_2{=}SH^+$ (m/z 47) + $C_2H_5^{\cdot}$ $\Delta H_r^\circ = 161\ kJ\ mol^{-1}$ (1)

14% →  (m/z 61) + $CH_3^{\cdot}$ $\Delta H_r^\circ = 125\ kJ\ mol^{-1}$ (2)

80% → $(CH_3)_2CH^+$ (m/z 43) + $HS^{\cdot}$ $\Delta H_r^\circ = 119\ kJ\ mol^{-1}$ (3)

74% → $CH_3CH{=}CH_2^{+\cdot}$ (m/z 42) + H_2S $\Delta H_r^\circ = 119\ kJ\ mol^{-1}$ (4)

The α-cleavage reaction of thiol radical cations is normally more endothermic than α-cleavage of the analogous alcohol molecular ions as exemplified by the formation of $CH_2{=}SH^+$ from the *n*-propanethiol ion, which is associated with an enthalpy change of *ca* 161 kJ mol^{-1} (equation 1), whereas formation of $CH_2{=}OH^+$ from the *n*-propanol radical cation is only *ca* 90 kJ mol^{-1} endothermic[13]. The main part of the stable $C_2H_5S^+$ ions formed by β-cleavage of the molecular ions of *n*-propanethiol (equation 2) and longer chain aliphatic thiols has the structure of protonated thiirane[14]. Formation of this species ($\Delta H_f^\circ = 798\ kJ\ mol^{-1}$)[13] is energetically favored over generation of protonated thioacetaldehyde, $CH_3CH{=}SH^+$ ($\Delta H_f^\circ \approx 823\ kJ\ mol^{-1}$)[13], which is formed only to a minor extent by the β-cleavage reaction[14]. The loss of HS$^{\cdot}$ with formation of an *i*-propyl carbenium ion[15] (equation 3) and the elimination of H_2S (equation 4) are less endothermic than the other reactions and give rise to intense peaks in the 70 eV EI spectrum of *n*-propanethiol.

The formation of negative ions from thiols has been reviewed earlier[4,16,17]. The RS$^{\bullet}$ and ArS$^{\bullet}$ radicals possess high electron affinities[13] and dissociative electron capture by aliphatic and aromatic thiols leads mainly to RS^- and ArS^- anions, which are formed also by deprotonation of the parent compounds (see Section II.B.2). Other ions than thiolate anions may be formed by dissociative electron capture by a thiol as exemplifed by the additional formation of $CH_2S^{-\bullet}$, HS^- and S^- ions from methanethiol[4].

2. *Decomposition of the methanethiol radical cation*

The mass spectrometric behavior of methanethiol has been the subject of several experimental[18–23] and theoretical[24–26] studies. The main reactions of the molecular ion of this compound are: (i) loss of a hydrogen atom, (ii) elimination of a hydrogen molecule and (iii) loss of an HS$^{\bullet}$ radical. The relative abundances of the product ions of these reactions have been determined as a function of the internal energy of the molecular ion leading to a so-called breakdown diagram of the methanethiol system[19,23]. One of the main features of the breakdown diagram is a relatively sharp cross-over from the molecular ion to the product ion of H atom loss at an internal energy of *ca* 2.16 eV. The loss of an H atom results exclusively in ions with a $CH_2{=}SH^+$ structure (equation 5) as revealed by CID experiments[21] and indicated by an ICR[27] study of the energetics of proton transfer between the product ion of this reaction and various reference bases[22].

$$\underset{m/z\,48}{CH_3SH^{+\bullet}} \longrightarrow \underset{m/z\,47}{CH_2{=}SH^+} + H^{\bullet} \quad \Delta H_r^{\circ} \approx 192\,\text{kJ mol}^{-1} \tag{5}$$

Elimination of H_2 is important only at internal energies $\geqslant 2.16$ eV, while loss of HS$^{\bullet}$ with formation of CH_3^+ requires an internal energy > 3.6 eV. The elimination of H_2 from the methanethiol molecular ion can proceed, in principle, by a 1,2-elimination leading to $CH_2{=}S^{+\bullet}$ (equation 6) and/or by a 1,1-elimination yielding ions with a $HC{=}SH^{+\bullet}$ structure. The obtained photoionization curve for H_2 loss shows a relatively weak threshold at a photon energy of 10.61 eV and a pronounced increase in the ion yield beginning at 11.51 eV[23]. Based on these results and thermochemical considerations, it was suggested that the $CH_2{=}S^{+\bullet}$ ion is generated at the onset for H_2 loss, whereas the possibly less stable $HC{=}SH^{+\bullet}$ species may be formed at higher photon energies.

$$\underset{m/z\,48}{CH_3SH^{+\bullet}} \longrightarrow \underset{m/z\,46}{CH_2{=}S^{+\bullet}} + H_2 \quad \Delta H_r^{\circ} \approx 107\,\text{kJ mol}^{-1} \tag{6}$$

The $CH_2{=}SH^+$ ion fragments further by H_2 loss[19,23] if generated from methanethiol molecular ions with an internal energy of $\geqslant 4.1$ eV. The structure of the product ion from this reaction is likely to be HCS^+ (equation 7)[23], which according to calculations should be more stable than the isomeric $C{=}SH^+$ ion[28].

$$\underset{m/z\,47}{CH_2{=}SH^+} \longrightarrow \underset{m/z\,45}{HC{=}S^+} + H_2 \quad \Delta H_r^{\circ} \approx 156\,\text{kJ mol}^{-1} \tag{7}$$

Even though the loss of a hydrogen atom from the methanethiol ion yields the $CH_2{=}SH^+$ ion, this process involves not only a hydrogen atom from the methyl group, but also the hydrogen atom from the thiol function as shown by the ratio of about 2 for loss of a D and an H atom from the $CD_3SH^{+\bullet}$ ion if generated by 70 eV EI[18]. The photoionization threshold for loss of a D atom from $CD_3SH^{+\bullet}$ is determined to be 0.11 eV higher than the threshold for loss of an H atom, while the threshold for H atom loss from $CH_3SD^{+\bullet}$ is 0.10 eV lower than the threshold for D atom loss[23]. The trend in the thresholds for H and D atom loss from either $CD_3SH^{+\bullet}$ or $CH_3SD^{+\bullet}$ was ascribed to the differences in the zero-point energies between the species involved in these

reactions[23] and concluded to be in accord with the formation of a single ion structure by H atom loss from the methanethiol molecular ion (equation 5)[21]. The generation of a single ion structure by loss of an H and a D atom from $CD_3SH^{+\cdot}$ is manifested also in the observation that the metastable ions generated by H atom loss eliminate D_2 with almost the same kinetic energy release (0.93 eV at half peak height) as for the loss of HD from the metastable ions generated by D atom loss (0.91 eV at half peak height)[20]. Elimination of D_2 from the $CD_2{=}SH^+$ ion is not observed implying that hydrogen–deuterium interchange is not occurring prior to dissociation.

The formation of a single ion structure in reaction 5 is corroborated further by *ab initio* MO calculations[24,25], which place the barrier for loss of an H atom from the methyl group in the methanethiol ion at 193 kJ mol^{-1} implying that α-cleavage can occur essentially at the thermochemical threshold. A similar barrier (190 kJ mol^{-1}) is predicted for a 1,2-H shift from the methyl group to the sulfur atom leading to the distonic ion[25,29], $^{\cdot}CH_2{-}\overset{+}{S}H_2$, which is calculated to be 76 kJ mol^{-1} less stable than the conventional ion. Subsequent loss of one of the hydrogen atoms bonded to the sulfur atom in the distonic ion is predicted to be associated with a barrier of 135 kJ mol^{-1} or 211 kJ mol^{-1} relative to the conventional ion. The calculations thus indicate that the energy requirements are similar for the formation of the $CH_2{=}SH^+$ ion by direct loss of an H atom from the methyl group and by the 1,2-H shift initiated loss of a sulfur-bonded H atom.

The distonic ion, $^{\cdot}CH_2{-}\overset{+}{S}H_2$, is formed by loss of formaldehyde from the molecular ion of 2-mercaptoethanol (equation 8)[30] as indicated by charge stripping[2] experiments. In particular, the charge stripping spectrum of the distonic ion shows an enhanced intensity of the peaks corresponding to formation of the dicationic species and the $CH_2^{+\cdot}$ and $H_2S^{+\cdot}$ ions as compared to the spectrum of the molecular ion of methanethiol[30].

$$\underset{m/z\,78}{HSCH_2CH_2OH^{+\cdot}} \longrightarrow \underset{m/z\,48}{^{\cdot}CH_2{-}\overset{+}{S}H_2} + CH_2O \qquad (8)$$

The relative stability of the $CH_2{=}SH^+$ ion and the isomeric thiomethoxy cation, CH_3S^+, has been discussed in a number of instances. The CH_3S^+ ion is reported to arise together with the $CH_2{=}SH^+$ isomer by cleavage of the S—S bond in the molecular ion of dimethyl disulfide (equation 9, see also Section III.A.1)[21,31].

$$\underset{m/z\,94}{CH_3SSCH_3^{+\cdot}} \longrightarrow \underset{m/z\,47}{CH_3S^+} + CH_3S^{\cdot} \qquad (9)$$

The highest yield (*ca* 60%) of the CH_3S^+ ion relative to the $CH_2{=}SH^+$ isomer was obtained at an electron energy of *ca* 18 eV. The competing formation of the $CH_2{=}SH^+$ ion at lower electron energies than *ca* 18 eV was suggested to occur by a 1,2-H shift assisted elimination of a $CH_3S^{\cdot}$ radical from the dimethyl disulfide ion. At higher electron energies, direct cleavage of the S—S bond in the dimethyl disulfide ion was proposed to yield CH_3S^+ ions, which subsequently isomerized to $CH_2{=}SH^+$ by a 1,2-H shift.

The ionization energy of the $CH_3S^{\cdot}$ radical has been determined recently to be 9.225 ± 0.014 eV[32]. This value places the heat of formation of the CH_3S^+ cation between 1021 and 1036 kJ mol^{-1} indicating that the thiomethoxy cation is *ca* 167 kJ mol^{-1} less stable than the $CH_2{=}SH^+$ ion[13]. *Ab initio* calculations[24,26] indicate that the CH_3S^+ ion is stable in its triplet state and that the energy of this state lies 131 kJ mol^{-1} above the energy of the singlet state of the $CH_2{=}SH^+$ ion, whereas the singlet state of the CH_3S^+ ion is predicted to be 269 kJ mol^{-1} less stable than singlet $CH_2{=}SH^+$. The calculations indicate further that the singlet CH_3S^+ ion rearranges to the $CH_2{=}SH^+$ isomer by a barrier-free 1,2-H shift in analogy with the conclusion reached for the CH_3O^+ species[33–35].

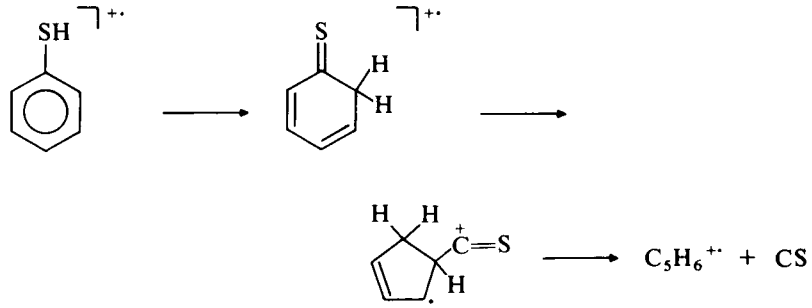
3. Dissociations of the thiophenol radical cation

The metastable molecular ions of thiophenol expel H$^{\cdot}$, C_2H_2 (equation 10) and CS (equation 11). Time-resolved photoionization/photodissociation[36] experiments place the threshold for C_2H_2 loss at an internal energy of 2.9 eV and the onset for CS loss at 3.2 eV. The photoionization curves cross at an internal energy of approximately 4 eV and at higher energies CS loss becomes more important than elimination of C_2H_2.

$$C_6H_5SH^{+\cdot} \ (m/z\ 110) \longrightarrow C_4H_4S^{+\cdot}\ (m/z\ 84) + C_2H_2 \quad (10)$$

$$C_6H_5SH^{+\cdot} \ (m/z\ 110) \longrightarrow C_5H_6^{+\cdot}\ (m/z\ 66) + CS \quad (11)$$

At an internal energy of 4.2 eV, the experimentally determined rate constant is $1.3 \times 10^5\ s^{-1}$ for C_2H_2 loss and $8 \times 10^4\ s^{-1}$ for CS loss. The value of the rate constant for C_2H_2 loss could be reproduced by RRKM (Rice–Ramsperger–Kassel–Marcus theory)/QET (Quasi Equilibrium Theory)[37,38] calculations assuming a relatively tight transition state for this process, whereas successful modelling of CS loss could be achieved only by postulating a loose transition state[36]. Tentatively, the rate determining step in the reaction sequence was proposed to be loss of CS from a thiacylium ion generated by isomerization of the thiophenol radical cation to the thioketo form followed by ring-contraction (Scheme 1).



SCHEME 1. Proposed mechanism for the loss of CS from the $PhSH^{+\cdot}$ ion[36]

The elimination of a CS molecule is also the main fragmentation mode of the $C_6H_5S^+$ ions generated by loss of a methyl radical from the molecular ions of methyl phenyl sulfide[39]. In addition to CS loss, the metastable $C_6H_5S^+$ ions react by competing loss of an H atom and a C_3H_4 molecule.

4. Collision-induced reactions of deprotonated thiols

The 8 keV ion kinetic energy CID mass spectra of $C_6H_5S^-$, 4-$CH_3C_6H_4S^-$ and $C_6H_5CH_2S^-$ have been recorded[40]. The major fragment ions formed from the $C_6H_5S^-$ ions are: C_4HS^-, C_3HS^-, C_2HS^- and HS^-, whereas fragment ions not containing a sulfur atom, i.e. $C_6H_5^-$, $C_6H_3^-$, $C_5H_5^-$ and C_4H^-, are of minor importance. Deuterium labelling indicates that the major product ions from the thiophenoxy anion are formed almost without prior loss of the positional identity of the hydrogen atoms, whereas a

minor extent of loss in the positional identity of the hydrogen atoms could not be excluded for the reactions leading to the C_4HS^- and C_4H^- ions. The predominant collision-induced reactions of $C_6H_5CH_2S^-$ are generation of $C_6H_5S^-$, $C_6H_5^-$, $C_6H_3^-$, $CH_2S^{-\cdot}$ and HS^- ions. All these processes are accompanied by partial loss of the positional identity of the hydrogen atoms, possibly proceeding by interchange between the benzylic hydrogen atoms and the hydrogen atoms at the *ortho*-positions[40].

Dissociative electron capture by thioglycollates, $HSCH_2CO_2R$, results in $^-SCH_2CO_2R$, $[M-2H]^{-\cdot}$ and HS^- ions[41]. The $^-SCH_2CO_2R$ ions eliminate CO_2 following collisional activation implying that a shift of the R group from the oxygen to the sulfur atom occurs prior to or during fragmentation possibly yielding a $RSCH_2^-$ carbanion. In addition to CO_2 loss, the $^-SCH_2CO_2CD_2Ph$ ions fragment by simple cleavages to form $PhCD_2O^-$ and $PhCD_2^-$ and by a rearrangement reaction to yield $PhCDS^{-\cdot}$ and $PhCD_2S^-$. The later ions in the unlabelled form are generated also in the collision-induced reactions of the homologous $^-SCH_2CH_2CO_2CH_2Ph$ ions. Elimination of CO_2 is not observed, however, for the $^-SCH_2CH_2CO_2R$ ions derived from β-thiopropionates[41].

B. Bimolecular Reactions

1. Positive ions

Thiols possess relatively high proton affinities (PA, see Table 1 for selected values) and are readily protonated under positive ion CI conditions. The RSH_2^+ ions may decompose if the protonation step leading to their formation is sufficiently exothermic as exemplified by the loss of H_2 and H_2S from the $CH_3SH_2^+$ ion generated under H_2/H_3^+ CI conditions (equations 12–14)[42]. Longer chain aliphatic thiols expel predominantly H_2S following protonation by H_3^+, in agreement with a more favorable thermochemistry for this process when larger and more stable carbenium ions than the CH_3^+ ion can be formed.

$$\underset{m/z\,3}{H_3^+} + CH_3SH \longrightarrow \underset{m/z\,49}{CH_3SH_2^+} + H_2 \qquad \Delta H_r^\circ \approx -361\,\text{kJ mol}^{-1} \qquad (12)$$

$$\underset{m/z\,49}{CH_3SH_2^+} \xrightarrow{ca\,80\%} \underset{m/z\,47}{CH_2{=}SH^+} + H_2 \qquad \Delta H_r^0 \approx 139\,\text{kJ mol}^{-1} \qquad (13)$$

$$\underset{m/z\,49}{CH_3SH_2^+} \xrightarrow{ca\,20\%} \underset{m/z\,15}{CH_3^+} + H_2S \qquad \Delta H_r^0 \approx 350\,\text{kJ mol}^{-1} \qquad (14)$$

The molecular ions of 2-mercaptoethanol and 1,2-ethanedithiol are reported to react with their corresponding neutral precursors by a variety of reactions[43]. Among other processes, the molecular ion of 2-mercaptoethanol, $C_2H_6OS^{+\cdot}$, reacts with its parent compound to form $C_3H_7OS^+$ and $C_4H_9OS^+$ ions. Similarly, the 1,2-ethanedithiol ion, $C_2H_6S_2^{+\cdot}$, reacts with its neutral precursor to form $C_3H_7S_2^+$ and $C_4H_9S_2^+$ ions.

2. Negative ions

Thiols are in the gas phase—as in the condensed phase—more acidic than aliphatic alcohols (see Table 1 for selected gas-phase acidities, ΔH_{acid}°) and deprotonation of thiols by negative ions in the gas phase provides an easy entry to RS^- or ArS^- ions. Other processes may occur, however, as exemplified by the formation of $C_6H_5S^-$ ions in the

TABLE 1. Selected proton affinities (PA) and gas phase acidities (ΔH°_{acid}) of thiols, sulfides and the related oxygen compounds[a-c]

Compound	PA	ΔH°_{acid}
	in kJ mol^{-1}	
CH_3OH	761	1592
C_2H_5OH	799	1579
CH_3OCH_3	804	1703
CH_3SH	784	1493[d]
C_2H_5SH	798	1486
CH_3SCH_3	839	1645
$PhSCH_3$	—	1597[e]

[a] All values from Ref. 13.
[b] The proton affinity is defined as the enthalpy change for the reaction: $BH^+ \rightarrow B + H^+$.
[c] The gas-phase acidity is defined as the enthalpy change for the reaction: $AH \rightarrow A^- + H^+$.
[d] See also text.
[e] This value refers to the acidity of the methyl group in $PhSCH_3$ (see Section III.B.2).

reaction of the conjugate base of 1,2-dehydrobenzene, $C_6H_3^-$, with 2-methyl-2-propanethiol (equation 15)[44].

$$\underset{m/z\,75}{C_6H_3^-} + (CH_3)_3CSH \longrightarrow \underset{m/z\,109}{C_6H_5S^-} + C_4H_8 \qquad (15)$$

Deprotonation of thiols in the gas phase results exclusively in the formation of thiolate anions. The α-thiocarbanion, $^-CH_2SH$, has been generated recently by collision-induced fragmentation of $HSCH_2CH_2S^-$ (equation 16) and $HSCH_2CH_2CO_2^-$ ions[45]. Distinction between the $^-CH_2SH$ ion and the isomeric CH_3S^- species was achieved by 8 keV ion kinetic energy collision-induced charge reversal[2] experiments[45]. Notably, the charge reversal mass spectrum of the carbanion displays more intense peaks corresponding to formation of $CH_2^{+\cdot}$ and HS^+ ions than the charge reversal spectrum of the CH_3S^- ion.

$$\underset{m/z\,93}{HSCH_2CH_2S^-} \xrightarrow{CID} \underset{m/z\,47}{^-CH_2SH} + CH_2{=}S \qquad (16)$$

The $^-CH_2SH$ ion is reported to arise also in the reaction of F^- with $(CH_3)_3SiCH_2SH$ (equation 17)[46], which proceeds mainly by simple proton transfer to yield $(CH_3)_3SiCH_2S^-$ ions. Under the reaction conditions some CH_3S^- ions (*ca* 25%) were generated in addition to the $^-CH_2SH$ ions, possibly as a result of an isomerization of the α-thiocarbanion in a secondary ion/molecule reaction with $(CH_3)_3SiCH_2SH$.

The $^-CH_2SH$ ion reacts with N_2O by hydride ion transfer and to form HO^- and HS^- ions, whereas the CH_3S^- isomer is unreactive towards this substrate. Hydride ion transfer occurs also with the substrates, O_2, CS_2, COS, CO_2 ans SO_2, whereas the reaction with D_2O proceeds by deuteron abstraction (equation 18) and isomerization to the methylthiolate anion (equation 19).

$$\underset{m/z\,19}{F^-} + (CH_3)_3SiCH_2SH \longrightarrow \underset{m/z\,47}{^-CH_2SH} + (CH_3)_3SiF \qquad (17)$$

The gas-phase acidity of the methyl group in CH_3SH is determined to be 1649 ± 12 kJ mol^{-1} and thus close to the value for the gas phase acidity of CH_3SCH_3

$$^{-}CH_2SH + D_2O \begin{cases} \longrightarrow DO^{-} + CH_2DSH \quad (18) \\ \qquad m/z\,18 \\ \longrightarrow CH_2DS^{-} + HDO \quad (19) \\ \qquad m/z\,48 \end{cases}$$
$$m/z\,47$$

(see Table 1 and Section III.B.2). The resulting heat of formation of the $^{-}CH_2SH$ ion is *ca* 96 kJ mol^{-1}, while the heat of formation of CH_3S^{-} is *ca* -60 kJ mol^{-1} revealing that a 1,2-proton shift in the carbanion is *ca* 156 kJ mol^{-1} exothermic. The distribution of the $^{-}CH_2SH$ and CH_3S^{-} ions appeared to be constant between temperatures from -40 °C to 100 °C in the flow tube of the Flowing Afterglow (FA)[47] instrument used for these experiments showing that isomerization by a 1,2-proton shift is not a facile process in spite of a favorable enthalpy change.

3. *Reactions of metal ions with thiols*

Various transition metal (M) positive ions react with thiols in the gas phase[48]. Formation of metal sulfide ions, MS^{+}, MSH^{+} or MSH_2^{+}, is a general process and is reported for the reaction of Ni^{+} with CH_3SH[49], the reaction of Ti^{+} and V^{+} with CH_3CH_2SH[50] and the reaction of Fe^{+} with C_6H_5SH[51], which yields only FeS^{+} ions. The reactions between Co^{+} and aliphatic thiols give rise to $CoSH_2^{+}$ (equation 20) and $Co(RCHCH_2)^{+}$ ions (equation 21)[52] possibly as a result of initial insertion of the metal ion into the relatively weak C—S bond of the substrates [the C—S bond dissociation energy (BDE) in CH_3SH is *ca* 315 kJ mol^{-1}][13]. Insertion into a C—C bond is reported only for 2-methyl-1-propanethiol as the substrate and leads to $CoC_3H_6^{+}$ and $CoCH_4S^{+}$ ions.

$$\underset{m/z\,59}{Co^{+}} + RCH_2CH_2SH \longrightarrow$$

$$[RCH_2CH_2—Co—SH]^{+} \begin{cases} \longrightarrow CoSH_2^{+} + RCH{=}CH_2 \quad (20) \\ \qquad m/z\,93 \\ \longrightarrow Co(RCH{=}CH_2)^{+} + H_2S \quad (21) \end{cases}$$

The reactions between the metal negative ions, Fe^{-} and Co^{-}, and aliphatic thiols[53] result in the metal sulfide ions: MS^{-}, MSH^{-} and MSH_2^{-}. In analogy with the chemistry of the metal positive ions, the initial step in the reaction sequence is considered to be insertion into the C—S bond of the thiol.

III. SULFIDES AND DISULFIDES

A. Unimolecular Reactions

1. *General characteristics*

The unimolecular reactions of sulfide radical cations have been discussed and compared with the reactions of the related ethers in earlier reviews[5,12]. In brief, the main reactions of sulfide radical cations are: (i) α-cleavage, (ii) cleavage of a S—C bond with charge retention either on the alkyl part or on the sulfur-containing fragment and (iii) elimination of an alkene if one or both alkyl groups contain a β-hydrogen atom. These processes are shown in equations 22–25 for the molecular ion of diethyl sulfide

together with the associated enthalpy changes as estimated from data in Reference 13 and with the relative intensities of the corresponding peaks in the 70 eV EI mass spectrum of this compound.

$$
\begin{array}{l}
{}^{\beta}CH_3{}^{\alpha}CH_2\overset{+\cdot}{S}CH_2CH_3 \\
m/z\,90
\end{array}
\begin{cases}
\xrightarrow{100\%} C_2H_5\overset{+}{S}{=}CH_2 + CH_3^{\cdot} \quad m/z\,75 & \Delta H_r^{\circ} \approx 204\,\text{kJ mol}^{-1} \quad (22) \\
\xrightarrow{55\%} CH_3CH{=}\overset{+}{S}H + C_2H_5^{\cdot} \quad m/z\,61 & \Delta H_r^{\circ} \approx 212\,\text{kJ mol}^{-1} \quad (23) \\
\xrightarrow{60\%} C_2H_5^{+} + C_2H_5S^{\cdot} \quad m/z\,29 & \Delta H_r^{\circ} \approx 273\,\text{kJ mol}^{-1} \quad (24) \\
\xrightarrow{50\%} C_2H_5SH^{+\cdot} + C_2H_4 \quad m/z\,62 & \Delta H_r^{\circ} \approx 173\,\text{kJ mol}^{-1} \quad (25)
\end{cases}
$$

The product ion of α-cleavage is formulated as $C_2H_5\overset{+}{S}{=}CH_2$ in equation 22 on the basis of CID experiments, which show that the nondecomposing ions formed by this reaction retain their structure[54]. By contrast, the main portion of the metastable $CH_3CH_2\overset{+}{S}{=}CH_2$ ions are reported to isomerize to a $CH_3CH_2CH{=}\overset{+}{S}H$ structure prior to elimination of H_2S or C_2H_4[55,56].

The α-cleavage of aliphatic dialkyl sulfide radical cations is normally more endothermic than α-cleavage of the analogous ether ions. For example, α-cleavage of the diethyl ether molecular ion is *ca* 75 kJ mol^{-1} endothermic, while reaction 22 is *ca* 204 kJ mol^{-1} endothermic[13]. As a result, other reactions such as cleavage of a C—S bond compete effectively with α-cleavage during decomposition of aliphatic sulfide radical cations and give rise to intense peaks in the 70 eV EI mass spectra of these compounds[12]. Cleavage of a C—S bond in the molecular ion of diethyl sulfide (equation 23) results in ions with a $CH_3CH{=}\overset{+}{S}H$ structure, implying that this process is accompanied or succeeded by a 1,2-H shift from the α-position to the sulfur atom (see also Section II.A.2)[14,57,58].

The molecular ions of dialkyl disulfides eliminate an alkene molecule if the alkyl group is ethyl or larger (see Section II.A.2)[12,59,60]. This reaction may be repeated, leading to a characteristic peak corresponding to $H_2S_2^{+\cdot}$ (m/z 66) in the EI mass spectra of aliphatic disulfides. Simple cleavage of a S—C or S—S bond may also occur. The appearance energy (AE) for the formation of $C_4H_9^{+}$ by simple cleavage of a S—C bond in the molecular ions of a series of $RSSC(CH_3)_3$ compounds [R = CH_3, C_2H_5, $CH(CH_3)_2$ and $C(CH_3)_3$] (equation 26) is reported to be largely independent of the nature of the R group[61]. The AE measurements result in an average S—C bond dissociation energy for dialkyl disulfides of 226 kJ mol^{-1} and in a dissociation energy of 135 ± 4 kJ mol^{-1} for the central S—S bond in dialkyl tetrasulfides.

$$
RSSC(CH_3)_3 + e^{-} \longrightarrow \underset{m/z\,57}{C_4H_9^{+}} + RS_2^{\cdot} + 2e^{-} \qquad (26)
$$

2. *Aliphatic sulfides and disulfides*

The dissociations of the dimethyl sulfide molecular ion have been examined as a function of internal energy by the PEPICO (Photo Electron Photo Ion Coincidence)[62] method and expressed in a breakdown diagram[63]. Formation of $CH_2{=}S^{+\cdot}$ by methane

elimination (equation 27) is associated with an AE of 10.436 ± 0.018 eV and dominates at low internal energies of the molecular ion. The AE for $CH_2{=}SH^+$ formation by methyl radical loss (equation 28) is determined to be 10.670 ± 0.018 eV, whereas the AE for generation of $CH_3{-}\overset{+}{S}{=}CH_2$ by α-cleavage is 10.914 ± 0.020 eV (equation 29). Methyl radical loss dominates at internal energies ranging from 2.4 to 4.1 eV and, at higher internal energies, α-cleavage is the main reaction of the $CH_3SCH_3^{+\cdot}$ ion.

$$\begin{array}{l} \longrightarrow CH_2{=}S^{+\cdot} + CH_4 \quad \Delta H_r^0 \approx 131\ \text{kJ mol}^{-1} \quad (27) \\ \qquad m/z\ 46 \\ CH_3\overset{+}{S}{\cdot}CH_3 \longrightarrow CH_2{=}\overset{+}{S}H + CH_3^{\cdot} \quad \Delta H_r^0 \approx 207\ \text{kJ mol}^{-1} \quad (28) \\ m/z\ 62 \qquad\quad m/z\ 47 \\ \longrightarrow CH_3\overset{+}{S}{=}CH_2 + H^{\cdot} \quad \Delta H_r^0 \approx 229\ \text{kJ mol}^{-1} \quad (29) \\ \qquad m/z\ 61 \end{array}$$

The stable ions formed by loss of a methyl radical from the dimethyl sulfide molecular ion are reported to have only the $CH_2{=}\overset{+}{S}H$ structure (equation 28)[21]. At a sufficiently high internal energy this process may involve direct cleavage of a C—S bond with formation of CH_3S^+ ions, which subsequently undergo a 1,2-H shift to the more stable $CH_2{=}SH^+$ species (see Section II.A.2). The lowest energy pathway for methyl radical loss is predicted to involve a 1,2-H shift in the dimethyl sulfide molecular ion yielding a distonic ion[25,29], which then dissociates (equation 30). According to *ab initio* MO calculations[24], this ion is $82\ \text{kJ mol}^{-1}$ less stable than the conventional isomer, $CH_3SCH_3^{+\cdot}$. The calculations indicate further that the barrier separating the conventional ion from the distonic species is $202\ \text{kJ mol}^{-1}$. By analogy, the pronounced loss of $CF_3^{\cdot}$ from the $CH_3SCF_3^{+\cdot}$ ion[64] may be initiated and/or accompanied by a 1,2-H shift, thus yielding the $CH_2{=}\overset{+}{S}H$ species.

$$\underset{m/z\ 62}{CH_3\overset{+}{S}{\cdot}CH_3} \xrightarrow{1,2\text{-H}} {\cdot}CH_2{-}\overset{+}{\underset{\displaystyle H}{\underset{|}{S}}}{-}CH_3 \longrightarrow \underset{m/z\ 47}{CH_2{=}SH^+} + CH_3^{\cdot} \quad (30)$$

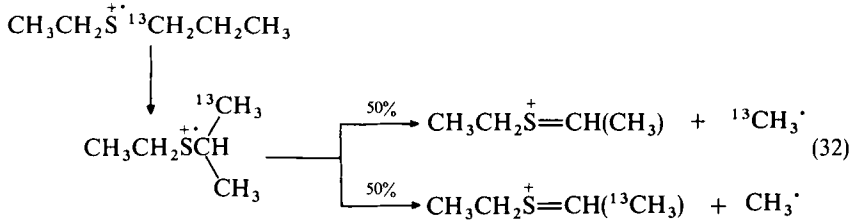
The elimination of an alkene (equation 25) is a common reaction of the molecular ions of dialkyl sulfides with an alkyl group which is larger than ethyl and contains β-hydrogen atoms[5,59]. This process can be typified by the loss of propene from the molecular ion of ethyl *n*-propyl sulfide (equation 31)[65].

$$\underset{m/z\ 104}{CH_3CH_2\overset{+}{S}{\cdot}CH_2CH_2CH_3} \longrightarrow \underset{m/z\ 62}{CH_3CH_2SH^{+\cdot}} + CH_3CH{=}CH_2 \quad (31)$$

$$\Delta H_r^{\circ} \approx 155\ \text{kJ mol}^{-1}$$

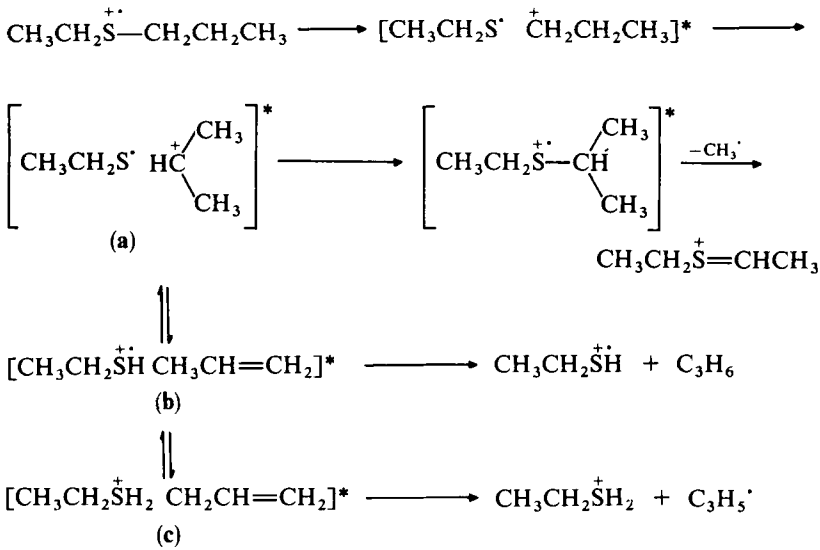
In addition to propene loss, the metastable molecular ions of ethyl *n*-propyl sulfide expel an allyl radical and methyl radical originating from the propyl chain as indicated by the exclusive loss of $CH_3^{\cdot}$ from the radical cations of ethyl *n*-propyl sulfides labelled with deuterium in the ethyl group. Equal amounts of $CH_3^{\cdot}$ and $^{13}CH_3^{\cdot}$ are eliminated from the metastable molecular ions of $CH_3CH_2S^{13}CH_2CH_2CH_3$ (equation 32) revealing that the *n*-propyl group can isomerize to an *i*-propyl group prior to methyl radical loss.

Extensive loss of the positional identitiy of the hydrogen atoms of the propyl group occurs prior to fragmentation, as shown by site-specific labelling of this entity. However,



(32)

complete randomization of the atoms of this group is not occurring and a certain specificity for transfer of a hydrogen from the β-position of the propyl group to the sulfur atom is noted in the elimination of propene in the ion source and is maintained to some extent in the reactions of the metastable ions. The initial step in the reactions of the metastable ions has been formulated as a 1,2-hydride shift assisted heterolytic cleavage of the bond between the S atom and the α-C atom of the propyl group (Scheme 2). This results in an ion-neutral complex[66,67] composed of a thioethoxy radical and an *i*-propyl carbenium ion (**a** in Scheme 2) and held together by ion-dipole/ion-induced dipole interactions. Subsequently, recombination of the particles in the complex can occur and lead to the molecular ion of ethyl *i*-propyl sulfide, which then expels a methyl radical by α-cleavage. Proton transfer between the constituents results in a complex (**b**) of the ethanethiol radical cation and propene. This complex can dissociate or react by hydrogen atom transfer to form complex **c** prior to formation of an allyl radical and a $C_2H_5SH_2^+$ ion. The partial loss of positional identity of the hydrogen atoms of the propyl entity was concluded to be a result of reversible proton transfers between the constituents of complexes **a** and **b**, which compete effectively with 1,2-hydride shifts in the *i*-propyl carbenium ion[15] and to some extent with the loss of a methyl radical, a propene molecule or an allyl radical[65].

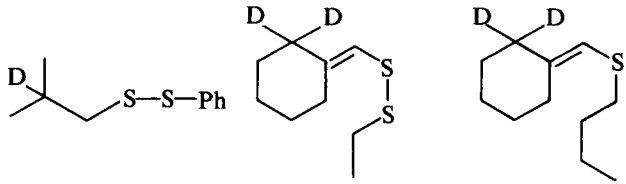


SCHEME 2. Proposed mechanism for the reactions of the metastable molecular ions of ethyl *n*-propyl sulfide[65]

Elimination of an alkene is also a common reaction of dialkyl and alkyl aryl disulfide radical cations[12,59,60]. Deuterium labelling reveals the occurrence of competing transfer of a hydrogen from the α- and β-positions in the elimination of ethene from the molecular ion of diethyl disulfide (equation 33)[68].

$$\underset{m/z\,122}{{}^{\beta}CH_3{}^{\alpha}CH_2SSCH_2CH_3}{}^{+\cdot} \longrightarrow \underset{m/z\,94}{C_2H_6S_2{}^{+\cdot}} + C_2H_4 \qquad (33)$$

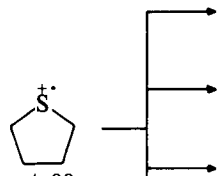
Transfer of a hydrogen from a γ-position is noted for the loss of C_4H_8 from the molecular ion of the disulfide, 1-phenyl-4-deuterio-4-methyl-1,2-dithiapentane (**1**)[69]. The possibility for a H-shift from the γ-position with respect to the nearest sulfur atom in a disulfide ion is reflected also in the formation of nearly equal amounts of $C_2H_5DS_2{}^{+\cdot}$ and $C_2H_6S_2{}^{+\cdot}$ ions during fragmentation of the molecular ion of 1-(2′,2′-dideuteriocyclohexyl)-2,3-dithiapent-1,1′-ene (**2**). Only minor amounts of $C_4H_9SD^{+\cdot}$ and $C_4H_9SH^{+\cdot}$ ions are formed from the molecular ion of the related monosulfide 1-(2′,2-dideuteriocyclohexyl)-2-thiahex-1,1′-ene (**3**) revealing that a 1,4-D/H-shift from the γ-position to sulfur atom is not occuring to any significant extent during decomposition of ionized **3**. This suggests that the additional sulfur atom in the disulfide (**2**) is essential for the occurrence of the reaction leading to the $C_2H_5DS_2{}^{+\cdot}$ or $C_2H_6S_2{}^{+\cdot}$ ions and that the H/D-shift occurs to the sulfur atom, which is bonded to the ethyl group in **2**[69].



(1) (2) (3)

3. Cyclic sulfides

The molecular ions of cyclic sulfides undergo a number of characteristic reactions including ring-opening followed by loss of a hydrocarbon fragment, a HS· radical and a H_2S molecule as exemplified in equations 34–37 for thiolane[5,70]. According to PEPICO measurements[71] the relative order of the rate constants of the reactions shown in equations 34–37 are: $k_{34}(E) > k_{37}(E) > k_{36}(E) > k_{35}(E)$ (E = internal energy) at photon energies from 10.5 to 10.7 eV.



$$\rightarrow \underset{m/z\,60}{C_2H_4S^{+\cdot}} + C_2H_4 \qquad (34)$$

$$\rightarrow \underset{m/z\,59}{C_2H_3S^{+}} + C_2H_5{}^{\cdot} \qquad (35)$$

$$\rightarrow \underset{m/z\,57}{C_4H_7{}^{+}} + HS^{\cdot} \qquad (36)$$

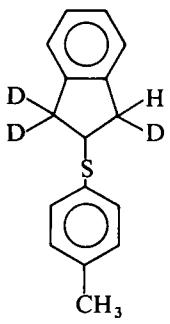
$$\rightarrow \underset{m/z\,56}{C_4H_6{}^{+\cdot}} + H_2S \qquad (37)$$

Photoionization threshold experiments[71] indicate that the heat of formation of the $C_2H_4S^{+\cdot}$ ion formed by elimination of C_2H_4 from the thiolane ion is about 916 kJ mol^{-1}. This value is close to the heat of formation expected for the molecular ion of thioacetaldehyde and much lower than the heat of formation of the molecular ion of thiirane (961 kJ mol^{-1})[13] implying that elimination of C_2H_4 at threshold yields the thioacetaldehyde ion, $CH_3CHS^{+\cdot}$. This is in contrast to an earlier report[70] in which the generation of the thiirane ion or the ring-opened species, $^{\cdot}CH_2—S—CH_2^+$, was suggested. The elimination of C_2H_4 from the thiolane radical cation is preceded by extensive rearrangement of the carbon-skeleton as shown by the competing losses of $^{13}CH_2{=}{}^{13}CH_2$, $CH_2{=}{}^{13}CH_2$ and $CH_2{=}CH_2$ from the metastable ions of thiolane labelled with ^{13}C at the 2- and 5-positions[72]. This rearrangement may involve the formation of methyl substituted thietane radical cations as indicated by the similar dissociation behavior of the metastable molecular ions of 2-methyl thietane and thiolane[73].

4. *Aromatic sulfides*

The elimination of an alkene molecule is a common reaction for the molecular ions of alkyl phenyl sulfides as noted in the early mass spectrometry literature[12,5]. This process and heterolytic cleavage of a C—S bond with charge retention on the hydrocarbon fragment dominate in the decomposition of the molecular ions of 2-indanyl aryl sulfides[74]. In the former reaction, an H-shift from the β-position of the indanyl group occurs as indicated by the formation of $C_7H_7DS^{+\cdot}$ ions from the molecular ion of **4**.

The dissociations of the molecular ions of the phenyl styryl sulfides **5** and **6** have been examined and compared to the fragmentations of the molecular ions of the isomeric compounds: benzyl phenyl thione (**7**), 1,2-diphenylthiirane (**8**) and 2-phenyl-2,3-dihydrobenzo[*b*]thiophene (**9**)[75–77]. The metastable molecular ions of **5–9** all undergo competing losses of $CH_3^{\cdot}$, $HS^{\cdot}$, $CHS^{\cdot}$, $C_6H_5^{\cdot}$, C_6H_6 or $C_7H_7^{\cdot}$ although the relative importance of these channels differs for the different molecular ions. Notably, the loss of $CHS^{\cdot}$ is significantly more pronounced for the metastable molecular ions of **5** than for the metastable ions of **6**. Labelling with ^{13}C and deuterium reveals the occurrence of extensive rearrangements of the metastable molecular ions of **5** and **6** possibly involving the radical cations of **7** and **8** as intermediates[75–77].



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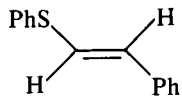

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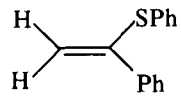

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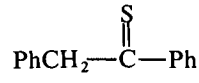

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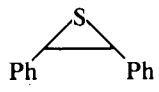

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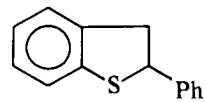


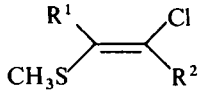
(9)

5. *Sulfides with additional functional groups*

The mass spectra of a series of *erythro* and *threo* 1,2-dimethyl- and 1,2-diphenyl-1-methylthio-2-Y-ethanes with the general formula RCH(Y)-CH(SCH$_3$)R [Y = F, Cl, Br, I,

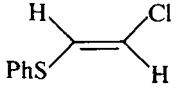
OH, OCH_3, OAc, NH_2 and $N(CH_3)_2$] are characterized by peaks corresponding to the formation of $RCHY^+$ and $RCH{=}\overset{+}{S}CH_3$ ions by cleavage of the central C—C bond[78]. The former ions are generated in a lower yield than the latter species when Y = F, Cl, Br, I and OH, while the $RCHY^+$ ions give rise to the main peak in the mass spectra of the compounds with Y = OCH_3, NH_2 and $N(CH_3)_2$. Loss of Y$^\cdot$ is significant only for R = CH_3 and Y = Cl, Br and I. In these instances, the process may be anchimerically assisted by the —SCH_3 group and possibly lead to a sulfur-methylated 1,2-dimethylthiirane species[78].

The possibility for anchimerically assisted cleavage of the C—Cl bond in the molecular ions of 2-chlorovinyl methyl sulfides (**10**) and the related phenyl 2-chlorovinyl sulfide (**11**) has been examined in an attempt to generate thiirenium ions in the gas phase along a route comparable to the one leading to these species in the condensed phase[79–81]



R^1 = H, alkyl, Ph R^2 = H, alkyl, Ph

(10)



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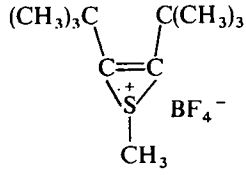
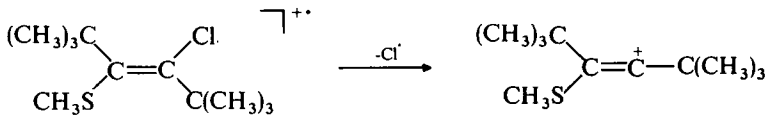


(12)

No conclusive evidence was obtained for the generation of thiirenium ions by the loss of a Cl$^\cdot$ atom from the molecular ions of **10** and **11**. This loss is associated with a narrow metastable peak typical for a simple cleavage reaction, suggesting that loss of Cl$^\cdot$ leads initially to a vinylic carbenium ion as illustrated in equation 38 for ionized **10** and $R^1 = R^2 = C(CH_3)_3$. The MIKE (mass-analyzed ion kinetic energy)[2] and CID spectra of the product ion of Cl$^\cdot$ loss are reported to be almost identical to the spectra of the cationic part of the BF_4^- salt of the isomeric thiirenium ion **12** (brought into the gas phase by Fast Atom Bombardment) indicating that a common ion structure and/or a mixture of ions is generated in both instances[82].



m/z 220 *m/z* 185 (38)

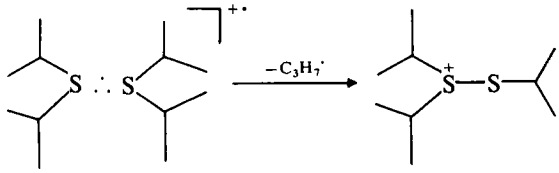
Finally, *ortho*-effects are reported for the EI induced fragmentation of methoxy-substituted diaryl sulfides[83], *o*-carboxyphenyl *ω*-carboxyalkyl sulfides[84], *o*-nitro substituted aromatic sulfides containing, for example, a pyridyl group[85], allyl *o*-nitrophenyl sulfides[86], allenyl *o*-nitrophenyl sulfides[87] and *o*-nitrophenyl phenylethynyl sulfides[88]. Notably, the molecular ions of allyl *o*-nitrophenyl sulfides[86] and *o*-nitrophenyl phenylethynyl sulfides[88] react in part by double oxygen atom transfer from the nitro group to the sulfur atom followed by expulsion of a $HSO_2^\cdot$ radical.

B. Bimolecular Reactions

1. Positive ions

Sulfides are readily protonated under positive ion CI conditions (see Table 1 for selected PA values). The metastable MH^+ ions formed by proton transfer from CH_5^+ to 2,3-dimethylthiirane, 2-methylthietane, thiolane and allyl methyl sulfide all eliminate H_2 and H_2S[73]. Loss of H_2S dominates over loss of H_2 for the MH^+ ions from the three former compounds, whereas protonated allyl methyl sulfide also reacts by loss of C_2H_4 and C_3H_6, possibly as a result of competing proton transfer from the CH_5^+ ion to the carbon–carbon double bond and the sulfur atom[73].

The bimolecular chemistry of the radical cations of simple dialkyl sulfides has not been studied in great detail. The di-*i*-propyl sulfide molecular ion is reported to form a dimeric species with its own precursor under conditions where collisional deactivation of the encounter complex occurs[89]. Loss of a $C_3H_7^{\bullet}$ radical is the main collision-induced reaction of the dimeric species (equation 39), while dissociation to the di-*i*-propyl sulfide ion is less important. The occurrence of both these reactions was taken as evidence for the formation of a two-center, three-electron S—S bond[90,91] with a strength comparable to that of the S—C bond in the dimeric species.



(39)

m/z 236 *m/z* 193

Interestingly, the molecular ion of methyl 1-phenylethyl sulfide reacts with its neutral precursor by overall transfer of CH_3S^+ leading to a thiosulfonium ion (equation 40)[92].

$$\underset{m/z\ 152}{PhCH(CH_3)\overset{+\cdot}{S}CH_3} \xrightarrow[-PhCHCH_3]{PhCH(CH_3)SCH_3} \underset{m/z\ 199}{PhCH(CH_3)—\overset{+}{S}(CH_3)—SCH_3} \qquad (40)$$

Although the precise mechanism of reaction 40 is unknown, it may be anticipated that the initial step in the reaction sequence is the formation of a three-electron two center S—S bond followed by loss of a benzylic radical. Formation of such a S—S bond may be thought also to be involved in the reaction of the molecular ion of thiirane with its own precursor, which is reported to yield a $C_2H_4S_2^{+\cdot}$ ion by loss of C_2H_4 from the collision complex[43,93].

The ability of SR and OR (R = H and alkyl) groups to stabilize an adjacent carbenium ion center has been the subject of a number of theoretical studies[94–96]. At the highest level of theory applied in the calculations, the OR group is predicted to stabilize an α-carbenium center slightly better than a SR group (about 5 kJ mol^{-1} when R = H)[94–96] suggesting that hydride ion transfer between the $CH_3SCH_2^+$ ion and CH_3OCH_3 is slightly exothermic (equation 41).

$$\underset{m/z\ 61}{CH_3SCH_2^+} + CH_3OCH_3 \not\longrightarrow CH_3SCH_3 + \underset{m/z\ 45}{CH_3OCH_2^+} \qquad (41)$$

Thermoneutral or exothermic hydride ion transfer reactions are often slow in the gas phase[97] and the reaction in equation 41 is reported not to occur under ICR conditions[98].

However, chloride ion transfer from $ClCH_2SCH_3$ to $CH_3OCH_2^+$ (equation 42) occurs readily and is observed to be reversible with the equilibrium being displaced to the right[98].

$$\underset{m/z\,45}{CH_3OCH_2^+} + ClCH_2SCH_3 \rightleftharpoons CH_3OCH_2Cl + \underset{m/z\,61}{CH_3SCH_2^+} \qquad (42)$$

The free energy change for the chloride ion transfer reaction (equation 42) is determined to be about $-10\,kJ\,mol^{-1}$. According to a theoretical analysis, the exoergic nature of this reaction is a result of anomeric effects in the neutral molecules[96], which stabilize the oxygen relative to the sulfur compound by $25\,kJ\,mol^{-1}$. These effects in the neutral molecules compensate for the less efficient stabilization of the carbenium ion center in the $CH_3SCH_2^+$ ion than in the $CH_3OCH_2^+$ ion. Notwithstanding that a SR group should stabilize an adjacent carbenium ion center slightly less than an OR group, the $CH_3SCH_2^+$ ion is reported to abstract exclusively a deuteride ion from $CH_3OCH_2CD_2SCH_3$ yielding the sulfur stabilized cation[98].

The $CH_3OCH_2^+$ ion transfers a methyl cation to dimethyl sulfide and dimethyl disulfide[92]. In the reaction with methyl allyl sulfide attack on the terminal carbon atom of the double bond by the methylene group of the reactant ion occurs and is succeeded by the competing eliminations of CH_2O, CH_3OH or CH_3SH[99]. The reaction of $CH_3OCH_2^+$ with dimethyl disulfide leads to a thiosulfonium ion, $(CH_3)_2\overset{+}{S}SCH_3$, whereas dithiosulfonium ions are formed in the reaction of protonated dimethyl disulfide with neutral dimethyl disulfide (equation 43)[49]. Both thio- and dithiosulfonium ions react in the gas phase by transfer of CH_3S^+ to neutral sulfides or alkenes, e.g. 2-methoxypropene, by analogy with their chemistry in solution.

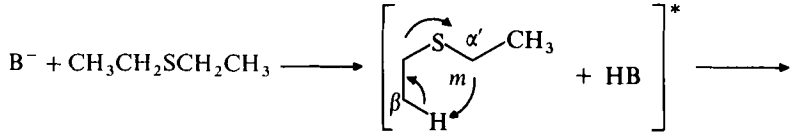
$$\underset{m/z\,95}{CH_3-\overset{+}{S}(H)-SCH_3} \xrightarrow[-CH_3SH]{CH_3SSCH_3} \underset{m/z\,141}{\begin{matrix} CH_3S \\ CH_3S \end{matrix}\!\!>\!\overset{+}{S}-CH_3} \qquad (43)$$

2. *Negative ions*

The reactions of negative ions with sulfides and disulfides are described in a recent review[11]. The stabilizing influence of a sulfur atom on an adjacent carbanionic center is reflected directly in the finding that CH_3SCH_3 is *ca* $58\,kJ\,mol^{-1}$ more acidic than CH_3OCH_3 in the gas phase (see Table 1)[100–102]. The strongly basic amide ions, NH_2^-, $C_2H_5NH^-$ and $(CH_3)_2N^-$, abstract a proton from the methyl group as well as the phenyl group in $PhSCH_3$, whereas selective abstraction of a proton from the methyl group occurs in the reaction with CH_3O^- ions[100]. The enhanced acidity of sulfides in comparison to ethers is manifested also in the mechanism of gas-phase base-induced elimination reactions of dialkyl sulfides[103], cyclic sulfides[104], 1,3-thiolanes[105], 1,3-dithianes[105,106] and 1,3-dithiane-1-oxides[106].

Amide anions react with diethyl sulfide preferentially by a *syn* α',β-elimination reaction in which the initial step is abstraction of a proton from the α'-position (Scheme 3)[103]. The weaker bases, HO^- and CH_3O^-, react with diethyl sulfide by an E2 elimination leading to $C_2H_5S^-$ ions and with F^- as the reactant ion, HF solvated ethylthiolate anions, $[C_2H_5S^-, HF]$, are formed also. The reactions of anions with the cyclic sulfides, thiepane, thiolane, thietane and thiirane, proceed by (i) E2 elimination, (ii) α'-proton abstraction partly followed by an α',β-elimination and (iii) S_N2 substitution[104]. The HO^-, CH_3O^- and F^- anions react with thiepane and thiolane only by E2 elimination. The S_N2 substitution pathway competes effectively with the E2 elimination in the reactions of the HO^- and CH_3O^- ions with thietane and thiirane, whereas the F^- ion is unreactive

towards these sulfides. Abstraction of an α′-proton followed by elimination dominates in the reaction of NH_2^- with thiepane, but is less important than E2 elimination in the reaction with thiolane.

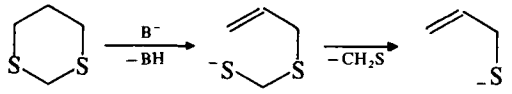


$C_2H_4 + HB + C_2H_5S^-$

$B^- = NH_2^-, CH_3NH^-, C_2H_5NH^-$ and $(CH_3)_2N^-$

SCHEME 3. Mechanism of the α′, β-elimination reaction of diethyl sulfide[103]

Anions react with 1,3-dithiane in the gas phase by deprotonation and an elimination reaction which, to some extent, is followed by fragmentation of the initially generated thiolate anion (equation 44). Introduction of two methyl groups at the 5-position in 1,3-dithiane leads to the sole occurrence of proton abstraction, indicating that the process in equation 44 requires the presence of hydrogen atoms at this position.



(44)

Deuterium labelling at the 2-position in 1,3-dithiane results in the occurrence of D^+ and H^+ abstraction, revealing that deprotonation of 1,3-dithiane in part takes place from this position[105]. Deprotonation from the 2-position as well as other positions occurs in the reactions of HO^- and CH_3O^- with *cis*-2,2-dideuterio-4,6-dimethyl-1,3-dithianes in addition to extensive fragmentation of the initially generated ions with formation of thiolate anions[106]. Stereoselective deuterium labelling reveals that the axial proton at the 2-position is removed as readily or more so than the equatorial proton, in contrast to the results for the corresponding condensed phase reactions, which indicate a strong preference for abstracting the equatorial proton at the 2-position[106] Exclusive deprotonation at the 2-position is achieved by introduction of a phenyl group at this position[107], whereas blocking of this position with a methyl group and an aryl function leads to competing deprotonation of the methyl group and the 4- and 5-positions, in the 1,3-dithiane system[108].

The reactions of negative ions with dimethyl disulfide proceed by proton abstraction, elimination across the C—S bond and attack on a sulfur atom[109]. No evidence has been obtained for the formation of a carbanion by proton abstraction from dimethyl disulfide. Instead, this process was suggested to lead to an $[CH_3S^-CH_2{=}S]$ ion-neutral complex, which recombines with the formation of a $CH_3SCH_2S^-$ ion[109] Elimination across the C—S bond results either in CH_3S^- ions or cluster ions and dominates in the reactions of charge localized anions, which are at least as basic as the methoxide ion in the gas phase. The charge delocalized anions, $CH_3COCH_2^-$, $^-CH_2CN$ and $^-CH_2NO_2$, react mainly by attack on a sulfur atom followed by loss of CH_3SH from the collision complex (equation 45).

$$\underset{m/z\,60}{^-CH_2NO_2} + CH_3SSCH_3 \longrightarrow \underset{m/z\,106}{CH_3S\bar{C}HNO_2} + CH_3SH \qquad (45)$$

Competing attack on a sulfur atom and elimination across a C—S bond may be held responsible also for the formation of CH_3S^- in the reaction of the $^-$·CHNC radical anion with dimethyl disulfide[110]. By contrast, in the reactions with the isomeric radical anion, $^-$·CHCN, loss of a CH_3S· radical and a CH_3SH molecule from the collision complex compete effectively with CH_3S^- formation, thus distinguishing this radical anion from the isomeric $^-$·CHNC species[110].

3. *Reactions with metal ions*

The Co^+ ion reacts with dimethyl sulfide with elimination of methane from the collision complex (equation 46)[50]. With thiirane as the substrate, the Co^+ ion reacts by sulfur atom abstraction, a reaction also observed for Ti^+, V^+, Fe^+ and Ta^+ ions[48].

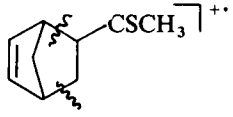
$$\underset{m/z\ 59}{Co^+} + CH_3SCH_3 \longrightarrow \underset{m/z\ 105}{Co(CH_2S)^+} + CH_4 \qquad (46)$$

The metal negative ions, Co^- and Fe^-, react with dimethyl disulfide mainly by insertion into a C—S bond leading to MS_2^- and $M(S_2CH_3)^-$ ions by loss of ethane and a methyl radical, respectively, from the collision complex[53]. Insertion into the S—S bond is less important than insertion into the C—S bond and yields CH_3S^- as well as $M(SCH_3)^-$ ions.

IV. THIOCARBONYL COMPOUNDS

A. Unimolecular Reactions

The 70 eV mass spectra of dialkyl, alkyl cycloalkyl, dicycloalkyl and cyclic thioketones exhibit more intense molecular ion peaks than the spectra of the related ketones[111,112]. The molecular ions of the aliphatic thioketones fragment to a large extent along the same routes as the oxygen compounds, i.e. α-cleavage, McLafferty rearrangement and double McLafferty rearrangement. In addition, cleavage of a remote C—C bond with respect to the C=S function can take place. Notably, the molecular ions of the different thioketones appear to expel a HS· radical by a process, which may involve the enol form of the radical cation of the thioketone and/or a transfer of a hydrogen atom to the sulfur atom from other sites than the α-position[111]. The molecular ions of cyclopropyl methyl thioketone, dicyclopropyl and dicyclobutyl thioketone fragment predominantly by α-cleavage, loss of a hydrogen atom and loss of HS·, while the molecular ion of the thioketone **13** undergoes a retro Diels–Alder-type reaction to form $C_5H_6^{+\cdot}$ (equation 47) and $C_4H_6S^{+\cdot}$ (equation 48) ions[112].

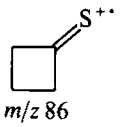


(13) *m/z* 152

$$\xrightarrow{} \underset{m/z\ 66}{C_5H_6^{+\cdot}} + C_4H_6S \qquad (47)$$

$$\xrightarrow{} \underset{m/z\ 86}{C_4H_6S^{+\cdot}} + C_5H_6 \qquad (48)$$

The molecular ion of cyclobutanethione reacts, as the related oxygen species, by α-cleavage accompanied by rupture of the $C_{(2)}$—$C_{(3)}$ bond leading to a sulfur containing fragment ion (equation 49). The molecular ions of methyl substituted cyclobutanethiones reacts likewise, but ionized alkenes are formed in addition to the complementary sulfur containing fragment ions. In contrast to the cyclobutanones, whose molecular ions expel CO, loss of CS is not observed for ionized cyclobutanethiones[112].

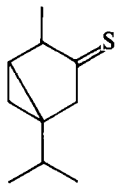


m/z 86

$$\longrightarrow \quad C_2H_2S^{+\cdot} + C_2H_4 \qquad (49)$$

m/z 58

Loss of a HS$^{\cdot}$ radical is the main reaction of the molecular ions of cyclopentanethione and cyclohexanethione, while the loss of $C_3H_7^{\cdot}$ dominates in the decomposition of the molecular ions of the bicyclic thioketones **14**, **15** and **16**[112,113]. For the latter compound, thiocampher (**16**), deuterium labelling of the bridging group indicates that this entity is expelled together with a hydrogen atom, which may originate from the 3-position with respect to the C=S function[113].



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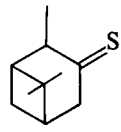
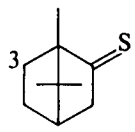
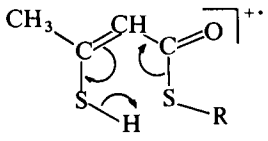


(15)



(16)

The mass spectra of β-thioketo thiolesters exhibit characteristic peaks corresponding to the formation of $RSH^{+\cdot}$ and $C_4H_4SO^{+\cdot}$ ions by a reaction, which may involve the enolic form (**17**) of the molecular ions (equations 50 and 51)[114].



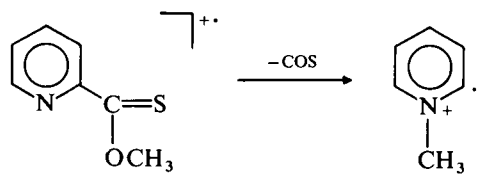
(17)

$$\longrightarrow \quad RSH^{+\cdot} + C_4H_4SO \qquad (50)$$

$$\longrightarrow \quad C_4H_4SO^{+\cdot} + RSH \qquad (51)$$

m/z 100

The molecular ions of the 3- and 4-pyridine carbothioic acid *O*-methyl esters expel a $CH_3O^{\cdot}$ radical, while the 2-isomer eliminates a $CH_2{=}O$ molecule[115]. In addition, the molecular ions of 2-pyridine carbothioic acid *O*-methyl ester eliminate a COS molecule with formation of a $C_6H_7N^{+\cdot}$ ion, possibly with the structure shown in equation 52. The related pyridine carbodithioic methyl esters behave similarly, that is, loss of $CH_3S^{\cdot}$ dominates in the EI induced fragmentation of the 3- and 4-substituted compounds, while the molecular ion of 2-pyridine carbodithioic methyl ester eliminates $CH_2{=}S$ and, to a minor extent, a CS_2 molecule with formation of a $C_6H_7N^{+\cdot}$ ion[115].



m/z 153 m/z 93 (52)

The electron affinity of thioformaldehyde is measured to be 0.465 ± 0.023 eV[116] and stable negative molecular ions are formed by electron capture of $ArCS_2R$ compounds[16], with formation of a $C_6H_7N^{+\cdot}$ ion, possibly with the structure shown in equation 52. The thioanilides[16], thiobenzamides[16] and are reported also for the β-thioketo thiolesters (**17**)[114]. The molecular negative ions of the latter compounds fragment by (i) loss of RCOS$^{\cdot}$ to form $CH_3C(S)CH_2^-$ ions, (ii) loss of R$^{\cdot}$ and (iii) loss of RSH to form $C_4H_4SO^{-\cdot}$ ions by analogy with the reaction of the positive ions shown in equation 51[114].

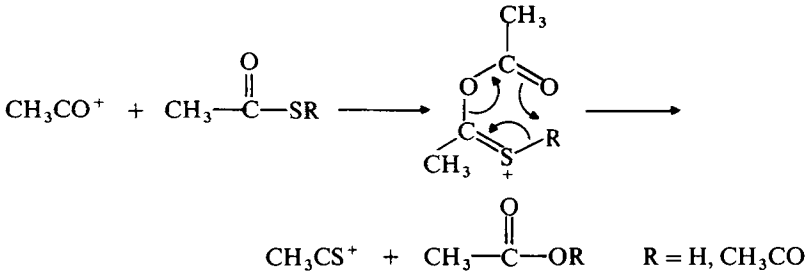
Thiocarboxylate anions, $RCOS^-$ (R = alkyl or aryl), are formed by dissociative electron attachment to, for example, thioacetic anhydride, thiolpropanoic acid or thiolbenzoic acid[117]. Collision-induced charge reversal of the thiocarboxylate anions with N_2 as the collision gas results in extensive fragmentation with formation of ions such as R^+, $COS^{+\cdot}$, and RCO^+. Nondecomposing $RCOS^+$ ions are not observed following collision of CH_3COS^- or $C_2H_5COS^-$ ions with N_2 and only minor amounts of stable $PhCOS^+$ ions are generated from $PhCOS^-$.

B. Bimolecular Reactions

The thioacylium ion, CH_3CS^+, is reported to be formed by simple cleavage of the molecular ions of $CH_3C(S)OCH_3$ and $CH_3C(S)SCH_3$[118]. The CH_3CS^+ ions react with their neutral precursors by proton transfer, while the reaction with $(CH_3CO)_2S$ or $CH_3CO_2CH{=}CH_2$ proceeds by elimination of ketene from the collision complex. The $C_2H_3S^+$ ions fomed in the reactions of CH_3CO^+ with $CH_3C(O)SH$, $CH_3C(S)OCH_3$ (equation 53) or $(CH_3CO)_2S$ react likewise, indicating that thioacylium ions are generated also by this route. Similarly, the $C_2H_5CS^+$ ion is formed by the reaction between $C_2H_5CO^+$ and $C_2H_5C(O)SH$ or $C_2H_5C(S)OCH_3$.

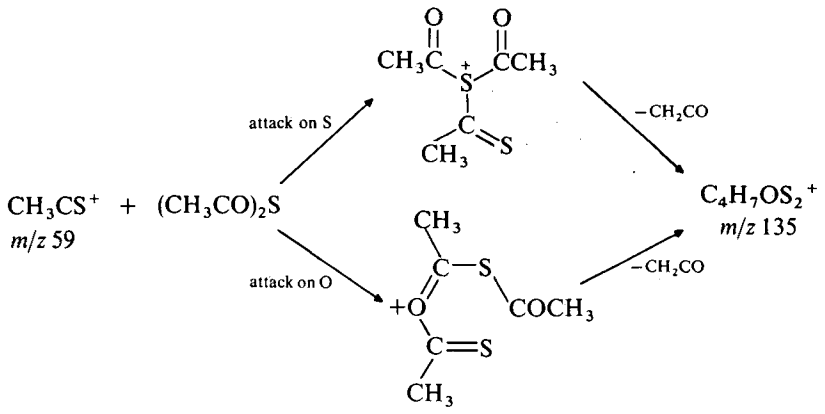
$$\underset{m/z\,43}{CH_3CO^+} + CH_3C(S)OCH_3 \longrightarrow \underset{m/z\,59}{CH_3CS^+} + CH_3C(O)OCH_3 \qquad (53)$$

The formation of the thioacylium ions in the reaction of CH_3CO^+ with $CH_3C(O)SR$ may proceed by attack on the oxygen atom of the substrate followed by a shift of the R group concomitant with dissociation to the separated products (Scheme 4) in line with the observation that the reaction between CD_3CO^+ and $CH_3C(O)SH$ yields almost exclusively CH_3CS^+ ions[118].



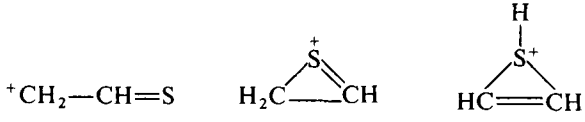
SCHEME 4. Proposed mechanism for the formation of the CH_3CS^+ ion[118].

The elimination of ketene from the collision complex in the reactions of CH_3CS^+ with $(CH_3CO)_2S$ corresponds to a thioacylation reaction, which has been suggested to proceed by electrophilic attack on either the sulfur atom or one of the oxygen atoms with formation of the intermediate structures shown in Scheme 5.



SCHEME 5. Proposed mechanism for thioacylation of $(CH_3CO)_2S$[118]

The CH_3CS^+ ion is predicted to be more stable than the isomeric $CH_2{=}C{=}SH^+$ ion, indicating that the thermodynamically preferred site of protonation of thioketene is at the β-carbon atom[118,119]. According to *ab initio* MO calculations, the acylium ion is also more stable than other conceivable $C_2H_3S^+$ isomers, for instance α-carbon protonated thioketene (**18**), the thiiranyl cation (**19**) and the thiirenium ion (**20**) (see also Section III.A.5)[119].



(**18**) (**19**) (**20**)

Simple cleavage of the molecular ion of $CH_3C(S)NHPh^{+\cdot}$ is expected to yield the thioacylium ion. This $C_2H_3S^+$ isomer is reported to react with 3-methylanisole by adduct formation, charge exchange, proton transfer and, to a very minor extent, by the competing losses of $H_2C{=}S$ and $HS^{\cdot}$ from the collision complex[120]. The $C_2H_3S^+$ ions formed in the decomposition of ionized 1,3-dithiolane and 1-methylthiirane react with 3-methylanisole along the same routes, but the losses of $H_2C{=}S$ and $HS^{\cdot}$ from the collision complex occur to a more significant extent than in the reaction of the thioacylium ion. This implies that the $C_2H_3S^+$ ions derived from 1,3-dithiolane and 1-methylthiirane have a different structure than CH_3CS^+. This conclusion is in line with the results of high kinetic energy CID experiments, which indicate that the thiiranyl cation (**19**) can arise by EI induced decomposition of 1,3-dithiolanes and 1,3-oxathiolanes[121]. However, earlier studies[122,123] indicated that the $C_2H_3S^+$ ions formed by EI induced decomposition of different sulfur containing compounds [for example $CH_3C(S)NHPh$, thiirane, methyl-substituted thiophenes, ethyl methyl sulfide and diethyl disulfide] attain the same structure(s) prior to CID or surface induced decomposition.

Thioenolate anions are formed in the reactions of negative ions with 1,3-dithiolanes, 1,3-oxathiolanes[105] and ethyl vinyl sulfides[24] (equation 54; see also Section III.B.2). Based on the occurrence/nonoccurrence of proton transfer in the reactions between the thioenolate anions and reference acids of known acidity the ΔG°_{acid} of $CH_3CH{=}S$ and

$(CH_3)_2C{=}S$ has been determined to be $1427 \pm 12\,kJ\,mol^{-1}$ and $1439 \pm 12\,kJ\,mol^{-1}$, respectively[124].

$$F^- + CH_3CH_2SC(R){=}CH_2 \longrightarrow CH_2{=}C(R){-}S^- + C_2H_4 + HF \qquad (54)$$
$$R = H,\ CH_3$$

V. SULFOXIDES AND SULFONES

A. Unimolecular Reactions

1. General characteristics

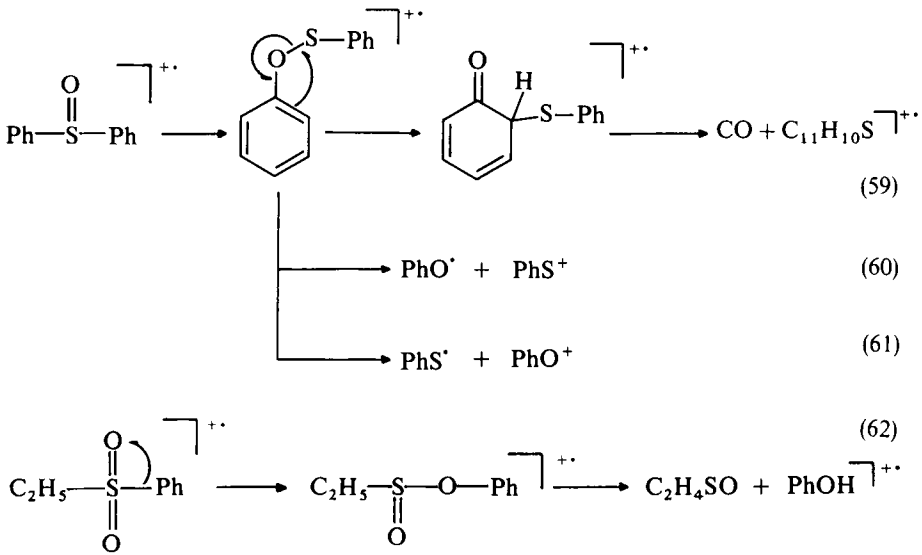
The typical fragmentation modes involved in the electron impact induced decomposition of sulfoxides and sulfones are documented in a number of reviews[6–8,125–128]. As for the sulfides, the decomposition of the ionized *alkyl sulfoxides and sulfones* is dominated by C—S bond cleavage with competing charge retention on either the hydrocarbon (equation 55) or the sulfur containing fragments (equation 56). Alternatively, C—S bond cleavage may be accompanied by migration of a hydrogen from the alkyl group to the electron-deficient oxygen atom, which results formally in the elimination of an alkene molecule and formation of ionized sulfenic (equation 57) and sulfinic acids in case of sulfoxides and sulfones, respectively. In addition, ionized sulfones show a tendency to eliminate the alkyl group with associated double hydrogen migration to the oxygen atoms as the size of the alkyl group is increased.

$$C_nH_{2n+1}{-}\overset{\overset{O}{\|}}{S}{-}C_nH_{2n+1}\ ]^{+\cdot} \longrightarrow C_nH_{2n+1}{-}\dot{S}{=}O + C_nH_{2n+1}^{+} \qquad (55)$$
$$\longrightarrow C_nH_{2n+1}^{\cdot} + C_nH_{2n+1}{-}\overset{+}{S}{=}O \qquad (56)$$
$$\longrightarrow C_nH_{2n} + C_nH_{2n+1}{-}S{-}OH\ ]^{+\cdot} \qquad (57)$$
$$\longrightarrow HO^{\cdot} + C_nH_{2n+1}{-}S{-}C_nH_{2n}^{+} \qquad (58)$$

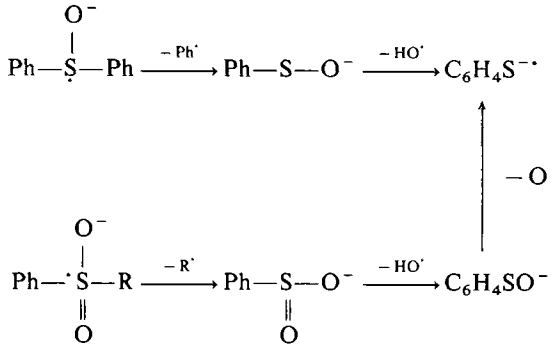
Further, migration of a hydrogen from the alkyl group to the oxygen atom may be accompanied by a cleavage of the S—O bond resulting in the loss of an HO· radical (equation 58).

In contrast with the alkyl sulfoxides and sulfones, *aryl and vinyl sulfoxides and sulfones* undergo abundant skeletal rearrangements upon electron impact. These skeletal rearrangements are revealed by the competing losses of CO, SO, HSO· and H_2SO from the sulfoxides and the competing losses of CO, SO_2, $HSO_2^{\cdot}$ and H_2SO_2 from ionized sulfones. Loss of CO is associated with 1,2-migration of an aryl or vinyl group from the sulfur to an oxygen atom, resulting in an ionized sulfenic (equations 59–61) and sulfinic ester (equation 62), respectively. The EI induced rearrangements of sulfoxides and sulfones to sulfenic and sulfinic esters, respectively, gain importance if the migrating aryl or vinyl groups are substituted with electron-donating groups and are also disclosed in the formation of fragments arising from cleavage of the S—O bond in the rearranged species (see equations 60–62).

Alternatively, EI may result in the capture of an electron, resulting in the formation of negative molecular ions of sulfoxides and sulfones, while dissociative electron capture yields negative fragment ions[129,130]. In contrast to the positive molecular ions, the negative molecular ions show no tendency to undergo skeletal rearrangements. Cleavage of the S—C bond constitutes the prominent fragmentation route and yields only



sulfur-containing fragment ions. When both alkyl and aryl substituents are present, the alkyl radical is lost from the molecular radical anion. The resulting fragment ions may lose HO• and O as shown in Scheme 6.



SCHEME 6. Dissociative electron capture of sulfoxides and sulfones[129]

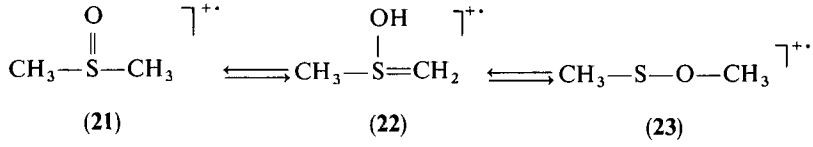
The low-energy resonance electron capture is related to the σ^* orbital of the S—C bond, while the oxidation state of the sulfur atom in sulfides, sulfoxides and sulfones has no marked effect on the major processes involved in the formation of negative ions.[130,131].

2. *Isomerization of ionized dimethyl sulfoxide*

Although dimethyl sulfoxide (DMSO) is the simplest sulfoxide, the nature of the decomposition of its radical cation is still debatable. The decomposition of metastable DMSO radical cations is characterized by retention of the sulfur atom in the ionic fragments[132]. The dominant fragmentation processes are the losses of CH_3• and HO•,

while skeletal rearrangements followed by the loss of an ethyl radical and the competing eliminations of ethylene, ethane and formaldehyde occur to a minor extent. Isotopic substitution does not have a marked effect upon the relative rates of the loss of $CH_3^{\bullet}$ and $HO^{\bullet}$[132].

The relatively low kinetic energies released during loss of $CH_3^{\bullet}$ and $HO^{\bullet}$ (19 and 22 meV, respectively) are considered to be indicative of isomerization of the radical cation of DMSO (**21**) to *aci*-DMSO (**22**) (Scheme 7)[132]. Fragmentation of the radical cation of DMSO and *aci*-DMSO can account for the formation of CH_3SO^+ and $CH_3—\overset{+}{S}=CH_2$, respectively.

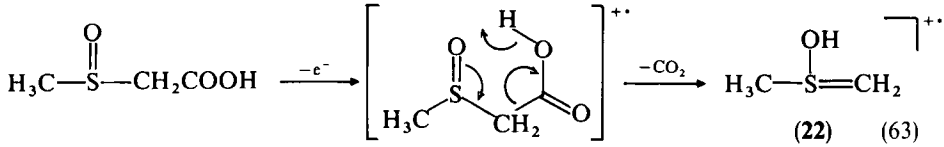


(21) (22) (23)

SCHEME 7. Isomerizations of $C_2H_6SO^{+\bullet}$

Irradiation of the electron impact generated molecular ions of DMSO with photons of energy 2.40 and 2.54 eV results exclusively in the loss of $CH_3^{\bullet}$[132]. Since no significant difference in the absorptivities in the visible region for the radical cations of DMSO and *aci*-DMSO is anticipated, it is concluded that **21** is the most dominant form and that tautomerization to **22** is followed by rapid loss of $HO^{\bullet}$. Apparently, photodissociation of the molecular ion of DMSO competes favorably with tautomerization to ionized *aci*-DMSO.

The isomerizations of the molecular ion of DMSO are revealed by comparison of the decompositions of the $C_2H_6SO^{+\bullet}$ radical cations generated from different precursors[133]. The DMSO radical cation (**21**) as well as the methyl methanesulfenate radical cation (**23**) are obtained by electron ionization of the corresponding neutral species, while the radical cation of *aci*-DMSO (**22**) is obtained as an electron impact induced fragment ion of methyl carboxymethyl sulfoxide, as shown in equation 63.



(22) (63)

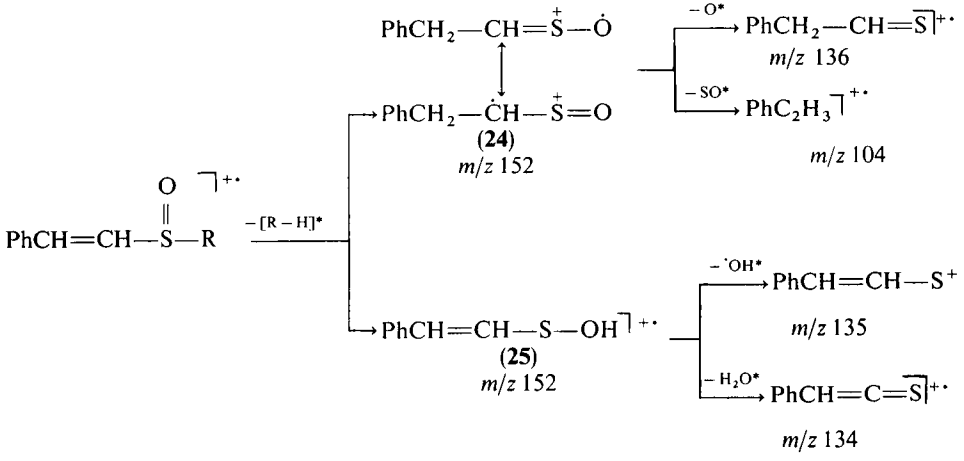
Assuming that ionized *aci*-DMSO (**22**) is the precursor for the loss of $HO^{\bullet}$, the decomposition of the specifically isotopically labelled isomeric ions indicates that reversible interconversion between the ionized DMSO and *aci*-DMSO can compete with the loss of the methyl and hydroxy radicals[133]. No significant deuterium isotope effect is encountered for the toutomerization, in contrast with the nitromethane/*aci*-nitromethane tautomerization, where the isotope effect is estimated to be more than 50[134]. Although isomerization of the methyl methanesulfenate radical cation (**23**) to *aci*-DMSO (**22**) can be held responsible for the loss of $HO^{\bullet}$, no conclusive evidence is obtained for the isomerization of ionized DMSO to methyl methanesulfenate. Interestingly, direct loss of a methyl radical occurs from all three isomeric $C_2H_6SO^{+\bullet}$ radical cations[133].

A semiquantitative analysis of the potential energy surface for the isomerizations and decompositions is reported on the basis of kinetic energy release data and fragment ion

appearance energies[133]. However, the uncertainty in the analysis may be quite large as illustrated by the appearance energies (derived from plots of ion currents *vs* nominal energy of the ionizing electrons) for the product ions resulting from the loss of $CH_3^{\bullet}$ and $HO^{\bullet}$ from DMSO which are 0.8 and 1.0 eV higher than the IE of DMSO[133], respectively. These values are significantly lower than the 1.63 and 1.54 eV obtained from threshold photoelectron photoion coincidence (TPEPICO) measurements on DMSO[135]. The TPEPICO results on the loss of $CH_3^{\bullet}$ and $HO^{\bullet}$ from the molecular ion of DMSO are reproduced by RRKM/QET[37,38] calculations.

3. *Hydrogen rearrangements in ionized styryl alkyl sulfoxides and sulfones*

Although the electron impact induced decompositions of styryl alkyl sulfoxides and sulfones can be accommodated within the framework of a few basic reaction types, the introduction of the additional styryl functionality reveals an interesting competition between hydrogen migration from the alkyl group to the sulfoxide/sulfone and to the styryl functionality. For ionized styryl alkyl sulfoxides, PhCH=CH—(SO)—R, with short alkyl chains (R = CH_3, C_2H_5), direct cleavage of the sulfur–alkyl bond constitutes a major fragmentation together with the fragmentations of the ionized sulfenic esters which are formed by migration of the styryl or alkyl group from the sulfur to the oxygen atom[136]. For the styryl alkyl sulfoxides with longer alkyl chains, hydrogen rearrangements become prominent as revealed by the formation of an abundant fragment ion with *m/z* 152. This ion results from a migration of a hydrogen from the alkyl group to either the benzylic carbon atom or the oxygen atom concomitant with cleavage of the sulfur–alkyl bond as shown in Scheme 8.



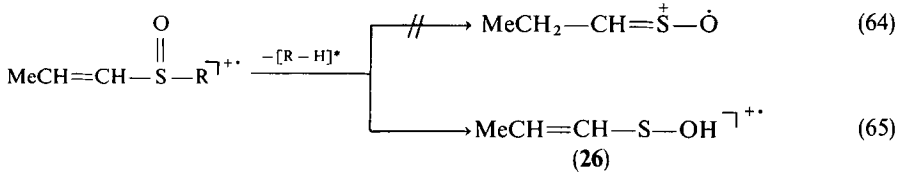
SCHEME 8. Hydrogen rearrangements in ionized styryl alkyl sulfoxides[136]

The individual contribution of alkyl loss associated with hydrogen migration to the benzylic carbon atom and the oxygen atom yielding the isomeric ions **24** and **25** is roughly estimated from the distribution of the fragment ions formed in the subsequent decompositions of these ions[136]. Loss of O and SO from the common ion with *m/z* 152 is ascribed to the decomposition of the fragment ion **24** resulting from an initial hydrogen migration to the benzylic carbon atom. Loss of $HO^{\bullet}$ and H_2O is ascribed to the decomposition of the ion **25** resulting from an initial hydrogen migration to the oxygen atom

as depicted in Scheme 8. For all the above mentioned, subsequent fragmentations of the primary fragment ion with *m/z* 152 metastable ion transitions are detected[136]. The product ion distribution indicates that hydrogen migration to the benzylic carbon atom and the oxygen atom occurs to a comparable extent. No appreciable difference is experienced between the (*E*) and (*Z*) isomers in all major fragmentations of the styryl alkyl sulfoxides, which is rationalized by a rapid electron impact induced interconversion between the geometric isomers prior to or during fragmentation[136].

From the decomposition of the specifically deuterium-labelled alkyl styryl sulfoxides[137], it follows that for alkyl groups with α- and β-hydrogen atoms, the alkyl group is lost exclusively with migration of a β-hydrogen. For alkyl groups with α-, β- and γ-hydrogen atoms, about equal migratory probability is encountered for the β- and γ-hydrogens.

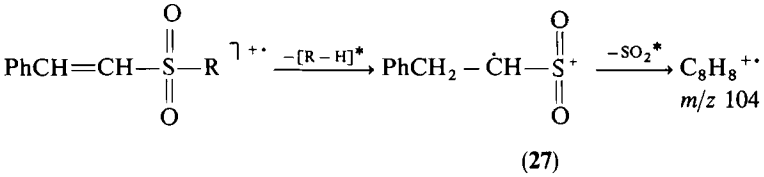
Probably owing to the large difference between the ionization energies of styrene and propene, hydrogen migration occurs only from the alkyl group to the oxygen atom in the decomposition of radical cations of propenyl alkyl sulfoxides, MeCH=CH—(SO)—R[137]. No evidence is obtained for the migration of a hydrogen from the alkyl group to the alkene functionality (equation 64). Again alkyl α-hydrogen atoms are not involved in the rearrangement leading to the fragment ion **26** (equation 65), which exclusively retains a hydrogen atom originating from either the β- or γ-position of the alkyl group.



$$MeCH{=}CH{-}\overset{\overset{O}{\|}}{S}{-}R^{\cdot+} \xrightarrow{-[R-H]^{*}} \begin{cases} \not\longrightarrow\ MeCH_2{-}CH{=}\overset{+}{S}{-}\dot{O} & (64) \\ \longrightarrow\ MeCH{=}CH{-}S{-}OH^{\cdot+} & (65) \end{cases}$$

(26)

The electron impact induced decomposition of styryl alkyl sulfones, PhCH=CH—(SO_2)—R, with large alkyl chains is dominated by the formation of a fragment ion with *m/z* 104[138,139]. Formation of this ion is associated with hydrogen migration from the alkyl group to the benzylic carbon atom accompanied by sulfur–alkyl bond cleavage generating the ion **27** in a low abundance. Subsequent elimination of a SO_2 molecule (for which a metastable ion transition is detected) yields the common fragment ion $C_8H_8^{\cdot+}$ with *m/z* 104 (equation 66). Deurerium labelling reveals that the migrating hydrogen may originate from either the alkyl β- or γ-position[139]. No fragment ions are detected, which in a relatively simple way can be related to fragmentation processes involving the migration of a hydrogen from the alkyl group to an oxygen atom[138,139]. Yet, a minor contribution to the electron impact induced decompositon of styryl alkyl sulfones can be related to the loss of the alkyl group with a double hydrogen migration to the sulfone group.[139]



$$PhCH{=}CH{-}\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}{-}R^{\cdot+} \xrightarrow{-[R-H]^{*}} PhCH_2{-}\dot{C}H{-}\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}{}^{+} \xrightarrow{-SO_2^{*}} C_8H_8^{\cdot+} \quad (66)$$

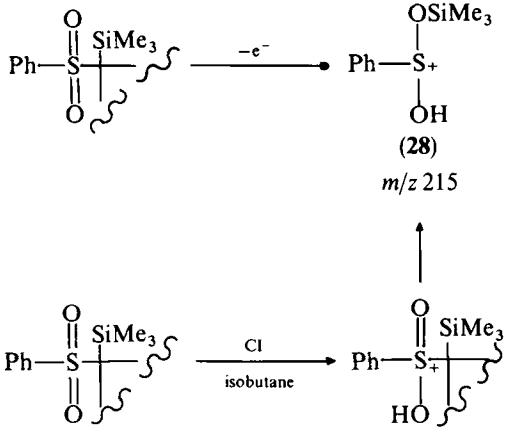
(27) *m/z* 168 — *m/z* 104

4. Migration of trimethylsilyl to the sulfone group

The ability of the silicon atom of a trimethylsilyl group to form a strong new bond with an oxygen atom of a remote functionality is well known[128]. This process is encountered

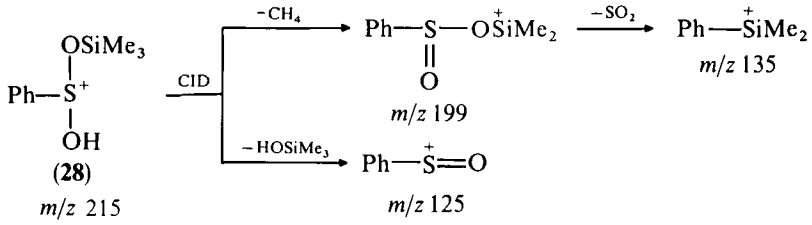
frequently as a transfer of intact trimethylsilyl groups to a carbonyl oxygen atom in the molecular ions. The remarkable similarity between the trimethylsilyl group and the hydrogen atom with respect to these specific transfers has been emphasized[140].

Migration of a trimethylsilyl group in the reactions of the molecular ions of substituted α-trimethylsilylalkyl phenyl sulfones is disclosed by the formation of a fragment ion with *m/z* 215[141,142]. This product ion is associated with a complex process involving trimethylsilyl migration from the α-position to a sulfone oxygen atom and additional hydrogen migration from the alkyl group to the remaining sulfone oxygen atom accompanied by sulfur–alkyl bond cleavage to form the ion **28** (Scheme 9).



SCHEME 9. Migration of the trimethylsilyl group to the sulfone functionality[141,142]

Furthermore, the ion with *m/z* 215 appears to be the main decomposition product of the protonated substituted α-trimethylsilyl alkyl phenyl sulfones, generated in an *iso*-butane CI plasma[141,142] (Scheme 9). Characterization of the product ion with *m/z* 215 follows from low-energy (5 eV) CID[141], which shows that this ion undergoes two competing reactions as depicted in Scheme 10.



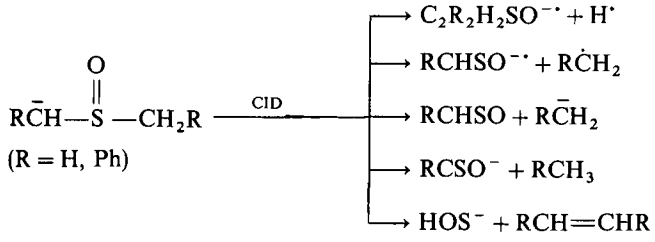
SCHEME 10. Characterization of the $PhS(OH)(OSiMe_3)^+$ fragment ion with CID[142]

5. Decomposition of deprotonated sulfoxides and sulfones

High-energy (8 keV) CID of deprotonated dimethyl sulfoxide and dibenzyl sulfoxide exhibits a competition between a number of fragmentations[143].

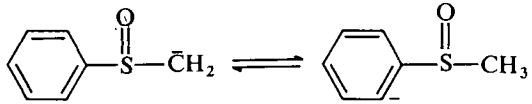
Loss of a hydrogen atom (equation 67) occurs for both deprotonated sulfoxides.

Homolytic cleavage of the S—C bond results in the loss of a methyl and benzyl radical, respectively (equation 68), while heterolytic cleavage is an important process in the decomposition of deprotonated dibenzyl sulfoxide, generating the benzyl anion (equation 69). Further, cleavage of the S—C bond leads also to the elimination of methane and toluene, respectively (equation 70). Finally, unlike the corresponding uneven electron molecular anions, the even electron deprotonated sulfoxides show the tendency to undergo a skeletal rearrangement as revealed by formation of the common HOS^- ion[143] (equation 71).



(67)
(68)
(69)
(70)
(71)

Except for this skeletal rearrangement, the collision-induced decomposition of deprotonated methyl phenyl sulfoxide is very similar to that of the deprotonated dimethyl and dibenzyl sulfoxides[143]. In addition, isotopic labelling shows that all major fragmentations of deprotonated methyl phenyl sulfoxide are preceded by a reversible proton transfer between the phenyl and methyl entities, revealing a reversible interconversion between the isomeric deprotonated methyl phenyl sulfoxides **29** and **30** (equation 72).



(72)

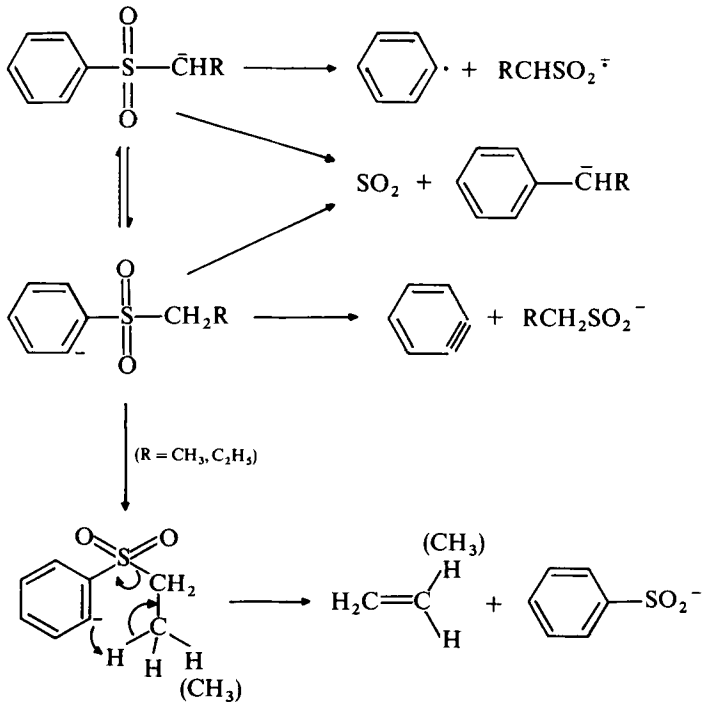
(29) **(30)**

A similar interconversion is considered to be operative in the low-energy CID of deprotonated alkyl phenyl sulfones[144], which involves the reactions shown in Scheme 11.

B. Bimolecular Reactions

1. Gas-phase basicity and acidity of sulfoxides and sulfones

Surprisingly, reports on positive and negative chemical ionization of sulfoxides and sulfones are very scarce and only limited data on the gas-phase basicity and acidity are available[13,145]. [See Table 1 for the definition of gas-phase basicity or proton affinity (PA) and the gas-phase acidity (ΔH^0_{acid}).] The lack of PA data may be due to the premise that, as for electron ionization, protonation on oxygen results in a considerable weakening of the sulfur–alkyl or aryl bond, leading to facile decomposition of the protonated molecules. In fact, only the PA for dimethyl sulfoxide has been determined. The obtained value of 884 kJ mol^{-1} indicates that sulfoxides are stronger bases in the gas phase than, for instance, ammonia [PA(NH_3) = 854 kJ mol^{-1}][13]. Further, it follows that oxidation of dimethyl sulfide to dimethyl sulfoxide results in an increase of the PA by 45 kJ mol^{-1}. On the other hand, the lack of gas-phase acidity data may be due to the premise that

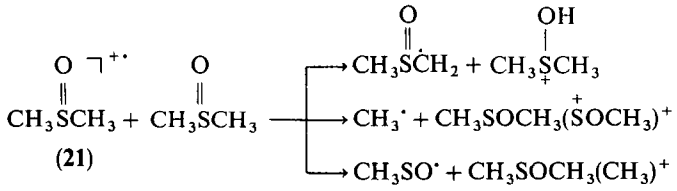


SCHEME 11. CID of deprotonated alkyl phenyl sulfones[144]

base-induced deprotonation yielding α-sulfoxyl and α-sulfonyl carbanions suffers from a competing base-induced 1,2-alkene elimination reaction if β-hydrogen atoms are present, resulting in the formation of stable sulfoxyl and sulfonyl anions, similar to the formation of thiolate anions in the base-induced reactions of alkyl sulfides (see Section III.B.2)[103,104]. Gas-phase acidity data are available for dimethyl sulfoxide, dimethyl sulfone and for some alkyl phenyl sulfones[146]. From these data it appears that the sulfoxide group in dimethyl sulfoxide stabilizes the α-carbanion slightly less efficiently than the carbonyl group in acetone, which in turn stabilizes the α-carbanion slightly less efficiently than the sulfone group in dimethyl sulfone as may be evident from the gas-phase acidities, ΔH°_{acid}, of 1563, 1544 and 1531 kJ mol^{-1} for dimethyl sulfoxide, acetone and dimethyl sulfone, respectively. It follows that oxidation of dimethyl sulfide to dimethyl sulfoxide results in an increase of the acidity by 82 kJ mol^{-1}, whereas further oxidation to dimethyl sulfone increases the acidity by an additional 32 kJ mol^{-1}.

2. *Reaction between dimethyl sulfoxide and ionized dimethyl sulfoxide*

The overall bimolecular rate constant for the gas-phase reaction between DMSO and its molecular ion, generated selectively by photoionization, is determined to be 1.0×10^{-9} cm^3 molecule^{-1} s^{-1} at 300 K. This rate constant is calculated to correspond to an efficiency of about 40%, meaning that 40% of the collisions between DMSO and its molecular ion result in the formation of product ions[147]. The efficiency is reported to be independent of the energy of the ionizing photons.



Reaction between DMSO and its molecular ion is dominated by a competing formation of protonated DMSO (equation 73) and methyl sulfenyl cationized DMSO (equation 74).

A minor contribution to the reaction is due to a methyl cation transfer, yielding the methyl cationized DMSO (equation 75). All primary product ions react rapidly with a second DMSO molecule to form the proton-bound dimer of DMSO, $(CH_3SOCH_3)_2H^+$, while progressive solvation leading to $(CH_3SOCH_3)_nH^+$, with $n = 2$–5, occurs under relatively high pressure conditions[147].

Introduction of water to the reaction atmosphere results in a very limited mixed solvation of the proton. This mixed solvation gains importance if water is replaced by methanol[147]. However, exclusive solvation of the proton by DMSO molecules is most dominant due to the higher PA of DMSO in the gas phase ($PA = 854\,kJ\,mol^{-1}$) relative to methanol ($PA = 761\,kJ\,mol^{-1}$) and water ($PA = 697\,kJ\,mol^{-1}$). It follows that the above behavior is consistent with the hypothesis that mixed solvation of the proton becomes energetically more favored if the difference in PA of the different solvents is minimized[152].

3. *Progressive solvation of a proton by dimethyl sulfoxide*

The energetics of progressive solvation of a proton by DMSO molecules, as determined from the temperature dependence of the gas-phase association equilibria shown in equation 76, give insight into the nature of DMSO as an important dipolar aprotic solvent[151].

$$(\text{Solvent})_n\overset{+}{\text{H}} + \text{Solvent} \rightleftharpoons (\text{Solvent})_{n+1}\overset{+}{\text{H}} \tag{76}$$

For comparison, data on the energetics of progressive solvation of a proton by water, acetonitrile, dimethyl ether, acetone and dimethyl sulfoxide molecules are compiled in Table 2. Within this series the PA represented by $-\Delta H^\circ_{0,1}$ varies over a wide range from $697\,kJ\,mol^{-1}$ for H_2O to $884\,kJ\,mol^{-1}$ for DMSO. Yet, the binding enthalpies for the solvent molecule, $-\Delta H^\circ_{1,2}$, of around $130\,kJ\,mol^{-1}$ are similar for all solvents in the

TABLE 2. Enthalpy change, $-\Delta H^0_{n,n+1}$ ($kJ\,mol^{-1}$), associated with the progressive solvation of a proton

$n, n+1$	H_2O^a	CH_3CN^b	$(CH_3)_2O^c$	$(CH_3)_2CO^d$	$(CH_3)_2SO^d$
0,1	697	787	804	823	884
1,2	132	126	128	126	129
2,3	82	39	42		89
3,4	73				

[a]Data taken from Reference 148.
[b]Data taken from Reference 149.
[c]Data taken from Reference 150.
[d]Data taken from Reference 151.

series. In contrast, the binding enthalpies for the third solvent molecule, $-\Delta H^{\circ}_{2,3}$, are very different. For DMSO and water the enthalpies of 89 and 82 kJ mol^{-1}, respectively, are relatively large. However, for dimethyl ether and acetonitrile these binding enthalpies are reduced to 42 and 39 kJ mol^{-1}, respectively. Since both the aprotic acetonitrile and DMSO have large permanent dipole moments of the same magnitude of 3.92 and 3.96 *D*, respectively, the significant difference in binding enthalpies for the third solvent molecule is rationalized in terms of differences in specific electrostatic interactions due to the actual distribution of atomic charges[151]. This is qualitatively revealed by the net atomic charges on the 'electron donor' end of the solvent molecules: the N atom in acetonitrile is calculated to have only 0.185 negative charges, while the O atom in DMSO has 0.441 negative charges[153].

From the calorimetrically obtained solvation enthalpies of a proton in liquid water and DMSO of 1129 and 1155 kJ mol^{-1}, respectively[154], and the energetics of progressive solvation listed in Table 2, it follows that the first three solvent molecules account for about 80% of the total solvation of a proton in water and for 92% in DMSO[151]. On the basis of the above results it is concluded that the greater solvation of a proton in DMSO relative to water is due to much higher PA of DMSO.

4. *Attachment of cations to sulfoxides and sulfones*

Attachment of ions to sulfoxides and sulfones is achieved readily in an ammonia chemical ionization plasma[155]. The metastable $[M + NH_4]^+$ and $[M + N_2H_7]^+$ ions undergo exclusively desolvation of an ammonia molecule (equations 77 and 78) indicating that ammonia molecules are weaker bound to the proton than the sulfoxide and sulfone molecules.

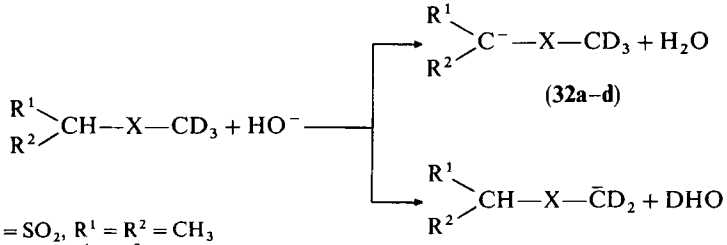
$$[M + NH_4]^+ \rightleftharpoons NH_3 + [M + H]^+ \tag{77}$$

$$[M + N_2H_7]^+ \rightleftharpoons NH_3 + [M + NH_4]^+ \tag{78}$$

Further, both diphenyl sulfoxide and sulfone are shown to undergo attachment to benzyl and propargyl cations in a CI plasma of benzyl and propargyl chloride, respectively[156].

5. *Regiospecificity of the deprotonation of sulfones*

A priori, deprotonation of asymmetric sulfoxides and sulfones can result in a mixture of isomeric α-sulfoxyl and α-sulfonyl carbanions. This is demonstrated for the hydroxide-induced reaction of d_3-methyl isopropyl sulfone **31a** which proceeds by proton and deuteron abstraction resulting in a mixture of the tertiary, **32a** (equation 79), and primary, **33a** (equation 80), α-sulfonyl carbanions[157]. The preference of deuteron over



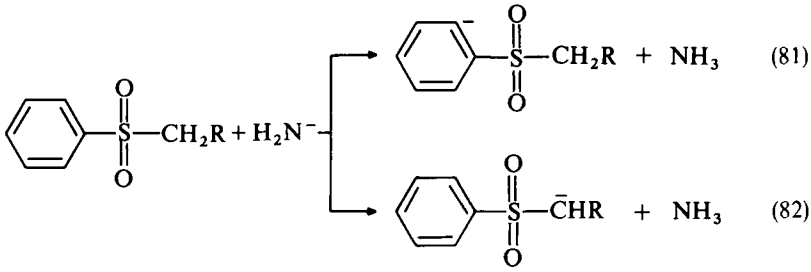
(79)

(80)

(**31a**) X = SO_2, $R^1 = R^2 = CH_3$
(**31b**) X = CO, $R^1 = R^2 = CH_3$
(**31c**) X = SO_2, R^1 = H, R^2 = Ph
(**31d**) X = CO, R^1 = H, R^2 = Ph

proton abstraction by a factor of 1.4 indicates that the primary α-sulfonyl carbanion is slightly more stable than the tertiary α-sulfonyl carbanion. This is more pronounced for the ketone analogue **31b**, which in spite of a similar gas-phase acidity (*vide supra*) shows a strong preference for deuteron over proton transfer by a factor of 10.4.

Further, d_3-methyl benzyl sulfone **31c** favors formation of the benzylic sulfonyl carbanion, **32c**, which follows from the preference of proton over deuteron abstraction by a factor of 2.2. For the ketone analogue **31d** this preference is enhnaced to a factor of 3.8. It appears that the regiospecificity of the deprotonation of ketones and sulfones agrees with the view that resonance stabilization plays a more important role in enolate anions than in α-sulfonyl carbanions[157].



(81)

(82)

If reaction of an alkyl phenyl sulfone, Ph—(SO_2)—CH_2R, is promoted by the strongly basic amide ion, both the proton abstraction from the aryl group and from the α-position of the alkyl group become energetically accessible. This results in competing formation of aryl carbanions (equation 81) and α-alkyl sulfonyl carbanions (equation 82) as illustrated for deprotonation of methyl, ethyl and *iso*-propyl phenyl sulfone, where the relative yield of *ortho* aryl carbanions (equation 81) amounts to 20, 24 and 37%, respectively[144].

VI. SULFENIC, SULFINIC AND SULFONIC ACIDS AND ESTERS

A. Unimolecular Reactions

1. General characteristics

A general synopsis of mass spectromeric research on sulfinic acids, esters and their derivatives[9] and on sulfonic acids and their derivatives[10] is given in earlier reviews.

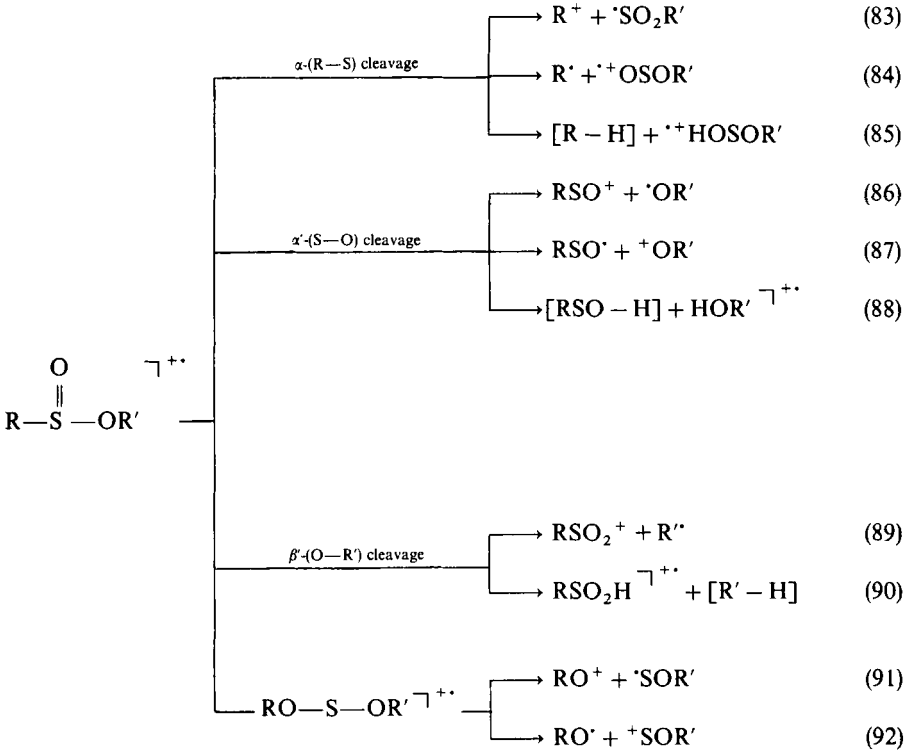
The characterization of the EI induced decompositions of the gaseous sulfenic, sulfinic and sulfonic acids and esters is hindered by their thermal and/or kinetic instability. Consequently, the limited conclusive data available do not allow unambiguous analysis of all fragmentation modes involved in the electron impact induced decomposition of these classes of compounds.

Upon electron impact, sulfenic acids, R—S—OH (R = CH_3, H_2C=CH, HC≡C, C_6H_5)[158] afford abundant molecular ions. Decomposition of these molecular ions exhibits competing R—S and S—OH cleavages, with and without associated hydrogen migrations (see also Section V.A.1).

Electron impact on gaseous methanesulfinic acid[159], H_3C—(SO)—OH, yields also abundant molecular ions. Decomposition of these molecular ions is dominated by C—S bond cleavage, which may result either in the loss of a $CH_3^{\bullet}$ radical or lead to the elimination of a molecule of methane. Of less importance is the cleavage of the S—OH bond resulting in the loss of an $HO^{\bullet}$ radical or the elimination of a molecule of water.

Gaseous arenesulfonic acids[160–164], Ar—(SO_2)—OH, can undergo characteristic desulfonation upon electron impact, yielding Ar^+ fragment ions. In addition, loss of a $SO_2H^\bullet$ radical and elimination of a SO_2 molecule are considered to be preceded by a rearrangement of the molecular ion to the ionized sulfite, ArO—(SO)—$OH^{+\bullet}$.

The electron impact induced decomposition of methyl methanesulfenate[133], H_3C—S—O—CH_3, shows competing S—C and O—C bond cleavages both resulting in the loss of a $CH_3^\bullet$ radical, while cleavage of the S—O bond leads to the elimination of a formaldehyde molecule (see also Section V.A.1). The low yield of molecular ions resulting from electron impact on gaseous sulfinates, R—(SO)—OR′, is probably due to the relatively low energy required for their decompositions, in which the competition between possible fragmentation processes is governed by the nature of both the R and R′ groups (R = alkyl, R′ = alkyl)[165,166], (R = aryl, R′ = alkyl)[166,167–169], (R = alkyl, R′ = aryl)[167], (R = benzyl, R′ = alkyl)[167].



Alpha-(C—S)-cleavage occurs with retention of the charge on either the hydrocarbon (equation 83) or the sulfur containing fragment (equation 84). Typically for the sulfinates with longer R alkyl groups, this C—S bond cleavage proceeds with a concomitant hydrogen migration from the R alkyl group to either one of the chemically distinct oxygen atoms (equation 85).

For methyl arenesulfinates (R = aryl, R′ = CH_3) α′-(S—O)-cleavage gains importance, resulting in the loss of a $CH_3O^\bullet$ radical (equation 86) with subsequent elimination of a CO molecule[167]. The resulting characteristic fragment ions are not encountered in the decomposition of the isomeric molecular ions of aryl methyl sulfones, Ar—(SO_2)—CH_3, which instead can rearrange to ionized aryl methanesulfinates, Ar—O—(SO)—CH_3,

leading to the formation of ArO^+, or $ArOH^{+\cdot}$ fragment ions, depending on the nature of the arene group (see also Section V.A.1). In agreement herewith, these fragment ions are the only significant ionic products formed in the EI induced decomposition of aryl methanesulfinates[167], (R = CH_3, R′ = aryl) (equations 87 and 88).

Further, ionized methyl arenesulfinates (R = aryl, R′ = CH_3) can undergo β'-(O—R′)-cleavage, resulting in the loss of a methyl radical[167] (equation 89), whereas β'-(O—R′)-cleavage in ethyl[166,169] and isopropyl[168] arenesulfinates (R = aryl, R′ = C_2H_5, i-C_3H_7) leads to the elimination of an ethylene and propene molecule, respectively (equation 90). Finally, formation of RO^+ (equation 91) and the complementary $^+SOR'$ ions (equation 92) are indicative of a skeletal rearrangement of the molecular ions involving migration of the R group from the sulfur atom to the oxygen atom, followed by cleavage of the formed RO—S bond. A related process is also detected in the decomposition of electron ionized sulfoxides and sulfones (Section V.A.1).

Also, the EI induced decomposition of gaseous sulfonates, R—(SO_2)—OR′, exhibits many competing fragmentation reactions of which the individual importance is governed by the nature of the R and R′ groups (R = alkyl, R′ = alkyl)[170,171], (R = aryl, R′ = alkyl)[129,172–175], (R = alkyl, R′ = aryl)[171,176], (R = aryl, R′ = aryl)[177], (R = CH_3, R′ = vinyl)[178]. In general, the decomposition of ionized sulfonates involves analogous fragmentation reactions which are encountered also for the decomposition of sulfinates (equations 83–92). However, a number of additional fragmentations are characteristic for ionized sulfonates.

Ionized sulfonates with large R alkyl groups show a tendency to undergo α-(R—S)-cleavage with associated double hydrogen migration (equation 93).

Characteristic for the sulfonates with γ-hydrogen atoms is a McLafferty-type process, where the hydrogen migration is accompanied by β-cleavage[170] (equation 94).

Typically for the methyl esters, α'-(S—O)-cleavage is associated with hydrogen migration, resulting in the elimination of a formaldehyde molecule yielding an ionized sulfinic acid[170,171] (equation 95).

Higher ester homologues undergo facile β'-(O—R′)-cleavage with associated double hydrogen migration, yielding protonated sulfonic acids[170–175] (equation 96).

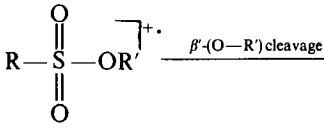
Alternatively, these esters may undergo γ'-cleavage without (equation 97) or with (equation 98) double hydrogen migration[171–173].

Resonant electron capture of ethyl benzenesulfonate[129], Ph—(SO_2)—OC_2H_5, yields

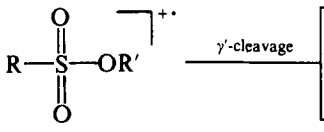
$$R{-}\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}{-}OR' \xrightarrow{\alpha\text{-(R—S) cleavage}} [R-H_2]^{\cdot} + {}^+H_2O_2SOR' \qquad (93)$$

$$R{-}\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}{-}OR' \xrightarrow{\beta\text{-cleavage}} [R-CH_3] + H_2C{=}\overset{\overset{OH}{|}}{\underset{\underset{O}{\|}}{S}}{-}OR' \qquad (94)$$

$$R{-}\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}{-}OCH_3 \xrightarrow{\alpha'\text{-(S—O) cleavage}} RSO_2H + H_2CO \qquad (95)$$

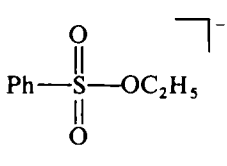


$$\xrightarrow{\beta'\text{-(O—R')cleavage}} RSO_3H_2^+ + [R' - H_2]^{\cdot} \quad (96)$$



$$\xrightarrow{\gamma'\text{-cleavage}} R(SO_2)—\overset{+}{O}=CH_2 + [R' - CH_2]^{\cdot} \quad (97)$$

$$\xrightarrow{\gamma'\text{-cleavage}} R—S(OH)_2—\overset{+}{O}=CH_2 + [R' - CH_4]^{\cdot} \quad (98)$$



$$\xrightarrow{-Ph^{\cdot}} {}^{-}O_2SOC_2H_5 \quad (99)$$

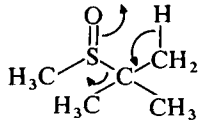
$$\xrightarrow{-{}^{\cdot}OC_2H_5} PhSO_2^- \quad (100)$$

abundant negative molecular ions, while dissociative electron capture results in Ph—S and S—OC_2H_5 bond cleavages with loss of a phenyl radical (equation 99) and an ethoxy radical (equation 100), respectively.

Dissociative electron capture of *p*-toluenesulfonate esters[179], $CH_3C_6H_4$—(SO_2)—OR, shows exclusive cleavage of the aryl–S bond resulting in the loss of a *p*-tolyl radical. In marked contrast to this, the photochemically generated negative molecular ions undergo cleavage of the S—O bond in alcoholic solution, yielding alkoxy anions[180].

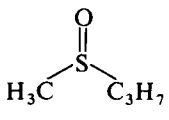
2. *Isomerizations of ionized methanesulfenic acid*

The molecular ion of methanesulfenic acid (**34**) can be generated by EI of the neutral methanesulfenic acid formed as a transient species by flash-vacuum pyrolysis of methyl *tert*-butyl sulfoxide[158,181] as shown in equation 101.

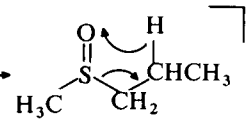


$$\xrightarrow[-C_4H_8]{\Delta} CH_3SOH \xrightarrow{-e^-} CH_3SOH^{+\cdot} \quad (101)$$

(**34**)



$$\xrightarrow{-e^-}$$



$$\xrightarrow{-C_3H_6} CH_3SOH^{+\cdot} \quad (102)$$

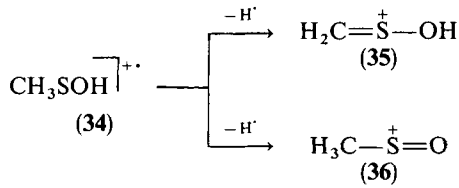
(**34**)

Alternatively, these ions can be generated by dissociative electron impact on methyl *n*-propyl sulfoxide[181] (equation 102). High-energy collisional activation of the molecular

ions **34**, generated via both routes, reveals an identical decomposition behavior. This behavior indicates strongly that the ions have the assigned structure[181].

The metastable molecular ions of methanesulfenic acid react by loss of a hydrogen atom. Deuterium labelling reveals that a hydrogen atom is lost preferentially from the methyl group with formation of the product ion **35** (equation 103), whereas loss of a hydrogen atom from the hydroxy group to form the isomeric product ion **36** (equation 104) is of minor importance, consistent with thermochemical considerations[181].

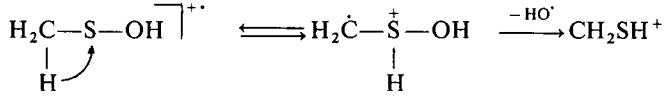
Moreover, the loss of a hydrogen atom originating from the hydroxy group is accompanied by a relatively large kinetic energy release, indicating that O—H bond cleavage may involve a substantial reverse activation energy.



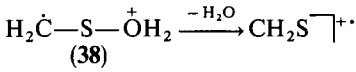
(103)

(104)

Further, loss of a hydroxy radical and elimination of a water molecule from the molecular ion of methanesulfenic acid is shown to give rise to CH_2SH^+ and $CH_2S^{+\cdot}$, respectively. Analogous to the proposed mechanism of methyl radical loss from ionized dimethyl sulfide[24,25] (equation 30) (see Section III.A.2), it is considered that formation of CH_2SH^+ (equation 105) proceeds via rearrangement of the molecular ion to the ylid ion **37**, while further hydrogen migration from the sulfur atom to the oxygen atom forming another distonic intermediate (**38**) is held responsible for the formation of $CH_2S^{+\cdot}$ (equation 106).



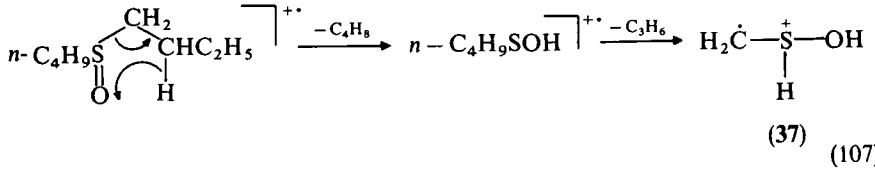
(105)



(106)

Consistent with this additional hydrogen migration, a large deuterium isotope effect is encountered which reduces the water loss relative to the hydroxyl loss. Since the original hydroxy hydrogen is lost selectively with the water molecule, it appears that the rearrangement of the distonic intermediate **37** to **38** is irreversible.

To substantiate the intermediacy of the ylid ion **37**, this isomer is generated as a distinct stable species by the consecutive losses of C_4H_8 and C_3H_6 from the molecular ion of di-*n*-butyl sulfoxide[181] (equation 107).



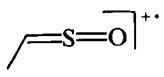
(107)

Incorporation of deuterium atoms in the water molecule eliminated from site-specifically deuterium labelled ylid ion **37**, generated in this way, reveals that reversible isomerization between the ylid ion **37** and the molecular ion of methanesulfenic acid **34** occurs prior to water loss (equation 106).

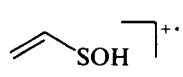
The relative stabilities of the ionized methanesulfenic acid (**34**) and the isomeric distonic ions **37** and **38** are estimated by MNDO calculations[181]. These calculations find the ylid ion **37** as a stable species in a potential energy minimum, destabilized against ionized methanesulfenic acid **34** by 104 kJ mol^{-1}. This is consistent with the calculated lower stability of $^{\cdot}CH_2SH_2^+$ relative to $CH_3SH^{+\cdot}$ by 76 kJ mol^{-1} [24,25] (see also Section II.A.2). By contrast, the distonic isomer **38** is calculated to have an ion–molecule complex character with a long S—O bond (0.319 nm) and a small C—S—O bond angle (90°), and its decomposition to $CH_2S^{+\cdot}$ and H_2O is only slightly endothermic[181].

3. *Isomerization of ionized ethenesulfenic acid*

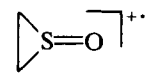
Radical cations with the elemental composition $C_2H_4SO^{+\cdot}$ can be synthesized by different routes[182] as depicted in Scheme 12. Route A represents the pyrolytic elimination of an isobutene molecule from vinyl *tert*-butyl sulfoxide yielding ethanethial-*S*-oxide either by direct retro-ene dissociation or via the intermediacy of ethenesulfenic acid. Electron ionization of the resulting transient ethanethial-*S*-oxide is considered to yield primarily the molecular ion of ethanethial-*S*-oxide (**39**).



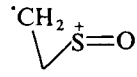
(**39**)



(**40**)



(**41**)



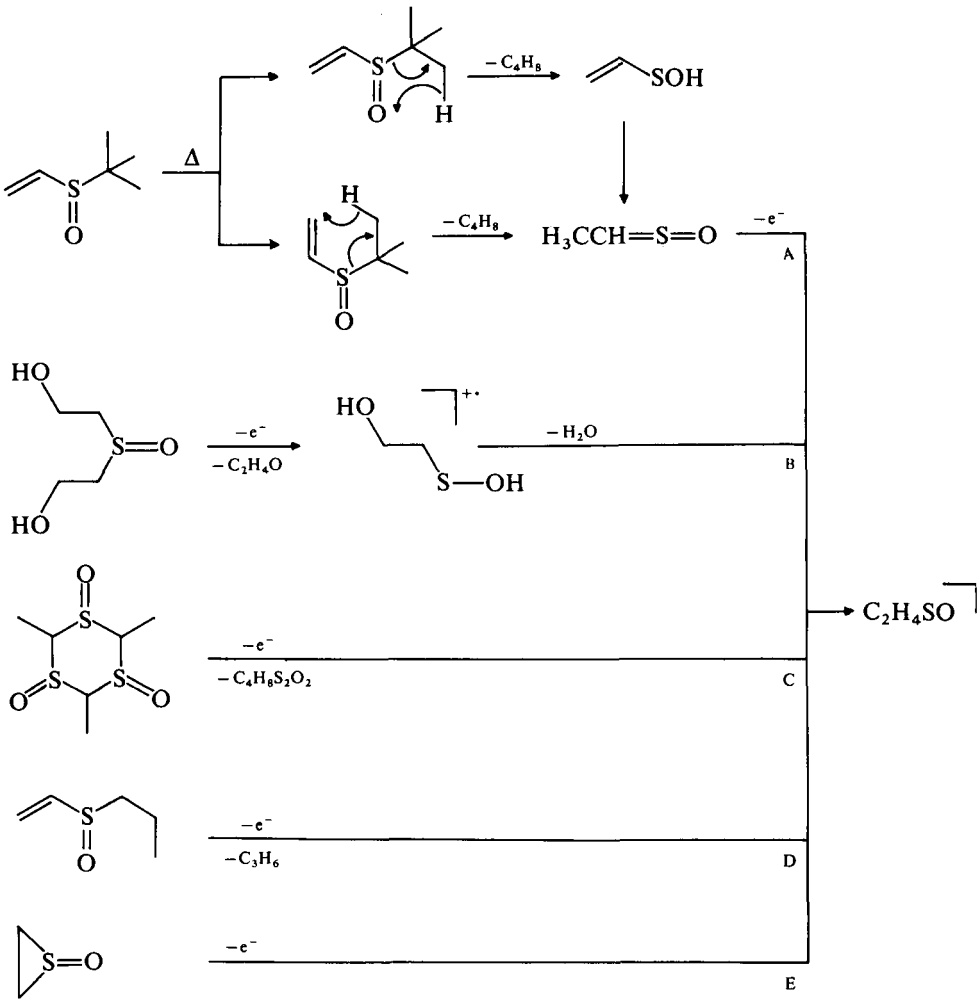
(**42**)

Route B represents the subsequent electron impact induced eliminations of C_2H_4O and a water molecule from bis(2-hydroxyethyl) sulfoxide. Route C shows a dissociative electron ionization of *syn*-trimethyltrithiane-*S*-oxide, which is assumed to yield primarily the molecular ion of ethanethial-*S*-oxide (**39**).

Route D involves the electron impact induced elimination of a propene or cyclopropane molecule from *n*-propyl vinyl sulfoxide where cleavage of the *S*-*n*-propyl bond is accompanied by competing hydrogen migration to the terminal vinyl carbon atom and the sulfoxide oxygen atom, resulting in a mixture of ionized ethanethial-*S*-oxide (**39**) and ethenesulfenic acid (**40**). Analogous processes are postulated for the dissociations of alkyl styryl and propenyl sulfoxides[136,137] (see Section V.A.3). Finally, route E implies electron impact on thiirane-*S*-oxide, which is considered to yield primarily both the molecular ion (**41**) and its ring-opened distonic isomer (**42**).

The decompositions of the metastable $C_2H_4SO^{+\cdot}$ ions, generated by the above routes, are very similar and are dominated by the competing losses of CO, HCO and H_2CO. This suggests that the differently generated metastable $C_2H_4SO^{+\cdot}$ ions can undergo a skeletal rearrangement to a common intermediate. High-energy CID shows significant differences, which are indicative for the existence of distinct $C_2H_4SO^{+\cdot}$ isomers. However, the CID results do not allow quantitative assessment of the isomeric admixtures. Yet, the collisionally induced loss of HO$^{\cdot}$ versus DO$^{\cdot}$ from the specifically deuterium labelled $C_2H_4SO^{+\cdot}$ ions generated via route D is fitted with an isomeric mixture containing 86% ionized ethenesulfenic acid (**40**) and 14% ionized ethanethial-*S*-oxide (**39**).

Total energies and zero-point energies for various C_2H_4OS molecules and their molecular ions are determined using high-level theoretical calculations[182]. From this



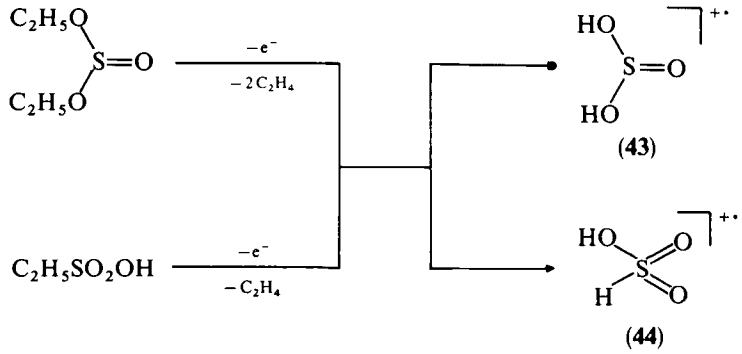
SCHEME 12. Generation of $C_2H_4SO^{+\cdot}$ ions[182]

theoretical study it appears that ethanethial-*S*-oxide, $CH_3CH{=}S{=}O$, is 12 kJ mol^{-1} more stable than ethenesulfenic acid, $H_2C{=}CHSOH$, while ionization reverses the relative stability, i.e. the ionized ehtanethial-*S*-oxide (**39**) is 96 kJ mol^{-1} less stable than the ionized ethenesulfenic acid (**40**). The differences in relative stabilities of the ionic and neutral molecules are quantitatively similar to the differences observed for simple keto/enol systems[183–185]. Indeed, ethanethial-*S*-oxide and ethenesulfenic acid can be viewed as sulfur-extended analogs of acetaldehyde and vinyl alcohol, respectively. There are significant barriers separating the isomers for both neutral and ionic systems. Conversion of ethenesulfenic acid to its more stable isomer, ethanethial-*S*-oxide, requires 137 kJ mol^{-1}, while conversion of ionic ethanethial-*S*-oxide (**39**) to its more stable isomer,

ionic ethenesulfenic acid (**40**), requires 90 kJ mol^{-1}. The thiirane-*S*-oxide ion (**41**) is calculated to lie 114 kJ mol^{-1} higher in energy than the most stable isomeric ethenesulfenic acid ion (**40**). Finally, the ring-opened distonic ion (**42**) is calculated to exist in a local minimum on the potential energy surface, lying 190 kJ mol^{-1} above the ethenesulfenic acid ion (**40**).

4. Generation of ionized sulfurous acid from ethanesulfonic acid

General textbook knowledge takes sulfurous acid to be nonexistent in the free state. Yet, the molecular ion of sulfurous acid can be generated readily by an electron impact induced dissociation of diethyl sulfite or ethanesulfonic acid[186] (Scheme 13).

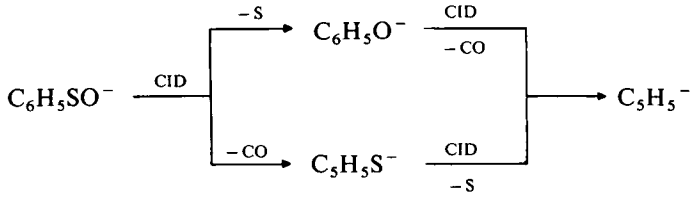


SCHEME 13. Generation of ionized sulfurous acid[186]

High-energy CID of specifically deuterium labelled sulfurous acid ions, generated by EI on the correspondingly labelled ethanesulfonic acid, shows the losses of HO$^{\cdot}$ and DO$^{\cdot}$, providing evidence that the generated ionized sulfurous acid has structure **43**, rather than **44**. These findings are substantiated by *ab initio* MO calculations[186], which show that structure **43** is 156 kJ mol^{-1} more stable than structure **44**, while interconversion from structure **44** to structure **43** is hindered by a barrier of 186 kJ mol^{-1}.

5. Decomposition of deprotonated sulfenic and sulfinic acids

A series of deprotonated sulfenic and sulfinic acids, generated by dissociative electron capture of corresponding sulfoxide and sulfone derivatives, has been subjected to high-energy CID[40].



SCHEME 14. CID of deprotonated benzenesulfenic acid[40].

The decomposition of deprotonated benzensulfenic acid is dominated by skeletal rearrangements, leading to the eliminations of S and CO yielding $C_6H_5O^-$ and $C_5H_5S^-$, respectively. Subsequent decomposition of these primary fragments involves the loss of CO and S, respectively, so that both decomposition pathways terminate with the formation of the cyclopentadienyl anion (Scheme 14).

Deprotonated benzylsulfenic acid, $C_6H_5CH_2SO^-$, behaves very differently.[40] The decomposition is dominated by the elimination of a water molecule, while simple C—S bond cleavage yields both $C_7H_7^-$ and $SO^{-\bullet}$ ions. Deuterium labelling reveals that the hydrogen atoms in the eliminated water molecule may originate from both the phenylic and benzylic positions.

Deprotonated arylsulfinic acids, $ArSO_2^-$, eliminate SO, presumably by the rearrangement $ArSO_2^- \rightarrow ArOSO^- \rightarrow ArO + SO$. Other fragmentations occur generally by simple cleavages to form, e.g., Ar^- and $SO_2^{-\bullet}$[40].

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CHAPTER 7

Carbon acidity resulting from sulfur substituents

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Supplement S: The chemistry of sulphur-containing functional groups
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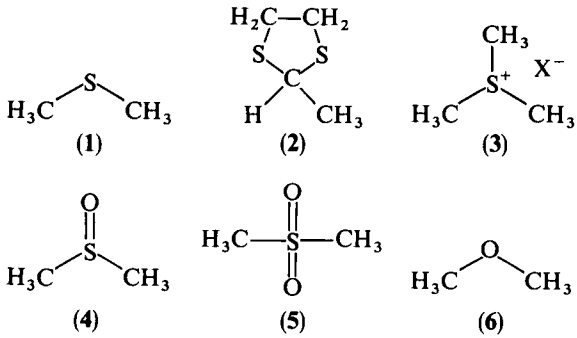
I. INTRODUCTION

The comparatively high acidity of carbon–hydrogen bonds in thioethers (e.g. **1**), dithioacetals (e.g. **2**), sulfonium salts (e.g. **3**), sulfoxides (e.g. **4**) and sulfones (e.g. **5**) was recognized very early and the facile formation of the corresponding 'anions' is widely used in synthesis[1–11]. Similarly, many chemists have been intrigued over the years by the reason for the high acidity of a thioether (such as **1**) as compared to its oxygen analogue **6**[1–13], or, more specifically, whether there is a 'd-orbital effect' and a 'π(pd) bonding' in the sulfur compound which is responsible for the difference. We wish to address this question here not so much from a historical perspective[1–13], but rather in the context of recent results from theoretical calculations which will be compared with recent experimental data, mostly of crystal structure investigations. This procedure tells us about the quality of the calculations and thus about the importance of d-orbitals as found in these calculations. We note how general agreement was reached on the topic in the 1980s.



In the first part we concentrate on the stabilization of a negative charge by an —SH(R) group. Next we compare the —SH(R) results with those for the —OR group, a comparison which shows nicely the difference between first- and second-row substituents in their ability to stabilize a negative charge. Finally, we discuss comparatively the substituents —SR, —S^+R_2, —S(O)R and —SO_2R, and their ability to stabilize a negative charge. Supplementary material on unpublished calculations of several compounds discussed in Section IV, such as total energies and geometries (given as coordinates), is summarized in the Appendix (Section V).

II. THE STABILIZATION OF A NEGATIVE CHARGE BY THE —SH(R) GROUP: MODEL CALCULATIONS AND EXPERIMENTAL RESULTS

After a number of earlier publications by various authors[14–26] Wolfe, Bernardi and coworkers in 1983 again tackled the problem of the stabilization of a negative charge by sulfur substituents using more advanced theoretical methods[27]. When they studied the transformations **7** → **8** and **1** → **9** (equations 1 and 2) it was found necessary to include

$$H_3C—S—H \longrightarrow H_2\bar{C}—S—H \qquad (1)$$

(7) (8)

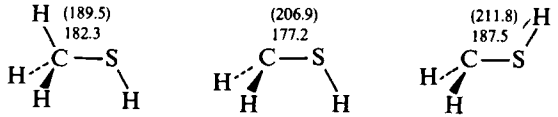
$$H_3C—S—CH_3 \longrightarrow H_2\bar{C}—S—CH_3 \qquad (2)$$

(1) (9)

d-orbitals in the calculations in order to obtain a proper description of the *geometries* of the anions **8** and **9**. This is first exemplified by the formation of the anion **8** from methylthiol **7**. With the 3-21G basis set (no d-orbitals on sulfur), the calculated H_3C—S bond length in **7** is 189.5 pm, which is too long compared with the experimental value of 181.9 pm[28]. With 3-21G(d)—now d-orbitals on sulfur are used—a value of 182.3 pm is calculated. In the anion **8** the C—S bond length calculated *without d-orbitals* is increased considerably to 211.8 pm, and the anti conformation *anti*-**8** is calculated to be more stable than *syn*-**8** (C—S 206.9 pm) by 1.0 kcal mol^{-1} (Figure 1).

With d-orbitals on sulfur [3-21G(d)] a dramatic change is observed in the anion **8**: C—S in *syn*-**8** decreases to 177.2 pm, and *syn*-**8** is more stable than *anti*-**8** by 4.38 kcal mol^{-1}; in *anti*-**8** C—S is 187.5 pm long. Wolfe, Bernardi and coworkers attribute the decrease in the C—S bond length to 'conjugative stabilization of the carbanion by the —SH moiety'[27a].

A rather similar situation is observed in the deprotonation of dimethyl sulfide **1** to give the anion **9**. The 3-21G(d) data are given in Figure 2. Deprotonation of **1** (H_3C—S 181.3 pm) again leads to a remarkable *shortening* of the $H_2\bar{C}$—S bond (172.8 pm) along with a *lengthening* of the S—CH_3 bond (187.5 pm) of **9**. The anionic carbon is pyramidal. It can be seen from the orbital representations in Figure 2 that the HOMO of **9** is π-bonding in the $H_2\bar{C}$—S and σ-antibonding in the S—CH_3 region. The dominant d-orbital contribution to the HOMO results from the $3d_{xz}$ atomic orbital of sulfur. Mixing-in leads to an *increased* bonding between H_2C^- and S, and a decreased



(7)	*syn*-**8**	*anti*-**8**
experimental value: 181.9	0.0 (+1.0)	+4.38 (0.0)

FIGURE 1. Geometries (bond lengths in pm) and relative energies (kcal mol^{-1}) of **7** and **8**; 3-21 G (in parentheses) and 3-21 G(d) values

(**1**) (**9**)

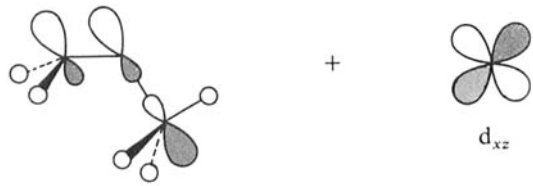


FIGURE 2. 3-21G(d) Geometries (bond lengths in pm) of **1** and **9**, and the HOMO of **9** with the d_{xz} orbital of sulfur

antibonding between S and CH_3. Both effects lower the energy of the HOMO and, according to Wolfe, Bernardi and coworkers[27], stabilize the anion. The d-orbital of sulfur operates as a polarization function. (Indeed, in a more recent work, Magnusson[29] has shown that 'd-orbitals' do not even have to be placed on sulfur in 'hypervalent sulfur compounds'. By putting enough functions on the atoms connected to sulfur rather than on sulfur itself he has obtained similar results, showing that 'd-orbitals' are simply polarization basis functions.)

The changes in the carbon–sulfur bond lengths on going from **1** to **9** are reminiscent of the PMO treatment of the anomeric effect[30]. In the present case one has to focus on the interactions of the lone pair at carbon in **9**, n_c, with the σ and σ^* orbitals of the S—CH_3 bond.

If the sulfur d-orbitals mix into σ^*, a lowering of the energy of σ^* and an increase of its overlap with n_c result. At the 3-21G(d) level this stabilization amounts to $-16.34\,kcal\,mol^{-1}$ while the destabilizing interaction of n_c with σ is $15.39\,kcal\,mol^{-1}$, leading to a small overall stabilization (Figure 3). When the d-orbital is removed, the σ^* orbital energy increases, the overlap between n_c and σ^* decreases and the stabilizing interaction decreases to $-12.40\,kcal\,mol^{-1}$; now the destabilization (+17.77) dominates[27]. To reduce this destabilization the $H_2\bar{C}$—S bond *lengthens*: optimization of the structure without d-orbitals leads to a bond length greater than 200 pm (as in the case of *syn*- and *anti*-**8**).

The results and conclusions of Wolfe, Bernardi and coworkers[27] in their 1983 papers can be summarized as follows: the effect of the sulfur d-orbital leads to a *shortening* of the $\bar{C}H_2$—S bond and a *lengthening* of the S—CH_3 bond in the $\bar{C}H_2$—S—CH_3 anion **9**; the d-orbital operates as a polarization function; the bond lengthening of S—CH_3 is due to negative hyperconjugation; the anion **9** is slightly *stabilized* by d-orbitals on sulfur. Thus, d-orbitals influence strongly not only the *geometry* of (R)HS-substituted anions, but are also somewhat important with regard to their *energy*[31].

In a comprehensive paper on structures and stabilities of α-hetero-substituted anions, organolithium and organosodium compounds, Schleyer, Clark, Houk and coworkers in 1984 also addressed the situation of α-sulfur-substituted compounds (geometries, energies) and hence the effect of d-orbitals on the stabilization of a negative charge[32].

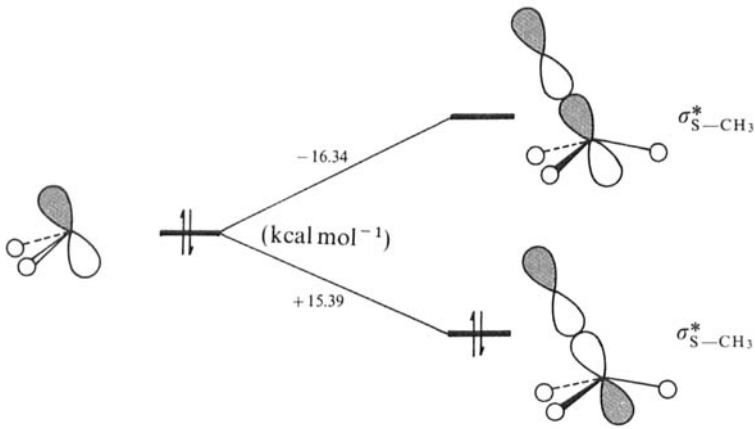


FIGURE 3. Interactions of the lone pair at carbon with σ_{S-CH_3} and $\sigma^*_{S-CH_3}$ orbitals. The + and − signs are according to Reference 27

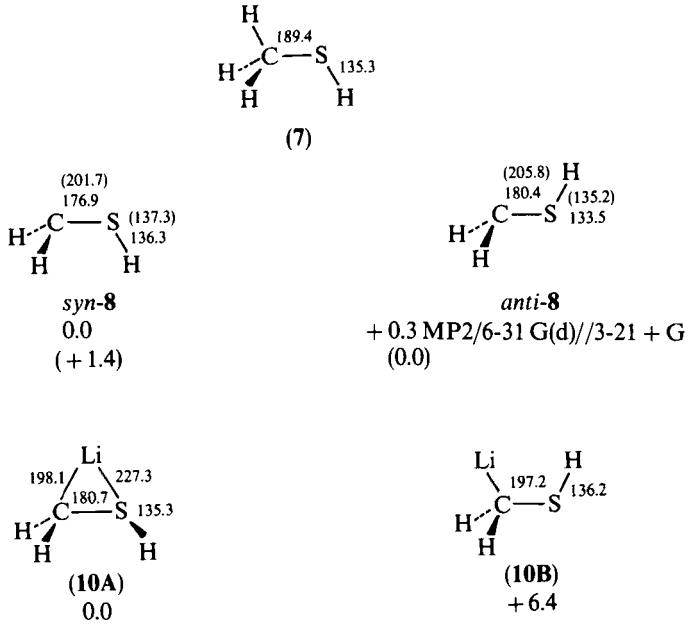
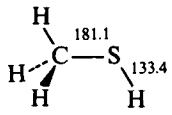


FIGURE 4. Geometries (bond lengths in pm) and relative energies (kcal mol^{-1}) of **7**, **8** and **10**. Basis sets: 3-21 G for **7** and **10**; 3-21 + G (values in parentheses) and 3-21 + G(d) for **8**[32]

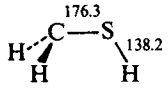
They first calculated the structure of methylthiol **7** and the two structures of $LiCH_2$—SH, **10A** and **10B**, at the 3-21G level, while the two anions *syn*-**8** and *anti*-**8** were calculated with the 3-21 + G and 3-21 + G(d) basis sets (+ indicates the use of diffuse functions). As far as the effect of sulfur d-orbitals on the *geometry* of the sulfur-stabilized anions is concerned, their results agree well with those of Wolfe, Bernardi and coworkers which we have discussed above [27] (see Figure 4).

One can see from Figure 4 that the geometry of *anti*-**8** shows no evidence for S—H hyperconjugation on the 3-21 + G level (values in parentheses; compare with **7**). In contrast, *syn*-**8** has a slightly lengthened S—H and a shortened $H_2\bar{C}$—SH bond if compared to the values of *anti*-**8** (and in agreement with a better n_c-σ^*_{S-H} interaction in the *syn* isomer). In comparison to the nondeprotonated **7** the $H_2\bar{C}$—SH bonds in *anti*- and *syn*-**8** are *shortened*, but only when d-orbitals have been included. The *syn*/*anti* preference is not very strong: *syn*-**8** is more unstable (+ 1.4 kcal mol^{-1}) on the 3-21 + G level while on the MP2/6-31G(d)//3-21 + G level it is slightly more stable (−0.3 kcal mol^{-1}) than *anti*-**8**.

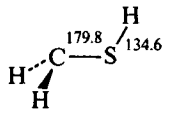
If Li^+ is added to the anion $H_2\bar{C}$—SH the $LiCH_2SH$ structures **10A** and **10B** were obtained. On the 3-21G level the bridged isomer **10A** is 6.4 kcal mol^{-1} more stable than **10B** with lithium only attached to the anionic carbon atom. Because of the importance of the $LiCH_2SH$ structures **10** for a comparison of theoretical with experimental results (crystal structures of *lithiated* thioethers), we also calculated the structures of the $LiCH_2SH$ isomers **10A,B** on the MP2/6-311 + + G(d,p)//MP2/6-311 + + G(d,p) level; similarly H_3C—SH **7** and the anions *syn*- and *anti*-**8** were calculated on this level (Figure 5).



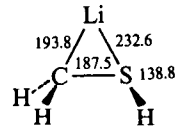
(7)



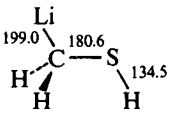
(*syn*-**8**)
0.0



(*anti*-**8**)
+1.1



(10A)
0.0

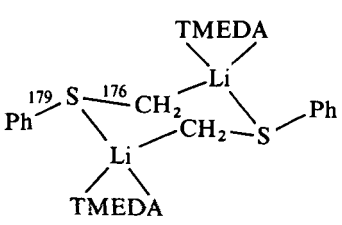


(10B)
+2.7

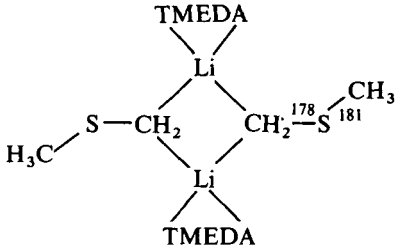
FIGURE 5. Geometries (bond lengths in pm) and relative energies (kcal mol^{-1}) of **7**, **8** and **10** on the MP2/6-311 + +G(d,p)//MP2/6-311 + +G(d,p) level

It can be seen from Figure 5 that the bridged **10A** is again the most stable one. However, the energy difference between **10A** and nonbridged isomer with Li only attached to carbon, **10B**, is rather small (+2.7 kcal mol^{-1}). The C—S bond is slightly shortened in **10B** (180.6 pm) if compared to the C—S bond in the nonlithiated **7** (181.1 pm). The S—H bond in **10** is generally longer than in **7** (133.4 pm): e.g. in **10B** it amounts to 134.5 pm. In the anions *syn*-**8** and *anti*-**8** the *shortening* of the H_2C—S bonds (176.3 and 179.8 pm) and the *lengthening* of the S—H bonds (138.2 and 134.6 pm) are much more pronounced than in the Li compounds **10A,B**. The *syn*-anion *syn*-**8** is 1.1 kcal mol^{-1} more stable than its *anti* isomer *anti*-**8**.

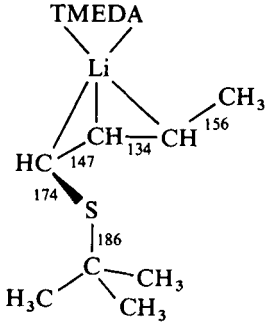
Two important outcomes of these calculations are, first, the small energy differences between the lithiated isomers **10A** and **10B**, and second, that the strong effects of —SH(R) substituents on the geometry of the *anions* (**8**) are essentially reduced to residual effects in the corresponding lithium compounds (**10**). At this point it is significant to raise the question about the experimental results on the structures of sulfur-substituted Li compounds, and how they compare with the calculated ones. Until now, crystal structure determinations of the following lithiated thioethers have been published (Figure 6): (phenylthio)methyllithium **11** crystallizing as a dimer with two tetramethylethylene diamine (TMEDA) molecules [**11**·TMEDA]$_2$[33]; (methylthio)methyllithium **12**, also crystallizing as a TMEDA dimer [**12**·TMEDA]$_2$[33]; (*E*)-1-(*tert*-butylthio)-2-butenyllithium **13**, which forms a monomer with TMEDA, **13**·TMEDA[34]; and α-(phenylthio)-benzyllithium **14**, which crystallizes as a monomer with three tetrahydrofuran (THF) molecules, **14**·3THF[35,36]. Bond lengths are given in Figure 6.



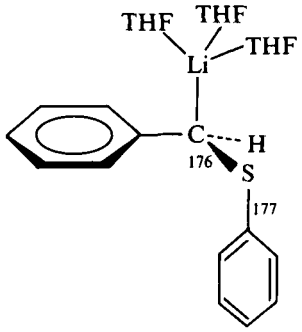
([**11**·TMEDA]$_2$)[33]



([**12**·TMEDA]$_2$)[33]



(**13**·TMEDA)[34]



(**14**·3 THF)[35]

FIGURE 6. Crystal structures of lithiated thioethers

Most significantly, in none of the four solid state structures of Figure 6 does Li *bridge* the anionic carbon atom and sulfur atom! This documents nicely the low tendency of second-row elements like sulfur to be bridged by lithium[32]. As shown in Section III, an entirely different situation is observed in the case of lithiated *ethers*. Indeed, the calculations of the $LiCH_2SH$ isomers **10A** and **10B** (Figure 5) did not give a strong preference for the bridged structure **10A**. As far as the bond lengths are concerned, one observes in [**11**·TMEDA]$_2$ a *shortening* of the $H_2\bar{C}$—S bond (176 pm) and a lengthening of the S—C_{phenyl} bond (179 pm) if compared to the mean values of H_3C—S (182.1 pm) and S—C_{aryl} bonds (176.8 pm)[37]. Similarly, in [**12**·TMEDA]$_2$ the $H_2\bar{C}$—S bond (178 pm) is *shorter* than the S—CH_3 bond (181 pm). In **13**·TMEDA the S—*t* butyl bond is exceptionally *long*: with 186 pm it is the longest known to date; for the bond from sulfur to the allyl anion carbon atom (174 pm) it is difficult to find a proper comparison. Although in the benzyl compound **14**·3THF the S—C_{phenyl} bond is only slightly lengthened (177.1(9) pm) if at all—the mean value for S—C_{phenyl} bonds is 177.1 pm[37]—the bond from the anionic carbon to sulfur again is *shortened* (176 pm) if compared to the mean value of H_3C—S bonds (182.1 pm)[37].

In summary, the experimentally determined overall structures and bond lengths as observed in the crystal structures of [**11**·TMEDA]$_2$, [**12**·TMEDA]$_2$, **13**·TMEDA and **14**·3THF agree nicely with the results of model calculations on sulfur-substituted carbanions like $H_2\bar{C}$—SH (**8**), $H_2\bar{C}$—S—CH_3 (**9**) and especially the lithiated species

10A,B. A lithium atom bridging the anionic carbon and sulfur atoms is not observed; the bond between the anionic carbon and sulfur is generally (slightly) *shortened*; the bond between sulfur and the neutral carbon atom is somewhat *lengthened* (except for **14**·3THF). Agreement between experimental results and model calculations is only observed if d-orbitals are used to calculate the *geometry* of sulfur-substituted anions.

Indeed, it is generally agreed now that a proper calculation of the *geometry* is only possible with d-orbitals on sulfur. There has been, however, disagreement between Wolfe, Bernardi and coworkers[27] and Schleyer, Clark, Houk and coworkers[32] whether or not d-orbital effects are important *energetically*. Schleyer, Clark, Houk and coworkers[32] make the statement that Wolfe, Bernardi and coworkers[27a] 'imply but do not demonstrate that d-orbital effects are important *energetically* provided geometries optimized with such functions are employed'. We have indicated this aspect of the work of Wolfe, Bernardi and coworkers[27a] above.

However, d-orbitals are not important *energetically* in the case of sulfur-substituted carbanions as clearly shown by Schleyer, Clark, Houk and coworkers[32] by means of the following example: $H_2\bar{C}$—SH **8** is more stable than $H_3\bar{C}$ by 39.9 kcal mol^{-1}. This value is too large because of the 3-21G basis set used. 3-21 + G does not improve the geometry appreciably, but the diffuse functions reduce the stabilization energy to 23.8 kcal mol^{-1}. With d-functions on sulfur [3-21 + G(d)] optimization leads to a change in the preferred conformation (*syn* is more stable than *anti*) and a remarkable *shortening* of the $H_2\bar{C}$—SH bond—but the stabilization energy actually becomes smaller: 21.3 kcal mol^{-1}! This is because the d functions on sulfur lower the energy of H_3C—SH ' *more* than the energy of the anion **8**. Higher-level single-point calculations using the 3-21 + G(d) geometries without electron correlation [6-31 + G(d): 21.3 kcal mol^{-1}] and with electron correlation [MP2/6-31 + G(d): 20.9 kcal mol^{-1}] do not change the stabilization energy.

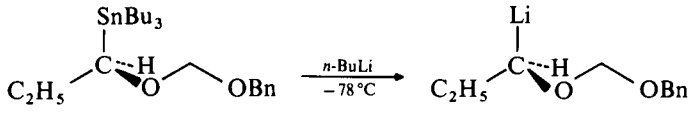
In conclusion, a thorough examination by means of theoretical methods leads to the conclusion that *d-orbitals on sulfur do not contribute to an energetic stabilization of the corresponding anions.*

III. THE STABILIZATION OF A NEGATIVE CHARGE BY THE —SH(R) AND THE—OH(R) GROUPS: A COMPARISON OF THEORETICAL AND EXPERIMENTAL RESULTS

In contrast to the —SH(R) group which stabilizes an adjacent negative charge very effectively (Section II), this is not the case with the —OH(R) group. Although α-lithiated ethers were prepared long ago by Lüttringhaus and coworkers[38] and by Wittig and Löhmann[39], they were only easily accessible if the negative charge was additionally stabilized by, e.g., an *aryl* group. For example, benzyl phenyl ether **15** reacts with phenyllithium **16** to give the lithiated ether **17** and benzene (equation 3)[38,39]. A general synthesis of *alkyl*-substituted α-lithiated ethers like **19** was only available after Still had described an access via tin–lithium exchange as, e.g., in the preparation of **19** from **18** (equation 4).[40]

$$\underset{\textbf{(15)}}{Ph{-}CH_2{-}O{-}Ph} + \underset{\textbf{(16)}}{Ph{-}Li} \xrightarrow[-\,Ph{-}H]{} \underset{\textbf{(17)}}{Ph{-}\overset{\displaystyle Li}{\overset{|}{C}}H{-}O{-}Ph} \qquad (3)$$

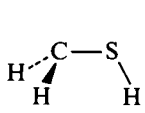
In a recent *ab initio* study, Bernardi and coworkers[41] compared at an extended level the effects of *thio*- and *oxy*-substituents on the stabilities of α-substituted carbanions. In the following we describe their work and summarize other calculations on structures of



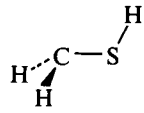
(18) (19) (4)

α-lithiated ethers. Then we examine whether the calculated data are in agreement with experimantal results. The fundamental differences between the second-row —SH(R) and first-row —OH(R) substituents on the energies and geometries of the corresponding anions and lithio compounds will then be evident.

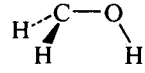
The systems chosen for the discussion are the *syn* and *anti* conformers *syn*-**8**, *anti*-**8**, *syn*-**20** and *anti*-**20**. In all cases the authors computed the stabilization energies SE,



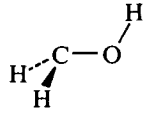
(*syn*-**8**)



(*anti*-**8**)



(*syn*-**20**)



(*anti*-**20**)

which were then decomposed into the component terms associated with the various types of effects that are assumed to play a role in the stabilization: σ-effects (SE_σ), nonbonded interaction effects (SE_{NB}), d-orbital effects (SE_d) and correlation effects (SE_{CE}).

The stabilization energies SE associated with the substituents —SH and —OH have been computed on the basis of equation 5:

$$SE = [E_T(H_3C—XH) + E_T(\bar{C}H_3)] - [E_T(H_2\bar{C}—XH) + E_T(CH_4)] \quad (5)$$

with E_T = SCF-MO total energy. Positive values of SE mean that the substituent stabilizes a negative charge more than H, while negative values mean the reverse.

Neutral molecules were optimized with the 3-21G basis set; sulfur compounds have also been calculated with the 3-21G(d) (including d-orbitals), and in the case of $H_2\bar{C}$—SH **8**, with the 3-21 + G(d) (diffuse functions and d-orbitals) versions.

In order to obtain more accurate *energy* values, single-point computations were performed on the 3-21G and 3-21 + G optimized geometries at the 6-31 + G level. Similar computations have also been performed with the 6-31 + G(d) basis set on the 3-21G(d) and 3-21 + G(d) optimized geometries of **7** and **8**. Finally, in order to estimate the effect of the electron correlation, MP2/6-31 + G(d) single-point calculations have been carried out. The total energy values in the absence of nonbonded interactions as well as the PMO estimates of the energy effects associated with these interactions have been calculated by methods described in Reference 42. The stabilization energy values SE calculated at the various levels are summarized in Table 1.

It is evident from Table 1 that the —SH group stabilizes a negative charge at all

TABLE 1. Stabilization energies SE (kcal mol^{-1}) of the *syn* and *anti* conformations of the sulfur anions **8** and oxygen anions **20**

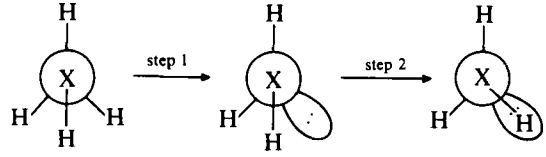
	6-31 + G //3-21 + G	6-31 + G(d) //3-21 + G	MP2/6-31 + G(d) //3-21 + G(d)
syn-**8**	18.81	18.63	27.95
syn-**20**	−2.23	—	0.24
anti-**8**	19.75	17.43	26.74
anti-**20**	3.76	—	5.30

levels of theory much better than an —OH group. A comparison of the results *without* (first column) and *with* d-orbitals (second column) led Bernardi and coworkers in their 1986 publication[41] also to the reasoning that the inclusion of d-orbitals has only minor effects on the stabilization energy, a result which agrees well with the findings of Schleyer, Clark, Houk and coworkers[32] as outlined in Section II. It is thus superfluous to further discuss this point in any length.

In order to understand the energetic effects involved in the formation of $H_2\bar{C}$—XH (X = O, S) the authors *decomposed* the formation of $H_2\bar{C}$—XH from H_3C—XH into two steps. In Figure 7 the formation of the isomer *anti*-$H_2\bar{C}$—XH with optimized geometry from *anti*-$H_2\bar{C}$—XH with frozen geometry (the same geometry as in H_3C—XH) is shown. In a similar fashion the formation of *syn*—$H_2\bar{C}$—XH has been studied. Since the results for the *anti* and *syn* isomers of $H_2\bar{C}$—XH are rather similar (see Table 1), and since the differences are not important for an understanding of the effects involved in the stabilization of a negative charge, we restrict ourselves in the further disscussion to a description of the situation of the *anti* isomers $H_2\bar{C}$—XH.

The results of calculations giving the —SH and —OH stabilization energies SE and the contributions associated with the σ and nonbonded interactions (NB), namely SE_σ and SE_{NB}, are listed in Tables 2 and 3.

The trend according to which the —SH group stabilizes a negative charge much better than an —OH group is not only found at the level of the optimized geometries, but already in the frozen conformations, as shown by the SE values in Tables 2 and 3. In order to understand the various contributing factors to the stabilization energy SE, the results calculated *without d-orbitals on sulfur (6-31 + G)* are investigated first. If one compares the results of Table 2 (*anti*-$H_2\bar{C}$—SH **8**, 6-31 + G level) with those of Table 3



anti-$H_2\bar{C}$—XH frozen geometry *anti*-$H_2\bar{C}$—XH optimized geometry

FIGURE 7. Formation of *anti*-$H_2\bar{C}$—XH (X = O, S) with frozen geometry from H_3C—XH, and its transformation into *anti*-$H_2\bar{C}$—XH with optimized geometry

TABLE 2. —SH stabilization energies (SE) of *anti*-**8** calculated at the 6-31 + G (without d-orbitals) and 6-31 + G(d) (including d-orbitals) levels, and related contributions associated with the σ (SE_σ) and nonbonded interaction effects (SE_{NB}); bond lengths in pm, energies in kcal mol^{-1}

	anti-$H_2\bar{C}$—SH (*anti*-**8**)			
	without d-orbitals (6-31 + G)		including d-orbitals [6-31 + G(d)]	
	frozen	optimized	frozen	optimized
C—X	189.4	205.8	182.5	180.4
SE	12.16	19.75	9.52	17.43
SE_σ	61.41	−2.20	51.53	37.15
SE_{NB}	−49.26	21.95	−42.01	−19.72

TABLE 3. —OH stabilization energies (SE) of *anti*-**20** (6-31 + G), and related contributions associated with the σ (SE_σ) and nonbonded interaction effects (SE_{NB}); bond lengths in pm, energies in kcal mol^{-1}

	anti-$H_2\bar{C}$—OH (*anti*-**20**) (6-31 + G)	
	frozen	optimized
C—X	144.0	155.9
SE	−4.24	3.76
SE_σ	39.92	−29.64
SE_{NB}	−44.16	33.40

(*anti*-$H_2\bar{C}$—OH **20**, 6-31 + G), one realizes that in the case of the *frozen* carbanions the SE_{NB} contribution is destabilizing and favors —OH over —SH; in contrast, SE_σ is stabilizing and favors —SH over —OH. Since the SE_σ contributions dominate, the —SH carbanions **8** are more stable than the —OH carbanions because of a more favorable σ effect in the former ones.

The negative sign of SE_{NB} indicates that the removal of a proton from the carbon in H_3C—XH is accompanied by an increase in the replusive effects associated with the nonbonded interactions. To reduce these large effects the geometry tends to change in the anions $H_2\bar{C}$—XH: a comparison of the bond lengths C—X in Tables 2 and 3 shows that in the optimized structures, C—X is much longer than in the frozen ones. The lengthening of the C—X bonds, however, is also associated with a *decrease in the C–X bond stability* (SE_σ) (Tables 2 and 3). Since both energy changes, SE_{NB} and SE_σ, are of the same order of magnitude, the overall stabilization energy SE remains almost unchanged with the relaxation of the $H_2\bar{C}$—XH geometry. Therefore, at the optimized geometry again SE_σ determines the trend of the stabilization energy, which means that the —SH anion *anti*-**8** is more stable than the —OH anion *anti*-**20** because of the different C—X σ-bond effects. With d-orbitals on sulfur [Table 2, 6-31 + G(d) level] the C—S bond length again shortens significantly. It is even slightly shorter than

in H_3C—SH **7** (exp. value 181.9 pm[28]) which agrees well with the theoretical and experimental results outlined in Section II. Including d-orbitals, however, has only a marginal effect on the overall stabilization energy SE (supporting again the results given in Table 1 and in Section II) since SE_σ and SE_{NB} again vary in opposite directions to roughly the same extent. Therefore, also with d-orbitals on sulfur, the —SH anion *anti*-**8** is more stable than the —OH anion *anti*-**20** because of the σ-effect.

The comparative analysis of the C—X σ-bond weakening associated with the removal of a proton in the H_3C fragment of H_3C—XH to give $H_2\bar{C}$—XH thus leads to the conclusion that it is much more significant for X = O than for X = S, and that this differential bond weakening effect of C—X is the source of the relative stability of the anions $H_2\bar{C}$—SH **8** and $H_2\bar{C}$—OH **20**. Most significantly, this is also reflected in the bond length of the C—O bond in *anti*-$H_2\bar{C}$—OH (*anti*-**20**): the calculated value (155.9 pm) means that the C—O bond in the anion $H_2\bar{C}$—OH **20** is *remarkably longer* (!) than in H_3C—OH (experimental value: 142.5 pm[43]). One should remember that the C—S bond in **8** is *shorter* than in H_3C—SH (Table 2 and Section II). We will return to this important difference between —SH(R) and —OH(R) stabilized 'anions'.

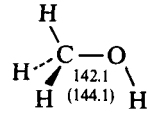
Besides the large SE_σ and SE_{NB} effects and a negligible d-orbital effect SE_d, the authors also discuss correlation effects[41]. In short, they find small effects of SE_{CE} in the case of the oxy-anion *anti*-**20** (1.54 kcal mol^{-1}) while these effects are more pronounced in the case of the sulfur anion *anti*-**8** (9.31 kcal mol^{-1}); see Table 1. This type of energy component can be considered as a polarization effect arising from low-lying excited states involving, in addition to the sulfur d-orbitals, other types of empty orbitals such as σ^*_{C-X} and σ^*_{C-H}. Since these orbitals are at lower energy when X = S, SE_{CE} favors second-row over first-row substituents.

In conclusion, an —SH group stabilizes a negative charge better than an —OH group because of the different σ effects: in the anion $H_2\bar{C}$—XH the C—S bond is less weakened than the C—O bond; the effect of the nonbonded interactions (SE_{NB}) favors the oxygen- versus the sulfur-substituted anion; the contribution of the sulfur 3d orbital on the stabilization energy SE_d is unimportant; more significant is the contribution associated with the correlation energy effects which favor —SH over —OH. With regard to the geometry it is of interest that the C—S bond is slightly shortened, while the C—O bond should be lengthened in the 'anion'.

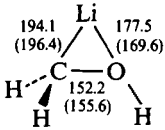
Since it was shown above and in Section II that the results of calculations of *sulfur*-substituted anions **8** and lithium compounds **10** agree well with crystal structure data of respective Li compounds, the calculationally predicted bond lengthening of the C—O bonds in the oxygen-substituted anions **20** raises the question about C—O bond lengths in α-lithiated ethers. Again we consider the experimental confirmation of the calculated data to be of great importance for evaluating the significance of the calculations which are used in this section to analyze the different effects of sulfur and oxygen substituents on the stabilization of a negative charge.

Before crystal structures of α-lithiated ethers are examined, we must refer to earlier model calculations of H_3COH **21** and lithiated ethers performed on $LiCH_2OH$ **22** by Clark, Schleyer, Houk and Rondan[44]. It is of interest that these investigations have been stimulated by NMR investigations of Seebach and coworkers[45] and by theoretical studies first performed by Schleyer and coworkers[46] on Li/halide carbenoids of the type $LiCH_2Hal$. The results of the calculations of H_3COH **21** and $LiCH_2OH$ **22**, which we have repeated on a higher theoretical level and which show overall agreement between $LiCH_2Hal$ and $LiCH_2OH$ **22**, are listed in Figure 8.

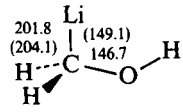
The carbon–oxygen bridged Li compound **22A** is by far the most stable isomer, especially if compared with the situation observed in the case of the Li–sulfur compounds **10**. The energy difference between **22A** and **22B** amounts to 13.6 kcal mol^{-1}. In contrast, the Li-bridged sulfur analogue **10A** is only 2.7 kcal mol^{-1} more stable than the non-



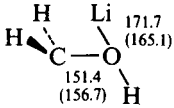
(21)



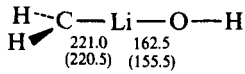
(22A); 0.0



(22B); 13.6 (13.8)

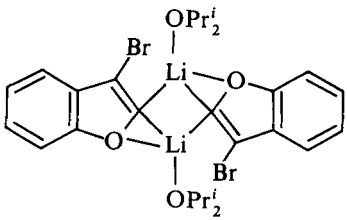


(22C); 16.4 (19.6)

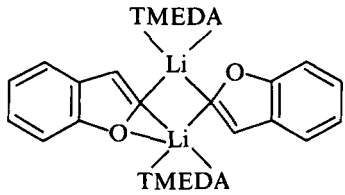


(22D); 44.4 (50.0)

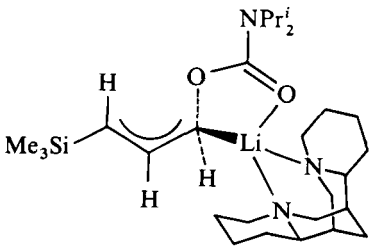
FIGURE 8. MP2/6-311++G(d,p)//MP2/6-311++G(d,p) calculated structures (bond lengths in pm) and relative energies (in kcal mol^{-1}) corrected to zero-point vibration of H_3COH and $LiCH_2OH$ **22**; earlier MP2/6-31G(d)//3-21G data[32,44] are listed in parentheses



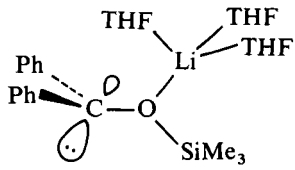
([23·OPr$^i_2$]$_2$)[47]



([24·TMEDA]$_2$)[48]



(25·sparteine)[49]



(26·3THF)[50]

FIGURE 9. Crystal structures of lithiated ethers

bridged **10B** (see Figure 5). The C—O bond in **22A** is appreciably lengthened to 152.2 pm (H_3COH **21**: 142.1 pm; experimental value: 142.5 pm[43]). In the nonbridged isomer **22B** the C—O bond is elongated to 146.7 pm; **22C** is 16.4 kcal mol^{-1} higher in energy than **22A**, and has also a longer C—O bond (151.4 pm); in this isomer Li is only bonded to the oxygen atom. **22D** is rather energy-rich (+44.4 kcal mol^{-1}). It indicates an electrophilic character of the oxygen-substituted carbon atom, a property which is well known for $LiCH_2Hal$ carbenoids.

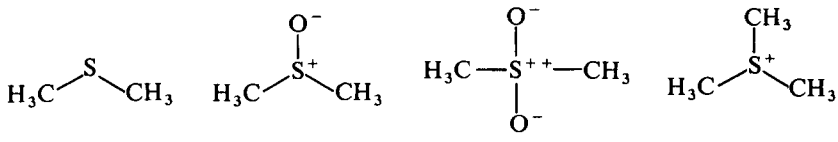
The crystal structures of the α-lithiated ethers known to date are shown in Figure 9. The overall structures of [**23**·OPr^i_2]$_2$[47], [**24**·TMEDA]$_2$[48], **25**·sparteine[49] and **26**·3THF[50] agree perfectly well with those of the calculated structures **22A–C**. Similarly, in the crystal structures the C—O bonds are remarkably lengthened if compared to appropriate nonlithiated compounds[50].

Thus, in [**23**·OPr^i_2]$_2$ lithium bridges twice the C—O bonds. This is at least the case in one-half of the dimer [**24**·TMEDA]$_2$, although the corresponding Li thereby adopts a penta-coordination instead of the usual tetra-coordination. As mentioned in Section II, a similar bridging of lithium is not observed in the crystal structures of lithiated thioethers (see Figure 6). These experimental findings nicely confirm the results of the calculations mentioned above, i.e. the tendency of first-row elements like oxygen to bridge, and the absence of bridging in the case of second-row elements like sulfur[32]. The C—O bonds in [**23**·OPr^i_2]$_2$ and [**24**·TMEDA]$_2$ are 147.0 and 145.3 pm long; since the mean value of the corresponding bond in benzofuran amounts to 138.5 pm[37], one recognizes the remarkable elongation of the C—O bonds in these two lithiated ethers. As one recalls the situation in the lithiated thioethers (Figure 6) this situation was exactly the reverse there: the C—S bonds are *shorter* than in nonlithiated thioethers. The energetically less favorable $LiCH_2OH$ isomers as modelled by **22B** (Li only at carbon) and **22C** (Li only at oxygen) (Figure 8) obviously can only be realized if the energy difference from the most stable bridged structure **22A** is compensated by other effects. In **25**·sparteine this is the chelation of Li by the carbamoyl group, and in **26**·3THF it is the stabilization of the negative charge at the anionic carbon atom by two phenyl groups. In both cases the C—O bonds are again much longer (147.6 and 148.8 pm, respectively) than in the corresponding nonlithiated species. This is exactly what theory[32,41,42,50] had predicted[51].

In conclusion, the theoretical studies outlined in this section confirm the results of Section II with regard to the stabilization of a negative charge by an —SH(R) group. d-Orbitals only play a role in determining the geometry of the anion as well as of the lithiated species; energetically they are unimportant. Deprotonation of a thioether destabilizes the C—S σ-bond much less than deprotonation of an ether destabilizes the C—O σ-bond. In the sulfur-subtituted anion the C—S bond becomes slightly shorter; in the oxygen-substituted case 'anionization' leads to a remarkably elongated C—O bond. Li bridging in lithiated thioethers is not observed while it is predicted and observed in lithiated ethers. Most importantly, the experimental verifications of the calculations in the case of —SH as well as —OH substituted 'carbanions' confirm that the theoretical analyses of the effects of —SH(R) substituents on the acidity of adjacent C—H bonds, and on the stability of the corresponding carbanions, including the importance of d-orbitals, are on safe ground.

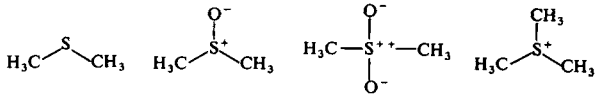
IV. THE CARBON ACIDITY OF THIOETHERS, SULFOXIDES, SULFONES AND SULFONIUM IONS: A COMPARATIVE ANALYSIS ON THE BASIS OF THEORY AND EXPERIMENT

The acidity of thioethers like **1**, sulfoxides like **4**, sulfones like **5** and sulfonium ions like **3** increases in the order **1** < **4** < **5** < **3** as shown by the pK_a values below[53]. This is nicely reflected in the calculated deprotonation energies. Table 4 summarizes the results at



	(1)	(4)	(5)	(3)
pK_a	45	35	31.3	18.2

TABLE 4. Deprotonation energies (kcal mol^{-1})



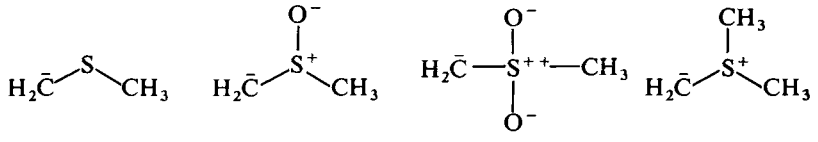
	(1)	(4)	(5)	(3)
HF/6-311 + + G(d,p)	413.2	396.9	382.4	284.0
HF/6-311 + + G(d,p) + ZPE[a]	402.3	386.8	372.5	274.4
MP2/6-311 + + G(d,p)	404.9	384.3	376.4	273.3
'Best' value[b]	394.0	374.2	366.5	263.7

[a] Uncorrected vibrational energies at 298 K.
[b] E(HF/6-311 + + G(d,p) + ZPE) − E(HF/6-311 + + G(d,p)) + E(MP2/6-311 + + G(d,p)).

different levels of calculation[54]. The reader will note that **4** and **5** (and later on also their deprotonated forms) are wtitten with charges, rather than in the conventional neutral form as in Section I. This is due to the results of the calculations.

One can see from Table 4 that each of the methods shows that the ease of removing a proton is in the same order (**3** > **5** > **4** > **1**) as observed experimentally. The qualitative jump on going from the sulfone **5** to the cationic sulfonium ion **3** is also reproduced by theory.

Next we compare bond lengths in the 'acids' **1**, **4**, **5** and **3**, and in the deprotonated compounds **9**, **27**, **28** and **29**. We also list covalent bond orders[55], bond ionicities[56] and



(9) **(27)** **(28)** **(29)**

atomic charges[57] in these species. The atomic and bond properties quoted here are obtained within the framework of the topological theory of atoms in molecules[57] and therefore avoid the bias inherent in some other population analyses[58] that equate basis functions with 'atomic orbitals'. One should note that the aforementioned rigorous interpretive tools have been previously employed in studies of sulfur compounds[54]. The results of our calculations are summarized in Tables 5–8. Earlier calculations on a sulfoxide, sulfone, sulfonium ion and their deprotonated species were performed at a lower level[27c]; sulfonyl anion and lithiated sulfones were also previously calculated[59].

An inspection of the individual bonds leads to the following conclusions:

TABLE 5. Bond lengths (pm), bond orders and bond ionicities (the degree of ionicity of the principal localized MO corresponding to the bond in question) of **1**, **4**, **5** and **3**, calculated at the MP2/6-311 + + G(d, p) level

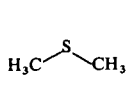
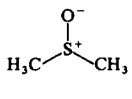
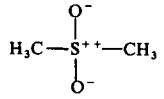
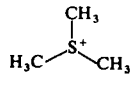
	 (1)	 (4)	 (5)	 (3)
Bond length				
C—S	180.1	180.5	178.2	179.7
S—O	—	150.7	145.9	—
Bond order				
C—S	1.091	1.002	0.957	1.016
S—O	—	1.297	1.158	—
Degree of ionicity (%)				
C—S	1.7	0.7	3.9	16.4
S—O	—	50.5	60.4	—

TABLE 6. Bond lengths (pm), bond orders and bond ionicities (the degree of ionicity of the principal localized MO corresponding to the bond in question) of the deprotonated **9**, **27**, **28** and **29**, calculated at the MP2/6-311 + + G(d, p) level. The ylid **29** has C_1 symmetry and thus two different S—CH_3 bonds

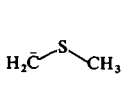
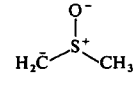
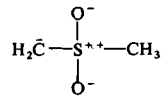
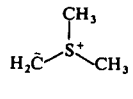
	 (9)	 (27)	 (28)	 (29)
Bond length				
$H_2\bar{C}$—S	172.0	170.3	166.4	165.7
S—CH_3	186.5	181.5	182.7	180.7; 184.2
S—O	—	155.7	148.4	—
Bond order				
$H_2\bar{C}$—S	1.369	1.331	1.293	1.432
S—CH_3	1.070	0.981	0.900	1.023; 1.021
S—O	—	1.238	1.099	—
Degree of ionicity (%)				
$H_2\bar{C}$—S	9.6	11.5	18.1	18.9
S—CH_3	10.7	6.8	9.5	3.9;4.0
S—O	—	51.5	60.4	—

TABLE 7. Bader atomic charges of **1**, **4**, **5** and **3**, calculated at the MP2/6-311 + + G(d,p) level

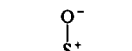
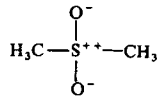
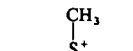
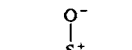
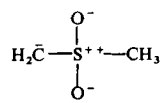
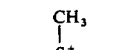
Atom	(1)	 (4)	 (5)	 (3)
C	−0.113	−0.177	−0.176	−0.141
H	0.036	0.057	0.085	0.113
H	0.022	0.037	0.061	0.095
H	0.022	0.054	0.061	0.113
CH_3 total	−0.033	−0.029	0.031	0.180
S	0.065	1.296	2.521	0.456
O	—	−1.236	−1.291	—
O	—	—	−1.291	—
$S(O_2)_{total}$	0.065	0.060	−0.061	0.456

TABLE 8. Bader atomic charges of the deprotonated **9**, **27**, **28** and **29**, calculated at the MP2/6-311 + + G(d, p) level; the ylid **29** has C_1 symmetry and thus two different CH_3 groups

Atom	(9)	 (27)	 (28)	 (29)
C	−0.531	−0.541	−0.484	−0.455
H	−0.076	−0.048	−0.019	0.017
H	−0.076	−0.051	−0.019	0.041
CH_2 total	−0.683	−0.640	−0.522	−0.397
S	−0.044	1.084	2.373	0.476
O	—	−1.299	−1.350	—
O	—	—	−1.350	—
$S(O_2)_{total}$	−0.044	−0.215	−0.327	0.476
C	−0.141	−0.145	−0.153	−0.143; −0.160
H	−0.055	−0.008	0.006	0.060; 0.044
H	−0.039	0.008	−0.002	0.029; 0.025
H	−0.039	−0.001	−0.002	0.042; 0.031
CH_3 total	−0.274	−0.146	−0.151	−0.012; −0.060

$H_2\bar{C}$—S bonds in the anions 9, 27, 28 and the ylid 29. The $H_2\bar{C}$—S bonds (Table 6) *shorten* on going from the deprotonated thioether **9** (172.0 pm) via the deprotonated sulfoxide **27** (170.3 pm) and the deprotonated sulfone **28** (166.4 pm) to the deprotonated sulfonium ion (sulfur ylid) **29** (165.7 pm). All of the $H_2\bar{C}$—S bonds are much shorter than the C—S bonds in the nondeprotonated compounds **1** (180.1 pm), **4** (180.5 pm), **5** (178.2 pm) and **3** (179.7 pm) (Table 5). In the case of **9** this corresponds to X-ray data of lithiated thioethers (see Section II). The bond orders of the $H_2\bar{C}$—S bonds, however,

do not follow the sequence found in the bond lengths of **9**, **27**, **28** and **29**: they go down from 1.369 in **9** via 1.331 in **27** to 1.293 in **28**, as these bonds shorten. In contrast, the ylid **29** has the highest bond order in the series and also the shortest $H_2\bar{C}$—S bond (see above). The ionicities of the $H_2\bar{C}$—S bonds increase from **9** (9.6%), via **27** (11.5%) and **28** (18.1%) to **29** (18.9%). Altogether this means that the bond shortening ('strengthening') on going from **9** via **27** to **28** is mostly due to electrostatic effects (the attraction between the negatively charged CH_2 unit and the positively charged S atom; see also below). On the other hand, taking into account the slight increase in the bond ionicity and the significant increase in the covalent bond order upon going from **28** to **29**, we conclude that the bond shortening in the latter molecule is caused by the increased covalent interactions. These interactions can be traced down to significant contributions from π-type orbitals that complement the σ-like bonding. These additional interactions are also present to a smaller extent in **9**, **27** and **28**, as reflected in the relevant covalent bond orders that are substantially greater than 1.000. This is especially the case for the ylid **29**. For comparison, the C—S bond orders in the nondeprotonated **1** (1.091), **4** (1.002), **5** (0.957) and **3** (1.016) are much closer to 1.000 (Table 5). The same applies for the bond orders of the S—CH_3 bonds in the deprotonated **9**, **27**, **28** and **29**, and for the S—O (!) bonds in **27** and **28** (Table 6).

S—CH_3 bonds in the anions 9, 27, 28 and the ylid **29**. The lengthening especially observed in the S—CH_3 bond of the deprotonated thioether **9** (186.5 pm; Table 6) corresponds to the findings described in Sections II and III, and is in agreement with crystal structure data of lithiated thioethers (Section II). In the case of the deprotonated sulfoxide **27** and the deprotonated sulfone **28** the S—CH_3 bonds are less lengthened, as shown by comparison of Tables 5 and 6. In agreement with the (slight) lengthening of the S—CH_3 bonds in the deprotonated **9**, **27** and **28**, the bond orders go somewhat down if compared to those in the nondeprotonated **1**, **4** and **5**.

In **29** both S—CH_3 bonds are lengthened [180.7 (slightly) and 184.2 pm] if compared to those in the sulfonium ion **3** (179.7 pm). **29** is highly unsymmetrical (C1), which might result from the interaction of the CH_2 lone pair with the CH_3 group having the longer S—CH_3 bond.

S—O bonds in the anions 27 and 28. The S—O bonds in the sulfone anion **28** are shorter (148.4 pm) than the S—O bond in the sulfoxide anion **27** (155.7 pm). In both cases the S—O bonds are slightly elongated if compared to those of the neutral species, namely the sulfone **5** (145.9 pm) and the sulfoxide **4** (150.7 pm). Correspondingly, the bond orders in the sulfoxide anion **27** (1.238) and sulfone anion **28** (1.099) are lower than those in the sulfoxide **4** (1.297) and sulfone **5** (1.158). The shorter S—O bonds in the sulfone **5** and the sulfone anion **28** as compared to those in the sulfoxide **4** and the sulfoxide anion **27** are due to the higher ionicities in the S—O bonds of the 'sulfones': for **5** and **28** 60.4% are calculated, while in the 'sulfoxides' **4** and **27** the values are 50.5% and 51.5%. This is because the charge on S is much higher in the sulfone species **5** (2.521) and **28** (2.373) than in the sulfoxide compounds **4** (1.296) and **27** (1.084). Thus the sulfur atom in sulfones and sulfone anions has essentially a charge of +2, while it is +1 in sulfoxides and their anions! This agrees with the result that the S—O bond orders of the sulfone species (see Tables 5 and 6) are lower than those of the sulfoxide compounds although the S—O bonds are shorter in the sulfone species. We have already mentioned that the shortening of the $H_2\bar{C}$—S bonds along the series **9**, **27** and **28** has the same reason, namely the electrostatic effect; should the bond shortening have its origins in increased conjugation, one would expect the covalent bond orders to be larger for shorter than for the longer bonds (Table 6).

How do the calculated data of the sulfoxide species **4** and **27**, the sulfone species **5** and **28** and the sulfonium ion/sulfur ylid pair **3** and **29** agree with X-ray structure investigations? The mean value for the $H_2\bar{C}$—S distance in the solid state structures of

two lithiated sulfoxides amounts to 166 pm[60]. This is much shorter than the C—S bond length in DMSO (180 pm)[61]. On the other hand, the S—O bond length in the lithiated sulfoxide amounts to 155 pm, which is considerably longer than the same bond in DMSO (147 pm)[61]. The corresponding calculated bond lengths agree nicely with these values (see Tables 5 and 6).

In the case of lithiated sulfones, the mean value from 7 structures leads to the following bond lengths: R_2C—S 165 pm and S—O 146 pm[37]. The mean value from 58 sulfones amounts to 181 pm for C—S and 143 pm for S—O[37]. The C—S bond in lithiated sulfones is thus strongly shortened with respect to the same bond in nonlithiated sulfones; the S—O bond, however, is only slightly elongated as compared to S—O bonds in sulfones. Once again the comparison between experimental and calculated bond lengths is very convincing, as one can see from these results and those in Tables 5 and 6.

Nice agreement between experiment and theory also holds for sulfonium ions and sulfur ylids. The mean value for C—S bonds in 58 sulfonium ions is 180 pm[37] while the calculations (Table 5) provided 179.7 pm. A comparison of calculated and experimental $\bar{C}$—S bond lengths in sulfur ylids (calculated: 165.7 pm; see Table 5), however, is hardly possible because essentially all the known X-ray structures of sulfur ylids are such that the anionic carbon atom is loaded with acceptor substituents, thereby reducing the charge at this carbon atom and thus the bond strength to sulfur; correspondingly, a mean value of 173 pm is found experimentally for the $\bar{C}$—S bond, a value which is longer than the calculated one. On the other-hand, completely different S—CH_3 bond lengths (180 and 183 pm) are observed in $(NC)\bar{C}$—$S^+(CH_3)_2$[62], which agrees perfectly with the results of the calculations in Table 6.

In conclusion, the difference in electronegativity of the sulfur and oxygen atoms is large enough to cause very substantial polarization of the S—O bond, which should be properly written as S^+—O^-. In consequence, the sulfur atoms in sulfoxides and their anions bear charges of approximately +1, whereas those in sulfones and their anions have charges of about +2. The electrostatic attraction between the positive charge on sulfur and the negatively charged CH_2 groups in the sulfoxide and sulfone anions causes the corresponding bond shortening.

As a result of the substantial S—O bond ionicities, sulfoxides, sulfones and their anions should not be regarded as hypervalent species. On the other hand, the electronegativity difference between the sulfur atom and the methylene group in the ylide **29** is much smaller, resulting in a partial double S—CH_2 bond. The sulfur atom in **29** is therefore hypervalent.

V. APPENDIX

In the following the coordinates of the atoms (in au) in the compounds listed as well as the total energies (in au) of formation are given (MP2/6-311 + + G(d, p)).

Structure		Total energy (au)	
CH_3SCH_3 **1**		−477.38952	
H	0.000000	4.331345	0.101075
C	0.000000	2.570640	−0.972851
S	0.000000	0.000000	1.257268
C	0.000000	−2.570640	−0.972851
H	1.687905	−2.529428	−2.161059
H	−1.687905	−2.529428	−2.161059

(*continued*)

Structure		Total energy (au)	
H	−1.687905	2.529428	−2.161059
H	1.687905	2.529428	−2.161059
H	0.000000	−4.331345	0.101075
$S(CH_3)_3^+$ **3**		−516.94584	
S	0.000000	0.000000	0.525764
C	−0.617859	1.489685	−0.266276
C	1.599035	−0.209761	−0.266276
C	−0.981176	−1.279924	−0.266276
H	0.000000	2.322182	0.072405
H	2.011069	−1.161091	0.072405
H	−2.011069	−1.161091	0.072405
H	−0.575047	1.386441	−1.351242
H	1.488216	−0.195215	−1.351242
H	−0.913169	−1.191226	−1.351242
H	−1.643550	1.640515	0.072419
H	2.242503	0.603098	0.072419
H	−0.598953	−2.243614	0.072419
CH_3SOCH_3 **4**		−552.44064	
H	−0.402424	−0.421688	4.300047
C	−0.491226	−1.478305	2.533049
S	−0.491226	0.805103	0.000000
C	−0.491226	−0.478305	−2.533049
H	−2.224590	−2.598138	−2.472298
H	1.184161	−2.670537	−2.352531
H	−2.224590	−2.598138	2.472298
H	1.184161	−2.670537	2.352531
H	−0.402424	−0.421668	−4.300047
O	2.080004	2.029839	0.000000
$CH_3SO_2CH_3$ **5**		−627.53446	
H	0.000000	4.313097	−0.516375
C	0.000000	2.644003	−1.726390
S	0.000000	0.000000	0.359734
C	0.000000	−2.644003	−1.726390
H	1.706424	−2.607816	−2.879709
H	−1.706424	−2.607816	−2.879709
H	−1.706424	2.607816	−2.879709
H	1.706424	2.607816	−2.879709
H	0.000000	−4.313097	−0.516375
O	−2.398370	0.000000	1.719533
O	2.398370	0.000000	1.719533
CH_3SH **7**		−438.17693	
C	0.049048	1.206761	0.000000
S	0.049048	−0.687638	0.000000
H	−1.289841	−0.872101	0.000000
H	1.087327	1.495865	0.000000
H	−0.438267	1.568938	0.889833
H	−0.438267	1.568938	−0.889833

(*continued*)

Structure		Total energy (au)	
$H_2\bar{C}$—SH *anti*-**8**		−437.52563	
C	−0.010405	1.205885	0.000000
H	−0.538299	1.554745	0.895767
H	−0.538299	1.554745	−0.895767
S	−0.010405	−0.591995	0.000000
H	1.305519	−0.872881	0.000000
$H_2\bar{C}$—SH *syn*-**8**		−437.52742	
C	0.088128	1.184297	0.000000
H	−0.364697	1.607106	0.903803
H	−0.364697	1.607106	0.903803
S	0.088128	−0.579161	0.000000
H	−1.209431	−1.053417	0.000000
$CH_3S\bar{C}H_2$ **9**		−476.74423	
H	−4.387873	−0.426688	−0.000588
C	−2.729754	0.831388	0.000009
S	0.211496	−1.110887	−0.000004
C	2.779994	0.881401	−0.000007
H	3.130253	1.931081	1.742987
H	3.130122	1.931221	−1.742942
H	−2.778646	2.031338	−1.685941
H	−2.779238	2.030508	1.686539
$LiCH_2SH$ **10A**		−445.03897	
C	−2.150300	−0.649283	0.107136
Li	−1.762976	2.989700	−0.033254
S	1.342919	−0.117785	−0.163987
H	1.762033	0.455142	2.262363
H	−2.616498	−1.528274	−1.714923
H	−2.441517	−2.115700	1.533290
$LiCH_2SH$ **10B**		−445.03424	
C	1.012511	−1.890928	0.000000
Li	0.000000	1.381936	0.000000
S	−2.599515	−2.494401	0.000000
H	−2.573196	1.154120	0.000000
H	2.148333	−2.218170	1.689005
H	2.148333	−2.218170	−1.689005
$CH_3SO\bar{C}H_2$ **27**		−551.82825	
H	−4.085492	−0.948291	−0.143630
C	−2.258475	−1.840247	0.216099
S	0.205634	0.336884	−0.760347
C	2.729317	−1.307601	0.372852
H	4.477634	−0.497057	−0.368388
H	2.717324	−1.462436	2.441547
H	−2.026397	−2.149895	2.248450
H	−2.078797	−3.621172	−0.805381
O	−0.639935	2.771974	0.657405

(*continued*)

Structure		Total energy (au)	
$CH_3SO_2\bar{C}H_2$ **28**		−551.82825	
H	−4.313988	−0.000079	0.203327
C	−2.744382	−0.000160	1.546854
S	0.217343	0.000026	−0.227128
C	2.755188	−0.000143	1.628185
H	3.019581	−1.761465	2.649049
H	3.019537	1.760959	2.649442
H	−2.800366	1.696820	2.719095
H	−2.800311	−1.697335	2.718817
O	0.020814	2.411339	−1.647019
O	0.020840	−2.411026	−1.647470
$H_2\bar{C}—S^+(CH_3)_2$ **29**		−516.51037	
H	0.000000	0.000000	0.000000
C	0.000000	0.000000	1.089146
S	1.729147	0.000000	1.614487
C	1.354827	−0.185869	3.408813
H	0.856302	−1.140417	3.599931
H	0.729549	0.648961	3.736254
H	−0.510764	−0.886102	1.472797
H	−0.480695	0.909929	1.455810
H	2.313649	−0.153936	3.927067
C	2.325004	1.486870	1.190925
H	1.866036	2.375539	1.612101
H	3.383939	1.479715	0.974315

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CHAPTER 8

Thiyl radicals

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I. INTRODUCTION

A large number of papers dealing with thiyl radicals, starting back in the twenties, have been published. From time to time review articles, describing some of their chemical characteristics, have also appeared. For this reason as well as for the availability of the space, this survey, which is not meant to be exhaustive, will reflect the scientific interest of the authors, dealing mainly with recent literature. Therefore, a few words about the exclusion of some specific subjects and the pattern of organization of this chapter will be useful.

In view of the importance and interest of thiyl radicals in biological systems, it is unthinkable to cover even part of this subject in this limited survey[1]. The alkanethiylperoxyl radicals, which are adducts of alkanethiyl radicals to molecular oxygen, will also not be considered, these transient species, which play important roles in a number of branches of chemistry, having recently been reviewed in Patai's series[2].

Thiyl radicals have the general structure: X—S·, where X represent a large variety of substituents. In this survey we will deal mainly with RS· and ArS· radicals, R and Ar

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being an alkyl and an aryl group, respectively. In the literature, several terminologies are used to indicate these species; for example, the PhS· radical is called (in order of popularity) phenylthiyl, phenylthio, thiophenoxy and benzenethiyl radical. Here, we will use alkylthio or alkanethiyl radical and arylthio or arenethiyl radical for RS· and ArS·, respectively. Structural properties are dealt with in Section II. For the first time we try to report and rationalize the data obtained by different spectroscopic techniques, including theoretical studies. In Section III, the most important elementary steps involving thiyl radicals, i.e. the formation of thiyl radicals by reaction of alkyl radicals with the corresponding thiols and the addition of thiyl radicals to carbon–carbon multiple bonds, are considered from a kinetic point of view. Some interesting chain processes involving mainly these reactions as propagation steps are then discussed. Finally, some of the general concepts of free radical chemistry are introduced at appropriate points throughout this article without reference.

II. STRUCTURAL PROPERTIES

A. Electronic Structure and Geometries

A knowledge of the energy and localization of the frontier molecular orbitals (MOs) is extremely important to interpret the magnetic (ESR) and electronic (UV-visible) properties of RS· radicals as well as their reactivity. The frontier MO orbitals of RS· and RSS· radicals are displayed in Figure 1[3].

The methanethiyl radical, CH_3S·, has an orbitally degenerate ^2E electronic ground state where the three outermost electrons occupy the degenerate 3p sulfur atomic orbitals

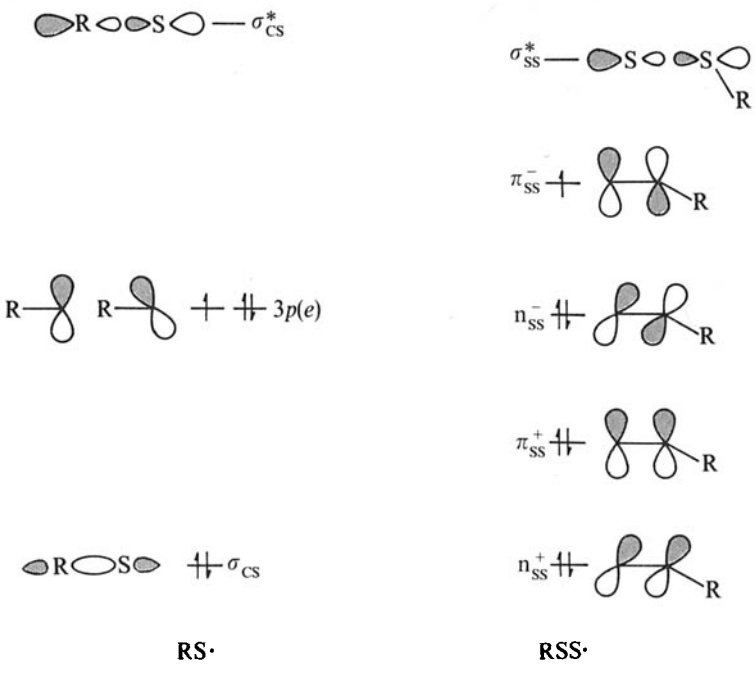


FIGURE 1. Frontier MO diagram of RS· and RSS· radicals

(AOs). Jahn–Teller distortion and asymmetric alkyl substituents slightly lift electronic degeneration. However, the Jahn–Teller distortion was found to be small by analyzing the $\tilde{A}^2A_1 \leftrightarrow \tilde{X}^2E$ laser-induced fluorescence excitation spectrum[4]. In particular, comparison between the spin–orbital splitting in $CH_3S\cdot$ and S (^3P) (-255.5 and $-396.1\,cm^{-1}$, respectively) and between the corresponding values in the oxygen analogs (-62.0 and $-158.5\,cm^{-1}$, respectively) suggests that distortion in $CH_3S\cdot$ is smaller than in $CH_3O\cdot$. The effect of the second sulfur in the perthiyl radical $RSS\cdot$ on the 3p degenerate sulfur AOs is found to be much stronger. The 3p AOs of the two sulfur atoms are strongly mixed with each other, giving rise to four substantially separate MOs, i.e. n_{SS}^{+}, π_{SS}^{+}, n_{SS}^{-}, π_{SS}^{-} in decreasing order of energy; π_{SS}^{-} is the singly occupied MO (SOMO). According to the Koopmans theorem MO energies can be approximated to ionization potentials (IPs) and electron affinities (EAs). The vertical[5] and adiabatic[6] IP of $CH_3S\cdot$ was found to be 8.1 and 7.7 eV, respectively. These values are similar to those determined for $CH_3O\cdot$ (8.1 and 7.4 eV, respectively)[7]. IP increases with the length of the alkyl group, the vertical IP value for $C_2H_5S\cdot$ and n-$C_3H_7S\cdot$ being 8.2 and 9.6 eV, respectively[8]. On the other hand, EA of alkanethiyl radicals slightly increases with increasing substitution at the alkyl group ranging from 1.86 eV for $CH_3S\cdot$ to 2.07 eV for t-$BuS\cdot$[9]. The same trend was observed in the oxygen analogs, EA being 1.59 eV for $CH_3O\cdot$ and 1.90 eV for t-$BuO\cdot$[10]. This finding was ascribed to increasing stabilization of the anion species because of the more effective $p\pi$–alkyl π^* mixing. This type of interaction is, however, weaker in thiyl than in alkoxyl anions. *Ab initio* calculations at the 4-31G level performed on CH_3X^- and $CH_3X\cdot$ (X = O, S) showed that the CH bond lengthens to a greater extent for X = O than for X = S on going from the radical to anion species. The phenyl group slightly increases EA, being 2.47 and 2.40 eV in the phenylthio[11] and phenoxy[12] radical, respectively. EA of the undetected $CH_2{=}CHS\cdot$ radical was computed to be positive (0.86 eV)[13] indicating that the $CH_2{=}CHS^-$ anion is stable as confirmed by negative ion mass spectroscopy[14]. IPs and EAs of thiyl radicals bearing an heteroatom in the α position are lacking, however, the IP of the perthiyl radical t-$BuSS\cdot$ was found to be 8.25 eV by measuring the appearance energy of t-$BuSS^+$ with a mass spectrometer[15].

The structural parameters of $CH_3S\cdot$ have been determined from the analysis of its rotational spectra[16]. The C—S bond was found to be significantly shorter (1.767 Å) than in CH_3SH (1.814 Å) as in the oxygen analogs. Unexpectedly, the $\angle$ HCH bond angle (102.5°) was found to be significantly smaller than the tetrahedral value. In contrast, *ab initio* calculations at the UHF/4-31G level, which closely reproduce the C—S bond length (1.76 Å), estimated the $\angle$ HCH bond angle (108°) to be *quasi-tetrahedral*[17]. In the excited ^2A state the $\angle$ HCH bond angle (107.1°) was computed to be nearly tetrahedral, whereas the C—S bond length (2.057 Å) increased dramatically. *Ab initio* calculations on $CH_3O\cdot$[18], where a similar trend was observed, suggest that this lengthening is due to excitation of an electron from the bonding σ_{CS} MO to the slightly antibonding e (3p) MO. The C—S bond length was computed to significantly decrease in the undetected vinylthio radical[13]. Its value (1.721 Å at the MCSCF/DZP level) is intermediate between the single (1.814 Å in CH_3SH) and double bond (1.611 Å in $CH_2{=}S$). The leading configuration of the MCSCF wavefunction corresponds to the sulfur-centered radical structure ($CH_2{=}CHS\cdot$), whereas in the oxygen analog the unpaired electron is located at the carbon atom ($\cdot CH_2{-}CH{=}O$). The C—S bond length (1.632 Å) in $HC{\equiv}CS\cdot$ was computed to be double bond in character[19]. The radical is *quasi*-linear at the UMP3/6-31G* level at variance with $HC{\equiv}CO\cdot$ which was computed to be strongly bent.

B. Thermodynamic Data

Thermodynamic data on sulfur-centered radicals are scarce. However, Benson determined them by using the group additivity method[20]. The data reported in his review

TABLE 1. Sulfur–hydrogen BDEs and gas-phase acidities (kcal mol^{-1}) of RSH and RSSH along with ΔH_f° (kcal mol^{-1}) and EAs (eV) of parent radicals[a]

Radical	BDE	Gas-phase acidity	ΔH_f°	EA
HS·	92.9[b]	353.4[c]	33.2	2.31[b]
MeS·	88.1[b]	359.0[c]	30.8	1.86[b]
EtS·	88.6[b]	357.4[c]	25.3	1.95[b]
i-PrS·	88.4[b]	355.6[c]	18.2	2.02[b]
t-BuS·	88.6[b]	354.7[c]	10.0	2.07[b]
PhS·	80.8		55.7	2.47[d]
HSS·	70.5		22.0	
MeSS·	70.5		16.4[e]	
EtSS·	70.5		10.3[e]	
i-PrSS·	70.5		3.3[e]	
t-BuSS·	70.5		−4.6[e]	

[a]Data are from Reference 21 unless otherwise stated.
[b]From Reference 9.
[c]From Reference 22.
[d]From Reference 11.
[e]From Reference 23.

were then updated by Griller and coworkers by taking into account more reliable values of heat of formation ΔH_f°, EA, and gas-phase acidity[21]. Relevant values of ΔH_f°, EA, and gas-phase acidity of thiyl and perthiyl radicals are reported in Table 1. ΔH_f° sizeably decreases on going from primary to tertiary alkyl substituents. The bond dissociation energy (BDE) of the S—H bond in thiols was determined by using available EAs and gas-phase acidity data (equation 1)[9]. Its value (*ca* 88.4 kcal mol^{-1}) was found to be nearly independent of the nature of the alkyl substituent as observed in aliphatic alcohols [BDE(RO—H) *ca* 102 kcal mol^{-1}][10]. Table 1 shows that the phenyl group decreases BDE by about 7.5 kcal mol^{-1} by stabilizing the PhS fragment. BDE(S—H) in polysulfides RS_nH(R = H, alkyl) sizeably decreases (*ca* 18 kcal mol^{-1}), its value being independent of R and *n*. This indicates that the unpaired electron in the RS_n fragment should be shared between the two terminal sulfur atoms.

$$\mathrm{BDE(RS—H)} = \mathrm{EA(RS\cdot)} + \Delta H^\circ_{298}(\mathrm{RSH} \rightarrow \mathrm{RS^-} + \mathrm{H^+}) - \mathrm{IP(H)} \qquad (1)$$

Table 2 shows that the S—S bond dissociation energy in disulfides RSSR (R = H, alkyl) is sizeably lower than BDE(S—H). Its value in the alkyl analogs (*ca* 68 kcal mol^{-1}) was found to be nearly independent of the nature of the substituent. This follows from the constancy of BDE(S—H) in thiols in conjunction with the good linear correlation found between ΔH_f°(RSSR,g) and ΔH_f°(RSH,g) (equation 2). BDE(S—S) of phenyl

TABLE 2. Sulfur–sulfur BDEs (kcal mol^{-1}) in polysulfides[a]

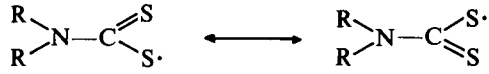
R	RS—SR	RS—S_2H	RS_2—S_2R
H	62.5	48.0	33.5
Alkyl	68.1	50.9	33.9 (32.3)[b]
Ph	53.3	43.5	<33.5

[a]From Reference 21.
[b]Mass spectrometric data (Reference 23).

disulfide can be estimated to be 52.8 kcal mol^{-1} since the linear correlation holds also for R = Ph. This value closely reproduces the one obtained from ΔH_f°(PhSSPh,g), i.e. 53.3 kcal mol^{-1}. As expected, the phenyl group stabilizes the PhS fragment by about 7.5 kcal mol^{-1}. By replacing an RS fragment with the RSS fragment BDE(S—S) decreases by 15–17 kcal mol^{-1} due to the larger stability of the RSS· radical (cf Table 2). This effect is found to be essentially additive. Thus, BDE of the S—S central bond in tetrasulfides is 34 kcal mol^{-1} lower than in disulfides. A similar lowering was found in the oxygen analogs, BDE(RO—OR) and BDE(ROO—OOR), being 36[24] and 8[25] kcal mol^{-1}, respectively. In general, the O—O bond is *ca* 30 kcal mol^{-1} weaker than the corresponding S—S bond.

$$\text{BDE(RS—SR)} = 2\text{BDE(RS—H)} + \Delta H_f^\circ\text{(RSSR)} - 2\Delta H_f^\circ\text{(RSH)} + 2\Delta H_f^\circ\text{(H)} \qquad (2)$$

The large stability of dialkylaminothiyl, sterically hindered arylthio, and dithiocarbamate radicals allowed one to determine the dissociation enthalpy and entropy of sulfur–sulfur bond by ESR spectroscopy (Table 3). In ortho substituted phenyl disulfides the low ΔH° value is due to destabilization of the disulfide by steric repulsion[26]. On the other hand, the absence of steric repulsion in thiuram disulfides[28] indicates that dithiocarbamate radicals are strongly stabilized by resonance (equation 3).



(3)

The BDE(S—S) of bis(1-pyrrolidino) disulfide was estimated to be 30.8 kcal mol^{-1} from the rate of thermal decomposition by assuming that the enthalpy of recombination was negligible. Radical concentration was determined by following the absorbance (at $\lambda = 473$ nm) of the stable Banfield's radical used as radical scavenger[29].

The sulfur–carbon BDE (*ca* 72 kcal mol^{-1}) in sulfides is slightly higher than the corresponding sulfur–sulfur BDE. Its value was found to be nearly constant in thiols and disulfides due to the constancy of BDE(RS—H). However, Table 4 shows that BDE slightly decreases on passing from primary to tertiary alkyl groups. The phenyl group decreases BDE(PhS—R) by about 7.5 kcal mol^{-1} as found for BDE(PhS—H) in thiophenol[21]. On the other hand, the sulfur–phenyl dissociation energy increases by

TABLE 3. Thermodynamic data of disulfides from ESR studies

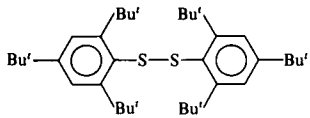
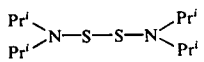
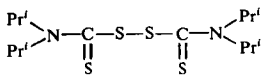
Compound	ΔH° (kcal mol^{-1})	ΔS° (eu)	Reference
	23.3	27.0	26
	24.0	16.0	27
	24.9	13.6	28

TABLE 4. Sulfur–carbon BDEs (kcal mol^{-1}) of some selected compounds[a]

R	R—SH	R—SR	R—SSR'[b,c]	RS—C(=O)Me
Me	73.9	74.8	58.1 (56.6)	
Et	72.7	73.6	57.6 (56.2)	74.1
i-Pr	71.5	72.2	56.2 (54.5)	73.6
t-Bu	70.0	65.7	55.0 (52.6)	71.9
Ph	85.3	79.4	69.8	

[a]From Reference 21.
[b]R' = H, alkyl.
[c]Values in parenthesis are taken from mass spectrometric studies (Reference 23).

TABLE 5. Redox potential (V) of sulfur-centered radicals[a]

RSSR/RS$^{\therefore}$SR$^-$	−1.57
RS$^{\therefore}$SR$^-$/RS$^-$	0.57
RS$^{\therefore}$SR$^-$ + H$^+$/RSH	1.72
RS·/RS$^-$	0.77
RS· + H$^+$/RSH	1.34

[a]From References 31 and 32.

about 12 kcal mol^{-1}. In disulfides BDE(S—C) displays the same trend as that observed in sulfides. However, BDE, in general, decreases by about 14.5 kcal mol^{-1} due to the larger relaxation energy of the RSS in respect to the RS fragment as observed for BDE(S—S). The additivity group method[20] suggests that BDE(S—C) in polysulfides should be essentially identical to that found in disulfides. BDE(S—C) in thioesters is slightly higher than in sulfides (see Table 4).

In disulfide anions RS$^{\therefore}$SR$^-$ ($^{\therefore}$ indicates a $\sigma^2\sigma^{*1}$ three-electron bond[30]) BDE of the S—S and S—C bond decreases dramatically to 15.5 and 46.6 kcal mol^{-1}, respectively, owing to the weakness of the three-electron bond. Indeed, Table 5 shows that the redox potential RSSR/RS$^{\therefore}$SR$^-$ is negative indicating that the S—S group can accept electrons only from strongly reducing species. On the other hand, the redox potential for (RS·, H$^+$)/RS$^-$ is largely positive. The nature of R slightly influences the redox potential which, however, increases with the electron-withdrawing capability of R. Also, the redox potential RS·/2RS$^-$ is positive. In fact, thiyl radicals rapidly accept electrons from biological molecules[33]. Interestingly, complexation of the thiyl radical with the thiolate anion turns an oxidant into a strongly reducing agent. The oxidative power of sulfur-centered radicals rises along the series[34] RS$^{\therefore}$SR$^-$ < RS· < RSSR$^+$ < R$_2$S$^{\therefore}$SR$_2^+$ < R$_2$S$^+$.

C. ESR Spectra

Thiyl radicals RS· are postulated to be intermediates in the radioprotection of biomolecules by means of thiols[35]. As a consequence, the ESR features observed during the photolysis or radiolysis of thiols were first attributed to thiyl radicals[36]. The ESR spectra detected in single crystals and in polycrystalline matrices are characterized by an anisotropic non-axial *g*-tensor which is not significantly affected by the environment, having components close to 2.060, 2.025, 2.002 (g_{av} = 2.029)[36]. Radical species having essentially the same *g*-factor were yielded by UV-irradiation of disulfides in solid solution[36]. This finding was used as a support to thiyl radical identification. However,

information from the sulfur hyperfine splitting (hfs) constants was lacking because it should have required the use of labelled ^{33}S compounds [the natural abundance of this magnetic isotope ($I = 3/2$) is 0.76%].

This assignment was later questioned[37] because the large orbital momentum about the C—S bond due to the (near) degeneracy of the sulfur 3pπ orbitals (see Figure 1) is expected to cause a line broadening which should prevent thiyl radicals from being observed in the liquid phase, while the components of the g-tensor in solid state should be difficult to determine since the ESR spectrum should exhibit only a weak broad band owing to the large anisotropy in the g-tensor.

The orbital angular momentum was quenched in solid solutions lifting the π-degeneracy by means of strong anisotropic interactions with the environment, such as hydrogen bonding[38,39], so that the g-tensor components were certainly determined. The g-tensor of radicals detected during radiolysis of thiols in rigid solution containing a protic solvent is indeed quite different. It has a *quasi*-axial symmetry and its anisotropy ($g_{\parallel}$-$g_{\perp}$) is large and depends on the strength of hydrogen bonding to sulfur[39], the $g_{\parallel}$-value being 2.30, 2.20, 2.16, 2.13 in HCl, *i*-PrOH, CD_3OD, $NaOH/H_2O$, respectively.

It was also suggested from chemical evidence[37] that the previous supposed RS· radicals are sulfuranyl species RS.∴S(H)R, which are formed in a combination process (equation 4). An analogous reaction was found to occur for the isostructural radical cations R(H)S.∴S(H)R^{+}[40] and anions RS.∴SR^{-}[41]. Indeed, the ^{33}S satellite features in γ-irradiated crystals of cysteine hydrochloride[42] indicate that the unpaired electron is delocalized over two non-equivalent sulfur atoms ($A_{iso} = 12.7$ and 21.3 G). However, the absence of proton hfs constants from hydrogens in the —S(H)R group could be interpreted as an argument against this identification[43]. Alternatively, formation of perthiyl RSS· radicals was also postulated[42,44]. This identification accounts for the observed proton hfs pattern. The non-axial g-tensor is however consistent with the non-linear structure of both the RS.∴S(H)R and RSS· radicals. Attempts to characterize the RSS· radical from thermal decomposition of RS_4R failed[43].

$$RS\cdot + RSH \longrightarrow RS.\therefore S(H)R \qquad (4)$$

Perthiyl radicals were observed in the photolysis of RSSCl in solution[45]. In this case the π-degeneracy is lifted by delocalization of the unpaired electron onto the second sulfur atom, the π_{SS}^{-}(SOMO) lying considerably high in energy relative to the n_{SS}^{-} doubly occupied MO (see Figure 1). The g-value ($g_{iso} = 2.025$) is very similar to that (2.0262) of the radical observed during the photolysis of di-*n*-butyl disulfide[46] and ascribed to the *n*-BuS· radical. Photolysis of *t*-butylthiosulphenyl chloride[45] in benzene matrix produces a radical species which has a non-axial g-tensor with components of 2.059, 2.026, 2.001 ($g_{av} = 2.029$) which are essentially identical to those observed in the photolysis of thiols and disulfides in solid solution. Identification of this radical species as a perthiyl rather than as a thiyl radical is consistent with the fact that thiyl radicals are expected not to be detected in solution (see above). Furthermore, perthiyl radicals were found on the basis of product studies[47] to be intermediates during the photosensitized decomposition of disulfides in solution. Thus, the radical species reported as thiyl radicals in the early work[36] are very likely perthiyl radicals. Since 1978 radical species displaying these ESR features have been identified as perthiyl radicals[48].

The sulfuranyl radical RS.∴S(H)R could be identified with the species generated from the γ-irradiation of single crystals of the disulfide cystine hydrochloride which was also identified first as RS·[36,42]. This radical species (g 2.066, 2.010, 2.000) displays large coupling to two hydrogens (17 and 21 G). On annealing it gives a transient species with $g_{av} = 2.029$, thus suggesting that formation of perthiyl radicals could arise from equation 5[43]. Support to these assignments follows from the low g-factor observed in

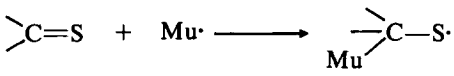
sulfuranyl radical $R_2S\therefore SCF_3$ ($g = 2.0133$)[49] and $R_2S\therefore SC(=O)R$ ($g = 2.014$)[50]. However, these low values could be caused by electronegativity of the substituents.

$$RS\therefore S(H)R \longrightarrow RSS\cdot + RH \tag{5}$$

In the liquid phase, oxidation of thiols and disulfides in continuous-flow systems using as oxidant Ti(III)—H_2O_2 and Ce(IV) in aqueous solutions produces broad line ESR spectra which were first attributed to thiyl radicals[36]. On the basis of chemical and spectroscopic [g_{iso} *ca* 2.01, a(1H) *ca* 9 G] evidence these radical species were subsequently identified as sulfinyl radicals[51].

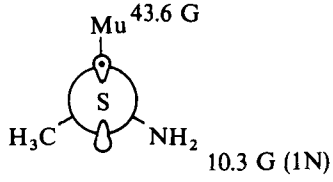
The formation of thiyl radicals in the liquid-phase radiolysis of thiols has been evidenced by means of the spin-trapping technique using as a trap *t*-BuNO·[52]. The coupling to three equivalent protons observed in *t*-BuN(O·)SCH_3 [$g = 2.0064$, a(1N) = 18.9 G, a(3H) = 1.2 G] was used as evidence for its identification. DMPO (5,5-dimethyl-1-pyrroline-*N*-oxide) was extensively employed in biological systems as a scavenger of thiyl radicals[53]. TMPO (3,3,5,5-tetramethyl-1-pyrroline-*N*-oxide) was shown to be of a greater utility for diagnostic use since it produces longer-lived adducts which have more characteristic spectral features[54].

Thiyl radicals were detected for the first time in solution using the transverse-field μ-SR technique[55] which provides the electron coupling to the muonium atom, a light hydrogen isotope. Addition of muonium to aliphatic thiocarbonyl compounds produces thiyl radicals (equation 6). Against all expectation, replacement of the hydrogen with

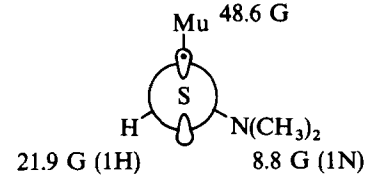


(6)

muonium atom strongly lifts the π-degeneracy, thus avoiding line broadening. The large muon hfs constant [A'_μ *ca* 50 G, the experimental value divided by the ratio between the gyromagnetic constant of μ and H (3.184)] and the negative temperature dependence observed in all adducts suggested that the muonium atom eclipses the 3pπ singly AOs at sulfur (structures **1** and **2**). This conformational assignment was further confirmed by the muon level-crossing resonance technique (μ-LCR)[56] in which the electron coupling to the other magnetic nuclei can be observed (cf **1** and **2**).



(1)



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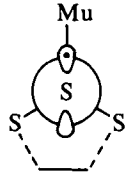

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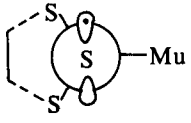


(4)

TABLE 6. g-Factors of thiyl and perthiyl radicals[a]

R	RS·	RSS·
Alkyl	2.07–2.09	2.025–2.029
Ph	2.010	2.030
R'_2N	2.015–2.018	2.029
$Ph_2C{=}N$	2.015	2.021
$(R'O)_2P(=S)$	2.019	
$(R'O)_2NC(=S)$	2.015	
$R'C(=O)$		2.024

[a]From References 36 and 48.

In radicals containing β-sulfur substituents the μ-hfs constant decreases significantly (A'_μ *ca* 40G). This suggested that the rotational barrier about the C—S bond decreases so that the staggered conformation (**4**) is populated to some extent. This finding is opposite to that found in β-sulfur substituted alkyl radicals where the C—S bond firmly eclipses the SOMO[57]. Thus, the hyperconjugative capability of β-bonds should follow the order $C{-}\mu > C{-}S > C{-}H$.

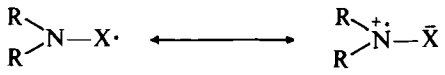
Substitution of alkyl with phenyl groups leads to the sulfur-bonded adduct $MuS{-}\dot{C}Ph_2$ which exhibits a small muon hfs constant ($A'_\mu = 7$ G) as found in muonium–carbonyl adducts bearing both alkyl and aryl substituents[58].

Partial delocalization of the unpaired electron onto aromatic systems lifts the π-degeneration. As a consequence the g anisotropy considerably decreases, making the arenethiyl radical detectable in solution. Photolysis of substituted thiophenols and phenyl disulfides in hydrocarbon solvents gives rise to a single line spectrum characterized by a relatively low g value (2.010). The g anisotropy remains however large ($g_\perp = 2.006$, $g_\parallel = 2.012$)[59]. ^{33}S labelled compounds show a sulfur coupling of *ca* 15 G[60].

Interaction of the $3p\pi$ sulfur, singly occupied atomic orbital with a π-lone pair in the α position reduces the anisotropy of the g-tensor more than in perthiyl radicals. The isotopic g-factors are in the range 2.01–2.02 (see Table 6).

Dialkylaminothiyl radicals were detected in solution from thermolysis[61] and photolysis[29] of corresponding bis(dialkylamino) disulfides. The spectra of unhindered dialkylaminothiyl radicals are however difficult to detect, being broadened probably because of an S_H2 exchange reaction (equation 7)[62]. The ESR spectra are characterized by a g-factor of *ca* 2.016 and a ^{14}N hfs of *ca* 11 G. In the *N,N*-diaryl derivatives the nitrogen hfs decreases to *ca* 8 G owing to delocalization of spin density onto the aromatic ring. The ^{14}N and β-^1H hfs constants in thionitroxides are smaller than in corresponding nitroxides. This was attributed to a larger localization of the unpaired electron on sulfur than on oxygen as a result of the lower electronegativity of the former. In fact, the contribution of the dipolar structure (**6**), which favors the delocalization of the unpaired electron to the amino group, is expected to be larger for X = O than for X = S. On the other hand, the g factor of thionitroxides is much higher compared with that of nitroxides. This is consistent with the larger spin–orbit coupling constant of sulfur (382 cm^{-1}) compared with that of oxygen (151 cm^{-1}) and nitrogen (76 cm^{-1}) in conjunction with a larger localization of the unpaired electron on sulfur. Photolysis of a frozen solution of bis(dialkylamino) disulfide produces also an anisotropic spectrum with principal g-values of 2.003, 2.033 and 2.051[27]. These values are essentially identical to those attributed to perthiyl radicals in solid solutions indicating that the N—S bond can be cleaved by photolysis in solid matrices.

$$R_2NS\cdot + R_2NSSNR_2 \rightleftharpoons R_2NSSNR_2 + R_2NS\cdot \qquad (7)$$



(5) (6)

$Ph_2C{=}NS\cdot$[a(1N) = 18.2 G, g = 2.015][27] and $(RO)_2P(=S)S\cdot$[a(P) *ca* 24.5 G, g *ca* 2.0188][63] radicals were generated by photolysis from the parent disulfides. Hfs and g-factors are insensitive to the structure of the alkyl groups, temperature and solvent. During photolysis of the bis(diphenylimino) disulfide a radical with no resolvable hfs and with a g-value of 2.0214 was also observed and was tentatively identified as an iminoperthiyl radical $Ph_2C{=}NSS\cdot$.

Thermolysis of thiuram disulfides in solution dissociates the S—S bond giving rise to a single line spectrum with a g factor of 2.015[28]. This value, which is in the range expected for sulfur-centered radicals, was attributed to dithiocarbamate radicals (equation 8). Similarly, photolysis of diacyl disulfides gives rise to a weak single line spectrum (g = 2.024) suggesting the formation of the perthiyl radical[50]. No spectra attributable to acylthio radicals were detected. Their formation was evidenced by the ESR features of their adducts with alkenes, trialkyl phosphites and dialkyl sulfides.

$$R_2NC(=S)SSC(=S)NR_2 \longrightarrow R_2NC(=S)S\cdot \qquad (8)$$

D. Absorption Spectra[64]

The $\tilde{A}^2A_1 \leftrightarrow \tilde{X}^2E$ transition in the $CH_3S\cdot$ has been extensively studied both in solution by UV absorption spectroscopy[65,66] and in the gas phase by emission[67], laser photodetachment[17] and laser-induced fluorescence spectroscopy[4,16,68–70]. The origin of the band in the gas phase is at 26525 cm^{-1} (377 nm) and the predissociation threshold was estimated to be at 28016 cm^{-1}. $\tilde{A} \leftrightarrow \tilde{X}$ laser-induced fluorescence of $MeS\cdot$[68], $EtS\cdot$[71] and i-$PrS\cdot$[72] shows a series of bands which were interpreted as due to transitions of the C—S stretching mode with a frequency of 403, 408 and 347 cm^{-1}, respectively. The origin of the band occurs at 377, 440 and 429 nm, respectively. The vibrational levels of the $\tilde{A}$ state are strongly predissociated in i-$PrS\cdot$ as the short lifetime (120 ns) of the $\tilde{A}$ state emission suggests.

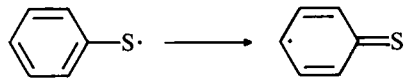
Substituted aliphatic thiyl radicals generated in the photolysis and pulse radiolysis of thiols, sulfides and disulfides have been more certainly identified by their UV-visible absorption spectra rather than by their ESR spectra even though their small extinction coefficients (ε = 290–580 $M^{-1}\,cm^{-1}$)[73] make it difficult to detect them. It is well established that photolysis of thiols at wavelengths below 300 nm cleaves the SH bond, producing thiyl radicals as primary species[74,75] which absorb at *ca* 330 nm[73].

Alkanethiyl radicals undergo reactions other than recombination (see below) so that occasionally secondary transient species, which absorb light with a greater extinction coefficient in the region of 400 to 450 nm, have incorrectly been identified as thiyl radicals. For example, photolysis of thiols in low-temperature hydrocarbon matrices produces an absorption band with $\lambda_{max} \sim 400$ nm ($\varepsilon \sim 7 \times 10^3\ M^{-1}\,cm^{-1}$) which was first attributed to thiyl radicals[44]. Later, this band was ascribed to sulfuranyl RS∴S(H)R radicals (equation 4)[76] since, for short exposure time, the UV spectra display only a weak band with a maximum at *ca* 330 nm[76]. Similarly, the absorption band observed at 420 nm during the pulse radiolysis of thiols in N_2O-saturated solutions at pH > 7 was attributed to the thiyl radical[77]. Again, the intensity of the absorption band depends on the concentration of the thiolate anion RS^- suggesting that the absorption could be due to formation of the sulfuranyl anion $RS{\therefore}SR^-$[73].

An unequivocal identification of perthiyl radicals is difficult to achieve from their UV-visible spectra in photolysis or radiolysis of polysulfides, since they give rise to a structureless absorption band as other sulfur-centered radicals[78,79]. The absorption band with $\lambda_{max} = 374\,nm$ and $\varepsilon = 1630\,M^{-1}\,cm^{-1}$ observed during pulse radiolysis of RS_3R was assigned to the perthiyl radical[80]. Laser flash photolysis of di-*t*-butyl tetrasulfides *t*-BuS_4Bu-*t* and *t*-butylthiosulfenyl chloride *t*-BuS_2Cl gives rise to the same absorption band, thus confirming this assignment[15]. In contrast, photolysis of disulfides yields thiyl radicals even though the S—S bond is *ca* 20 kcal mol^{-1} stronger than the S—C bond. In the presence of a sensitizer such as triplet benzophenone, a spectrum similar to that assigned to perthiyl radicals was however detected (equation 9)[47]. This indicates that the C—S cleavage can be achieved by using triplet sensitizers having a triplet energy lower than the S—S BDE.

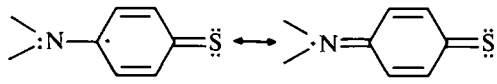
$$Ph_2CO^T + t\text{-BuSSBu-}t \longrightarrow Ph_2CO + t\text{-BuSS}\cdot + t\text{-Bu}\cdot \qquad (9)$$

Photolysis of phenyl disulfide or benzenethiol gives rise to two absorption bands, a strong band (ε *ca* $10^5\,M^{-1}\,cm^{-1}$)[81] around 300 nm and a weak band (ε *ca* $4 \times 10^3\,M^{-1}\,cm^{-1}$)[82] around 510 nm, which were ascribed to the phenylthio radical[83]. The weak band is generated by a transition which increases the carbon–sulfur double-bond character (equation 10)[82]. The quantum yield for the photolysis of phenyl disulfide was found to be 0.18 in isooctane solution[84]. This low value was interpreted as due to recombination of initial radical pairs which have singlet-spin state parentage[85]. The absorption spectra are significantly affected by polar solvents[82] as well as by



(10)

para-substituents[86]. Broadening of the weak absorption band was attributed to a weak charge-transfer interaction between the radical center and π-electrons of solvents[87]. The weak absorption band is strongly red-shifted in the *p*-aminobenzenethiyl radical (λ_{max} *ca* 570 nm)[88], while its intensity is enhanced by one order (ε *ca* $1\text{–}2 \times 10^4\,M^{-1}\,cm^{-1}$)[89,90]. This suggests that the carbon–sulfur double-bond excited structure is stabilized by electron donation from the amino group (cf **7** and **8**). Resonance CARS (coherent anti-Stokes Raman scattering) spectra of the *p*-aminobenzenethiyl radical and of the parent molecule suggest that in the radical ground state the C—S bond has a single-bond character[91].



(7) (8)

The *p*-aminobenzenethiyl radical has been extensively studied since luminescences in solution (quantum yield *ca* 0.05) were used to make the first free-radical laser[92]. The laser efficiency (1.5%) is due to the absence of primary loss processes via intersystem relaxation. By analyzing the spectral shift caused by solvents in the absorption and emission spectra, the dipole moment was estimated to be 4.3*D* and 7.3*D* in the ground and in the fluorescent state, respectively[82]. Subpicosecond time resolution of the transient absorption showed that photodissociation occurs in two stages[93]. In the first stage radical pairs are generated with a lifetime of 3.2 ps ($\lambda_{max} = 557.9$ nm), while in the second one radicals are separated by solvent ($\lambda_{max} = 572$ nm). Also, the absorption spectra of *p*-dialkylaminobenzenethiyl radicals display a strong band (ε *ca* $7 \times 10^3\,M^{-1}\,cm^{-1}$)

around 340 nm and a weak band (ε *ca* 300 $M^{-1}cm^{-1}$) around 525 nm which are red shifted with increasing solvent polarity[94]. Replacement of sulfur by oxygen causes a blue shift in λ_{max} (230 nm and 440 nm) and a decrease of the extinction coefficient (ε *ca* 2×10^3 and $5\ M^{-1}cm^{-1}$)[95]. The absorption spectrum of the diphenyliminothiyl radical shows only a band at 415 nm with an extinction coefficient of $5 \times 10^3\ M^{-1}cm^{-1}$[94].

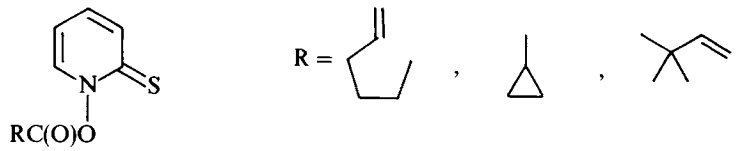
III. CHEMICAL PROPERTIES

A. The Reaction of Alkyl Radicals with Thiols

It is well known that thiols are very good hydrogen donors towards carbon-centered radicals, namely

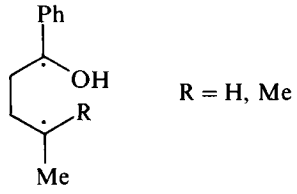
$$R\cdot + R'SH \longrightarrow RH + R'S\cdot \qquad (11)$$

Absolute rate constants for the reaction of alkyl radicals with alkanethiols have been a matter of controversy for many years since these values vary more than four orders of magnitude (3×10^4–$5 \times 10^8\ M^{-1}s^{-1}$) at room temperature[96]. However, Newcomb and coworkers[97] recently obtained Arrhenius parameters for the reaction of primary alkyl radicals with *t*-BuSH as a result of a careful study of *t*-BuSH/*N*-hydroxypyridine-2-thione esters. That is, radical chain reactions of the precursor esters **9** gave 5-hexenyl, cyclopropylcarbinyl and 2,2-dimethyl-3-butenyl radicals. These radicals either were trapped by *t*-BuSH or rearranged, and the rate constants for trapping were determined from the well-known rate constants for rearrangement and measured product yields. Arrhenius functions for the three primary alkyl radicals were quite similar and are given in Table 7.



(9)

It is well documented that radical centers in diradicals react in hydrogen-transfer reactions with the same rate constants as monoradicals with the same substitution at the radical center[98]. 1,4-Diradicals **10**, formed in Norrish type II cleavage, were found to react with $CH_3(CH_2)_7SH$ at 22 °C with a rate constant of $9.0 \times 10^6\ M^{-1}s^{-1}$ (for a tertiary center) and $11.3 \times 10^6\ M^{-1}s^{-1}$ (for a secondary center)[99]. Therefore primary, secondary and tertiary alkyl radicals react with alkanethiols with almost the same rate constants at ambient temperature.



(10)

Reliable absolute rate constants for the reaction of a variety of alkyl radicals with thiophenol are available. Franz and coworkers[100], using laser flash photolysis techniques,

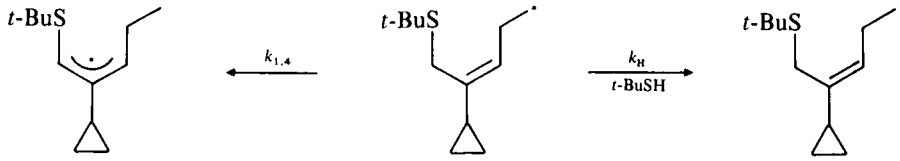
TABLE 7. Kinetic parameters for the reaction of alkyl radicals with thiols

Alkyl radical	Thiol	$\log A$ ($M^{-1}s^{-1}$)	E_a (kcal mol^{-1})	k_H(25 °C) ($M^{-1}s^{-1}$)
Primary	*t*-BuSH	8.37	2.00	8.0×10^6
Primary	PhSH	9.41	1.74	1.1×10^8
Secondary	PhSH	9.26	1.70	1.4×10^8
Tertiary	PhSH	9.26	1.50	1.5×10^8
Benzyl	PhSH	8.27	3.79	3.1×10^5
Benzyl	PhSD	8.49	4.89	8.0×10^4
α-(PhS)Benzyl	PhSH	8.60	6.64	5.8×10^3
Trityl	PhSH	7.84	9.54	7.0

were able to obtain Arrhenius expressions for the reactions of primary, secondary and tertiary alkyl radicals with PhSH (see Table 7). It is worth pointing out again that primary, secondary and tertiary alkyl radicals react with thiophenol with essentially the same rate constants despite changing thermochemistry for the reaction. Furthermore, Arrhenius parameters for the reaction of benzyl[101], α-(phenylthio)benzyl[102] and trityl[103] radicals with thiophenol were measured in competition with the self-termination of the benzyl radicals and in competition with the equilibrium constant for the dimerization of trityl radicals, respectively. These data are also given in Table 7. A value of $4.1 \times 10^9\ M^{-1}s^{-1}$ for abstraction of hydrogen by cyclopropyl radical from thiophenol at 25 °C has also been reported[104].

Kinetic results for hydrogen abstraction by carbon-centered radicals from thiols in aqueous solution are also known[96]. These data are largely obtained from the early work of pulse radiolysis studies. Rate constants for the reaction of methyl radical with ethanethiol, cysteine and glutathione are 4.7, 7.4 and $7.1 \times 10^7\ M^{-1}s^{-1}$, respectively, at pH = 7.0 and 25 °C[105].

Knowledge of the above-mentioned accurate rate expressions for the transfer of hydrogen from a thiol to an alkyl radical should be of great importance in measuring kinetic data of unimolecular radical processes using a 'radical clock' technique[106]. Griller and coworkers[107] measured the relative rate constant for the intramolecular 1,4-hydrogen atom transfer in competition with trapping by *t*-BuSH at 25 °C (Scheme 1). Combination



SCHEME 1

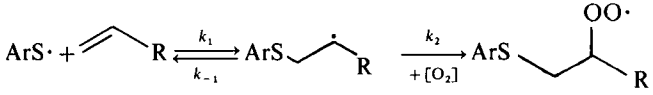
of $k_H/k_{1,4} = 2.9\ M^{-1}$ with the value for k_H taken from Table 7 leads to $k_{1,4} = 2.7 \times 10^6\ s^{-1}$ at 25 °C. Similarly, accurate temperature-dependent functions for the cyclopropyl–carbinyl radical ring-opening reaction[108] and for the neophyl-like 1,2-phenyl migration from sulfur to carbon-centered radical[102] (equation 12) were determined using PhSH for the hydrogen atom transfer.

$$PhCHSPh \longrightarrow Ph_2CHS\cdot \qquad (12)$$

B. Addition of Thiyl Radicals to Carbon–Carbon Multiple Bonds

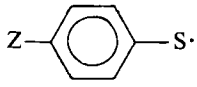
The reactions of arenethiyl radicals with a variety of alkenes have been investigated in considerable detail by Ito and Matsuda[109] and several hundreds of absolute rate constants are now available. Photolysis of diaryl disulfides proved to be a clean source of arenethiyl radicals that had UV-visible spectra (*vide infra*), which could be monitored using flash photolysis techniques. These authors were aware that addition to the double bonds was reversible and, to simplify the reaction kinetics, they ran their reactions in the presence of oxygen. This had no effect on the arenethiyl radicals formed by their addition to olefins. Under conditions of efficient scavenging, the rate of disappearance of the arenethiyl radicals, as monitored by flash photolysis techniques, was equal to their rate of addition to the olefin in question (equations 13 and 14). Thus, absolute rate

$$\mathrm{ArSSAr} \xrightarrow{h\nu} 2\,\mathrm{ArS}\cdot \tag{13}$$



(14)

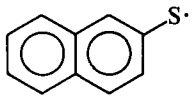
constants for the addition of *para*-substituted benzenethiyl radicals **11** to monosubstituted[110], *vic*-disubstituted[111], *gem*-disubstituted[112] olefins, cycloalkenes[113] and conjugated dienes[114] have been obtained. The reactivities have shown a wide range of values (5×10^2 to $5 \times 10^8\ M^{-1}s^{-1}$ at ambient temperature) and, consequently, the chemoselectivity can be anticipated. In a few instances relative equilibrium constants (Kk_2) were determined. The Hammett relations obtained by changing the substituents of the arenethiyl radicals were also investigated to obtain information about the polar transition state of the reactions. The ρ^+ values characterizing these reactions indicate an important contribution to the transition state of such polar structures as [p-$ZC_6H_4S^-$, $CH_2{=}CXY^{+\cdot}$]. Therefore, arenethiyl radicals behave in these reactions as electrophilic in character. Representative examples for the reaction of PhS· radical with some common alkenes are reported in Table 8.



Z = NH_2, OMe, Me, *t*-Bu, H, Cl, Br

(11)

Solvatochromic equations have been derived and successfully applied to the rate constants for the reversible addition of the *p*-aminobenzenethiyl radical to styrene[88,116] and α-methylstyrene[117]; these results, coupled with the known substituent effect in the *para*-substituted benzenethiyl addition reaction, have provided a detailed picture of the transition state. The absolute rate constant for the addition reactions of the 1- and 2-naphthalenethiyl radicals to vinyl monomers have been determined by means of flash photolysis[118]. For each vinyl monomer, the 2-naphthylthio radical (**12**) is less reactive than the phenylthiyl radical and more reactive than the 1-naphthylthio radical. Addition rates of benzothiazole-2-thiyl radical (**13**) to vinyl monomers have also been obtained[119].



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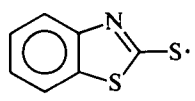
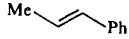


(13)

TABLE 8. Values of k_1 and Kk_2 for the addition of PhS· radical to some alkenes at 23 °C (cf equation 14)[a]

Alkene	$k_1(M^{-1}s^{-1})$	$Kk_2(M^{-1}s^{-1})$
	2.7×10^5	3.8×10^8
	6.7×10^4	5.0×10^7
	2.6×10^7	3.4×10^9
	1.6×10^4	4.0×10^6
	6.8×10^6	3.4×10^9
	5.2×10^6	—
	1.4×10^7	—
	3.3×10^3	2.0×10^5
	3.5×10^7	—

[a] $K = k_1/k_{-1}$ values may be estimated by taking an appropriate value for k_2 (cf Reference 115).

Studies on alkanethiyl radicals have been particularly difficult because these radicals are difficult to detect spectroscopically (*vide infra*). However, absolute rate constants for the reactions of *t*-BuS· radical with a few alkenes have been measured using a laser flash photolysis technique[120]. Thus, *t*-BuS· radicals add to 1,1-diphenylethylene, 1,1-dicyclopropylethylene and oct-1-ene with rate constants of 9.9×10^8, 2.4×10^8 and $1.9 \times 10^6\ M^{-1}s^{-1}$ at 25 °C. It is worth pointing out that the reaction with 1,1-dicyclopropylethylene is 130 times faster than with 1-octene, the reason probably being either the stabilizing effect of cyclopropyl rings or/and the destabilization of the starting olefin bearing the cyclopropyl rings. Absolute rate constants of the reaction of CH_3S· radical with unsaturated hydrocarbons have been measured in the gas phase, by using laser-induced fluorescence of the reactant radical as a probe[121].

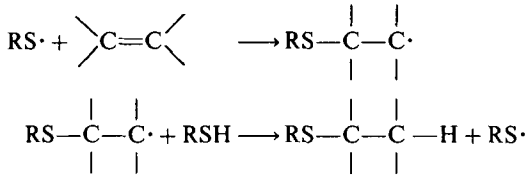
Absolute rate constants for addition of *para*-substituted benzenethiyl radicals **11** to a variety of monosubstituted acetylenes have been determined by flash photolysis techniques[122]. Also in this case, there is a large spread in the reactivities (rate constants varied by four orders of magnitude, i.e. 1×10^3 to $1 \times 10^7\ M^{-1}s^{-1}$ at ambient temperature).

Addition of thiyl radicals to carbon–carbon multiple bonds has occasionally been used for generating carbon-centered radicals and to study their behavior. Two examples are the thiyl radical-induced cleavage of ketoepoxides[123] and the direct observation by ESR of 1,4-hydrogen shift in vinyl radicals derived from the reaction of alkynes with thiyl radicals[124].

C. Addition of Thiols to Carbon–Carbon Multiple Bonds

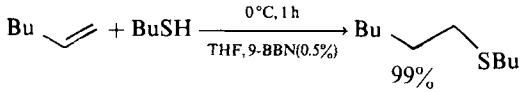
The free radical addition of a thiol to a carbon–carbon double or triple bond is a well-established reaction. It is one of the most useful methods for synthesizing sulfides,

under mild conditions. Since its discovery and its much later formulation as a free radical chain reaction (see Scheme 2 for the propagation steps), the anti-Markovnikov addition of thiols to unsaturated compounds has been the subject of many reviews[125–127].

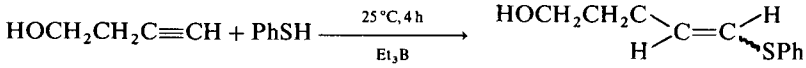


SCHEME 2

The radical addition reactions of thiols to carbon–carbon double or triple bonds were initiated by thermal decomposition of peroxides or azo compounds, by UV irradiation or by radiolysis[128]. More recently, organoboranes have been used as initiators. Thus, the radical addition of alkanethiols to alkenes under very mild conditions initiated by a catalytic amount of 9-borabicyclo[3.3.1]nonane (9-BBN) provides the corresponding dialkyl sulfides almost quantitatively[129] (equation 15), and thiols added easily to acetylenic compounds in the presence of Et_3B to give alkenyl sulfides in good yields (equation 16)[130].



(15)

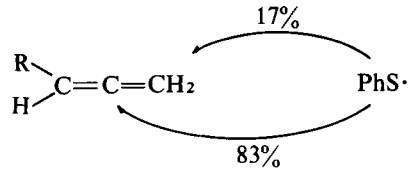


91% ($Z:E \approx 4:6$)

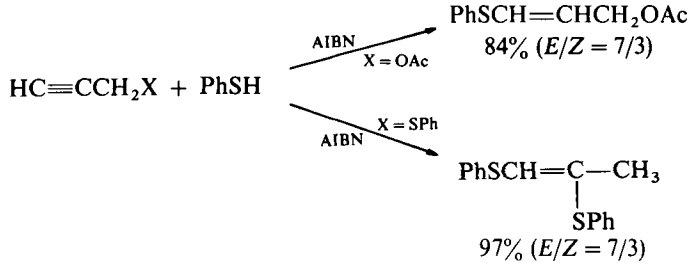
(16)

The fact that thiyl radicals are unreactive towards most organic functionalities indicates that thiols may add to C—C multiple bonds by tolerating other sensitive functionalities. For example, benzenethiol adds regiospecifically to isoprenoid chrom-3-enes to yield 3-phenylthiochromans, tolerating the free phenol and carbonyl functions and also the trisubstituted double bond[131].

The radical-chain addition of benzenethiol to a variety of substituted allenes has been studied and detailed chemo- and stereoselectivity aspects are described[132,133]. With monoalkylallenes the PhS· attack occurs at C-2 and C-3 in a ratio of 83:17 (increased attack of 25% at C-3 occurs with *tert*-butylallene), whereas with 1,1-dialkylallenes the attack occurs exclusively at C-2 (Scheme 3). Evidence that the addition of thiyl radical is not reversible under the reaction conditions (25 °C) is also presented[132]. However, the reversible addition of PhS· to terminal carbon has been invoked at 80 °C to explain the products formation in the reaction of PhSH with some alkynes[134]. Thus, Scheme 4 shows that the expected product is formed in 84% for X = OAc, whereas for X = SPh the 1,2-bis(phenylthio)-1-propene was obtained in almost quantitative yield. These results indicate that the intermediate vinyl radical eliminates PhS· prior to hydrogen abstraction



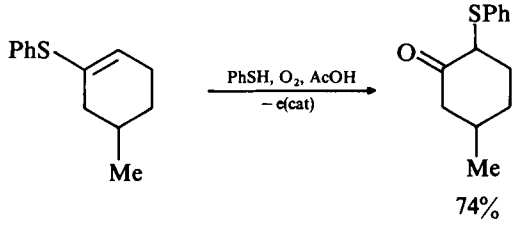
SCHEME 3



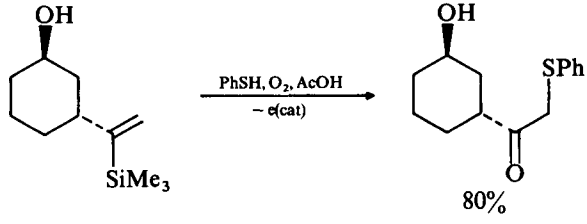
SCHEME 4

to form the corresponding allene, which then recombines with PhS· radical in a different fashion. Furthermore, based on kinetic and isotopic studies it was suggested that the addition of PhS· to substituted allenes occurs via a very early transition state in which little rotation around one end of the allene system has occurred[133]. Reaction of benzenethiol at 100 °C with neat alkyl- and dialkyl-acetylenes leads to virtually quantitative formation of isomeric mixtures of (*E*)- and (*Z*)-vinyl sulfide adducts in ratios which depend largely upon both the extent and the nature of alkyl substitution[135].

Based on the early work of the cooxidation of olefins and thiols with triplet molecular oxygen[136], a number of papers have appeared indicating the potentialities of this approach. For example, synthesis of α-phenylthio carbonyl compounds starting either from alkenyl sulfides[137] (equation 17) or alkenylsilanes[138] (equation 18) and of β-hydroxy



(17)



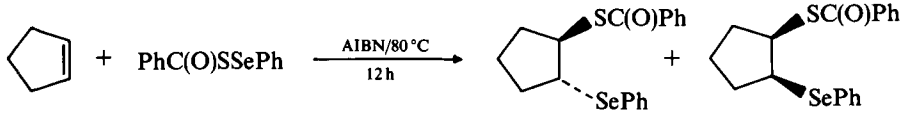
(18)

sulfoxides[139] (equation 19) have been reported to occur with good yields. Similarly, five- and six-membered cyclic peroxides have been obtained starting from appropriate alkenes and dienes[140]. Thus, the addition of a PhS· radical to an olefin followed by the reaction with molecular oxygen is a general method for the access of peroxy radicals.

$$AcOCH_2CH{=}CH_2 \xrightarrow{ArSH,\,O_2} AcOCH_2CH(OH){-}CH_2S(O)Ar \quad (19)$$

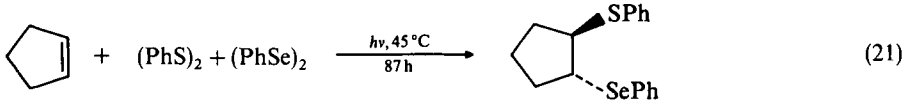
92%

There are no examples reported to date of the efficient free-radical addition of disulfides to olefins. *S*-Benzoyl phenylselenosulfide adds across the double bond of olefins to afford selenothiocarbonylated products (equation 20) with high regiospecificity but with lack of stereoselectivity[141]. Furthermore, an interesting thioselenation of olefins has been obtained by using a diphenyl disulfide/diphenyl diselenide mixed system (equation 21)[142]. The high regioselectivity observed in the thioselenation of the terminal olefins is due to the higher reactivity of PhS·, compared with PhSe·, toward carbon–carbon double bonds and the higher capture ability of $(PhSe)_2$, compared with $(PhS)_2$, toward carbon-centered radicals[142]. It is worth pointing out that reaction 21 shows higher stereoselectivity than reaction 20. A possible explanation is that the shielding effect of the PhC(O)S group is smaller than PhS, although the difference in temperature could be of great importance[143].



83%, *trans:cis* = 92:8

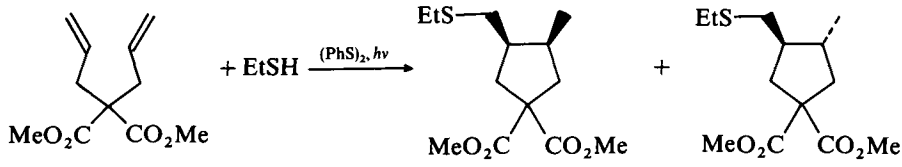
(20)



74%

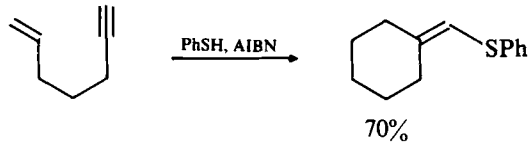
(21)

Geminal diallyl compounds undergo cyclization to cyclopentyl products in high yields on reaction with thiyl radicals. Thus, diallyl malonate gave good yield of *cis*- and *trans*-dimethylcyclopentanes (equation 22) and α-acoradiene was quantitatively converted



92%, *trans:cis* = 6:1

(22)

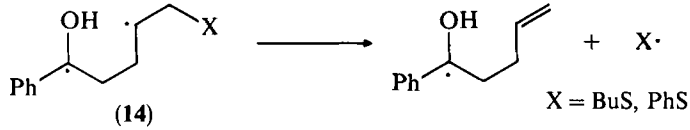


(23)

to cedrane[144]. Starting from dienylamides, this attractive methodology has recently been applied to lactam synthesis[145]. Thiophenol promoted also cyclization of enynes in the presence of free radical initiators (equation 23)[146]. Thus, vinyl radicals generated by addition of PhS· to 1-hepten-6-yne have been shown to cyclize regioselectively giving cyclohexylidene thioethers[146], probably through an equilibration of an initially formed cyclopentylmethyl radical with its more thermodynamically stable cyclohexyl isomer prior to hydrogen abstraction[147].

D. Addition–Elimination Methodology

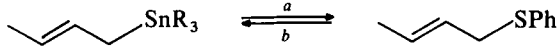
Since the early work on addition of thiols to olefins it has been clear that thiyl radicals add reversibly to double bonds[148]. From Table 8 we estimated that the rate constants, k_{-1}, for the β-elimination of PhS· radical (cf equation 14) range from *ca* 1×10^6 to $1 \times 10^8\ s^{-1}$ depending on the stabilizing effect of the α-substituent in the carbon-centered radical. Furthermore, rate constants of 2.7×10^5 and $1.9 \times 10^8\ s^{-1}$ have been measured for the β-elimination of *n*-BuS· and PhS·, respectively, from the 1,4-diradical **14** generated via the Norrish type II photoreaction (equation 24)[149,150]. In the light of the fact that photogenerated diradicals undergo typical monoradical rearrangements, the above data obtained by different techniques are in good agreement. Therefore, the β-elimination of thiyl radicals is generally a fast process, alkanethiyl radicals being much slower than arenethiyl radicals as leaving groups[149].



(24)

The *cis-trans* isomerization of olefins by the addition–elimination sequence of a PhS· radical[151] is now an established methodology in fine chemical synthesis. For example, the facile *cis–trans* interconversion of olefins caused by photochemically generated phenylthio radicals leading to the thermodynamic equilibrium is the key step for the syntheses of the antifungal macrocyclic lactone (−)-gloeosporone[152], of the antibiotic–antitumor agent (+)-hitachimycin[153] and other naturally occurring macrolides[154].

The interchange of heteroatom-containing groups by free radical substitution at an allyl group is a common and preparatively useful reaction that occurs by an addition–elimination mechanism. The PhS group is susceptible to such interchanges. Depending on reaction conditions, such substitutions can sometimes be conducted in either direction. An example is provided in equation 25[155].

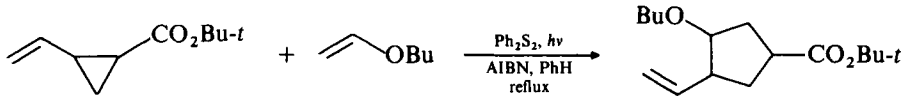


(25)

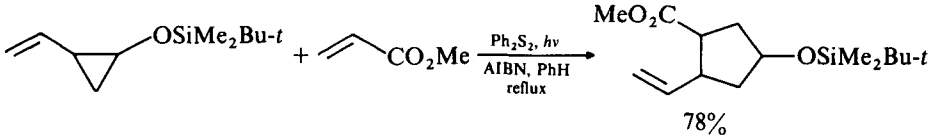
a: PhSH, Et_3B, 60 °C, 10 h, 75%

b: Ph_3SnH, Et_3B, 60 °C, 10 h, 19%

This addition–elimination concept has also been applied successfully to cyclopentanoid synthesis via [3 + 2] annulation[156–158]. Thus, the PhS· radical catalyzed reaction of substituted vinylcyclopropanes with functionalized alkenes affords the vinylcyclopentane derivatives. Two examples (equations 26 and 27)[156] show the judicious pairing of

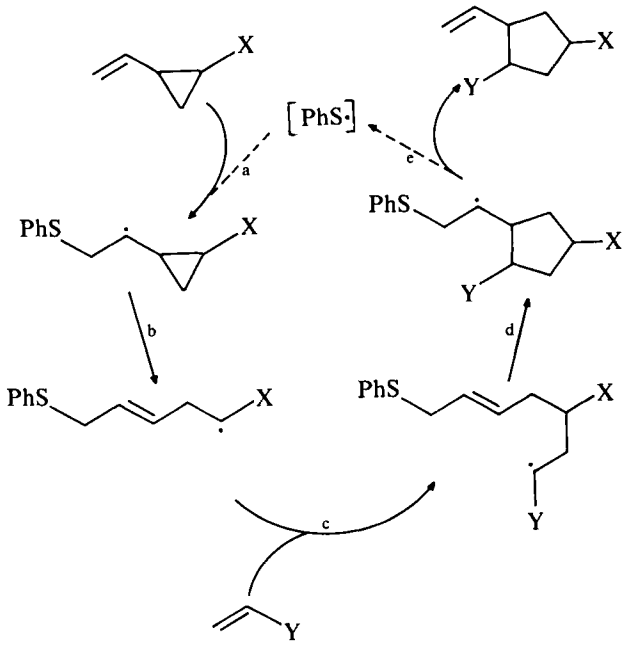


94% (26)



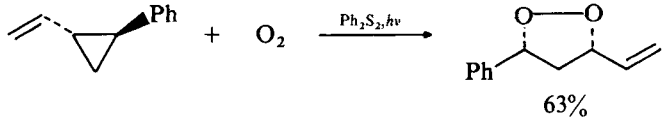
78% (27)

substituents on cyclopropane and alkene. These reactions proceed through a complex multistep mechanism as shown in Scheme 5[156,157]. That is, initiation occurs by PhS· radical addition to the vinylcyclopropane (step a), followed by ring opening to afford the homoallylic radical (step b), bimolecular addition of the alkene to produce the 5-hexenyl radical (step c), cyclization to the cyclopentanyl carbinyl radical (step d) and termination via ejection of the PhS· radical to afford the vinylcyclopentane product (step e).



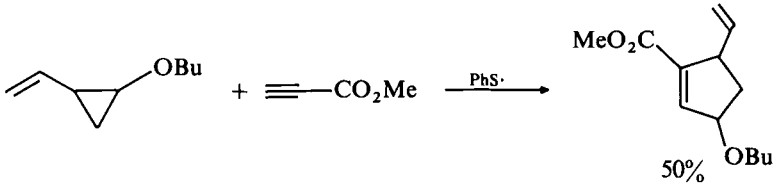
SCHEME 5

In a similar manner, opportunely substituted 1-vinylcyclopropanes when subjected to phenylthio radical catalyzed oxygenation afford the corresponding substituted 1,2-dioxolane products[159]. A typical example is given in equation 28. Convincing evidence that the reaction mechanism is similar to the multistep transformation reported in Scheme 5 has been obtained.

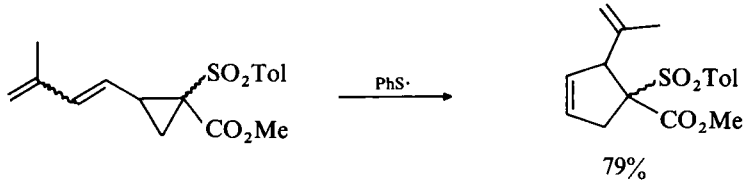


(28)

The addition–elimination approach has also been applied to the construction of vinylcyclopentene[160,161] and vinylcyclohexanone[162] skeletons. Examples are the PhS· radical catalyzed reaction of substituted vinylcyclopropanes with electron-deficient alkynes (equation 29)[160] and the isomerization of 2-(1,3-butadienyl)-cyclopropanes (equation 30)[161].

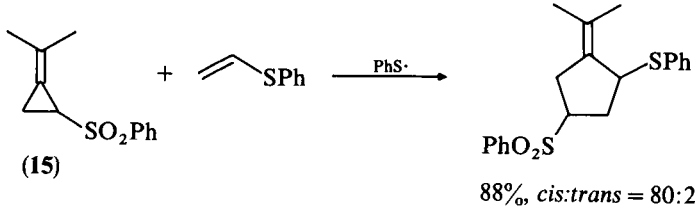


(29)



(30)

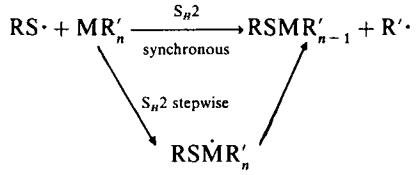
A variation of the above [3 + 2] annulation is the PhS· radical catalyzed reaction of methylenecyclopropane **15** with unactivated and electron-rich olefins affording methylenecyclopentanes[163]. An example is provided in equation 31. The mechanism of these reactions is easily envisioned as being analogous to that reported in Scheme 5.



(31)

E. S_H2 and S_H2' Reactions

Thiyl radicals react with a variety of organic and organometallic compounds via an S_H2 mechanism[164]. That is, the incoming thiyl radical displaces another group (Scheme 6) via a synchronous or stepwise S_H2 process. Some selected examples with available kinetic data are reported below (equations 32–35). Although alkylthio radicals react with



SCHEME 6

boranes by a synchronous S_H2 process (equation 32)[165], the displacement reaction of thiyl radicals with disulfides is shown to proceed via a transient adduct radical (stepwise S_H2) by using time-resolved pulse radiolysis techniques (equation 33)[166]. The reaction of alkanethiyl radicals with trivalent organophosphorus derivatives may give both substitution and oxidation products (equations 34 and 35)[165]. Thus, the reactions with phosphines and phosphites proceed through phosphoranyl radicals that ultimately undergo α- or β-fragmentation depending on the nature of the substituents[167].

$$t\text{-BuS}\cdot + \text{BEt}_3 \xrightarrow{k_3} t\text{-BuSBEt}_2 + \text{Et}\cdot \qquad (32)$$

$$k_3 = 1.3 \times 10^8\ \text{M}^{-1}\,\text{s}^{-1}$$

$$\text{MeS}\cdot + \text{MeSSMe} \underset{k_{-4}}{\overset{k_4}{\rightleftharpoons}} \text{MeS}\dot{\text{S}}(\text{Me})\text{SMe} \qquad (33)$$

$$k_4 = 3.8 \times 10^6\ \text{M}^{-1}\,\text{s}^{-1}$$
$$k_{-4} = 2.3 \times 10^4\ \text{s}^{-1}$$

$$t\text{-BuS}\cdot + \text{PBu}_3 \xrightarrow{k_5} t\text{-BuS}\dot{\text{P}}\text{Bu}_3 \longrightarrow t\text{-BuSPBu}_2 + \text{Bu}\cdot \qquad (34)$$

$$k_5 = 9.0 \times 10^8\ \text{M}^{-1}\,\text{s}^{-1}$$

$$t\text{-BuS}\cdot + \text{P(OEt)}_3 \xrightarrow{k_6} t\text{-BuS}\dot{\text{P}}(\text{OEt})_3 \longrightarrow \text{SP(OEt)}_3 + t\text{-Bu}\cdot \qquad (35)$$

$$k_6 = 3.1 \times 10^8\ \text{M}^{-1}\,\text{s}^{-1}$$

Free radical substitutions of allylic and vinylic substituted organometallic compounds with PhS· radicals generated either thermally or photochemically have been studied in detail (equations 36 and 37)[168]. For example, in the group 14 organometallics, alkenylstannanes and alkenylplumbanes undergo S_H2 and S_H2' substitution of the metal by a chain mechanism. Alkenylsilanes are unreactive whereas alkenylgermanes proceed under forced conditions[169]. In these chain processes, the propagation steps consist in the addition of the PhS· radical to the allylmetal (or vinylmetal), followed by elimination of a metal-centered radical, which perpetuates the chain by S_H2 displacement of a PhS· radical from PhSSPh. Analogous reactions occur with 1-alkynyl and propargyl derivatives[168].

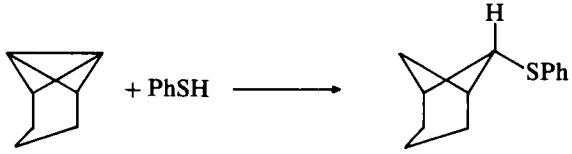
$$\text{CH}_2{=}\text{CHCH}_2\text{MR}'_n + \text{PhSSPh} \xrightarrow{S_H2'} \text{PhSCH}_2\ \text{CH}{=}\text{CH}_2 + \text{PhSMR}'_n \qquad (36)$$

$$(E)\text{-PhCH}{=}\text{CHMR}'_n + \text{PhSSPh} \xrightarrow{S_H2} (E)\text{-PhCH}{=}\text{CHSPh} + \text{PhSMR}'_n \qquad (37)$$

Bimolecular homolytic substitutions (S_H2) at sp^3-hybridized carbons are uncommon[164]. However, in the recent literature strained molecules, like bicyclo[1.1.0]butane (**16**) and [1.1.1]propellane (**17**), are found to undergo S_H2 displacement at bridge positions by

(16) (17)

free radicals. In particular, PhSH adds across the C-1/C-3 bond of a variety of substituted bicyclo[1.1.0]butanes via a radical pathway and relative rate constants have been obtained for the addition of PhS· radicals by competition experiments[170]. Benzenethiol adds also to tricyclo[4.1.0.0^{2,7}]heptane (**18**) and its analogs to give only the 6-*endo*-(phenylthio)norpinane (**19**), indicating the high stereospecificity of these reactions (equation 38)[171].



(38)

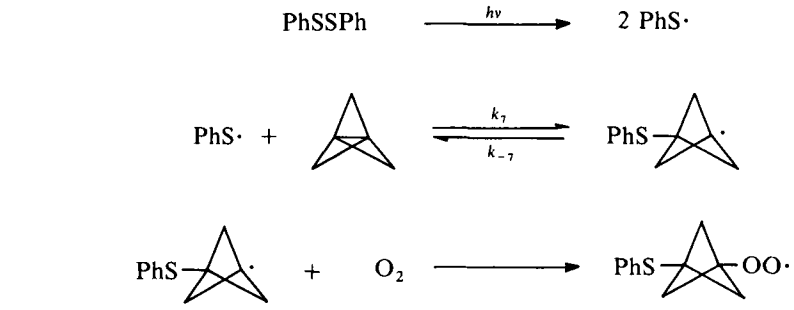
(18) (19)

The additions of thiophenol and diphenyl disulfide to [1.1.1]propellane proceed essentially quantitatively using equimolar quantities of the two reagents and occur across the central bond (equations 39 and 40)[172,173]. Scaiano and his coworkers[174] employed laser flash photolysis to study the reaction of the PhS· radical with propellane. By performing the reaction in the presence or absence of molecular oxygen, they have demonstrated that the S_H2 process is reversible. Scheme 7 shows the proposed mechanism. Kinetic analysis leads to $k_7 = 6.2 \times 10^7\ M^{-1}\ s^{-1}$ and $k_{-7} = 6.8 \times 10^7\ s^{-1}$ in Freon-113 as a solvent for the forward and reverse reactions, respectively. These data suggest that the addition of PhS· to propellane is thermoneutral or slightly exothermic.

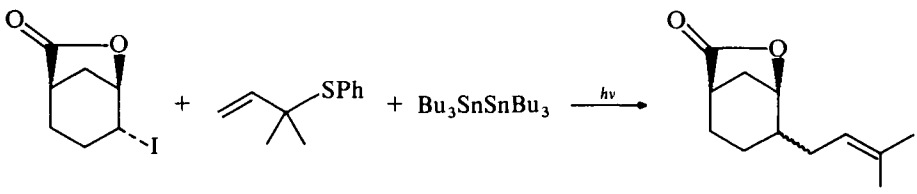
99% (39)

(40)

Radical allylation provides some of the mildest, most general methods to introduce allyl groups into functionalized molecules[175]. Among the possible allylating agents, allyl sulfides play an active role. Two examples are reported below (equations 41 and 42), where alkyl iodides were treated with two equivalents of an appropriate sulfide and one equivalent of hexabutylditin under sunlamp irradiation[176,177]. Scheme 8, which represents a plausible mechanistic rationalization of the results, shows the propagation steps of these chain reactions. According to this, the Bu_3Sn· radical, initially generated by photolysis of ditin, reacts with the alkyl halide to form an alkyl radical that attacks the allyl sulfide (S_H2' process) to give the desired product and a thiyl radical. Displacement reaction from ditin gives the Bu_3Sn· radical, thus completing the cycle of this chain reaction.

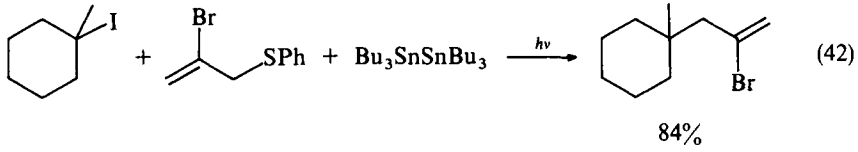


SCHEME 7



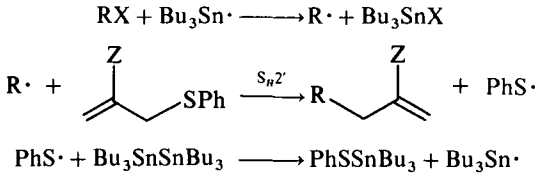
60%

(41)



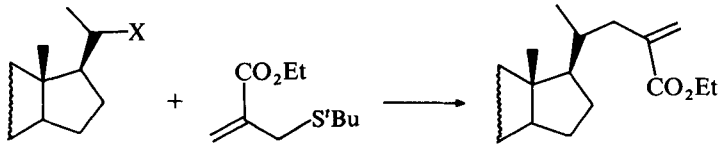
84%

(42)



SCHEME 8

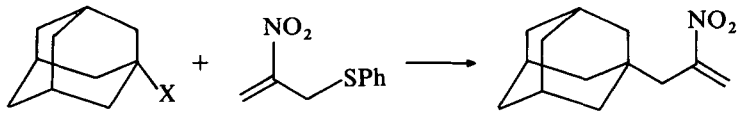
Free radicals derived from the esters of *N*-hydroxy-2-thiopyridone react with allyl sulfides to give moderate yields of the desired allylating products[178]. However, improved yields are obtained if the β-position bears an electron-withdrawing group (equations 43 and 44)[178,179]. A mechanistic scheme is proposed where the S_H2' step (cf Scheme 8) is the key step of these transformations[178].



(43)

74%

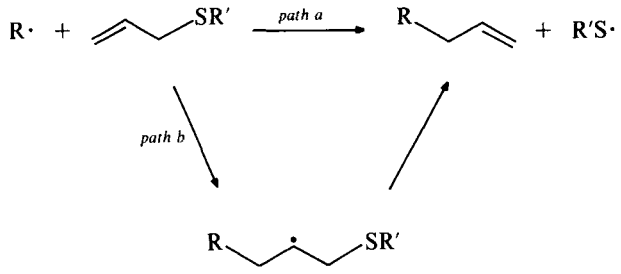
X = *N*-acyloxypyridine-2-thione



(44)

77%

There are two possible mechanisms for the S_H2' process, one in which the addition of the radical is concerted with the loss of the leading thiyl radical (Scheme 9, *path a*) and a second stepwise mechanism in which the adduct radical has a defined existence (Scheme 9, *path b*). A concerted addition and elimination process has been suggested[178] although the existing evidence cannot exclude the stepwise *path b*.



SCHEME 9

F. Thiols as Radical-based Reducing Agents

As we mentioned above, thiols are very good hydrogen donors towards carbon-centered radicals. The corresponding thiyl radicals are poor atom-abstracting agents and therefore do not support chain reactions analogous to common radical-based reducing agents such as $(Me_3Si)_3SiH$[180] and Bu_3SnH[181]. It has recently been demonstrated that trialkylsilanes, which are poor radical-based reducing agents for reasons opposite to those of thiols[180], can reduce alkyl halides and xanthates to the corresponding hydrocarbons in the presence of alkanethiols, which act as polarity reversal catalysts for hydrogen transfer from the silane to the alkyl radical[182]. The reaction is believed to consist of a chain process as shown in Scheme 10. This approach has also been applied for the hydrosilylation of chiral alkenes by Ph_2SiH_2[183]. However, there are several limitations and inconveniences in this otherwise attractive procedure such as structural restrictions in the starting materials, impracticability of C—C bond formation, unsuitability of arenes as solvents, the need for special workup of the reaction

$$R\cdot + XSH \longrightarrow RH + XS\cdot$$
$$XS\cdot + R'_3SiH \longrightarrow XSH + R'_3Si\cdot$$
$$R'_3Si\cdot + RZ \longrightarrow R'_3SiZ + R\cdot$$

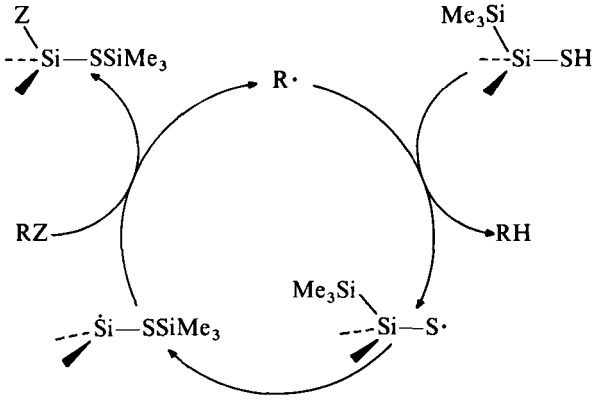
SCHEME 10

mixture, the choice of unusual initiators and much lower yields with respect to $(Me_3Si)_3SiH$[180] and Bu_3SnH[181] methods.

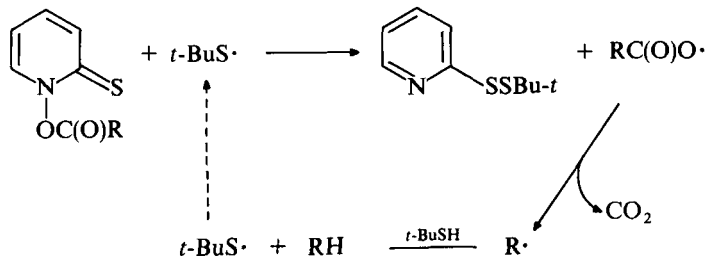
The facts that alkanethiols are good H-atom donors towards alkyl radicals and that silyl radicals are among the most reactive known species for abstraction and addition reactions[180] suggest that any class of compounds with an appropriate molecular arrangement which allows the transformation of a thiyl to a silyl radical via a fast intramolecular rearrangement will potentially be a good radical-based reducing agent. The silanethiols **20**[184] and **21**[185] are found to have this property. The reductions of

$(Me_3Si)_2Si(SH)Me$ **(20)** $(Me_3Si)_3SiSH$ **(21)**

organic bromides, iodides and isocyanides by tris(trimethylsilyl)silanethiol (**21**) are extremely efficient processes, and the reactions are completed in 5 minutes at 85 °C quantitatively[185]. The reaction mechanism is outlined in Scheme 11.

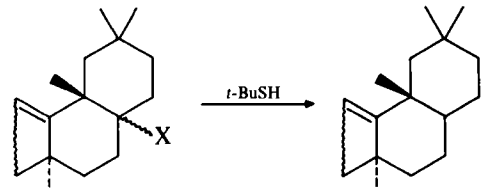


SCHEME 11

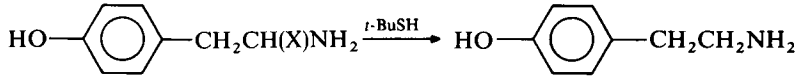


SCHEME 12

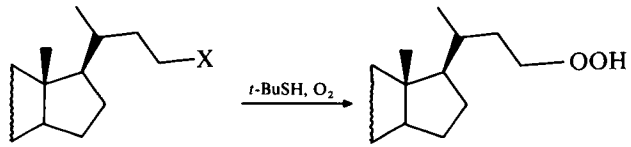
However, thiols can be used as reducing agents for the decarboxylation of acids via the acyl derivatives of *N*-hydroxy-2-thiopyridone either on heating to 80 °C or better, by irradiation with a tungsten lamp at room temperature or at any other temperature[186]. The reaction (Scheme 12) is initiated by addition of the *t*-BuS· radical to the thione's sulfur center. Normally, the RCO_2· radical decarboxylates rapidly yielding R·, which propagates the chain by abstracting a hydrogen, ultimately leading to the chain carrier *t*-BuS· radical. The following examples, taken from the original work of Barton and his coworkers, show the potentiality of this methodology (equations 45 and 46)[187,188]. If the reaction is run in the presence of oxygen, the intermediate carbon-centered radical could react with molecular oxygen prior to the hydrogen abstraction leading to a hydroperoxide (equation 47)[189]. The reduction of other thiohydroxamic acid esters has also been performed using *t*-BuSH in a similar fashion[190].



85% (45)



96% (46)



80% (47)

X = *N*-acyloxypyridine-2-thione

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CHAPTER 9

Pyrolysis of organosulphur compounds

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I. INTRODUCTION

In the last twenty years, the advances in synthesis and reaction mechanisms of sulphur chemistry[1-7] have prompted, in good extent, the use of new knowledge in industrial applications such as the production of pharmaceuticals[5-7], polymers[8], antioxidants[9] and fuels[10,11] among many others. Petroleum refining processes usually involve thermal treatments that induce reactions, in both vapour and condensed phases, affecting the content and composition of the organosulphur compounds present in the crude oil and its fractions. Thiols, sulphides, disulphides, thiophene and its derivatives, and high-molecular-weight asphaltenes are among these petroleum sulphur compounds[12,13]. A wide knowledge of sulphur chemistry requires an understanding of gas-phase reactions of compounds with sulphur functional groups. Under the conditions of homogeneous gas-phase pyrolysis, it is possible to study elementary molecular processes, their kinetics and thermochemistry. This information can be applied to the design of new hydrocarbon desulphurization methods and to the utilization of their sulphur-containing effluents in the production of the above-mentioned materials. The amount of published work in the field of organosulphur compounds pyrolyses is still small when compared with those for other types of molecules such as hydrocarbons[14,15], alkyl halides[15-18], esters[15-17,19], ethers[15,17], azoalkanes[20] etc. The present high predictability of the thermochemistry

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and kinetics of these compounds[21–23] rests on a wide base of experimental data. The present chapter describes the works published in the last twenty years of this largely unexplored field of organosulphur chemistry. Appropriate reference must be made to earlier work in order to place it within the new context. The experimental techniques used in most of these studies have been the static manometric[24], the flow[25], the stirred flow[26], the very low pressure pyrolysis[27], the flash pyrolysis[28] and the shock tube[29]. For the identification and quantitation of reaction products, instruments such as gas chromatographs, mass spectrometers, infrared spectrometers and photoelectron spectrometers, in line with or separated from the pyrolysis reactor, have been used along with more conventional analytical methods such as chemical trapping and titrations.

II. THIOLS

In 1933 Taylor and Layng[30] studied the pyrolyses of ethane and propanethiol in a static system at 400–435 °C and 100–300 Torr pressure. To explain the formation of the observed products H_2S, hydrocarbons, elemental sulphur and heavier sulphur compounds, intermolecular and unimolecular processes were hinted at. About that time, the Rice–Herzfeld mechanisms[31,32] for free radical chain reactions had begun to be applied to explain experimental kinetic results. In Taylor's work, however, no mention was made of these reactive species although two years earlier Malisoff and Marks[33] had used them in explaining the pyrolysis of 2-methyl-2-propanethiol. These earlier works showed the complexities that might be expected in any attempt to study sulphur compound pyrolysis. Twenty years later, Thompson, Meyer and Ball[34] studied 2-methyl-2-propanethiol in a flow system while Sehon and Darwent[35], also in a flow system using the toluene carrier technique developed by Szwarc and coworkers[25], examined phenylmethane, methane and ethane thiol at 300–500 °C and at sub-ambient pressures. The important conclusion from these latter works is that the formation of the reaction products may only take place by the intervention of sulphur and carbon centred free radicals in complex chain reactions. In 1964, Tsang[29] used the shock tube technique to study again the decomposition of 2-methyl-2-propanethiol at 677–957 °C in the presence of propene in a 1:4 ratio. He concluded that concurrent unimolecular elimination of H_2S and isobutene as represented by equation 1, via a four-centre cyclic transition state mechanism, and C—SH bond fission processes (equation 2) take place due to the small difference between the activation energy of the first (55 kcal mol^{-1}) and the C—S bond dissociation energy of the latter (69 kcal mol^{-1}).

$$t\text{-}C_4H_9SH \rightleftharpoons (CH_3)_2C\cdots SH \longrightarrow i\text{-}C_4H_8 + H_2S \qquad (1)$$
$$\qquad\qquad\quad \| \quad :$$
$$\qquad\qquad\quad H_2C\cdots H$$

$$t\text{-}C_4H_9SH \longrightarrow t\text{-}C_4H_9^{\bullet} + HS^{\bullet} \qquad (2)$$

For reaction 1, the Arrhenius equation $k(s^{-1}) = 10^{13.3} \exp[(-55\,\text{kcal mol}^{-1})(RT)^{-1}]$ was reported and has the expected frequency factor value for a unimolecular cyclic transition state mechanism. The propene was considered to suppress any radical-induced and thiol-consuming chain reaction. This same thiol was also studied by Bamkole[36] at 420–490 °C but in a static system using cyclohexene as radical chain inhibitor at a maximum ratio of 1.3 in respect of the thiol. The pyrolysis mechanism proposed by Bamkole, similar to that of Malisoff and Marks[33] and Thompson and coworkers[34], is initiated by equation 2, followed by the following steps 3–6:

$$t\text{-}C_4H_9^{\bullet} + t\text{-}C_4H_9SH \longrightarrow (CH_3)_2C(CH_2^{\bullet})SH + i\text{-}C_4H_{10} \qquad (3)$$

$$t\text{-}C_4H_9SH + HS^{\cdot} \longrightarrow (CH_3)_2C(CH_2^{\cdot})SH + H_2S \quad (4)$$

$$(CH_3)_2C(CH_2^{\cdot})SH \longrightarrow i\text{-}C_4H_8 + HS^{\cdot} \quad (5)$$

$$2\,HS^{\cdot} \longrightarrow H_2S + S \quad (6)$$

By applying the steady-state hypothesis to the concentrations of the free radicals, the following 1.5-order rate law was obtained:

$$-d[(CH_3)_3CSH]/dt = k_4(k_2/k_6)^{0.5}[(CH_3)_3CSH]^{1.5}$$

The Arrhenius equation for $k = k_4(k_2/k_6)^{0.5}$ was

$$k(\text{cm}^{1.5}\,\text{mol}^{-0.5}\,\text{s}^{-1}) = 10^{12.07\pm0.04}\exp[(-40.1\pm0.1\,\text{kcal mol}^{-1})(RT)^{-1}]$$

Bamkole also estimated $\Delta H^0_{298}(2) = 67$ and $\Delta H^0_{298}(4) = 7\,\text{kcal mol}^{-1}$. The same author similarly studied the pyrolyses of 1-butanethiol and 2-butanethiol for which he proposed the sequence of steps 7 to 11, where $R = CH_3(CH_2)_2CH_2^{\cdot}$ or $CH_3CH_2CH^{\cdot}CH_3$ and $R''SH = CH_3CH_2CH^{\cdot}CH_2SH$ or $CH_3CH^{\cdot}CH(SH)CH_3$, for the 1- and 2-butanethiol mechanisms, respectively.

$$RSH \longrightarrow R^{\cdot} + HS^{\cdot} \quad (7)$$

$$R^{\cdot} + RSH \longrightarrow RH + R''SH \quad (8)$$

$$HS^{\cdot} + RSH \longrightarrow H_2S + R''SH \quad (9)$$

$$R''SH \longrightarrow \text{olefin} + HS^{\cdot} \quad (10)$$

$$HS^{\cdot} + R''SH \longrightarrow R'(SH)_2 \longrightarrow \text{olefin} + H_2S + S \quad (11)$$

Again, the use of steady-state concentrations for the reactive species in equations 7–11 yield the first-order rate law $-d[RSH]/dt = (k_7k_9k_{10}/k_{11})^{0.5}[RSH]$. The following Arrhenius equations were obtained for $k = (k_7k_9k_{10}/k_{11})^{0.5}$:

$$\text{1-butanethiol: } k(\text{s}^{-1}) = 10^{9.34\pm0.05}\exp[(-42.6\pm0.2\,\text{kcal mol}^{-1})(RT)^{-1}]$$

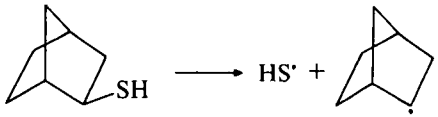
$$\text{2-butanethiol: } k(\text{s}^{-1}) = 10^{8.68\pm0.02}\exp[(-41.7\pm0.1\,\text{kcal mol}^{-1})(RT)^{-1}]$$

The orders predicted by the above rate laws agreed with those experimentally measured for the initial rates. The presence of cyclohexene prevented the formation of large amounts of sulphur. To explain this effect, Bamkole suggested that cyclohexene reduced the rates of steps 6 and 11 and possibly the interception of chains involving RS$^{\cdot}$ and H$^{\cdot}$ radicals leading to sulphur formation. The residual chain reaction of the predominant HS$^{\cdot}$ radicals, surviving in the presence of cyclohexene, corresponds to the above mechanisms.

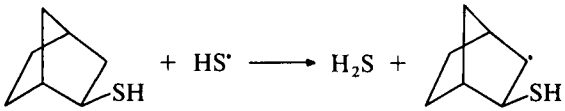
Yamada and coworkers[37] studied more recently the pyrolysis of 1-butanethiol using a mass spectrometric technique at pressures of 10^{-6} Torr and temperatures in the range 27–857 °C. According to their results, at pressures in the fall-off region[16] of the unimolecular rate coefficients, about 85% of the thiol molecules decompose to n-$C_4H_9^{\cdot}$ and HS$^{\cdot}$ radicals. The butyl radicals split ethylene to yield ethyl radicals, which in turn lose a hydrogen atom to form more ethylene. In the high-pressure range of the fall-off curve, 1-butene and hydrogen sulphide are formed by a unimolecular elimination mechanism. The pyrolysis was reported to be without surface effects.

Johnson and Dimian[38] studied the decomposition of *exo*- and *endo*-bicyclo[2.2.1]heptane-2-thiol using flash pyrolysis (500°C, 0.1 Torr) and flow pyrolysis at 400°C in a nitrogen stream at 1 atm. pressure. The flash pyrolysis yielded tricyclo[2.2.1.$0^{2,6}$]heptane and bicyclo[2.2.1]hept-2-ene as major products while the flow pyrolysis of benzene solutions of the thiols yielded cyclopentadiene, besides the same two hydrocarbons. The cyclopentadiene was found to be a pyrolysis product of the bicyclo[2.2.1]hept-2-ene. The flow pyrolysis product distribution was sensitive to hydrogen donor and radical

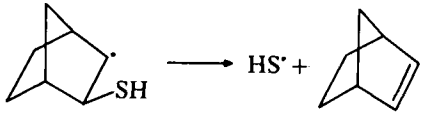
reaction initiator reagents. The results were found to be consistent with the formation of the bicyclo[2.2.1]hept-2-ene by a radical chain mechanism as represented in reactions 12–14. A 1,1-elimination of H_2S from the thiols forms bicyclo[2.2.1]heptan-2-ylidene, which rearranges to tricyclo[2.2.1.$0^{2,6}$]heptane as shown in reaction 15.



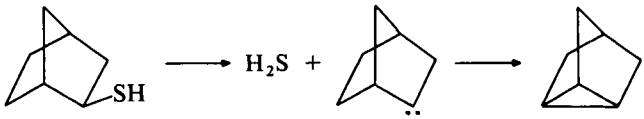
(12)



(13)



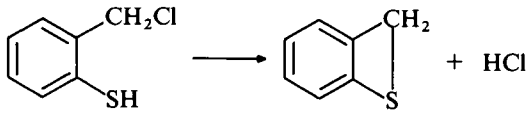
(14)



(15)

The presence of radical and carbene intermediates in the reaction was supported by experiments with the deuterium-labelled thiols. The authors concluded that the mechanisms of thiol thermal reactions are dependent on reaction conditions: in static and flow systems where high concentrations of reactants and radical intermediates are present, fast radical chain mechanisms forming H_2S dominate. Competing H_2S elimination mechanisms are kinetically unfavourable in the presence of such rapid chain reactions.

Bock and Rittmeyer[39] reported the dehydrochlorination of *o*-mercaptobenzyl chloride to benzothiete, at temperatures above 427 °C and pressures of 10^{-3} Torr, according to reaction 16.



(16)

Wazneh and coworkers[40] have shown that flash vacuum pyrolysis of thiocyanohydrins at 677 °C resulted in dehydrocyanation as shown in reaction 17 for R = H, CH_3. The methanethial and ethanethial were detected by mass spectra.

$$NCCH(R)SH \longrightarrow RCH{=}S + HCN \qquad (17)$$

Tanimoto and Saito[41] used a microwave cavity to study the formation of ethenethiol in the pyrolysis of 1,2-ethanedithiol at 600–1000 °C and pressures of 10^{-2} Torr. Other reaction products were H_2S and thiacyclopropane; the latter rearranges to ethene thiol above 700 °C. By studying mixtures of mono- and bideuteriated ethanedithiol, they concluded that elimination of H_2S from the dithiol to form ethenethiol and thiacyclopropane (equations 18 and 19) take different paths. In the formation of the latter, the hydrogen atoms in H_2S mainly come from those attached to the sulphur atoms, while in the formation of the ethenethiol, one of the hydrogen atoms attached

to the sulphur atoms remains on decomposition. The formation of the thiacyclopropane reached a maximum at 850 °C. Methanethial and ethanethial were also detected as products and their signals were strongest above 800 °C.

$$HSCH_2CH_2SH \longrightarrow H_2C\underset{S}{\overset{}{\diagdown\!\!\diagup}}CH_2 + H_2S \quad (18)$$

$$HSCH_2CH_2SH \longrightarrow H_2C{=}CHSH + H_2S \quad (19)$$

Barroeta and coworkers[42] investigated the pyrolysis of cyclohexanethiol in a static system at 420–497 °C following the reaction manometrically and by titrations of the produced H_2S and the unreacted thiol. In vessels seasoned by repeated pyrolyses of allyl bromide and the thiol, and with surface:volume ratios of up to 100 cm^{-1}, the consumption of the reactant behaved as a homogeneous reaction giving H_2S and cyclohexene as products up to about 70% conversion. At higher conversions, the products showed increased complexity. Addition of cyclohexene decreased considerably the rate of consumption of the thiol, with a maximum inhibitory effect at cyclohexene: thiol ratios of 2 to 2.5. Under these conditions, the consumption of the thiol showed first-order kinetics with rate coefficients following the Arrhenius equation

$$k = 10^{16.35 \pm 0.24} \exp[(-64.8 \pm 0.7\,\text{kcal mol}^{-1})(RT)^{-1}]$$

The inhibitory effect of cyclohexene suggested a radical chain process whose more relevant steps are represented by equations 20–25.

$$C_6H_{11}SH \longrightarrow C_6H_{11}^{\cdot} + HS^{\cdot} \quad (20)$$

$$C_6H_{11}SH + HS^{\cdot} \longrightarrow C_6H_{10}{}^{\cdot}SH + H_2S \quad (21)$$

$$C_6H_{10}{}^{\cdot}SH \longrightarrow C_6H_{10} + HS^{\cdot} \quad (22)$$

$$C_6H_{11}^{\cdot} + C_6H_{10}{}^{\cdot}SH \longrightarrow C_6H_{10} + C_6H_{11}SH \quad (23)$$

$$C_6H_{10} + HS^{\cdot} \longrightarrow C_6H_9^{\cdot} + H_2S \quad (24)$$

$$C_6H_{11}^{\cdot} + HS^{\cdot} \longrightarrow C_6H_{10} + H_2S \quad (25)$$

The cyclohexene should prevent the chain propagating step 21, so under maximum inhibition the observed products may be expected to be formed in step 25, which should be favoured by having an exothermicity of about 52 kcal mol^{-1}. For the initial C—S bond fission step 20 it was estimated $\Delta H^{\circ}_{298}(20) = 69.5\,\text{kcal mol}^{-1}$, a value in fair agreement with the experimental activation energy for the inhibited pyrolysis.

III. SULPHIDES

Shum and Benson[43] studied the pyrolysis of dimethyl sulphide in a static system at 400–450 °C and 35–198 Torr. The reaction is a complex free radical process, with small surface effects in conditioned vessels as well as small induction period and autocatalysis. The main reaction products were CH_4, C_2H_4, H_2S and CS_2. Minor products were C_2H_5SH and sulphur. These were formed according to the stoichiometries 26 to 28.

$$CH_3SCH_3 \longrightarrow C_2H_4 + H_2S\ (60\text{–}70\%) \quad (26)$$

$$CH_3SCH_3 \longrightarrow CH_4 + CH_2{=}S\ (20\text{–}30\%) \quad (27)$$

$$CH_3SCH_3 \longrightarrow C_2H_5SH\ \ (10\text{–}15\%) \quad (28)$$

Although methanethial was not observed, it was postulated as an important reaction intermediate. The formation of CS_2 was assumed to occur by a slow, complex radical process involving this intermediate in the latter stages of the reaction.

The sequence of steps 29 to 38 explain the main experimental features[43,44].

$$CH_3SCH_3 \longrightarrow CH_3^{\cdot} + CH_3S^{\cdot} \quad (29)$$

$$CH_3^{\cdot} + CH_3SCH_3 \longrightarrow CH_4 + CH_3SCH_2^{\cdot} \quad (30)$$

$$CH_3SCH_2^{\cdot} \rightleftharpoons CH_3^{\cdot} + CH_2{=}S \quad (31)$$

$$CH_3^{\cdot} + H_2S \longrightarrow CH_4 + HS^{\cdot} \quad (32)$$

$$HS^{\cdot} + CH_3SCH_3 \longrightarrow H_2S + CH_3SCH_2^{\cdot} \quad (33)$$

$$CH_3^{\cdot} + CH_2{=}S \longrightarrow CH_3CH_2S^{\cdot} \quad (34)$$

$$CH_3CH_2S^{\cdot} \rightleftharpoons CH_2^{\cdot}CH_2SH \quad (35)$$

$$CH_2^{\cdot}CH_2SH \longrightarrow C_2H_4 + HS^{\cdot} \quad (36)$$

$$CH_3CH_2S^{\cdot} + H_2S \rightleftharpoons C_2H_5SH + HS^{\cdot} \quad (37)$$

$$2\,HS^{\cdot} \longrightarrow \text{termination} \quad (38)$$

A chain I, formed by steps 30 and 31, accounts for CH_4 production. Another chain II, formed by steps 33–37, originates C_2H_4 and C_2H_5SH. Step 34 is required for C_2H_4 production and should be about 11 kcal mol^{-1} more exothermic than the competing step -31 and essentially irreversible at 427 °C. The 1,3 H-atom transfer in step 35 becomes rate-determining for C_2H_4 production if step 36 is fast compared to step -35. A steady-state treatment of the above kinetic scheme produced the following 0.5-order rate law for the consumption of the dimethyl sulphide:

$$-d\ln[CH_3SCH_3]/dt = k_{33}(k_{29}/k_{38})^{0.5}[CH_3SCH_3]^{0.5} \{1 + (k_{30}[CH_3SCH_3]/k_{32}[H_2S])\}$$

As $[CH_3SCH_3]$ becomes $\ll [H_2S]$, this rate law simplifies to

$$\text{rate} = k_{33}(k_{29}/k_{38})^{0.5}[CH_3SCH_3]^{0.5}$$

The experimentally measured reaction order was 1.43 at 407.9 °C and 1.53 at 449.4 °C, in agreement with the order predicted from the proposed mechanism. The rate coefficients for the consumption of the sulphide followed the Arrhenius equation

$$k(l^{0.5}\,mol^{-0.5}\,s^{-1})\ 10^{13.84\pm0.21}\exp[(-51.4\pm0.7\,kcal\,mol^{-1})(RT)^{-1}]$$

Benson[44] has suggested that an important process for all sulphur centred radicals is isomerization followed by decomposition as represented in equations 35 and 36 for the ethylthiyl radical. The Arrhenius equations estimated by Shum and Benson[43] for these were

$$k_{35}(s^{-1}) = 10^{13.3}\exp[(-32\,kcal\,mol^{-1})(RT)^{-1}]$$

$$k_{36}(s^{-1}) = 10^{13.2}\exp[(-9.7\,kcal\,mol^{-1})(RT)^{-1}]$$

These authors consider that those pyrolysis mechanisms for thiol, sulphides and disulphides proposed in the literature, in which alkylthiyl radicals are involved and do not take into account the above isomerization and subsequent decomposition steps, may be wrong because isomerization should be a common feature of all thiyl radicals. Other important thermochemical parameters relating to thiols and sulphides, such as S—H and C—S bond dissociation energies, and to thiyl radical reactions, have been estimated by Benson[45] and are a useful tool in choosing the most probable steps in a complex kinetic scheme.

Bock and Mohmand[46] used a photoelectron spectrometer to study the products of pyrolysis of diethyl sulphide, di-n-propyl sulphide and di-*t*-butyl sulphide at 647–818 °C and 10^{-1} Torr. A general scheme involving the homolytic fission of the C—S bond, followed by chain reactions of the thioalkyl radicals, was suggested to explain the formation of H_2S, alkene and free sulphur.

Martin and Barroeta[47] studied the pyrolysis of di-*t*-butyl sulphide in static and stirred flow systems over the temperature range 360–460 °C and pressures of 12–240 Torr. The measured order of the initial consumption of the reactant was 1.01 ± 0.03 at 380 °C. At this temperature, the stoichiometry of the reaction for 50% conversion was as shown in equation 39.

$$t\text{-}C_4H_9\text{—}S\text{—}C_4H_9\text{-}t \longrightarrow 1.72\, i\text{-}C_4H_8 + 0.88\, H_2S + 0.29\, i\text{-}C_4H_{10} + 0.11\, t\text{-}C_4H_9SH + 0.04\, S_2 \quad (39)$$

In the presence of 60% total pressure of cyclohexene, this stoichiometry changed as shown in equation 40.

$$t\text{-}C_4H_9\text{—}S\text{—}C_4H_9\text{-}t \longrightarrow 0.84\, i\text{-}C_4H_8 + 0.72\, t\text{-}C_4H_9SH + 0.36\, i\text{-}C_4H_{10} + 0.1\, H_2S \quad (40)$$

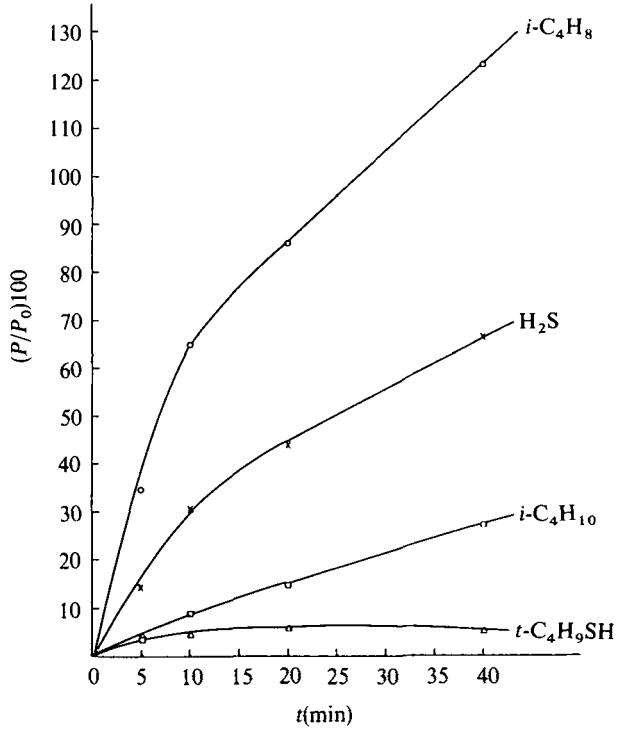


FIGURE 1. Product distribution in the pyrolysis of di-*t*-butyl sulphide at 380 °C: P denotes partial pressure and P_0 initial reactant pressure. Reproduced with permission from Ref. 47.

Figures 1 and 2 show the reaction product profiles at 380 °C for up to 70% conversion, as a function of time. In the absence of cyclohexene (Figure 1), the amount of the thiol is never higher than 3% of the total product. In the presence of cyclohexene (Figure 2) 2-methyl-2-propanethiol and isobutene are the major products, accumulating in equal amounts up to about 30% conversion. The ratio isobutane:isobutene varied in the ranges 0.10–0.22 and 0.35–0.48 in the absence and presence of cyclohexene, respectively. The analytical measurements indicated that about 3.0 mol of products were formed per mol of sulphide decomposed in the absence of cyclohexene. In the presence of the latter, and up to about 50% conversion, around 2.0 mol of gaseous products were formed. These relationships allowed the manometric measurement of the rate of consumption of the reactant in the static system. The first-order rate coefficients for the reaction in the absence of cyclohexene followed the Arrhenius equation

$$k_u(s^{-1}) = 10^{15.1 \pm 0.6} \exp[(-54.7 \pm 2\,\text{kcal mol}^{-1})(RT)^{-1}]$$

In the presence of cyclohexene, the Arrhenius equation was

$$k_i(s^{-1}) = 10^{16.7 \pm 0.2} \exp[(-59.7 \pm 0.5\,\text{kcal mol}^{-1})(RT)^{-1}].$$

The marked effect of the presence of cyclohexene as well as the complex product mixture are strong evidence of the free radical chain mechanism. The reactions 41–43 plus steps 3–6 were proposed for the uninhibited process.

$$t\text{-}C_4H_9\text{—}S\text{—}C_4H_9\text{-}t \longrightarrow t\text{-}C_4H_9S^{\cdot} + t\text{-}C_4H_9^{\cdot} \quad (41)$$

$$t\text{-}C_4H_9S^{\cdot} + t\text{-}C_4H_9^{\cdot} \longrightarrow t\text{-}C_4H_9SH + i\text{-}C_4H_8 \quad (42)$$

$$t\text{-}C_4H_9S^{\cdot} + t\text{-}C_4H_9SH \longrightarrow t\text{-}C_4H_9SH + (CH_3)_2(CH_2^{\cdot})CSH \quad (43)$$

Experiments carried out a 323 °C with mixtures of *t*-butyl sulphide and 2-methyl-2-

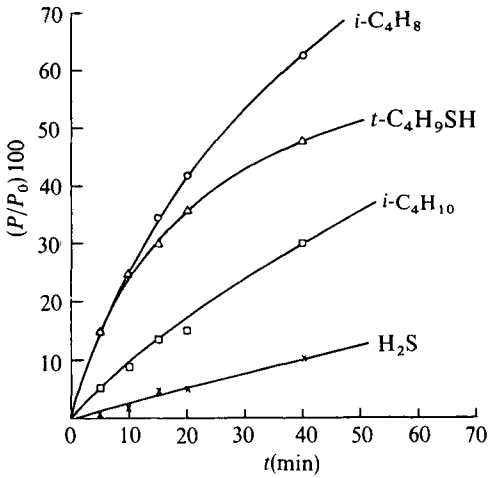


FIGURE 2. Product distribution in the cyclohexene inhibited pyrolysis of di-*t*-butyl sulphide at 380 °C: P denotes partial pressure and P_0 initial reactant pressure. Reproduced with permission from Ref. 47

propanethiol showed that at this temperature neither compound pyrolyses. However, the addition of a few Torr of di-isopropyl disulphide as a radical source caused the thiol to decompose at a rate very much faster than that of the sulphide. This fact together with the order one measured for the consumption of the sulphide suggested that the latter was not being consumed to a significant extent by a radical induced chain reaction, whereas the rapid disappearance of the thiol was due to a chain reaction involving steps 3–6. Step 42 was proposed as the key in the production of 2-methyl-2-propanethiol on the basis of the formation of equal amounts of this product and isobutene during the first stages of the reaction (Figure 2), the low production of isobutane and an estimated exothermicity of about 49 kcal mol^{-1}. By using appropriate literature values[21,22,36,43] of $\Delta H^0_{f\,298}$ for the species involved, it can also be estimated that steps 43, 3 and 4 are endothermic by about 12, 2 and 7 kcal mol^{-1}, respectively. The fact that not all the *t*-butyl radicals end up as isobutane, in the presence of cyclohexene, indicates an ineffectiveness of this inhibitor in intercepting the reactions of this radical. Thus, its effect is mainly the suppression to a large extent of steps 43, 3 and 6 particularly during the first 50% reaction. As the concentration of the 2-methyl-2-propanethiol increases, the attack of the free radicals on this product competes favourably with the attack on cyclohexene. The inhibiting effect of the cyclohexene is represented mainly by steps 44 to 46.

$$t\text{-}C_4H_9S^{\cdot} + c\text{-}C_6H_{10} \longrightarrow t\text{-}C_4H_9SH + c\text{-}C_6H_9^{\cdot} \quad (44)$$

$$t\text{-}C_4H_9^{\cdot} + c\text{-}C_6H_{10} \longrightarrow i\text{-}C_4H_{10} + c\text{-}C_6H_9^{\cdot} \quad (45)$$

$$HS^{\cdot} + c\text{-}C_6H_{10} \longrightarrow H_2S + c\text{-}C_6H_9^{\cdot} \quad (46)$$

The exothermicity of these steps can be estimated to be about 4, 15 and 11 kacl mol^{-1}, respectively. The cyclohexenyl radicals, being highly stable, are not expected to be chain carriers but either dimerize to a stable molecule or suffer further hydrogen atom abstraction to form benzene. For the C—S bond dissociation energies in alkyl sulphides, Benson[45] has quoted values in the range 71–77 kcal mol^{-1}. By combining the values[21,48,49] of $\Delta H^0_{f\,298}(t\text{-}C_4H_9)_2S = -50.1$ kcal mol^{-1}, $\Delta H^0_{f\,298}(t\text{-}C_4H_9^{\cdot}) = -11.6 \pm 0.4$ kcal mol^{-1} and $\Delta H^0_{f\,298}(t\text{-}C_4H_9S^{\cdot}) = 7$ kcal mol^{-1} we can obtain $\Delta H^0_{298}(41) = 69 \pm 4$ kcal mol^{-1}, a value about 10 kcal mol^{-1} higher than the experimental activation energy of the cyclohexene inhibited consumption reaction of di-*t*-butyl sulphide. The experimental activation parameters of the latter, in particular the high-frequency factor, are within the range expected for the bond fission process 41.

Colussi and Benson[50] used the very low pressure pyrolysis method to make a kinetic measurement of the C—S bond dissociation energy (BDE) in phenyl methyl and benzyl methyl sulphides as represented in equations 47 and 48, respectively. The temperature range of this study was 560–970 °C.

$$C_6H_5S\text{—}CH_3 \longrightarrow C_6H_5S^{\cdot} + CH_3^{\cdot} \quad (47)$$

$$C_6H_5CH_2\text{—}SCH_3 \longrightarrow C_6H_5CH_2^{\cdot} + CH_3S^{\cdot} \quad (48)$$

By adjusting the unimolecular rate-coefficient fall-off curves by means of the Kassel integral[16,51,52] they obtained the following high-pressure Arrhenius equations:

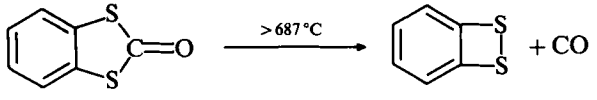
$$k_{47}(s^{-1}) = 10^{15.3} \exp[(-63.6\,\text{kcal mol}^{-1})(RT)^{-1}]$$

$$k_{48}(s^{-1}) = 10^{14.7} \exp[(-56.0\,\text{kcal mol}^{-1})(RT)^{-1}]$$

From the above activation energies they derived the thermochemical quantities (BDE) $\Delta H^0_{298}(47) = 67.5$, $\Delta H^0_{298}(48) = 59.4$ kcal mol^{-1} as well as the enthalpies of formation $\Delta H^0_{f\,298}(C_6H_5S^{\cdot}) = 56.8 \pm 2$, $\Delta H^0_{f\,298}(CH_3S^{\cdot}) = 34.2 \pm 2$ kcal mol^{-1}. Using these last two values they obtained also the following BDE. $CH_3S\text{—}H = 91.8 \pm 2$, $C_6H_5S\text{—}H = 82.2 \pm 2$, $(CH_3S\text{—}CH_3) = 77.4$ kcal mol^{-1}. These two sulphides had been studied much earlier by

Back and Sehon[53] and by Braye, Sehon and Darwent[54] at the lower temperature range of 470–706 °C, using the toluene carrier technique. In these studies, the main reaction products were methane and thiophenol from phenyl methyl sulphide while methane thiol and bibenzyl were formed from benzyl methyl sulphide. In both cases, H atom abstraction from toluene by the free radicals generated in steps 47 and 48 as well as dimerization of the benzyl radicals accounted for the formation of the products.

Reactions 49–53 show the thermal fragmentations observed[39] when 1,2-dithiobenzene derivatives are subject to flash vacuum pyrolysis. The reactants split off the favourable molecule to generate the corresponding benzene-1,2-dithiete product; the latter were identified by real-time photoelectron spectroscopy.



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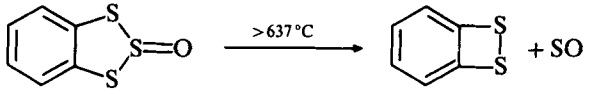

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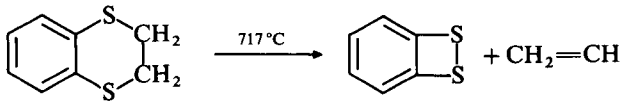

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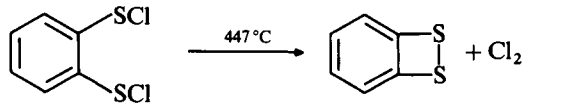

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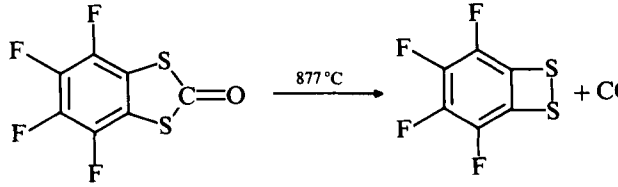
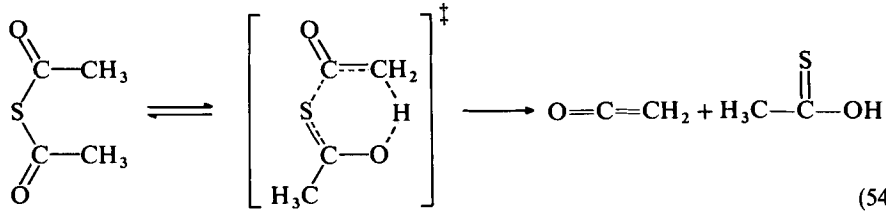


(53)

The gas-phase pyrolysis of diacetyl sulphide has been shown[55,56] to take place homogeneously, via a six-centre cyclic transition state, to produce ketene and thioacetic acid, as represented by reaction 54. For the latter, Taylor[55] reported the Arrhenius equation

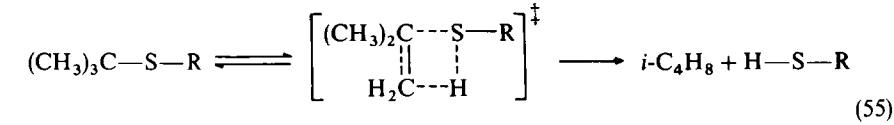
$$k(\mathrm{s}^{-1}) = 10^{12.5} \exp[(-42\,\mathrm{kcal\,mol}^{-1})(RT)^{-1}]$$

over the temperature range 529–655 °C.



(54)

At variance with the sulphides discussed previously, some of the structures t-C_4H_9—S—R, shown in Table 1, pyrolyse to isobutene and the corresponding thiol by a homogeneous, first-order reaction. The mechanism suggested is a unimolecular process via a four-centre cyclic transition state as represented in equation 55. These sulphides were studied using the toluene carrier technique in stirred flow reactors at pressures of 5–15 Torr.



(55)

The presence of some isobutane in the gaseous product distribution (Table 2) suggests a minor C—S bond fission process which is largest when R = C_6H_5. The arguments in favour of a unimolecular elimination are the formation of equal amounts of isobutene and thiol as primary products and the negative entropies of activation, corresponding to rigid transition states. Haugen and Benson[61,62] proposed a quadrupolar model for the transition state of equation 55 in which the heteroatom and one of the methyl C atoms bear partial negative charges while the tertiary C atom and the migrating H atom bear partial positive charges. This model allows the estimation of the activation energies for the addition and the reverse elimination reactions of H_2S or RSH, as well as of the homologous O, N and P systems, to an olefin. The increase in reactivity (Table 1) when R is group capable of stabilizing a charge in the heteroatom in the transition state, by inductive or resonance effects, supports this quadrupolar model. The effect is larger in the homologous ethers[58].

Alkyl allyl sulphides with H atoms bonded to the α—C atom of the alkyl moiety pyrolyse homogeneously and, with first-order kinetics, yield propene and a thiocarbonyl

TABLE 1. Kinetic parameters for $(CH_3)_3C$—S—R pyrolysis

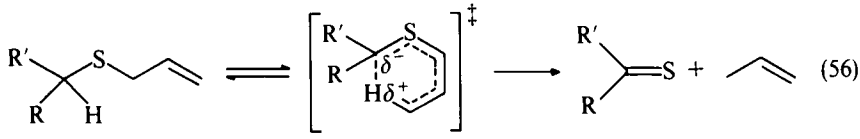
R	E_a(kcal mol^{-1})	log A	$k\cdot10^4$(s^{-1})[a]	T range (°C)	Reference
CH_3	56.9 ± 0.9	14.49 ± 0.28	6.5	509–540	57
$CH_2C{\equiv}CH$	48.5 ± 0.7	13.79 ± 0.24	522	430–490	58
CH_2CN	48.3 ± 0.9	12.63 ± 0.23	42	490–530	59
C_6H_5	44.9 ± 1	12.03 ± 0.39	117	460–500	60
$C_6H_5CH_2$	51.1 ± 1	13.82 ± 0.41	84	488–528	60
p-$O_2NC_6H_4$	44.2 ± 0.9	12.12 ± 0.27	240	489–529	58

[a]Rate coefficient calculated at 430 °C.

TABLE 2. Hydrocarbon product distribution from $(CH_3)_3C$—S—R pyrolysis

R	%i-C_4H_8	%i-C_4H_{10}	%C_2–C_3
CH_3	91 ± 3	6.7 ± 2.5	2.2 ± 0.7
$CH_2C{\equiv}CH$	95 ± 2	5 ± 2	trace
CH_2CN	97 ± 2	2.0 ± 0.3	trace
C_6H_5	78 ± 4	22 ± 4	trace
$C_6H_5CH_2$	98.6 ± 0.4	1.3 ± 0.4	trace
p-$O_2NC_6H_4$	97.9 ± 0.5	2.0 ± 0.3	trace

compound. This type of reaction has been used to generate these metastable molecules for their spectroscopic characterization[63–68]. The mechanism implies a retro-ene process involving a six-centre cyclic transition state. This reaction occurs also with alkyl allyl ethers[69] and amines[70–72]. The activation parameters for a series of these sulphides collected in Table 3 show an increase in reactivity when the group attached to the α—C atom can stabilize, through the resonance effect, a partial negative charge on it in a polar transition state, as described in equation 56. The acidity of the α—H atoms may therefore account for the higher reactivity of the allyl sulphides in comparison with the homologous ethers and amines[73].



(56)

The kinetic deuterium isotope effect for these sulphides[77] has a value of 2.6 ± 0.2 over a temperature range of 100 °C, a fact that supports the mechanism proposed and suggests also a non-linear path for the 1,5-H-atom transfer, different from the linear path proposed for the ether system[69b]. The allyl propargyl sulphide pyrolyses by two symmetrical reaction paths generating equal amounts of allene, propene, propenethial and propynethial[77]. The latter two thiocarbonyls react spontaneously to yield about 35% of a Diels-Alder adduct as represented in equation 57. The homologues allyl propargyl ether and amine[70], however, yield about 80% allene plus 20% propene. This suggests that, in the sulphide system, the energetic or conformational requirements for the α-H atoms of both the propargyl and allyl moieties to approach the p orbitals of the terminal

TABLE 3. Kinetic parameters of alkyl allyl sulphide R—S—C—C=C pyrolysis

R	E_a(kcal mol^{-1})	log A	$k \cdot 10^2$(s^{-1})[a]	Reference
CH_3	38.2 ± 0.7	11.23 ± 0.25	0.73	73
C_3H_7	37.5 ± 0.5	11.52 ± 0.16	3.7	74
n-C_4H_9	36.6 ± 0.2	11.16 ± 0.10	3.7	75
$(CH_3)_3CCH_2$	34.4 ± 0.7	10.54 ± 0.24	4.3	76
$ClCH_2$	34.4 ± 0.7	10.74 ± 0.23	6.9	76
i-C_3H_7[b]	37.0 ± 0.5	11.51 ± 0.14	10.5	77
$CH_3CH{=}CHCH_2$	33.7 ± 0.5	11.09 ± 0.19	13.4	78
c-C_6H_9[c]	33.5 ± 0.7	10.42 ± 0.12	14.6	79
$CH_3CH_2SCH_2$	33.9 ± 0.5	10.85 ± 0.18	15.8	80
$CH_2{=}CHCH_2SCH_2$	31.5 ± 0.9	10.45 ± 0.34	16.3	80
$C_6H_5CH_2$	33.7 ± 0.5	10.93 ± 0.18	19.0	73
$CH_2{=}CHCH_2$	33.0 ± 0.2	11.01 ± 0.10	19.2	73
$CH_3CH{=}CHCH_2$[b]	39.2 ± 0.7	13.11 ± 0.25	19.6	78
$C_6H_5SCH_2$	31.1 ± 1.0	10.09 ± 0.43	20.2	80
$HC{\equiv}CCH_2$	33.2 ± 0.7	11.22 ± 0.28	26.2	77
$CH_3C(O)CH_2$	29.4 ± 0.7	9.95 ± 0.29	37.8	81
$NCCH_2$	30.8 ± 0.5	10.20 ± 0.19	39.2	76
$NCCH(CH_3)$	33.9 ± 0.5	11.09 ± 0.18	48.8	76

[a] Calculated at 375 °C.
[b] *i*-Propyl propargyl sulphide and crotyl propargyl sulphide respectively.
[c] 3-Cyclohexenyl

allyl and acetylenic carbon atoms, respectively, in the transition state, are nearly the same. In the N and O systems these requirements must remain quite distinct.

(57)

The pyrolysis of neopentyl allyl sulphide[76] cleanly generates 2,2-dimethylpropanethial, the smallest stable thioaldehyde first reported by Vedejs and Perry[82]. The thermal stability of alkyl allyl and diallyl sulphides with branching at the α- and γ-C atoms has been investigated in relation to its relevance to rubber vulcanization[6,83]. In such branched sulphides, at temperatures above 180 °C, the decomposition proceeds slowly by homolytic C—S bond fission releasing allyl and allylthiyl radicals which form olefins, allyl thiols and allyl disulphides as products.

The pyrolysis of n-propyl 1-propenyl sulphide[84] in a stirred flow system over the temperature range of 442–491 °C at pressures of 1–9 Torr, yields propene, propene 1-thiol, hydrogen sulphide, propane and C_2 hydrocarbons. Due to the decomposition of the vinylic thiol, the pyrolysis becomes more complex than that of its allyl homologue, and possibly takes place by both molecular and free radical mechanisms.

IV. DISULPHIDES

Recent measurements[85] by an EI technique gave values of BDE(MeSS—R) = 56.6–52.6 kcal mol^{-1} for R = Me, Et, *i*-Pr and *t*-Bu, indicating a trend to a weaker bond with branching of R. For the symmetrical tetrasulphides BDE(RSS—SSR) fell within the narrow range 31.8–32.9 kcal mol^{-1}, indicating that the strength of the central S—S bond is quite independent of the nature of R. Table 4 presents some relevant enthalpies of formation for the estimation[49] of the BDE(C—S) and BDE(S—S) (ΔH^0_{298}, kcal mol^{-1}) of reactions 58–67. Although these enthalpies are approximate within about ±4 kcal mol^{-1}, the values suggest that both homolytic S—S and C—S bond fissions in

TABLE 4. Enthalpies of formation

Species	ΔH^0_{f298} (kcal mol^{-1})	Reference
$C_6H_5SS—C_4H_9$-*t*	−2.05	49
(*t*-$C_4H_9S)_2$	−47.5	21
$CH_3SS—C_4H_9$-*t*	−26.8	85
$(CH_2=CHCH_2S)_2$	30.9	86
$CH_2=CHCH_2SS—C_4H_9$-*t*	−8.7	86
CH_3SSCH_3	−5.8	85
t-$C_4H_9SS^{\cdot}$	−4.6	85
t-$C_4H_9S^{\cdot}$	7.0	49
$C_6H_5SS^{\cdot}$	49	49
$C_6H_5S^{\cdot}$	57 ± 2	50
$CH_3SS^{\cdot}$	16.4	85,45
$CH_3S^{\cdot}$	34 ± 2	50
$CH_3^{\cdot}$	35.1 ± 0.1	87
t-$C_4H_9^{\cdot}$	11.6 ± 0.4	48
$CH_2=CHCH_2SS^{\cdot}$	37.5	86
$CH_2=CHCH_2S^{\cdot}$	46.5	86
$CH_2=CHCH_2^{\cdot}$	39	87

disulphides would be feasible in a thermally energized disulphide molecule. Disulphide photolysis studies[88,89] have shown that both bond fissions are feasible in gas and condensed phases. Direct photolysis proceeds by S—S cleavage and thioalkyl radical formation. In liquid-phase sensitized photolysis, C—S bond cleavage is a major reaction path with the perthiyl radicals presumably ending up as disulphanes. For the latter radicals, RSS$^{\cdot}$, a stabilization energy of 21 ± 1 kcal mol^{-1} has been estimated[45] when considering that, within the S—S bond, there is some π-bond character.

$$CH_3SSCH_3 \longrightarrow CH_3SS^{\cdot} + CH_3^{\cdot} \quad 57.4 \quad (58)$$

$$\longrightarrow 2\,CH_3S^{\cdot} \quad 74.1 \quad (59)$$

$$(t\text{-}C_4H_9S)_2 \longrightarrow t\text{-}C_4H_9SS^{\cdot} + t\text{-}C_4H_9^{\cdot} \quad 54.5 \quad (60)$$

$$\longrightarrow 2\,t\text{-}C_4H_9S^{\cdot} \quad 61.4 \quad (61)$$

$$CH_3SS{-}C_4H_9\text{-}t \longrightarrow CH_3SS^{\cdot} + t\text{-}C_4H_9^{\cdot} \quad 55.0 \quad (62)$$

$$\longrightarrow CH_3S^{\cdot} + t\text{-}C_4H_9S^{\cdot} \quad 67.9 \quad (63)$$

$$(CH_2{=}CHCH_2S)_2 \longrightarrow CH_2{=}CHCH_2SS^{\cdot} + CH_2{=}CHCH_2^{\cdot} \quad 45.6 \quad (64)$$

$$\longrightarrow 2\,CH_2{=}CHCH_2S^{\cdot} \quad 62.4 \quad (65)$$

$$C_6H_5SS{-}C_4H_9\text{-}t \longrightarrow C_6H_5SS^{\cdot} + t\text{-}C_4H_9^{\cdot} \quad 62.9 \quad (66)$$

$$\longrightarrow C_6H_5S^{\cdot} + t\text{-}C_4H_9S^{\cdot} \quad 66.0 \quad (67)$$

Very few studies have been reported of the gas-phase pyrolysis of disulphides. Coope and Bryce[90] studied dimethyl disulphide in a static system at 316–373 °C and pressures of 24–230 Torr. The reaction was complex, forming one mole of methanethiol per mole of decomposed disulphide, together with a non-volatile product identified as a polymer of methanethial. There was a competing reaction forming a large amount of hydrogen sulphide and other products such as C_2 hydrocarbons, free sulphur, carbon disulphide and polysulphides. The mechanism proposed involved initial splitting of the S—S bond, originating thiomethyl radicals which induce a chain decomposition of the reactant. The estimated enthalpies for reactions 58 and 59, however, favour an initial C—S bond fission.

The pyrolysis of di-isopropyl disulphide[91] in a static system at 274–304 °C and 80–260 Torr produces 2-propanethiol, a mixture of propene (97%) and propane (3%), hydrogen sulphide and sulphur. The gas product distribution shown in Figure 3 indicates that 2-propanethiol is formed and consumed as the reaction proceeds. When the pyrolysis is carried out in the presence of 60% total pressure of cyclohexene, the rate of reaction decreases about one-half and the C_3 hydrocarbon proportion changes to 73% propene plus 27% propane and no free sulphur is formed. The corresponding gas product distribution is shown in Figure 4. A parallel study with 3,4-dithia-2,5-dideuterio-2,5-dimethylhexane, in the absence of cyclohexene, showed that only 2-deuterio-2-propanethiol, 2-deuteriopropene (89%) plus 2-deuteriopropane (11%) were formed. No deuterium scrambling was observed in the unreacted disulphide. The reaction mechanism proposed for this pyrolysis is represented by equations 68–76 plus reaction 6. By using literature values[85,87] for $\Delta H^0_{f298}(i\text{-}C_3H_7SS^{\cdot}) = 3.3$, $\Delta H^0_{f298}(i\text{-}C_3H_7^{\cdot}) = 18.2$ and estimated values of $\Delta H^0_{f298}(i\text{-}C_3H_7S^{\cdot}) = 15$ and $\Delta H^0_{f298}[(i\text{-}C_3H_7S)_2] = -32$ kcal mol^{-1}, BDE values for S—S and C—S bonds of 62 and 53 kcal mol^{-1}, respectively, may be obtained. The reaction scheme is complicated by the feasibility of both initial bond fissions and by the fact that the 2-propanethiol product reacts readily with the free radicals generating more chain carriers. The Arrhenius equation obtained for the consumption of the diisopropyl disulphide in the presence of cyclohexene was

$$k(s^{-1}) = 10^{14.34 \pm 0.38} \exp[(-46 \pm 1\,\text{kcal mol}^{-1})(RT)^{-1}]$$

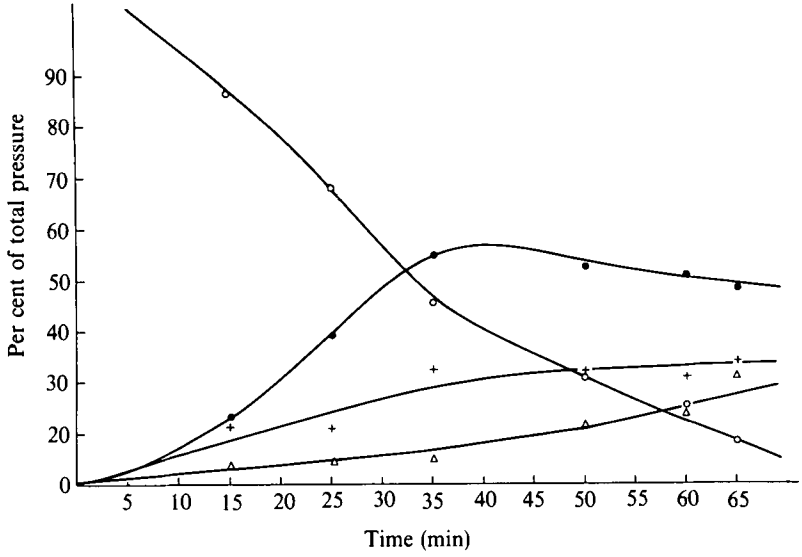


FIGURE 3. Product distribution in the pyrolysis of di-isopropyl disulphide at 274 °C: ○, di-isopropyl disulphide; ●, 2-propanethiol; +, C_3 hydrocarbons; Δ, H_2S. Reproduced with permission from Reference 91

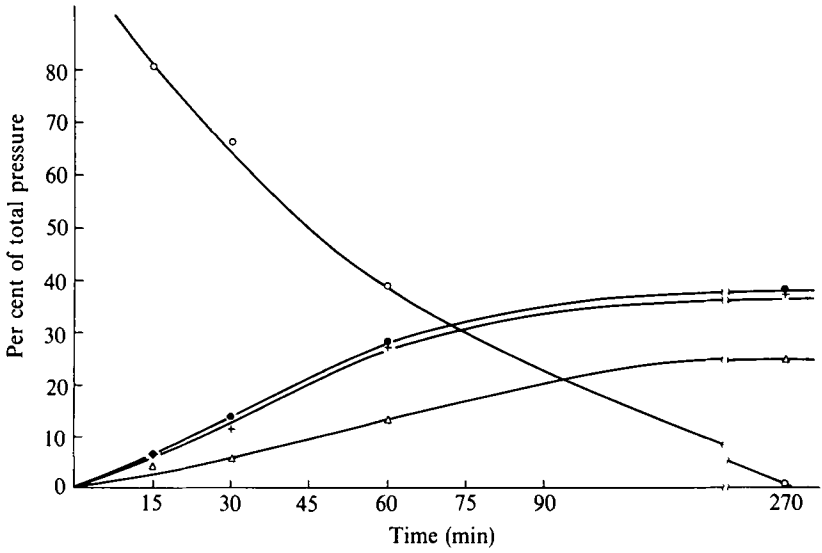


FIGURE 4. Product distribution in the cyclohexene inhibited pyrolysis of di-isopropyl disulphide at 274 °C: ○, di-isopropyl disulphide; ●, 2-propanethiol; +, C_3 hydrocarbons; Δ, H_2S. Reproduced with permission from Reference 91

The low value of E_a suggests a low efficiency of cyclohexene for impeding some consumption of the reactant by radical attack, such as step 70.

$$(C_3H_7S)_2 \longrightarrow 2\,C_3H_7S^{\bullet} \tag{68}$$

$$(C_3H_7S)_2 \longrightarrow C_3H_7SS^{\bullet} + C_3H_7^{\bullet} \tag{69}$$

$$(C_3H_7S)_2 + C_3H_7S^{\bullet} \longrightarrow C_3H_7SH + C_3H_7SSCH(CH_3)CH_2^{\bullet} \tag{70}$$

$$C_3H_7SSCH(CH_3)CH_2^{\bullet} \longrightarrow C_3H_6 + C_3H_7SS^{\bullet} \tag{71}$$

$$C_3H_7SS^{\bullet} + C_3H_7SH \longrightarrow C_3H_7SSH + {}^{\bullet}CH_2CH(CH_3)SH \tag{72}$$

$${}^{\bullet}CH_2CH(CH_3)SH \longrightarrow C_3H_6 + HS^{\bullet} \tag{73}$$

$$C_3H_7SSH \longrightarrow C_3H_7S^{\bullet} + HS^{\bullet} \tag{74}$$

$$C_3H_7S^{\bullet} + C_3H_7SH \longrightarrow C_3H_7SH + {}^{\bullet}CH_2CH(CH_3)SH \tag{75}$$

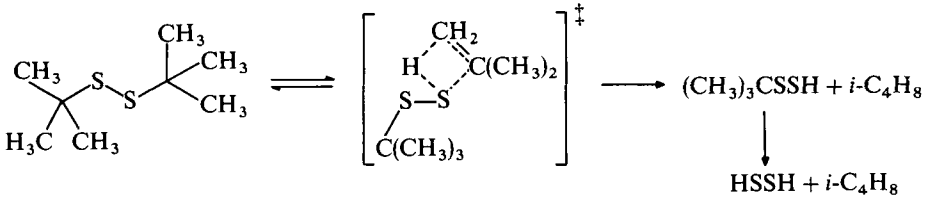
$$2\,C_3H_7^{\bullet} \longrightarrow C_3H_6 + C_3H_8 \tag{76}$$

Bock and Mohmand[46], in their study of the pyrolysis of alkyl sulphides and disulphides, observed that for the latter, the temperature of decomposition decreases with methyl substitution in the alkyl group. They conclude that the S—S bond is more easily split than the C—S bond. In the pyrolysis of di-*t*-butyl disulphide at 1127 °C they detected isobutene, hydrogen sulphide, carbon disulphide and acetylene as reaction products.

Martin and Barroeta[92] studied the pyrolysis of di-*t*-butyl disulphide in a stirred flow reactor at 300–400 °C and pressures of 8–15 Torr, using CO_2, cyclohexene and toluene as carrier gas. The consumption of the disulphide was a first-order reaction forming isobutene and hydrogen disulphide as primary products. Other products were about 5% isobutane and hydrogen sulphide, the latter being formed by the decomposition of the hydrogen disulphide on the glass surfaces. The Arrhenius equation obtained from the rate coefficients for isobutene production was

$$k(s^{-1}) = 10^{14.6\pm0.4}\exp[(-44 \pm 1\ \text{kcal mol}^{-1})\,(RT)^{-1}]$$

The reaction mechanism proposed involved two consecutive unimolecular eliminations via four-centre cyclic transition state as represented in equation 77.



(77)

Some evidence in relation to the transient formation of *t*-butyl disulphane comes from the mass spectrum of the di-*t*-butyl disulphide, where the peak of mass *m/z* 122 is evident. The formation of the species RSSH from alkyl disulphides by EI has been observed in many other cases[93]. A mechanism similar to equation 77 has been described[49] in the pyrolysis of the aryl *t*-butyl disulphides whose Arrhenius parameters are shown in Table 5. Over the temperature range 390–460 °C, these disulphides yielded 95 ± 1% isobutene, 5 ± 1% isobutane and the corresponding aryl disulphanes as reaction products. The latter have been synthesized and identified by NMR spectroscopy[94]. MINDO/3 calculations of the net atomic charges in the optimized molecular geometries of these

TABLE 5. Kinetic parameters for RSS—Bu-*t* pyrolysis

R	E_a (kcal mol^{-1})	log A	$k \cdot 10^2$(s^{-1})[a]	T range (°C)
C_6H_5	43.5 ± 0.9	13.49 ± 0.31	14	390–440
p-$O_2NC_6H_4$	44 ± 1	13.46 ± 0.32	8	420–460
p-ClC_6H_4	47 ± 2	14.44 ± 0.66	10	390–421
p-FC_6H_4	34.7 ± 0.5	10.80 ± 0.16	26	400–450
t-C_4H_9[b]	44 ± 1	14.6 ± 0.4	65	328–400
t-C_4H_9[c]	42.3 ± 0.5	13.57 ± 0.22	26	246–300

[a]Calculated at 390 °C.
[b]Flow system measurements.
[c]Static system measurements.

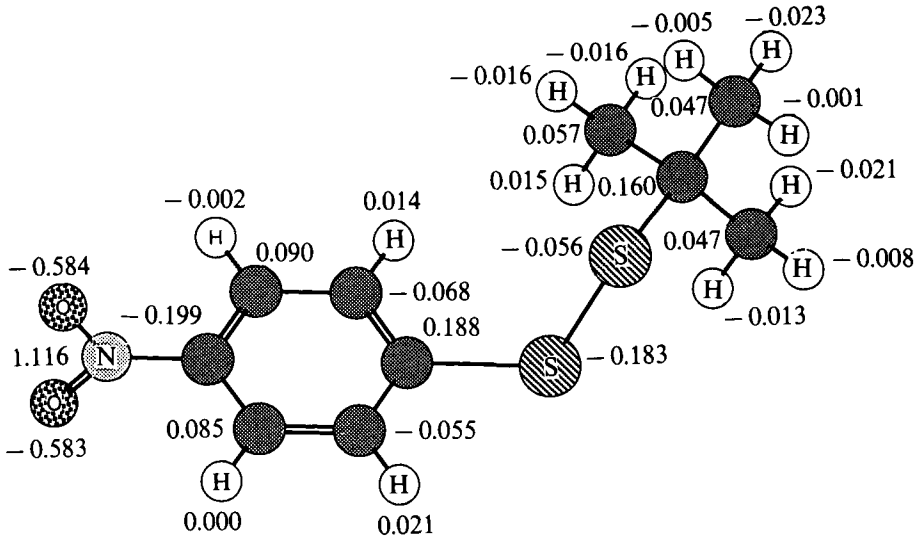


FIGURE 5. Net atomic charges in *p*-nitrophenyl *t*-butyl disulphide

aryl *t*-butyl disulphides, such as the one pictured in Figure 5, show that only one H atom in the *t*-butyl group bears a net positive charge and it is bonded to a methyl C atom having a positive charge lower than the tertiary C atom, which has the highest positive charge in the group; both S atoms have negative charges. The positively charged H atom is also the one with the shortest interatomic distance to the S atom bonded to the *t*-butyl group. The charge distributions resemble the expected one for the atoms, conforming the quadrupolar four-centre cyclic transition state model of Haugen and Benson[61]. The effect of the substituents on the reactivity (Table 5) suggests the possibility of such a polar transition state.

V. SULPHOXIDES

Thyrion and Debecker[95] studied the pyrolysis of dimethyl sulphoxide at 297–340 °C and 10–400 Torr in a static system. The reaction was found to be homogeneous and

the formation of the three main reaction products, methane, ethylene and sulphur dioxide, was first order with respect to the sulphoxide concentration. The Arrhenius equation for methane production was

$$k(s^{-1}) = 10^{14.57} \exp[(-49.4 \pm 1\,\text{kcal mol}^{-1})(RT)^{-1}]$$

The activation energies for sulphur dioxide and ethylene formation were 47.7 ± 2 and 47.2 ± 2 kcal mol^{-1}, respectively. Other products were carbon disulphide, dimethyl sulphide and propene. The experimental evidence suggested a complex radical chain mechanism involving the reactions 78–82. For the bond fission step 78, by using appropriate reported[21,45,87] enthalpy values, it can be estimated that $\Delta H^0_{298}(78) = 54$ kcal mol^{-1}. It was postulated that ethylene and sulphur dioxide originate mainly from sulphine by reactions 83 and 84. The detection of CH_2D_2 and CH_2CD_2 as products of the pyrolysis of equimolar mixtures of dimethyl sulphoxide and dimethyl sulphoxide-d_6 suggested the formation of methylene through reactions 85 and 86, despite the estimated high values $\Delta H^0_{298}(85) = 75$ and $\Delta H^0_{298}(86) = 98.5$ kcal mol^{-1}.

$$CH_3SOCH_3 \longrightarrow CH_3^{\cdot} + CH_3SO^{\cdot} \quad (78)$$

$$CH_3SO^{\cdot} \longrightarrow CH_3^{\cdot} + SO \quad (79)$$

$$CH_3^{\cdot} + CH_3SOCH_3 \longrightarrow CH_4 + {}^{\cdot}CH_2SOCH_3 \quad (80)$$

$${}^{\cdot}CH_2SOCH_3 \longrightarrow CH_2{=}SO + CH_3^{\cdot} \quad (81)$$

$$2\,CH_3^{\cdot} \longrightarrow C_2H_6 \quad (82)$$

$$2\,CH_2{=}SO \longrightarrow C_2H_4 + 2\,SO \quad (83)$$

$$2\,CH_2{=}SO \longrightarrow C_2H_4 + SO_2 + S \quad (84)$$

$${}^{\cdot}CH_2SOCH_3 \longrightarrow CH_2 + CH_3SO^{\cdot} \quad (85)$$

$$CH_2{=}SO \longrightarrow CH_2 + SO \quad (86)$$

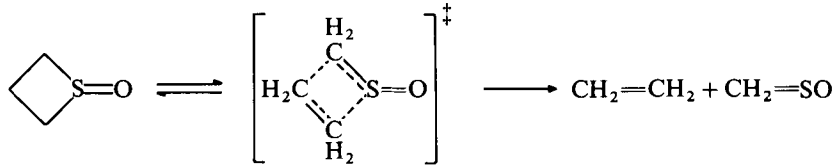
Other steps proposed to explain the formation of observed products are shown in equations 87–89.

$$SO + CH_3SOCH_3 \longrightarrow SO_2 + CH_3SCH_3 \quad (87)$$

$$CH_3SO^{\cdot} + CH_3SOCH_3 \longrightarrow CH_3SO_2^{\cdot} + CH_3SCH_3 \quad (88)$$

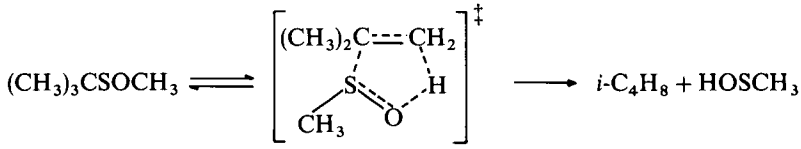
$$CH_3SO_2^{\cdot} \longrightarrow CH_3^{\cdot} + SO_2 \quad (89)$$

Block and coworkers[96,97] examined the pyrolysis of dimethyl sulphoxide at 650 °C using the flash vacuum pyrolysis–microwave spectroscopy technique. They also proposed a free radical mechanism initiated by reaction 78 and the formation of sulphine by reaction 81. They also studied[96] the pyrolyses of thietane *S*-oxide and 1,3-dithietane-1-oxide at 600 °C and 300 °C, respectively. These cleanly generate sulphine and alkene, possibly by a retro-ene mechanism as represented by reaction 90.



(90)

The pyrolysis of *t*-butyl methyl sulphoxide at temperatures above 250 °C was found to produce[97] methanesulphenic acid plus isobutene, as shown in reaction 91. Above 750 °C, the acid dehydrates to thiomethanal.



(91)

Allyl methyl sulphoxide, on the other hand, at temperatures above 250 °C, produces both sulphenic acid and sulphine, probably by both radical and retro-ene mechanisms. Similar results were reported by Davis and coworkers[98].

The study of dimethyl sulphoxide made by Carlsen and coworkers[99], using the same technique but coupled to a field ionization MS, showed that at 510–1131 °C the only products formed were dimethyl sulphide, methanethiol and methanal. Their findings support two possible mechanisms involving either atomic oxygen extrusion or rearrangement of the dimethyl sulphoxide to sulphenate, followed by its decomposition, as shown in reactions 92 and 93.

$$CH_3SOCH_3 \longrightarrow CH_3SCH_3 + O \tag{92}$$

$$\longrightarrow CH_3S(OCH_3) \longrightarrow CH_3SH + H_2CO \tag{93}$$

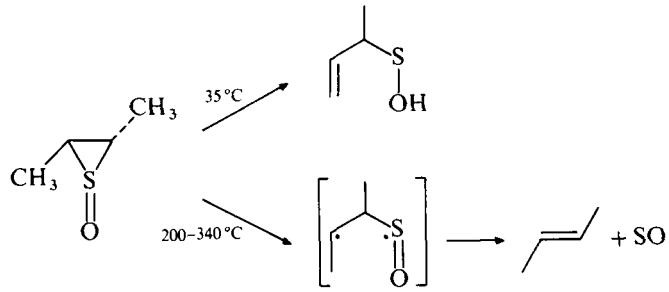
The pyrolysis of dimethyl sulphoxide-d_6 gave no evidence of either a reaction path leading to the initial loss of a methyl radical (reaction 78), or the formation of sulphine by loss of a hydrogen atom from $CH_3SO^{\cdot}$.

Saito[100] studied the flash pyrolysis of ethylene episulphoxide at temperatures up to 780 °C, reporting complete conversion above 560 °C. The microwave signals of the products indicated the presence of SO as well as SO_2, S_2O and methanal. The signal of SO was strongest at that temperature. The evidence suggested that SO extrusion (reaction 94) rather than atomic oxygen loss was the reaction path. The SO extrusion reaction was reported to be 39 ± 10 kcal mol^{-1} exothermic.

$$(CH_2)_2SO \longrightarrow CH_2{=}CH_2 + SO \tag{94}$$

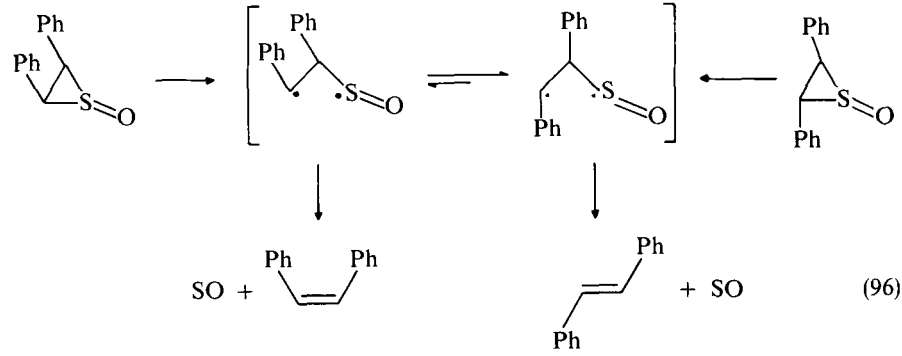
Hartzell and Paige[101] had previously reported that this episulphoxide decomposes at 100 °C to yield ethylene and SO. Its thermolysis in chlorobenzene solution was found to be a first-order reaction with an activation energy of 35 kcal mol^{-1}. The same authors studied[102] the stereochemistry of the pyrolyses of *cis*- and *trans*-2-butene episulphoxides at 150 °C in a gas chromatograph. At those experimental conditions, the *cis*-isomer yielded 89% *cis*-2-butene plus 11% *trans*-2-butene whereas the *trans*-isomer formed 58% *trans*-2-butene plus 42% *cis*-2-butene, the other product being always SO. The mechanism postulated was an E1-type elimination in which the intermediate species, formed by fission of the C—S bond, is capable of limited internal rotation about the internal C—C bond before the release of the SO moiety. Since the isomeric 2-butene episulphoxides do not yield the same product distributions, it is inferred that the corresponding intermediates cannot be equivalent and, further, that the activation energy for SO elimination from these intermediates should be comparable to the internal rotation energy barrier. Baldwin and coworkers[103] reported evidence of a lower activation energy path for these episulphoxides consisting in their rearrangement at 35 °C to the allyl sulphenic acid when the stereochemistry is favourable, as in the case of the *trans*-isomer. Over the temperature range 200–340 °C, their *cis*:*trans*-2-butene distribution was similar

to that reported by Hartzell and Paige[102], consequently they proposed that the intermediate in the high activation energy path leading to the 2-butenes and SO is a diradical species with limited internal rotation, as represented in reaction 95.



(95)

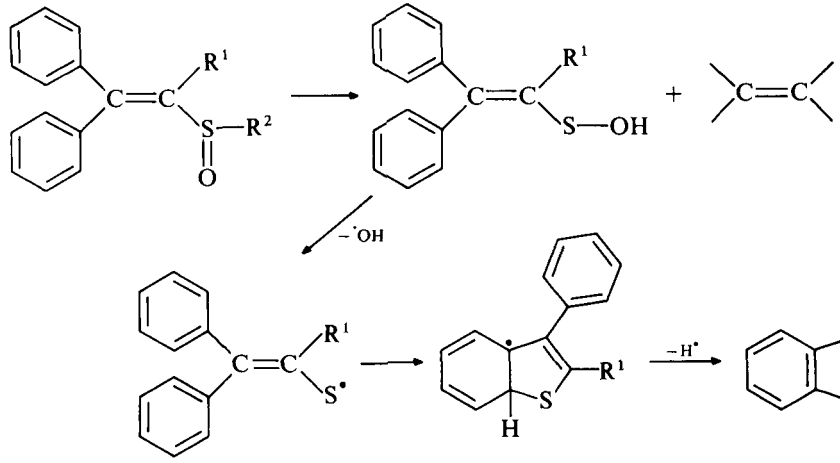
Kondo and coworkers[104] demonstrated that the pyrolysis of *trans*-stilbene episulphoxide proceeds almost stereospecifically over the temperature range 0–290 °C, yielding *trans*-stilbene plus SO, while the *cis*-isomer decomposes with complete loss of stereospecificity. By measuring the kinetics of their thermolyses in polar and non-polar solvents, in the presence of di-*p*-anisylthioketone as diradical trapping agent, it was concluded that these were first-order reactions involving homopolar species as reaction intermediates. The internal rotation in the latter, however, is restricted by the steric repulsion of the two phenyl groups. The mechanistic scheme is represented in reaction 96.



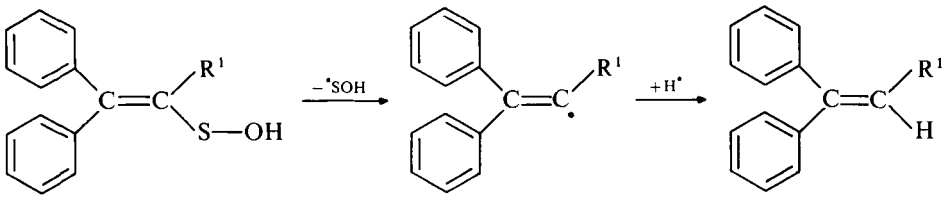
(96)

Ando[105] studied the pyrolyses of a series of α-phenyl styryl sulphoxides in a nitrogen flow system at 580 °C. The reaction mechanism involves the retro-ene type unimolecular elimination of the α-phenylstyrylsulphenic acid and alkene, similar to equation 91, followed by the decomposition of the acid by a S—OH bond cleavage as major path (47%). The styrylthiyl radical generated in the latter process undergoes cyclization to yield a substituted benzothiophene, as represented by equation 97 for $R^1 = H$, CH_3 and $R^2 = C_2H_5$, *i*-C_3H_7. As a minor reaction path (12%), the α-phenylstyrylsulphenic acid suffers a C—S bond cleavage forming an α-phenylstyryl radical which ends up as a diphenylethylene, as represented by equation 98. One more example of these mechanisms is the pyrolysis of 2-phenyl-1-cyclohexenyl ethyl sulphoxide, which gives the product yields presented in equation 99. The same author also reported that a series of homologous alkyl styryl sulphides and a styryl disulphide decompose also at 580°C by C—S bond fission forming the corresponding styrylthiyl radicals as major reaction

path. The latter radicals similarly undergo cyclization to the respective substituted benzothiophenes.



(97)



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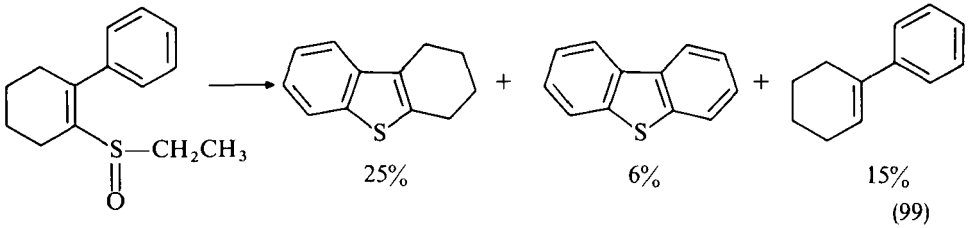
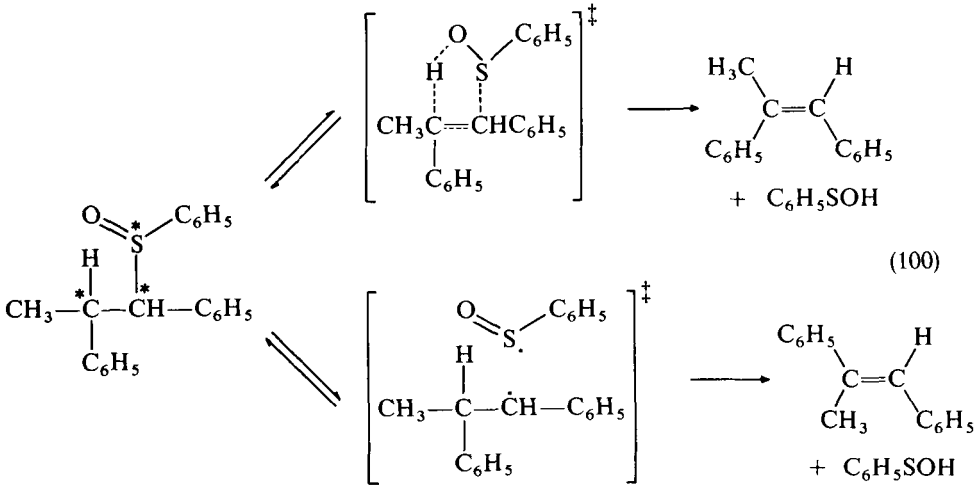


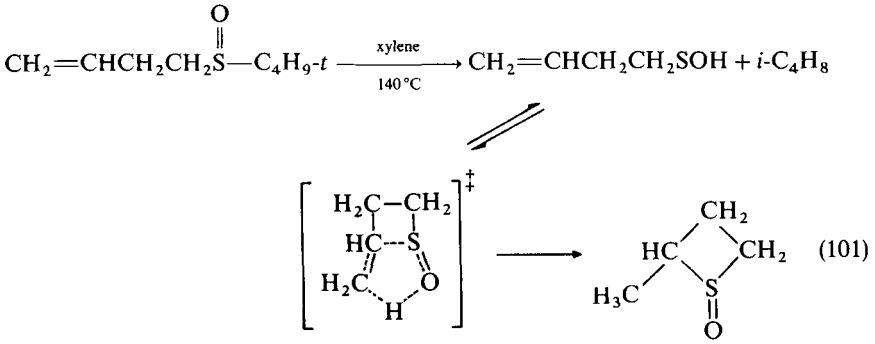
(99)

The thermolyses of sulphoxides in condensed phase, either pure or in solution, have been extensively studied and their mechanisms bear close resemblance to those discussed above. One of the first studies was made by Kingsbury and Cram[106], who thermolysed four diastereomeric 1,2-diphenyl-1-propyl phenyl sulphoxides at 80 and 120 °C in polar solvents. At 80 °C, these reactants undergo stereospecific elimination to yield the isomeric α-methylstilbenes plus phenylsulphenic acid, the product of the *cis*-elimination dominating by factors of 3 to 16 over the product of the *trans*-elimination. The results are consistent with a five-centre cyclic transition state mechanism. At 120 °C, however, a radical pair is formed which disproportionates by H atom transfer to yield predominatly the most thermodynamically stable olefin product. Both processes are presented in reaction 100.



(100)

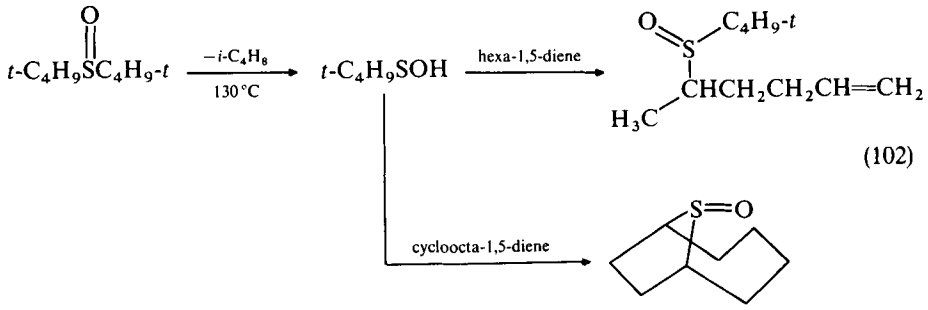
Emerson and coworkers[107] thermolysed a series of unsymmetrical dialkyl sulphoxides at 180 °C. The mechanism postulated involved the loss of a sulphenate moiety with any of the available β-H atoms via a similar cyclic transition state. Jones and coworkers[108] used the thermolyses of *t*-butyl alkenyl sulphoxides at 140 °C to study the regio- and stereospecific cyclization of the alkene-ω-sulphenic acids generated. An example is given in reaction 101.



(101)

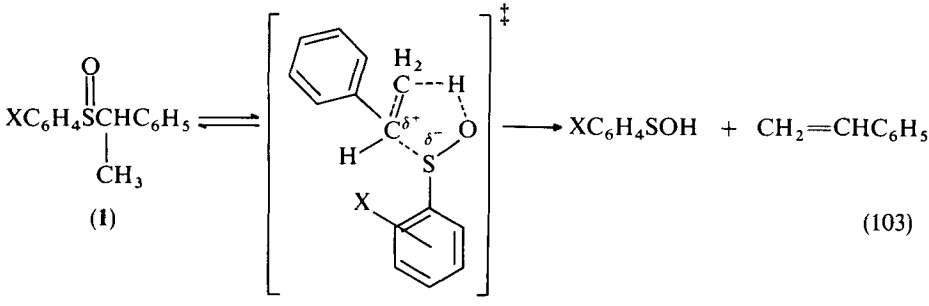
They also studied the intermolecular addition of the alkanesulphenic acids generated in these thermolyses to olefins, to give sulphoxides. For example, 2-methylpropane-2-sulphenic acid, generated by thermolysis of di-*t*-butyl sulphoxide at 130 °C, gave the products shown in reaction 102 in the presence of hexa-1,5-diene and cycloocta-1,5-diene, respectively. Several other examples were given with both linear and cyclic alkenes.

Kwart and coworkers[109] postulated a planar structure for the five-centre cyclic transition state involved in the sulphenic acid plus olefin elimination reaction from sulphoxides with β-H atoms. Such a structure was inferred from the temperature dependence of the kinetic deuterium isotope effect, over the temperature range 130–230°C, in the thermolyses of the protio and 2-deuteriohephyl phenyl sulphoxides in diglyme solution. These reactions gave $[E_a]^D$-$[E_a]^H = 1.15\,\text{kcal mol}^{-1}$ and $A_H/A_D = 0.76$, implying a linear path for the 1,4-H atom transfer in the transition state[110].



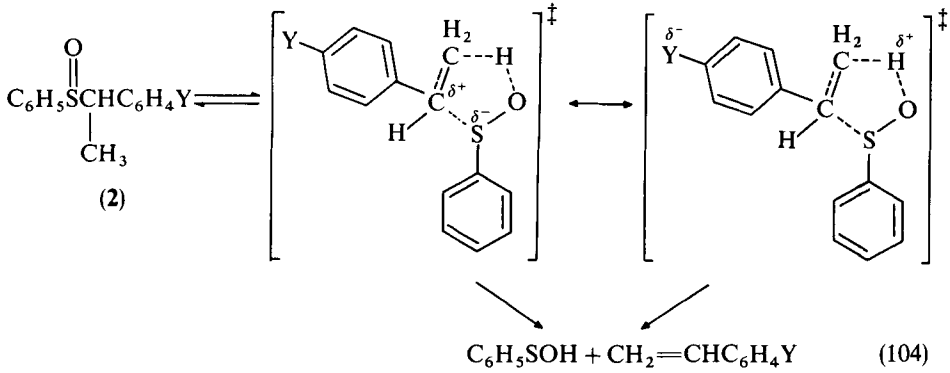
(102)

Yoshimura and coworkers[111] investigated the thermolysis kinetics, at 80–100 °C in dioxane, of *threo*- and *erythro*- $XC_6H_4S(O)CH(CH_3)C_6H_5$ (**1**) and $C_6H_5S(O)CH(CH_3)$-C_6H_4Y (**2**), where X and Y are H, and *p*- or *m*- substituents with either + M or − M effects. The rates for the *erythro* isomers were up to three times larger than those for the corresponding *threo* isomers. The Hammett plots of *threo*-**1** gave positive ρ values; those of the *threo*- and *erythro*-**2** were V-shaped with bottoms at $Y = m\text{-}OCH_3$. Large (4–6) kinetic isotope effects for *threo*- and *erythro*-$C_6H_5S(O)CH(CD_3)C_6H_4Y$ ruled out a radical-pair mechanism. The results suggested that the pyrolyses of these 1-arylethyl aryl sulphoxides proceed by a concerted mechanism, in which the five-centre cyclic transition state varies from an E1-like to a conjugated one. In the latter, conjugation of the phenyl group bearing a − M substituent with the developing π-bond electrons acidifies the β-H atoms. These transition states are represented in reactions 103 and 104.



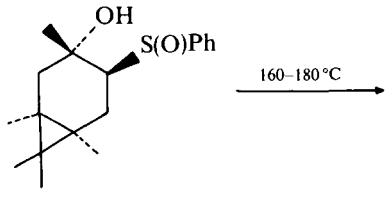
(103)

E1-like

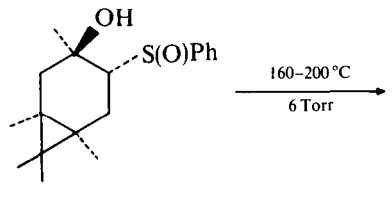


(104)

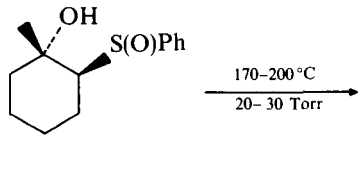
These unimolecular eliminations have been used to obtain synthetically importnt allylic alcohols in good yield. Several examples were given by Mitra and coworkers[112], some of which are shown in reactions 105–108.



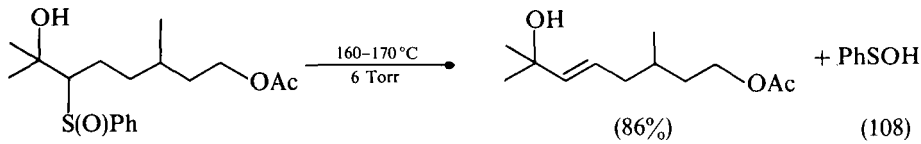
(105)



(106)



(107)



(108)

VI. SULPHONES

Dimethyl sulphone decomposes[113] at temperatures of 510–640 °C and pressures of 0.7 Torr by C—S bond fission, as represented in reactions 109 and 110.

$$CH_3SO_2CH_3 \longrightarrow CH_3SO_2^{\cdot} + CH_3^{\cdot} \tag{109}$$

$$CH_3SO_2^{\cdot} \longrightarrow CH_3^{\cdot} + SO_2 \tag{110}$$

In the presence of toluene as radical scavenger, the Me radicals form methane. Similar mechanisms were reported by the same authors for benzyl methyl sulphone and allyl methyl sulphone, which split benzyl and allyl radicals, respectively. The Arrhenius equation reported for step 109 was

$$k(s^{-1}) = 10^{14.3} \exp[(-60.6\,\text{kcal mol}^{-1})\,(RT)^{-1}]$$

For the similar steps in the latter two sulphones the equations were respectively.

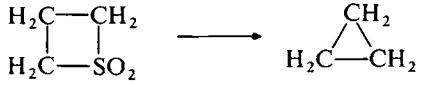
$$k(s^{-1}) = 10^{14.52} \exp[(-51.25\,\text{kcal mol}^{-1})(RT)^{-1}] \text{ and}$$

$$k(s^{-1}) = 10^{14.1} \exp[(-47.7\,\text{kcal mol}^{-1})(RT)^{-1}]$$

From these studies the value $\Delta H_f^0(CH_3SO_2^{\cdot}) = -58.0\,\text{kcal mol}^{-1}$ has been derived[15].

Cornell and Tsang[114] studied the pyrolysis kinetics of trimethylene sulphone and 3-methylsulpholane in a toluene flow system over the temperature range 365–405 °C. At low conversions, trimethylene sulphone decomposes into SO_2, cyclopropane and a trace of propene. At 100% conversion, increasing amounts of propene are formed, although SO_2 and the hydrocarbons are always formed in equal concentrations. The Arrhenius equation obtained for reaction 111 was

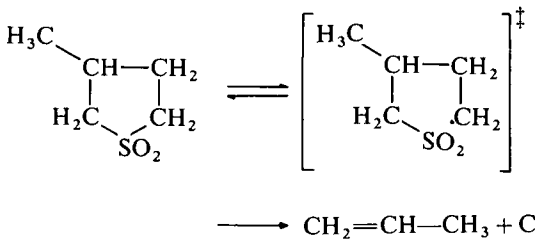
$$k(s^{-1}) = 10^{16.1 \pm 0.3} \exp[(-56 \pm 1\,\text{kcal mol}^{-1})(RT)^{-1}]$$



(111)

From the experimental data, no conclusive mechanism could be proposed for equation 111 since it might take place either through a biradical intermediate or a SO_2 ejection together with cyclopropane formation. 3-Methylsulpholane decomposes according to reaction 112 for which the Arrhenius equation was obtained.

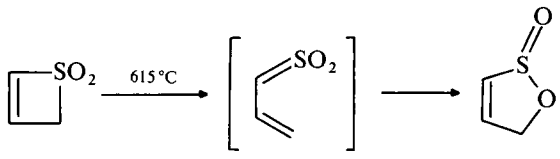
$$k(s^{-1}) = 10^{16.1 \pm 0.4} \exp[(-66 \pm 1\,\text{kcal mol}^{-1})(RT)^{-1}]$$



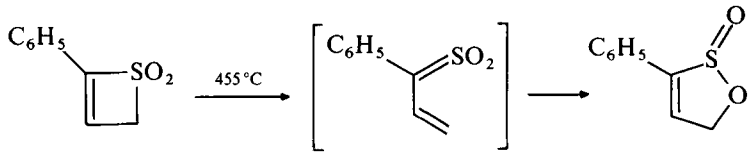
(112)

An initial C—S bond fission, followed by C—C bond cleavage and SO_2 ejection from the biradical, is the likely mechanism for the latter.

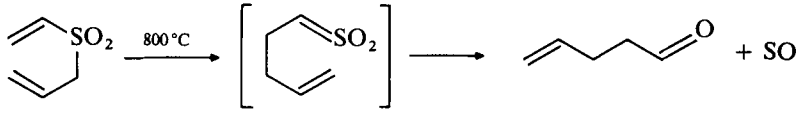
The flash vacuum pyrolyses of cyclic and linear sulphones have been extensively investigated by King, deMayo and coworkers[115–120], who have presented evidence of the formation of sulphenes as reaction intermediates. The thiete-1,1-dioxide rearrangements 113 and 114 have been postulated to occur via the corresponding vinylsulphenes. These authors have given evidence of sulphene intermediacy in reactions 115 and 116. The thietane-1,1-dioxide shown in reaction 117 undergoes SO_2 extrusion whereas the cyclic



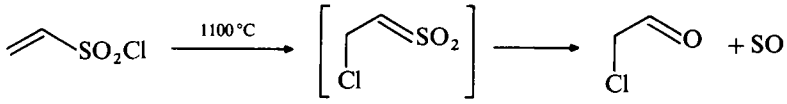
(113)



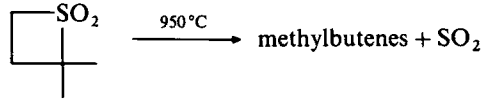
(114)



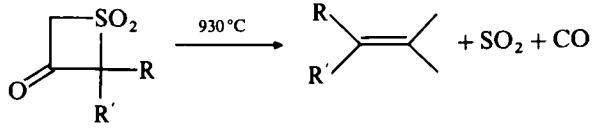
(115)



(116)



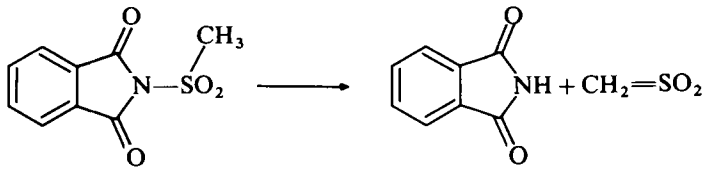
(117)



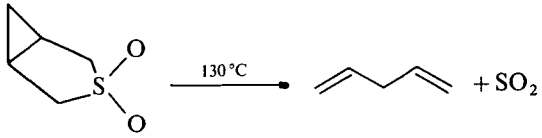
(118)

ketosulphones in reaction 118, in which R = R′ = H, R = R′ = Me and R = H, R′ = C_6H_5, respectively, lose CO and SO_2 quantitatively to give the respective alkenes. Formation of sulphene was also confirmed[121] in the vacuum pyrolysis at 600 °C of *N*-methylsulphonylphthalimide (reaction 119) in 36% yield.

Mock[122] investigated the stereochemistry of the SO_2 and diene formation by means of the pyrolyses of compounds with 3-thiabicyclo[3.1.0]hexane-3,3-dioxide ring system, such as those shown in reactions 120–124. These bicyclic sulphones should be free to adopt the geometries shown in reaction 125. The products formed and the kinetic evidence suggest that reaction 120 is a fully concerted $\sigma^2s + \sigma^2s + \sigma^2s$ process with



(119)



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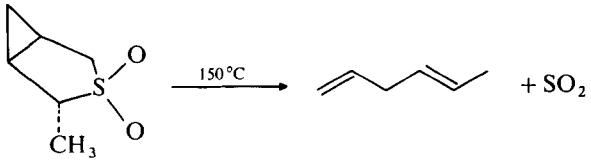
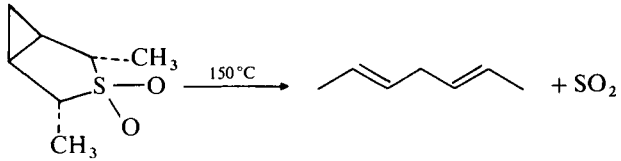
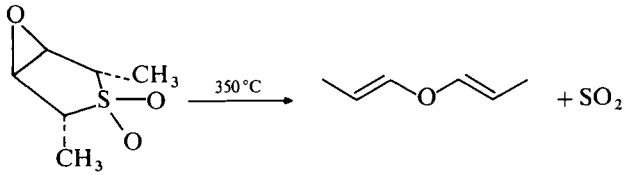


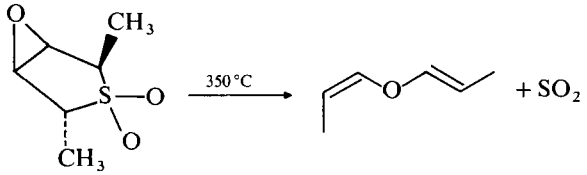
(121)



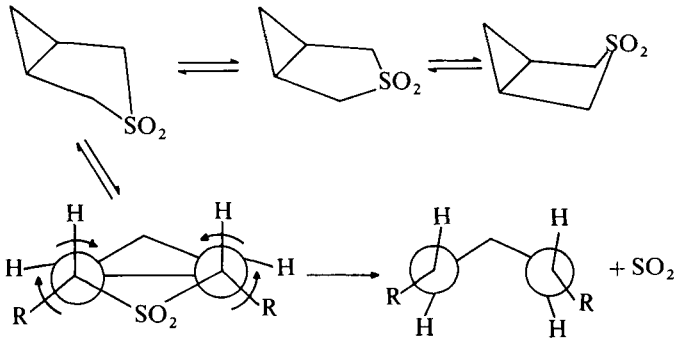
(122)



(123)



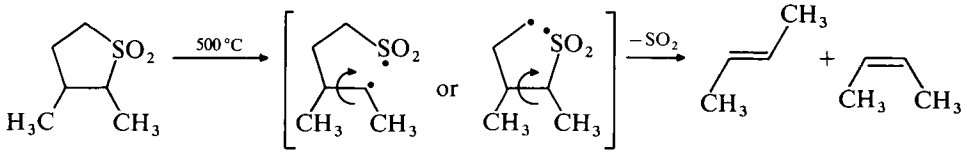
(124)



(125)

synchronous rupture of three σ bonds. Through the preferential disrotatory reaction course shown, the strain energy of the three-membered ring may be coupled to SO_2 departure to produce the observed facile reactions 120–122.

Sulpholanes like that shown in reaction 126[123] pyrolyse at much higher temperatures by a mechanism in which biradical intermediates exist for appreciable lifetimes. Internal rotation within them seems to be competitive with bond scission. Some residual stereospecificity, however, appears to be retained in equation 126 according to the 2-butene isomer distributions.

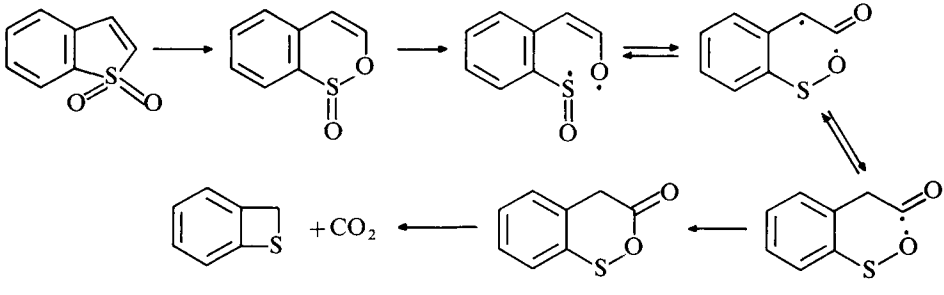


95% *cis* 90% *trans*

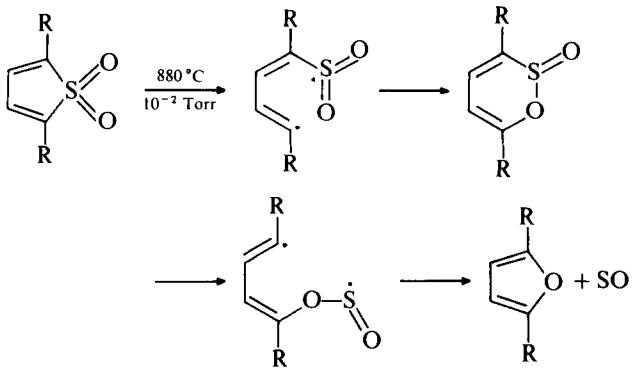
36 ± 6% 53 ± 3%
51 ± 6% 40 ± 3%

(126)

Tilborg and Plomp[124] obtained benzothiete (see reaction 16) by the flash vacuum pyrolysis of benzothiophene-1,1-dioxide at 1000 °C and 0.05 Torr. The mechanism should involve an initial sulphone–sulphinate isomerization, followed by S—O bond fission in the latter to generate a diradical which undergoes a sequence of rearrangements as shown in reaction 127.

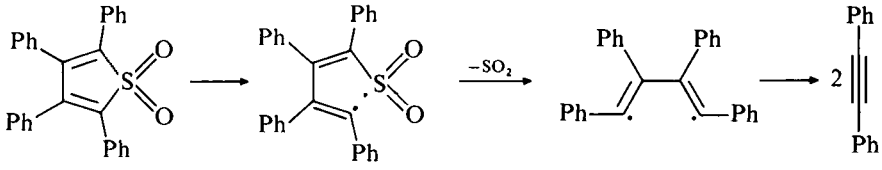


(127)



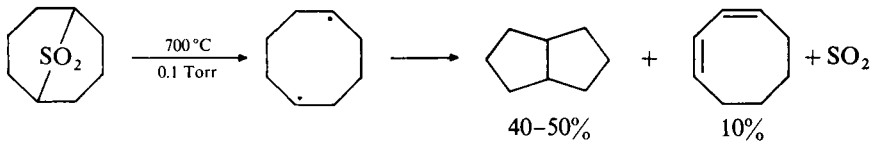
(128)

The flash vacuum pyrolysis of 2,4- and 2,5-alkyl substituted thiophene-1,1-dioxides[125] at 880 °C produces the corresponding alkyl-substituted furanes in over 50% yield. The mechanism similarly involves initial isomerization to the S-sultine (reaction 128) for R = Me, *t*-Bu and Ph. Dibenzothiophene-1,1-dioxide correspondingly forms dibenzofuran at 1000 °C in 89% yield. Tetraphenylthiophene-1,1-dioxide, however, pyrolyses at this temperature to form diphenylacetylene in 75% yield. The mechanism postulated[125] involves the loss of SO_2 and the splitting of the diradical formed into two molecules of the product, as shown in reaction 129.

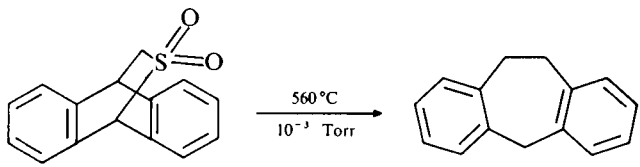


(129)

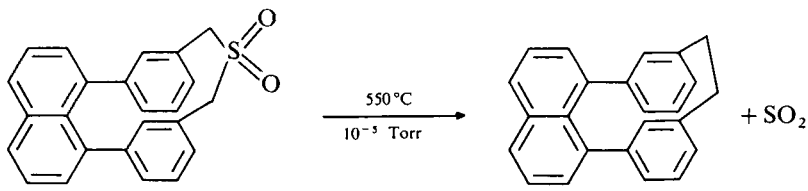
Vögtle and Rossa[126] published an excellent review on sulphone pyrolysis, covering the literature up to 1979, with the main stress on its synthetic application to obtain multi-membered, ring-strained cyclic compounds by SO_2 extrusion. A few of the many examples cited in the said publication are shown next, together with more recently reported work. Reactions 130–135[127–132] correspond to extrusion of a single SO_2 moiety from the respective sulphone.



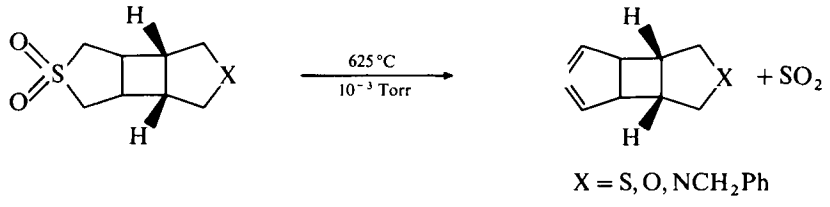
(130)



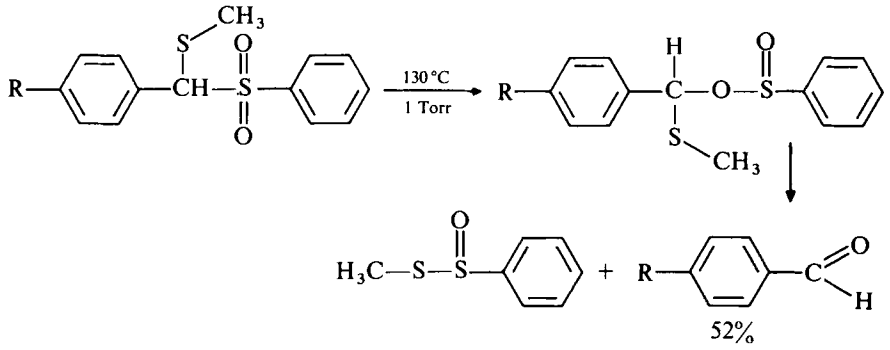
(131)



(132)



(133)



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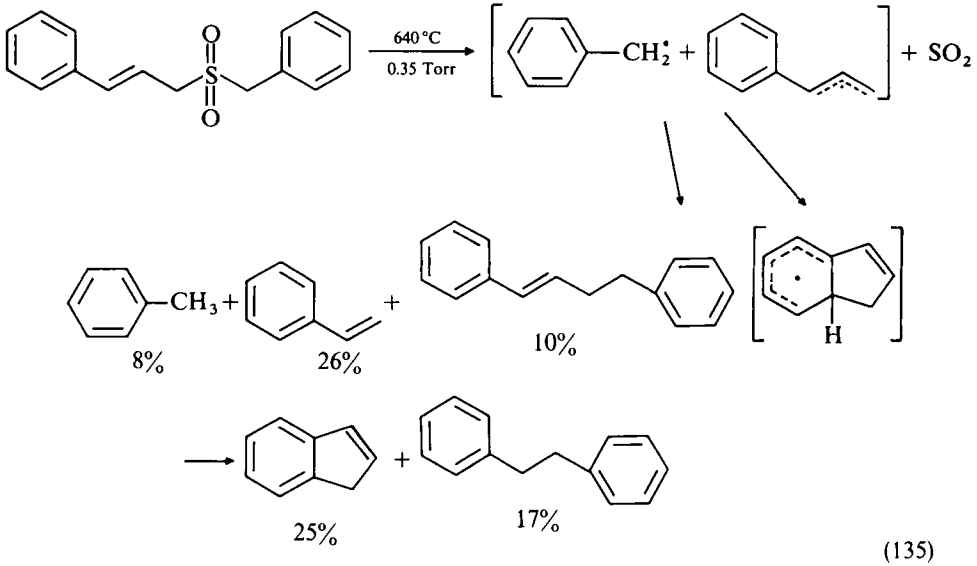
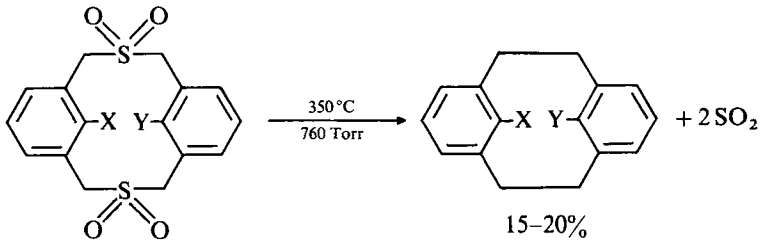


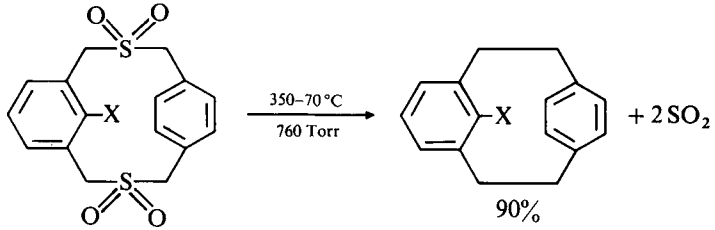
(135)

Double extrusion of SO_2 from cyclic bis-sulphones leads to multi-membered rings as shown in reactions 136–143[133–140].

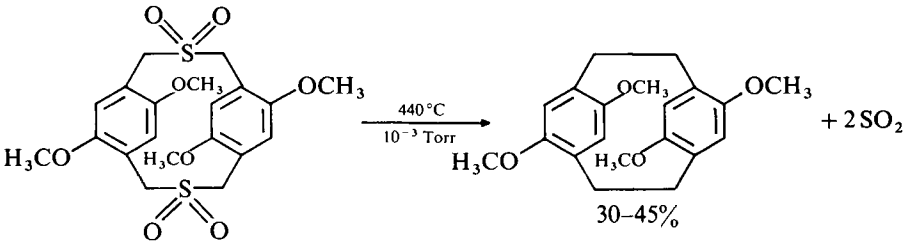
Triple SO_2 extrusion from tris-sulphones has been used to obtain triply-bridged benzophanes, some representative examples being reactions 144–146[141–143].



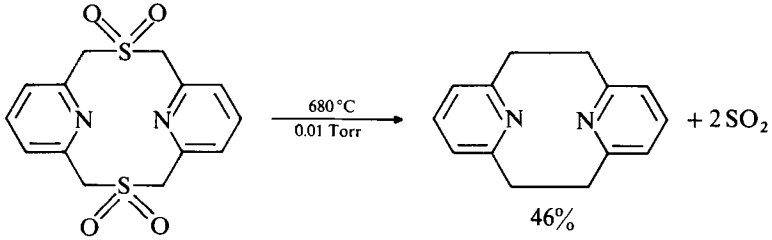
(136)



(137)



(138)



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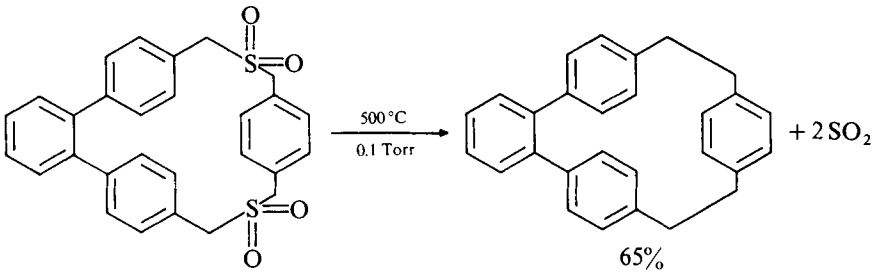
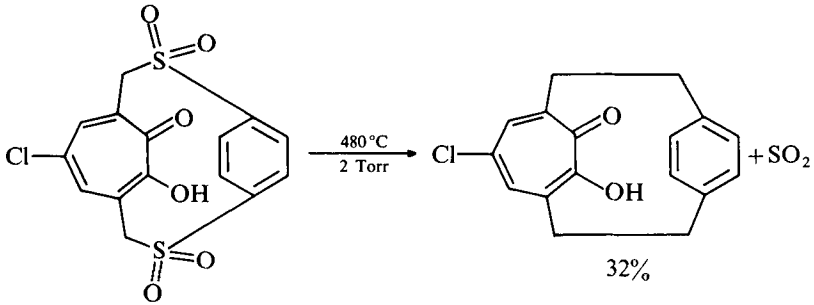
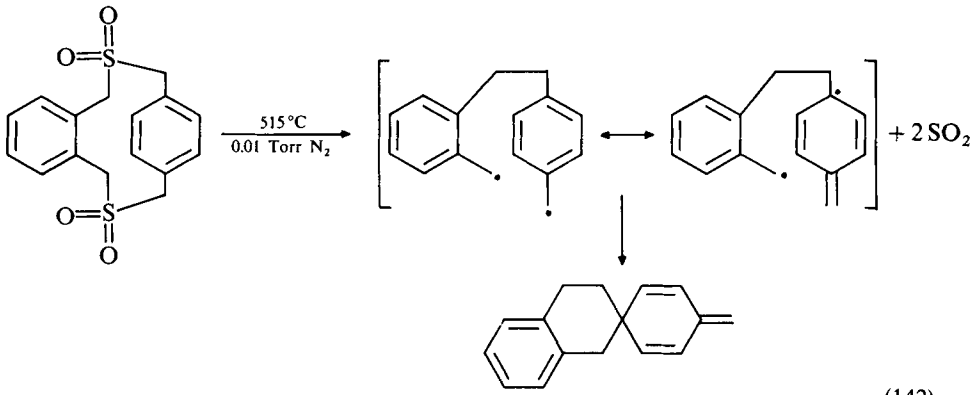


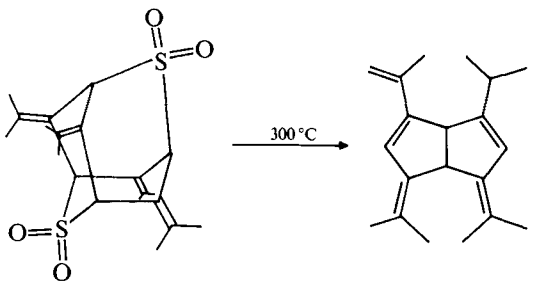
(140)



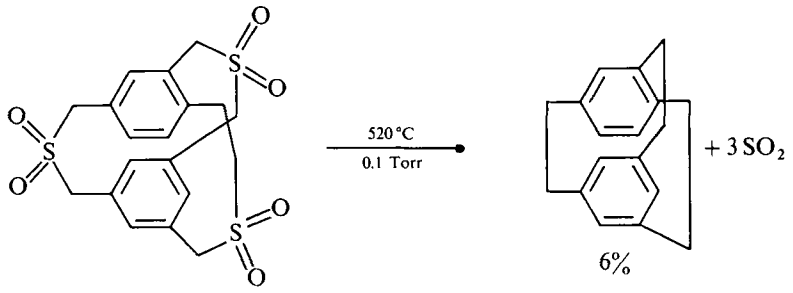
(141)



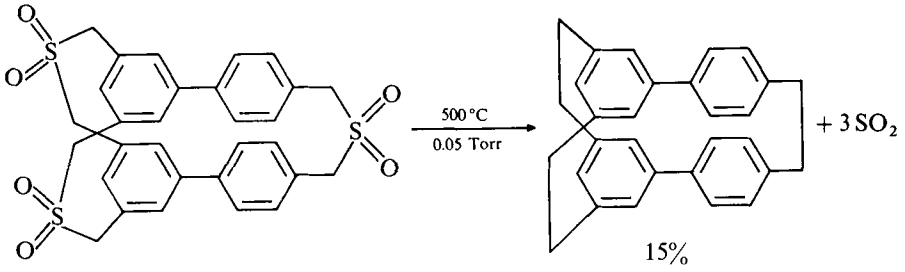
(142)



(143)



(144)



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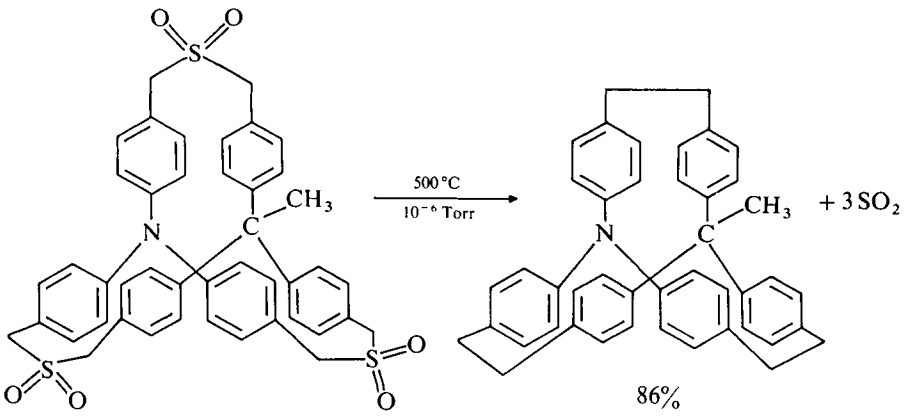
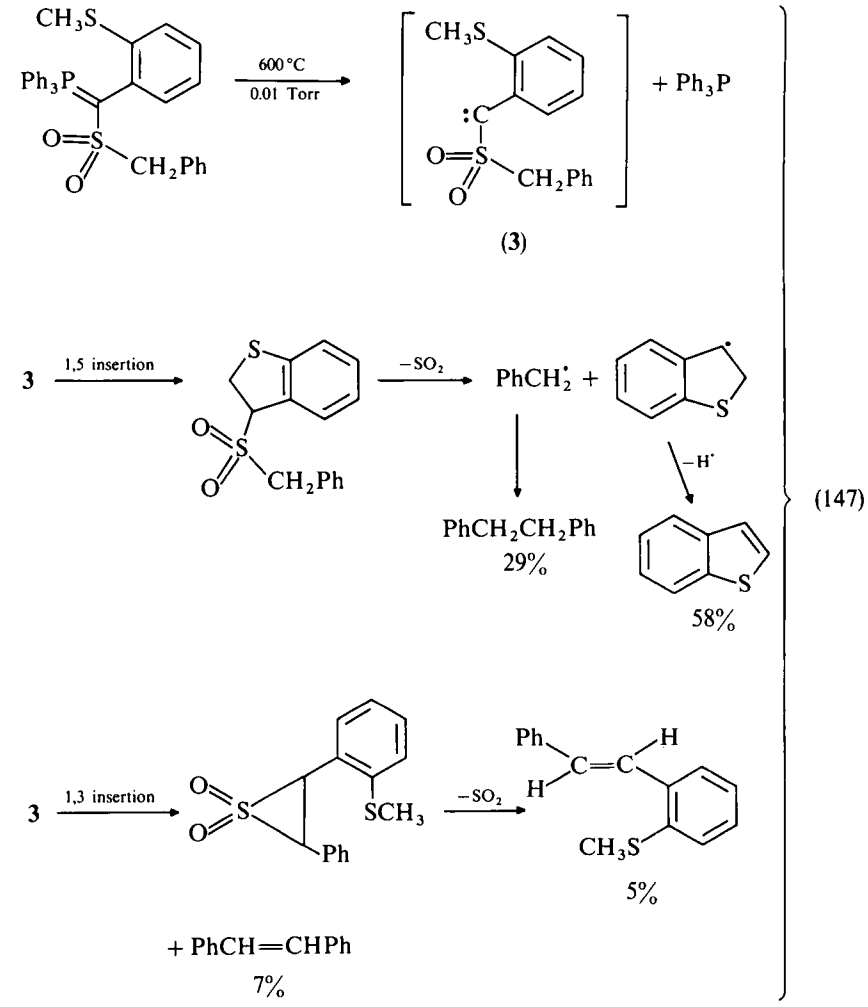
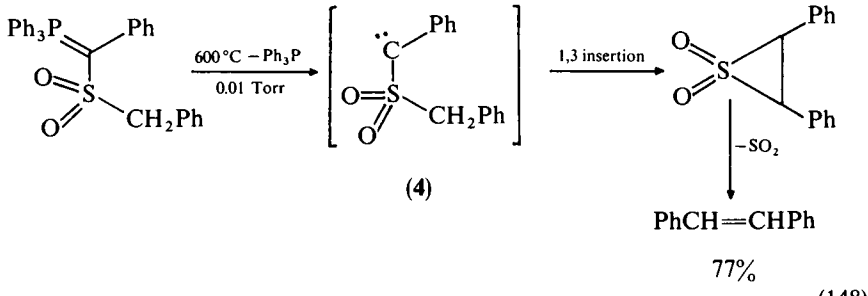
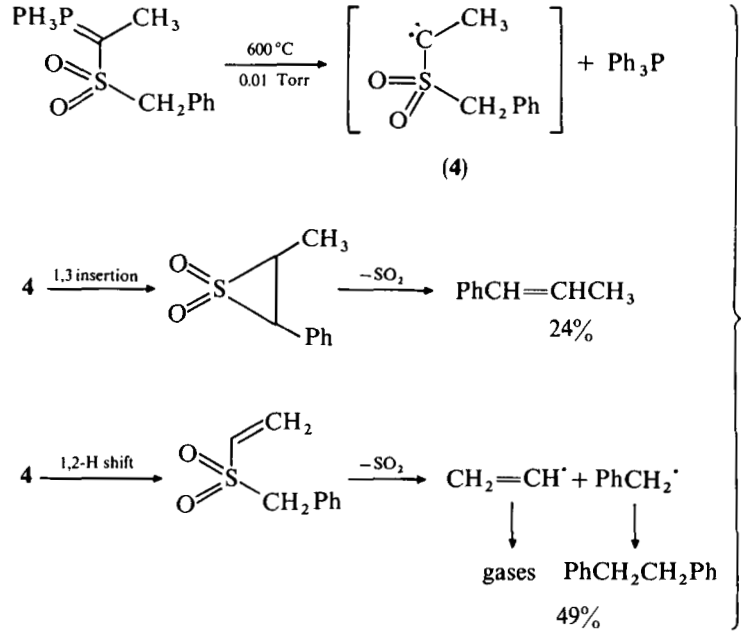


(146)

The flash vacuum pyrolysis of sulphonyl stabilized phosphorus ylides has been reported[144] to occur with loss of triphenylphosphine and SO_2. The postulated mechanism involves the formation of a sulphonyl carbene intermediate, by extrusion of Ph_3P, which may rearrange to a sulphone species. The latter splits SO_2 to give alkenes via radical intermediates. Some examples of these reactions are given in equations 147–149.


CH3S
Ph3P
O=S
O
CH2Ph
600 °C
0.01 Torr
:C
+ Ph3P
(3)
3
1,5 insertion
−SO2
PhCH2•
+
−H•
PhCH2CH2Ph
29%
58%
1,3 insertion
SCH3
Ph
−SO2
H
CH3S
5%
+ PhCH=CHPh
7%
(147)

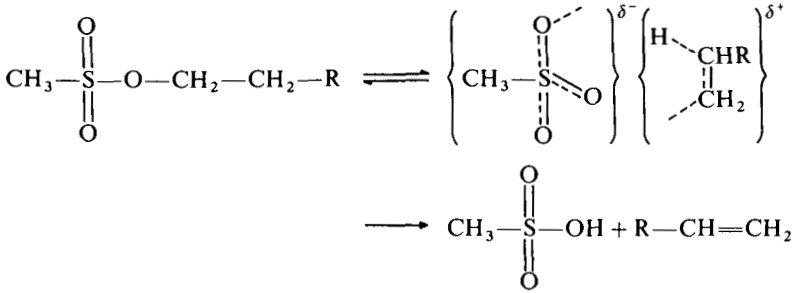

Ph3P
Ph
O=S
O
CH2Ph
600 °C − Ph3P
0.01 Torr
:C
(4)
1,3 insertion
−SO2
PhCH=CHPh
77%
(148)



(149)

VII. SULPHINATES AND SULPHONATES

The pyrolyses of sulphinates and other sulphinic acid derivatives have been recently reviewed in this series[145]. In regard to sulphonate pyrolysis, Chuchani and coworkers[146] have studied the gas-phase elimination kinetics of a series of alkyl and polar 2-substituted ethyl methanesulphonates (Table 6) in a static system and in the presence of the free radical inhibitors propene and toluene. The pyrolyses, examined in the temperature range of 280–360 °C, follow a first-order kinetics according to the stoichiometry presented by reaction 150.



(150)

The log k_{rel} of alkyl substituents versus σ^* values gave an approximate straight line with $\rho^* = -0.823 \pm 0.088$ at 320 °C. However, the Taft plot of the polar substituents listed in Table 6 gives an inflection point of the line at $\sigma^*(CH_3) = 0.00$ into another good

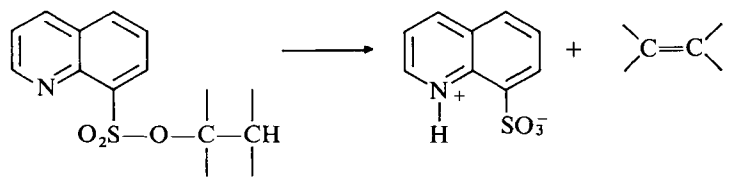
TABLE 6. Kinetic parameters for the pyrolysis of methanesulphonates $RCH_2CH_2OSO_2CH_3$

R	E_a(kcal mol^{-1})	log A	$k_{11} \cdot 10^4$(s^{-1})[a]
H	41.04 ± 0.31	12.18 ± 0.12	3.83
CH_3	41.01 ± 0.79	12.36 ± 0.28	8.89
CH_3CH_2	40.32 ± 0.55	12.16 ± 0.20	9.98
$CH_3CH_2CH_2$	40.49 ± 0.24	12.25 ± 0.09	10.7
$CH_3(CH_2)_3$	40.37 ± 0.79	12.21 ± 0.19	10.7
$(CH_3)_2CH$	41.75 ± 0.53	12.74 ± 0.19	11.2
$CH_3CH_2(CH_3)CH$	40.13 ± 0.45	12.28 ± 0.17	15.4
$(CH_3)_3C$	39.48 ± 0.31	12.14 ± 0.17	19.4
Br	41.30 ± 1.1	11.70 ± 0.43	1.51
Cl	41.56 ± 0.14	11.67 ± 0.50	1.13
CH_3CH_2O	40.00 ± 1.3	11.52 ± 0.52	3.02
$ClCH_2$	41.04 ± 0.62	12.01 ± 0.23	3.85
C_6H_5	39.93 ± 0.62	12.18 ± 0.24	14.4
$C_6H_5CH_2$	40.0 ± 1.0	11.87 ± 0.39	7.09
$C_6H_5CH_2CH_2$	40.37 ± 0.67	12.33 ± 0.26	14.1
CH_3OCH_2	39.03 ± 0.96	11.50 ± 0.36	6.61
$ClCH_2CH_2$	39.70 ± 0.84	11.78 ± 0.31	7.02

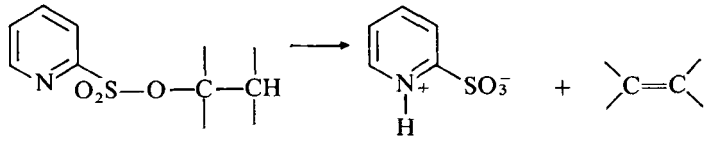
[a]Rate coefficient per β-hydrogen at 320 °C.

straight line with $\rho^* = -2.091 \pm 0.013$ at 320 °C. The result of one slope with electron-releasing alkyl groups and another slope with polar electron-withdrawing groups was thought to be due to a slight alteration in the polarity of the transition state due to changes of electronic transmission at the positive carbon reaction centre. The transition state was considered to be very polar in nature, where the C—O bond polarization, in the sense $C^{\delta+}\cdots O^{\delta-}$, is a determining factor. Because of this, the mechanism was explained in terms of an intimate ion-pair-type intermediate. Neighbouring phenyl participation has been described in gas-phase pyrolysis of ω-phenylalkyl methanesulphonates. The effect of the phenyl groups on the rate of pyrolysis of these substrates is shown in Table 6. The C_6H_5 substituent at the 2- and 4-position of the carbon chain with respect to the C—O bond of the methanesulphonate appeared to participate in the reaction and thus to affect the rate of elimination. In addition to this fact, the five-membered conformation which is a favourable structure for anchimeric assistance yielded to some extent a cyclic product, tetralin. Participation of an aromatic ring at the 3-position does not take place. The mechanism for the anchimeric assistance of the phenyl substituent was explained in terms of a tight ion pair with intramolecular solvation or autosolvation of the leaving CH_3SO_3 group.

The pyrolyses of the esters of 8-quinolinesulphonic acid and 2-pyridinesulphonic acid have been found[147] to produce cleanly high yields of olefin at temperatures of 100–230 °C and pressures of 0.3–27 Torr. The processes, represented by reactions 151 and 152, were

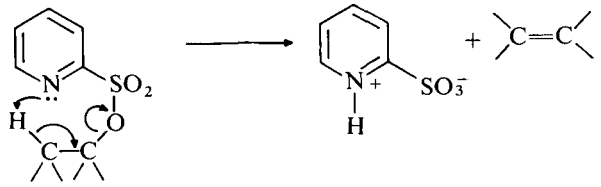


(151)

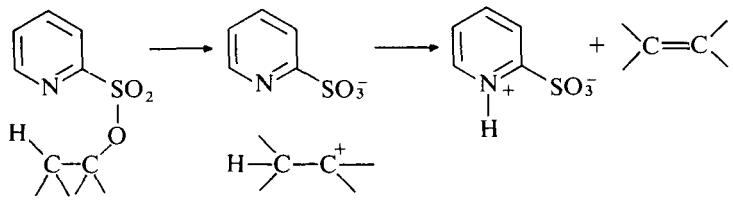


(152)

investigated with up to eight different sulphonates. Two possible mechanisms have been postulated. One would be a concerted elimination (reaction 153) and another one the formation of a carbocation intermediate as in an E1 elimination (reaction 154).

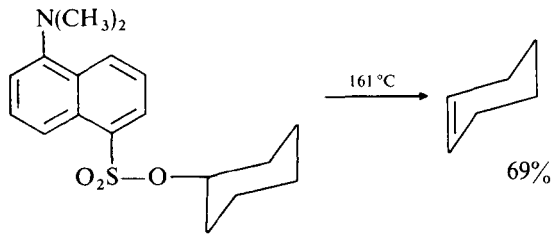


(153)

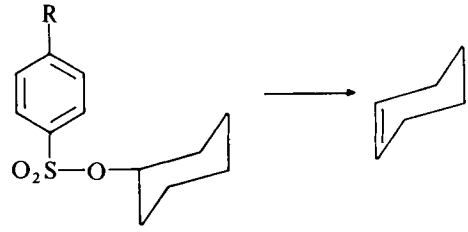


(154)

The pyrolyses of the primary alcohol esters are consistent with the mechanism of equation 154. They require temperatures about 100 °C higher than those for the secondary alcohol esters and produce also rearranged products. The ring nitrogen atom appears to be functioning as a base, since the pyrolyses of substituted benzene and naphthalene sulphonates that contain basic substituents in the ring give good yields of olefins while those without basic substituents give low yields of alkene and tar formation is observed. Some examples of these reactions are given in equations 155 and 156.



(155)

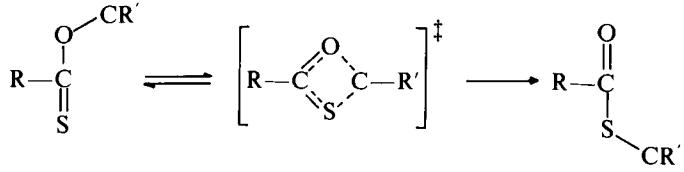


(156)

R	T(°C)	c-C_6H_{10} % Yield
$NHCOCH_3$	135	99
$NHCH_2CH_2CH_3$	175	91
CH_3	150	58
NO_2	100	29

VIII. THIOCARBOXYLIC ACID DERIVATIVES

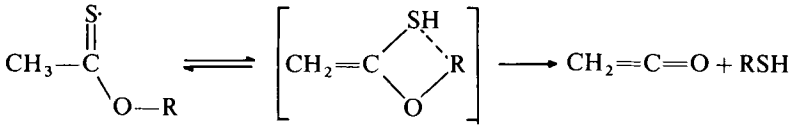
The pyrolyses of thiocarboxylic acid derivatives have been of interest in connection with differences in their mechanism and reactivity compared with their carboxylic acid homologues. The thiono–thiolo isomerization represented by reaction 157 has been studied by Carlsen and coworkers in thioacetates[148], thiocarbamates[149] and thiocarbonates[150] by means of the gas-phase Curie point pyrolysis technique, coupled to field ionization and collision activation mass spectrometry, at temperatures in the range 610–1231°C.



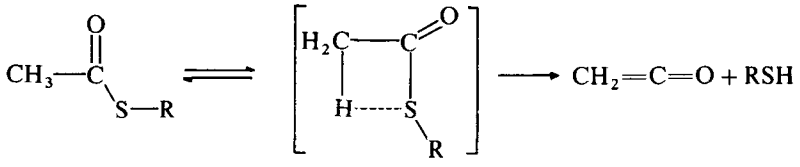
(157)

Such isomerization has been found to be displaced towards the thiolo structure, the driving force being the formation of the C=O bond instead of the much less stable C=S one. The evidence suggests that the reverse reaction does not take place. The methyl and ethyl thiono and thioloacetates pyrolyse at 610–1231 °C to form ketene and thiol almost exclusively without previous thiono–thiolo isomerization[148], as represented in reactions 158 and 159.

Bigley and Gabbott[151] measured the kinetic parameters shown in Table 7 for the thiono–thiolo isomerization of a series of alkyl thion acetates, as well as those for their



(158)



(159)

TABLE 7. Kinetic parameters for the isomerization of thionacetates $ROC(S)CH_3 \rightarrow RSC(O)CH_3$

R	E_a[a]	log A	$\Delta S^{\ddagger}$[b]	k_{rel}[c]
CH_3	45.8	12.9	−3.1	0.52
CH_3CH_2	45.3	12.7	−2.7	1
$CH_3(CH_2)_3$	41.5	11.9	−7.6	1.6
$(CH_3)_3C$	40.9	11.4	−8.9	1.4

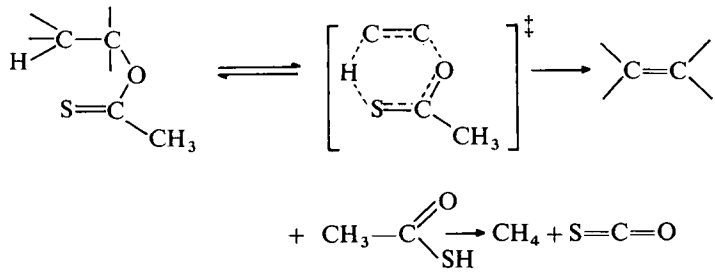
[a] kcal mol^{-1}.
[b] cal K^{-1} mol^{-1}.
[c] At 356 °C.

TABLE 8. Kinetic parameters for the pyrolysis of thionacetates $ROC(S)CH_3$

R	E_a[a]	log A	$\Delta S^{\ddagger}$[b]	k_{rel}[c]	k_{rel}[d]
CH_3CH_2	47.7	14.3	+4.7	1	138
$CH_3(CH_2)_3$	40.5	12.4	−5.2	1.88	132
$(CH_3)_2CH_2CH_2$	41.6	12.5	−4.6	1.13	438
$(CH_3)_2CH$	37.9	12.9	−3.0	44.5	218
$CH_3CH_2CH(CH_3)$	36.2	12.4	−5.1	63.7	562

[a] kcal mol^{-1}.
[b] cal K^{-1} mol^{-1}.
[c] At 356 °C.
[d] k(thionacetate):k(acetate) at 356 °C; activation parameters for acetates were the preferred values from Reference 15.

decomposition according to reaction 160 (Table 8) in a flow system at temperatures of 270–380 °C and pressures of 200–700 Torr. The thiolacetates are thermally more stable than the thionacetates and the latter decompose 130–560 times faster than the corresponding acetates. The negative $\Delta S^{\ddagger}$ values suggest the six-centre cyclic transition state, similar to the one proposed for the acetates, shown in equation 160.



(160)

TABLE 9. Kinetic parameters for the pyrolysis of thiolacetates $RSC(O)CH_3$

R	E_a[a]	log A	$\Delta S^{\ddagger}$[b]	k_{rel}[c]	T range (°C)	Reference
$CH_3(CH_2)_3$	46.5 ± 0.9	11.6	−10.5	6.4	507–537	152
$(CH_3)_2CHCH_2$	49.0 ± 1.5	11.8	−8.4	5.4	517–552	152
$CH_3CH_2(CH_3)CH$	44.0 ± 1.2	11.7	−8.8	8.5	441–470	152
$(CH_3)_3C$	41.6 ± 0.4	12.2	−6.2	55	377–407	152
$CH_3OCH(CH_3)$	39.6	13.0	−2.5	—	311–358	153
$CH_3SCH(CH_3)$	45.8	13.3	−1.1	—	367–425	153
$ClCH_2CH(OCH_3)$	44.0	13.3	−1.1	—	340–420	154

[a] kcal mol^{-1}.
[b] cal K^{-1} mol^{-1} at 356 °C.
[c] k(acetate):k(thiolacetate) at 356 °C.

TABLE 10. Kinetic parameters for the pyrolysis of dithioacetates CH_3CS_2R

R	$\Delta H^{\ddagger}$[a]	$\Delta S^{\ddagger}$[b]	E_a[c]	log A[d]	k_{rel}[e]
CH_3CH_2	43.9	−2.7	42.6	12.9	1
$CH_3(CH_2)_3$	43.4	−2.2	42.1	13.1	1.8
$CH_3CH_3(CH_3)CH$	38.9	−3.3	37.6	12.8	41
$(CH_3)_3C$	37.7	−2.4	36.4	13.0	172

[a] Enthalpy of activation, kcal mol^{-1}.
[b] cal K^{-1} mol^{-1}.
[c] $\Delta H^{\ddagger}$—R × 0.629.
[d] Calculated from $\Delta S^{\ddagger}$ at 356 °C.
[e] At 356 °C.

Tables 9 and 10 show the activation parameters for the pyrolyses of thiolacetates[152–154] and dithioacetates[155]. These are homogeneous, first-order reactions which occur via six-centre transition state mechanisms similar to equation 160. In the case of the dithioacetates, besides the alkene product, dithioacetic acid is produced and further decomposes into methane and carbon disulphide. The alkyl acetates are more reactive than the homologue thiolacetates while the dithioacetates are more reactive than their respective homologue acetates, thiolacetates and thionacetates.

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CHAPTER 10

Electrochemical behavior of organic molecules containing sulfur

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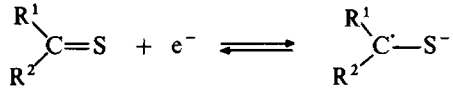
I. THIONES

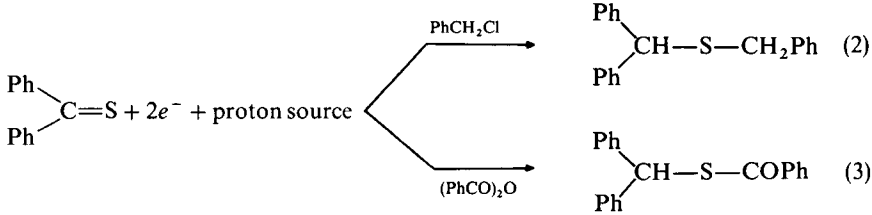
A. Cathodic Reduction

In general, it may be assumed that thiocarbonyl compounds are easier to reduce than the corresponding carbonyl structures. However, examples concerning aliphatic and aromatic thiones are not numerous owing to the limited stability of thiones in organic solution. In order to illustrate the difference in cathodic reactivity, Figure 1 shows voltammetries under the same experimental conditions of both thiobenzophenone and the parent ketone in a nonaqueous solvent. In the case where both R^1 and R^2 are aromatic it is possible to visualize[1] the formation of relatively stable anion radicals and then to have access to standard potentials values.



(1)

Such anion radicals may play the role of a nucleophile or/and a reducing species toward alkyl halides[1,2], tosylates[2] and acetyl chloride[1]. In this manner, thiobenzophenone was cathodically converted in the presence of benzyl chloride and benzoic anhydride to afford the corresponding products in 80% and 53% yield, respectively:



(2)

(3)

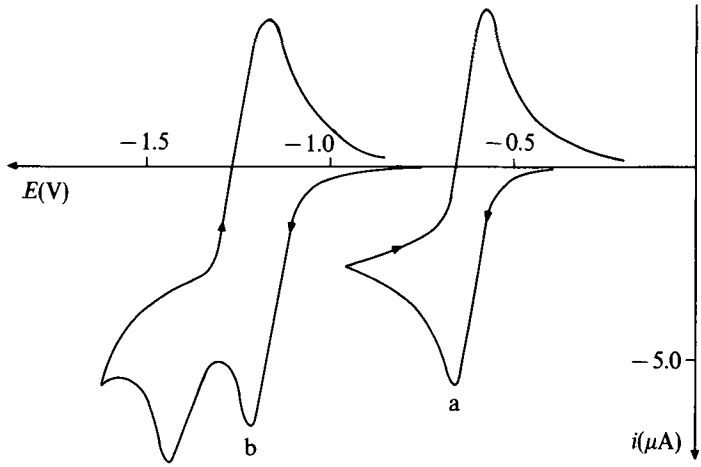
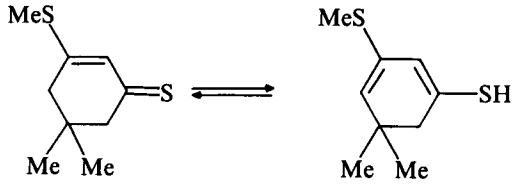


FIGURE 1. Comparison between the voltammetric responses of thiobenzophenone (curve a) and benzophenone (curve b) at a platinum stationary microcathode in DMF containing tetraethylammonium perchlorate 0.1 M. Substrate concentrations: 3×10^{-3} M. Sweep rate: 0.1 V s^{-1}. Reference system: Ag/AgI/I^- 0.1 M

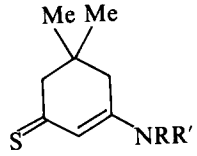
On the other hand, thiocamphor, which could be considered as a representative example among aliphatic thiones, exhibits in DMF a one-electron reversible step located at -1.38 V vs reference Ag/AgI/I^- 0.1 M. The gain in potential when compared to the reduction of relevant ketones is of the order of 0.9 volt.

The electronic reactivity of such anion radicals when reduced in the presence of primary alkyl halides was discussed on the basis of the obtained alkylated products. α,β-Unsaturated thio compounds such as **1** were also investigated polarographically[3] in protic solutions. Thus, it was shown that the protonated form of the unsaturated thione (when the study was carried out in an acidic solvent) yields, by means of electron transfer, a free radical which dimerizes. It was postulated that the tautomeric form **2** is the



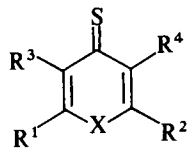
(1) **(2)**

electroactive one in alkaline media. Polarographic data on the oxidation of **1** are also available. Electrochemical properties of other unsaturated thiones such as **3**—determined by means of polarography—were also carried out. Electrochemical investigations[5] concerning 3-heterosubstituted 2-cyclohexene-1-thiones are available.



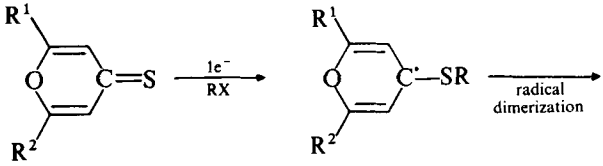
(3)

The cathodic coupling of heterocyclic activated thioketones such as 4*H*-pyran 4-thiones 4(X = O) was achieved[6,7] in nonaqueous media and allows the formation, sometimes in good or even high yields (45–90%), of π-donors such as bipyranylidenes. The reaction

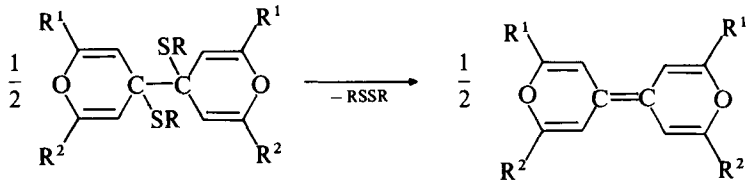


(4)

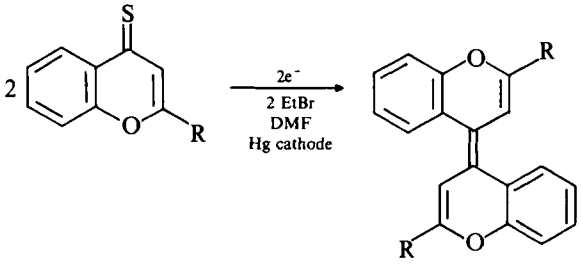
has to be conducted in the presence of an electrophile (e.g. in protic media or with primary alkyl halides) in order to allow anion radicals of **4** to react and lead more rapidly to a C—C bond formation. For example, in the presence of an electrophile RX (like EtBr) at a moderate concentration, the coupling of 4(X = O, $R^3 = R^4 = H$) may be formulated as follows:



(4)

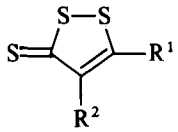


The ability of the electrochemical process to form π-donors can be easily checked analytically as demonstrated in Figure 2. Thus the two reversible steps of bipyranylidene can be observed easily within a sufficiently broad potential range. Such a coupling reaction was shown to be rather general (e.g. feasible with $R^1 = R^2 =$ thiophenyl). Thiocoumarines (R = H, Et or Ph) can be converted in one step into the corresponding π-donor dimers in reasonably good yields.



(yield: 40% with R = Ph)

Such a coupling reaction of activated thiones was shown[8] to be achievable with **4**, X = S and NR, however with lower yields. A series of 1,2-dithiole-3-thiones **5** possessing pharmaceutical interest were—and continue to be—frequently studied[9–15] in electrochemistry. Many papers deal both with analytical determinations and/or cathodic transformations of **5**. The cathodic behavior depends strongly on the nature of R^1 and R^2 substituents. Thus, OLTIPRAZ^R [4-methyl-5-(2-pyrazinyl)-1,2-dithiole-3-thione] leads after a four-electron reduction[9], to several metabolites, the transient species of which could endow the starting compound with its schistosomicidal activity. Generally speaking, when R^1 and R^2 are not directly involved in the reduction process, a first



(5)

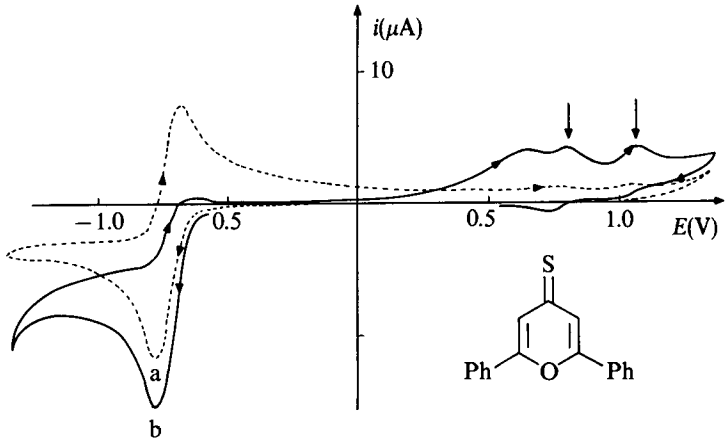


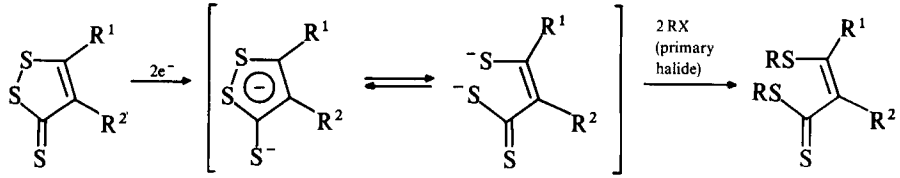
FIGURE 2. Typical cyclic voltammetry of 4-H-pyranthione (concentration: 3×10^{-3} M) in DMF/Bu_4NBF_4 0.1 M. Platinum microelectrode. Sweep rate: 0.2 V s^{-1}. Reference: Ag/AgI/I^- 0.1 M. Curve (a), thione alone; curve (b), after addition of an electrophile, e.g. phenol (2×10^{-2} M), as a proton donor. The two arrows show the appearance of the corresponding bipyranylidene during the reverse sweep (starting potential: −0.5 V)[7]

two-electron process affords the scission[12] of the S—S linkage. The open dianion can be readily[10] alkylated by common electrophiles RX (Scheme 1). On the other hand, the cathodic behavior was demonstrated to be more complex in cases when R^1 possesses some nucleophilic properties (e.g. with R^1 = 2-pyridyl—see Scheme 2—indolizine ring formation[11] is observed).

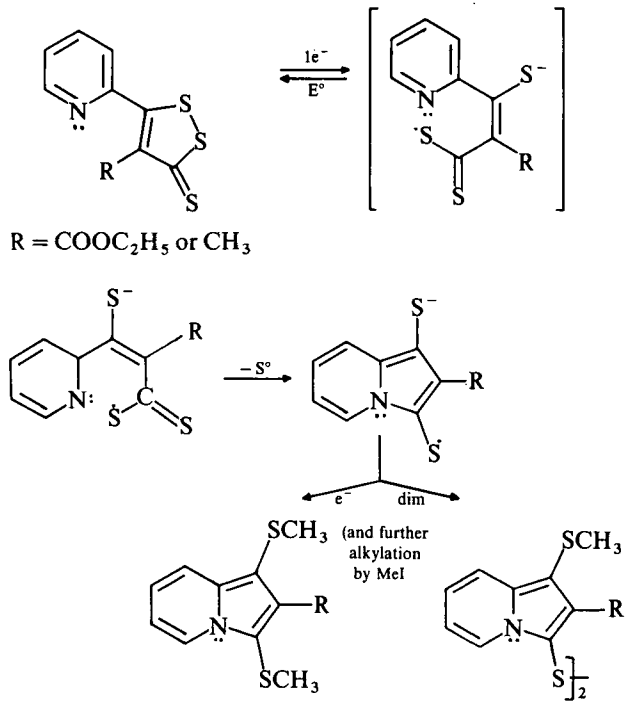
However, the nucleophilicity of the R^1 group towards the thione function (presumably activated at the stage of the anion radical as claimed[9] by Fleury's group) does not lead always to a loss of sulfur. As a matter of fact, when R^1 = 5-pyrimidinyl and R^2 = Me, electrolysis products of **5** can be methylated by MeI once the reduction is completed. In this manner, the fate of the electrochemically formed dianion is more satisfactorily explained (see Scheme 3).

Thiourea and related compounds like thioamides were studied polarographically in alcoholic buffered media. For example, benzotriazepine **6** leads cathodically[14] to a ring contraction affording the corresponding quinazoline **7**.

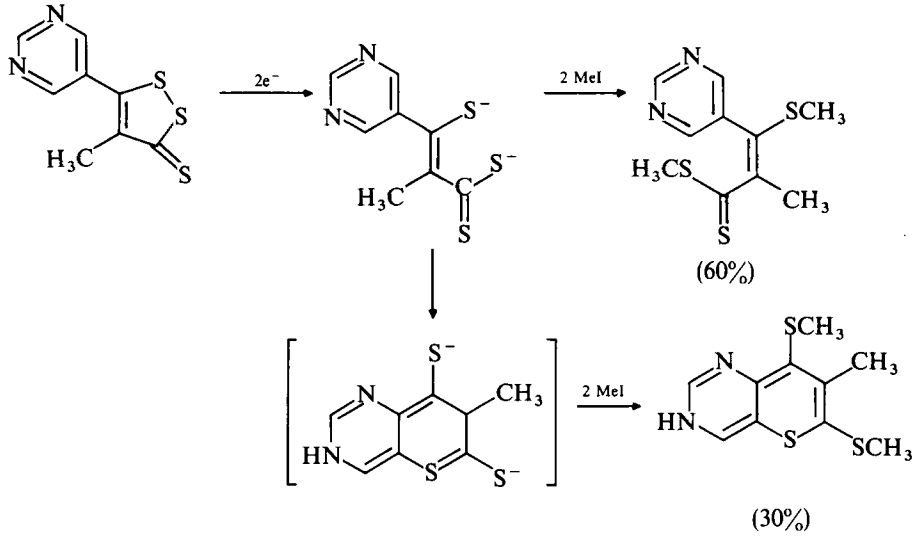
In nonaqueous solvents (DMF or acetonitrile), it is often postulated that the thione group is mainly involved in the two first charge transfers: substituted isothiazole-3-



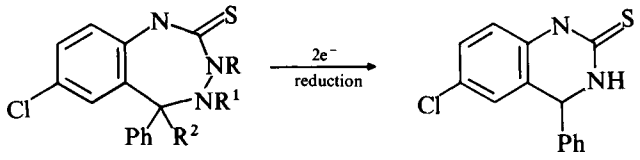
SCHEME 1



SCHEME 2

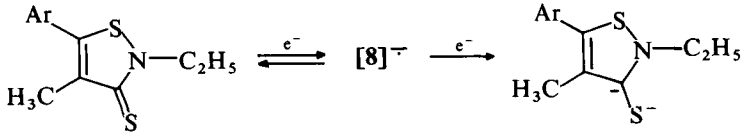


SCHEME 3



(6) (7)

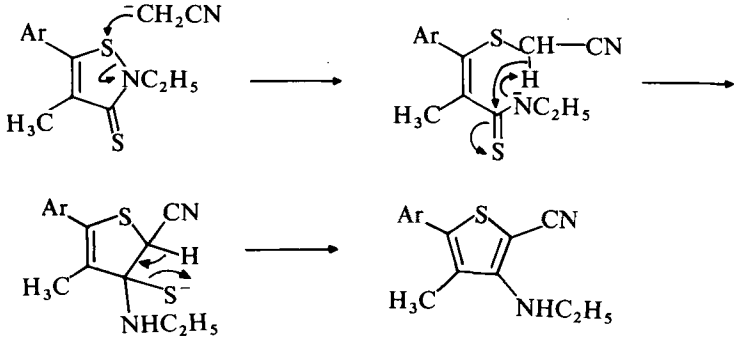
thiones **8** may thus furnish an example[15] of two successive electron transfers leading to the corresponding dianion.



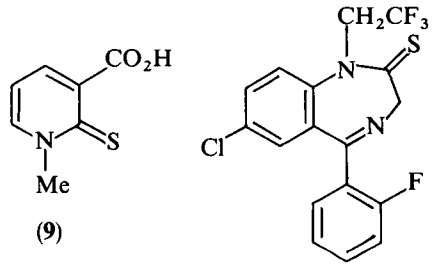
(8)

However, in the absence of an efficient proton source, acetonitrile may react slowly via its conjugated base $NCCH_2^-$ with the starting compound. The thione function then plays the role of an electrophilic center and further expels an HS^- anion. It is noteworthy that such reactions should be the source of many side products when there is no proton availability in the catholyte (Scheme 4).

The formation of such substituted thiophenes was mentioned in the cases where Ar



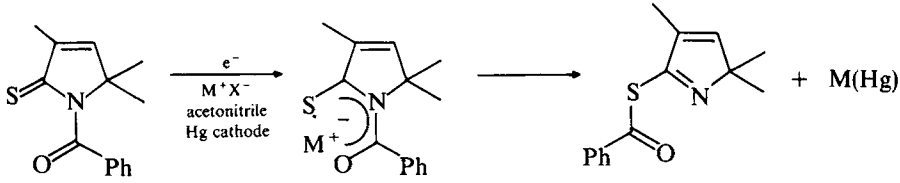
SCHEME 4



(9) (10)

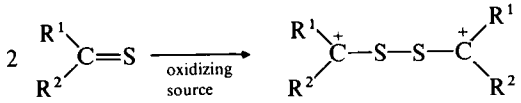
is pyrazin-2-yl or pyrimidin-5-yl. Lastly, cathodic reduction steps were observed[16] for thioamide-type compounds like **9** and for thiolactams[17] such as **10**.

The electrochemical reduction of 3-imidazolin-5-thiones in an electrolyte containing acetonitrile shows a rather unexpected migration of the electron-rich group from the nitrogen to the sulfur under electron transfer. Although this was not *stricto sensu* demonstrated by the authors[22], the process should occur under electron catalysis.



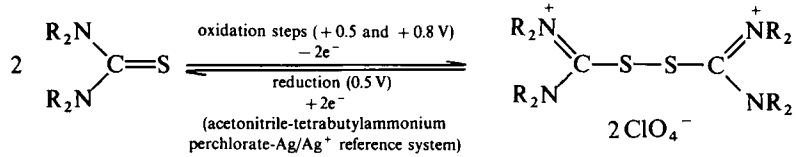
B. Oxidation

The activity of thiocarbonyl derivatives toward classical oxidants, especially nitrous acid, is now well established. Chemical oxidation of thioureas[18], thiocarbonates[19] and thiocarbamates[20] produces transient dimeric dications possessing a disulfur bridge (equation 4). Thus, the anodic behavior of those thiocarbonyl derivatives (tested in

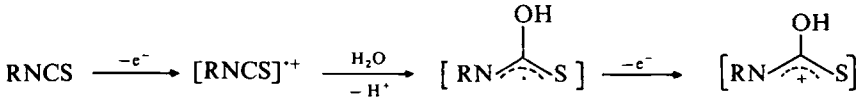


(4)

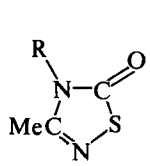
poorly nucleophilic electrolytes) including aromatic thioketones does confirm[21] the formation of such dicationic dimers. The reader's attention may be called to the reversible oxidation of thioureas demonstrated in cyclic voltammetry by studying the cathodic response of the anodically produced salt:



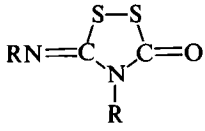
The anodic oxidation of alkyl isothiocyanates RNCS was rationalized[22] by Scheme 5 involving the formation of two possible transients (a free radical and the corresponding highly reactive cation in wet acetonitrile). The anodic behavior of RNCS appears to be strongly dependent on the nature of R. Thus, the exclusive formation of five-membered heterocyclic compounds as shown in structures **11**–**13** involves the reaction of transients



SCHEME 5



(11)



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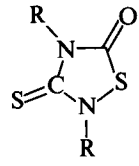
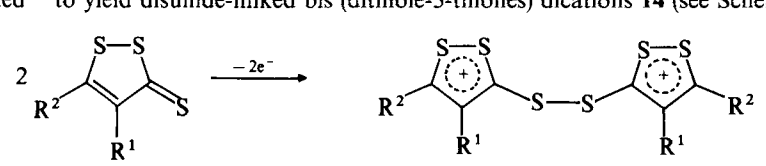


(13)

either with the starting product or with the nucleophilic solvent (e.g. acetonitrile renders possible the production of **11**). On the other hand, when R is a tertiary group (e.g. 1-adamantyl) the nitrogen bond scission (NCS$^{\cdot}$ being considered as the leaving radical) can be achieved[23] presumably at the stage of the radical cation. Since chloro and dichloro derivatives of adamantane were obtained as main products in dichloromethane as solvent, it was admitted that anodic solvent degradation could occur concomitantly with the oxidation of the isothiocyanate. However, a badly controlled diffusion of chloride ions obtained by cathodic degradation of methylene chloride through the separator could also satisfactorily explain the formation of such chlorinated products.

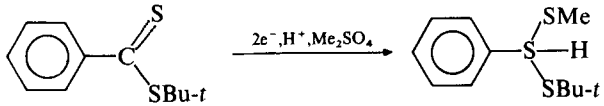
The anodic oxidation of 1,2-dithiole-3-thiones (R^1 and R^2 equal to H and phenyl) was reported[29] to yield disulfide-linked bis (dithiole-3-thiones) dications **14** (see Scheme 6).



(14)

SCHEME 6

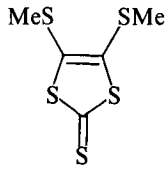
Thioesters and dithioesters are readily[26] reduced at a mercury cathode. In the presence of electrophiles[27] (primary alkyl halides, dimethyl sulfate) alkylated compounds may be formed in the following manner:



Benzenecarbodithio esters and carbothio-*S*-esters were shown to yield diphenylacetylene in aprotic media. The process was demonstrated[26] to go through coupling products, where the starting ester anion radical yields *Z* and/or *E* unsaturated didithioesters (namely 1,2-diphenyl-1,2-di(thiobenzylthio)ethylene), which in turn undergo a reductive elimination. Thus, the formation of diphenylacetylene involves four molecules of substrate. The cathodic reactivity of thioamides involving a similar alkylation of the C=S function in the presence of primary alkyl halides, was also reviewed[28] in the case of *N*,*N*-disubstituted derivatives.

C. Reduction of Carbon Disulfide

The electrochemical reduction of CS_2 under well-defined conditions (nonaqueous electrolytes such as DMF or acetonitrile) allowed the preparation[24] of several thiosubstituted derivatives of tetrathiafulvalene (formation *in situ* of C_6S_8 species).



(15)

Contrarywise, compound **15** was prepared[25] also (presumably using a methylation source) from CS_2 when the electrolyte is a chloride salt.

II. ORGANIC SULFIDES

A. Reduction

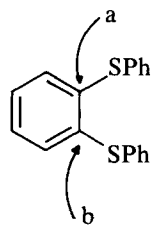
Dialkyl sulfides RSR′ are known[30] to be electrochemically inactive, probably because the level of their LUMO is too low in the absence of activation to permit any electron transfer. On the contrary, aryl sulfides ArSR and, even more, diaryl sulfides ArSAr in general exhibit[31] an irreversible two-electron cathodic step at fairly reductive potentials. As a matter of fact, diphenyl sulfide was reported to be polarographically reduced in DMF at a potential of $E_{1/2} = -2.549$ V with a Ag/Ag^+ electrode system while phenyl methyl sulfide, still under the same conditions, gave a wave at $E_{1/2} = -2.751$ V. Such negative potential ranges necessary to observe the reduction step of weakly activated organic sulfides (when Ar does not possess strongly electron-withdrawing groups) forbid in principle the use of acidic or protic organic solvents even when mercury, well known to exhibit a strong overvoltage to hydrogen evolution, is chosen as cathode material. It may be expected that the first electron transfer corresponds mostly to a $\pi \rightarrow \pi^*$ like transition, in principle reversible. The anion radical transient is readily cleaved. The free radical R$^\cdot$, owing the low potential necessary to its formation, is reduced rapidly.

$$ArSR \xrightarrow{e^-} ArSR^{\cdot -} \xrightarrow{k_c} ArS^- + R^\cdot \quad (5)$$

$$R^\cdot + ArSR^{\cdot -} \xrightarrow{\text{fast}} R^- + ArSR \quad (6)$$

$$R^- + \text{proton source} \longrightarrow RH \quad (7)$$

However, it is quite surprising that no quantitative study on the kinetics and mode of cathodic cleavage exists for the moment. Nevertheless, k_c values are probably very high when weakly activated ArSR compounds are considered.



(16)

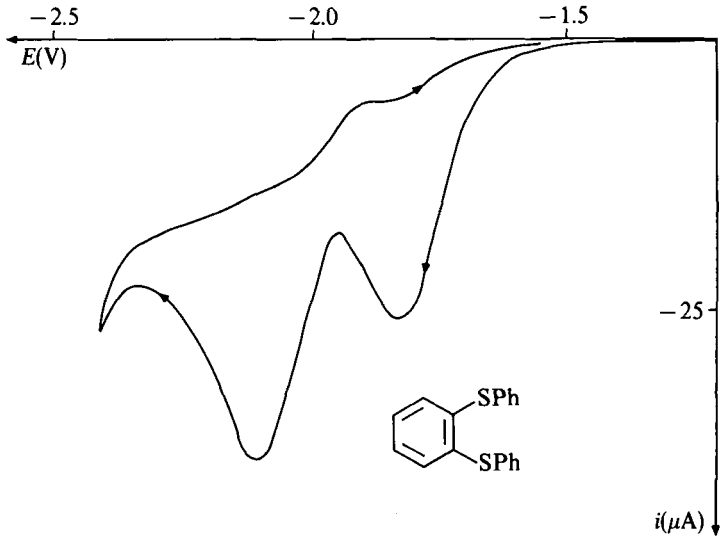
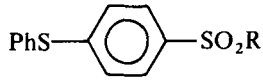


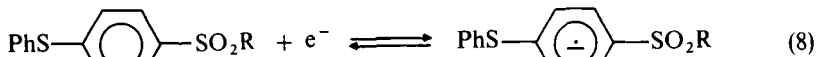
FIGURE 3. Typical cathodic response in voltammetry of an aromatic *ortho* disulfide (concentration: 3×10^{-3} M). Mercury microelectrode. Electrolyte: DMF + tetrabutylammonium tetrafluoroborate 0.1 M. Sweep rate: $0.2\,V\,s^{-1}$. Reference: Ag/AgI/I^- 0.1 M

In order to exemplify this kind of cathodic cleavage, Figure 3 exhibits clearly the two successive two-electron steps in reduction of **16**, taking place[32] successively at (a) $E_a = -1.82$ V and (b) $E_b = -2.11$ V vs Ag/AgI/I^- 0.1 M reference system. On the other hand, substitution by efficient electron-withdrawing groups may change[33] dramatically the cathodic behavior of ArSR-type compounds. In this manner the captodative character of substituents attached to the phenyl ring (see structure **17**) appears to reinforce strongly



(17)

the stability of the transient anion radical. Thus, the cathodic behavior of 4-(phenylthio)phenylalkyl sulfones (R = alkyl) was found[33] to be reversible. The rate of cleavage of the transient anion-radical was found to be rather low ($0.1 \leqslant k_c \leqslant 1\,s^{-1}$) including R = Ph; the cleavage mechanism was established to proceed as in equations 8–12:



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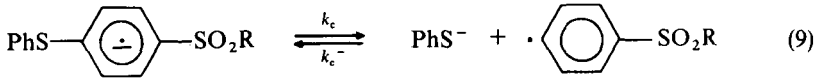
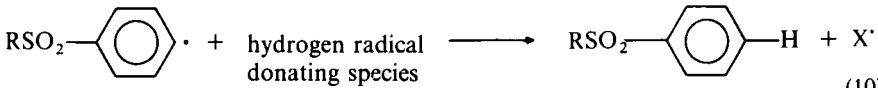
(17)



(9)



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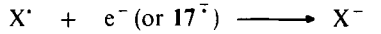

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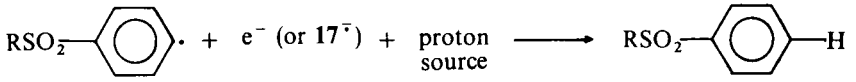
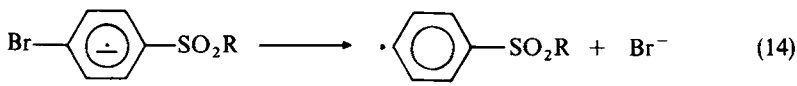


(12)

Reaction 9 of the process is an equilibrium with $k_c^- \gg k_c$. The fast reduction of the produced free radical (or/and its reaction with a strongly H-donor medium) draws definitively the electrochemical process to the two-electron cleavage. However, the same equilibrium may be (when now displaced to the left side) the basis of $S_{RN}1$ reactions when the nucleophile is the thiophenolate anion. Reactions of this type involving electrophilic aryl radicals produced electrochemically are extensively studied by Saveant's group[34]. To come back to compounds **17**, they were readily prepared[35] under the conditions of the radical aromatic substitution from the relevant bromosulfones **18** according to the scheme in equations 13–16 (with a nonelectroactive soft nucleophile such as $PhS^-R_4N^+$ added in excess or prepared *in situ* by cleavage of the S—S bridge in the catholyte solution).

(**18**) (**18**·⁻) (13)



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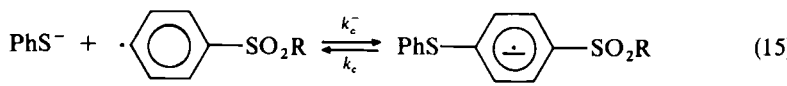

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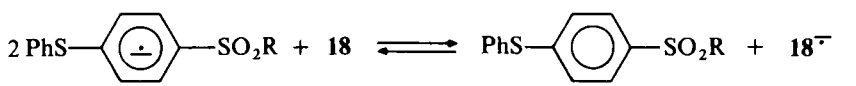
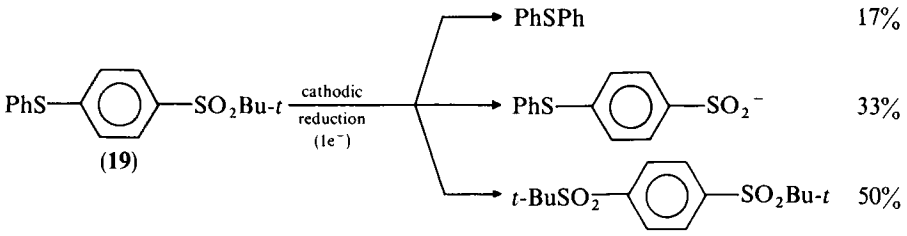


(16)

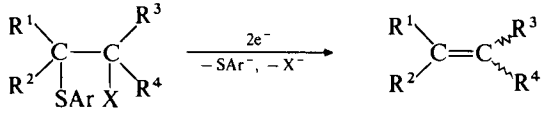
The scheme comprising equations 13–16 is electrocatalytic, in the absence of side reactions implying the transient aryl σ radical (see reaction 6). The electricity consumption is in principle—and often experimentally—very low. Only an inductive phase by electron transfer catalysis is necessary. Therefore, the $S_{RN}1$ process can be perceived as a S—C bond formation while, on the other hand, reduction of **17** is a cleavage process. This is essentially due to the thermodynamic unequality $E°\mathbf{17} < E°\mathbf{18}$ which renders the equilibrium 16 strongly shifted to the right side.



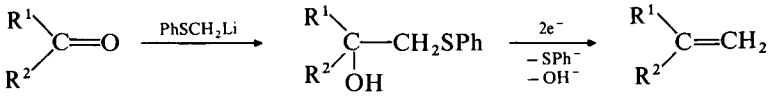
SCHEME 7

Unexpectedly, compound **19** (i.e., **17**, R^1 = Bu) behaves differently. The anion radical stability was found to be much lower (about 3 orders of magnitude) and the reduction process appears to proceed according to a rather complex mode of fragmentation and coupling (Scheme 7). The formation of the totally unexpected disulfone **20** can be explained (but not fully demonstrated) by means of a nucleophilic substitution by the *t*-butyl sulfinate onto the starting compound. All the reactions given above aim to demonstrate that the electrochemistry of organic sulfides in nonaqueous media (formation *in situ* by cleavage of soft nucleophiles) can be rather complex and conclusions have to be drawn carefully.

The cathodic elimination activated[36] by aryl sulfide groups:



can be used as a mild method for creating[37] ethylenic double bonds from ketones (X = OH) in fairly high yields:



The electrochemical method then allows one to create[37], by cleavage of a C—S bond in the course of a two-electron reaction in a well-chosen place, an anion which may lead either to an elimination or the formation of three-membered rings (thus methanesulfonates of γ-hydroxysulfides may be converted in good yield into cyclopropanes).

However, as mentioned above, the activation of anion elimination by cleavage of the C—S bond is usually achievable at rather reducing potentials. Under those conditions, the produced olefin, possibly substituted by unsaturated and/or aryl groups R^1, R^2, R^3 and R^4, can be *more* easily reduced than the starting sulfide. Thus, α,α′-disubstituted diphenylethanes may provide in aprotic solvents examples of self-catalyzed (in the sense of redox catalysis, now widely documented[38]) elimination. In such a process the anion radical of the unsaturated system readily formed at the potential necessary to cleave the C—S bond becomes progressively the reducing species of the starting product:

heterogeneous electron transfer ($t = 0$)

$$AX^1X^2 \xrightarrow{e^-} [AX^1X^2]^{\cdot -}$$

$$[AX^1X^2]^{\cdot -} \xrightarrow[\text{cleavage}]{-X^{1-}} [AX^2]^{\cdot}$$

$$[AX^2]^{\cdot} \xrightarrow{e^-} [AX^2]^-$$

$$[AX^2]^- \xrightarrow[[-X^2]^-]{\text{elimination}} A$$

$$A + e^- \xrightleftharpoons{\text{fast}} A^{\cdot -}$$

SCHEME 8

electron transfer and chemical reactions in solution ($t \gg 0$)

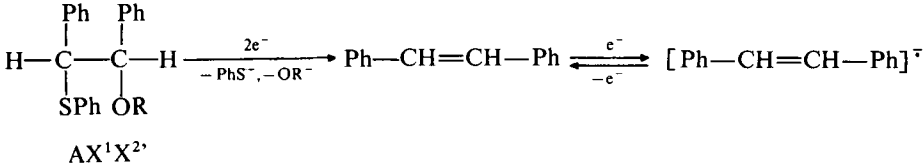
$$A^{\cdot -} + AX^1X^2 \rightleftharpoons A + [AX^1X^2]^{\cdot -}$$

$$[AX^1X^2]^{\cdot -} \longrightarrow [AX^2]^{\cdot} + [X^1]^-$$

$$[AX^2]^{\cdot} + A^{\cdot -} \xrightarrow{\text{fast}} [AX^2]^- + A$$

$$[AX^2]^- \longrightarrow A + [X^2]^-$$

SCHEME 9



The reduction mechanism has been shown[36] to depend on the rate of elimination of the transient anion after the transfer of two electrons.

At the start of electrolysis, the process follows Scheme 8 where X^1 is PhS^-, i.e. the best leaving group. During the electrolysis, Scheme 9 is operative since $E^\circ_A \gg E^\circ_{AX^1X^2}$. It can be demonstrated that the olefin concentration, and that of the relevant anion radical, grow continuously and then the electron exchange which takes place in solution is rendered faster and faster. Chronopotentiometric analysis curves (potential control of the working electrode in the course of a constant-current electrolysis) then exhibit a sudden increase in potential when the scheme takes place (Figure 4, curve A) as opposed to a slower elimination process (curve B) where the self-catalysis process in not foreseeable.

The reduction of α-carbonyl diphenyldithioacetals[39] (Scheme 10) was reported to be also self-catalyzed (formation in the course of the cathode process of the couple $PhSSPh/PhS^-$ which acts as a redox catalyst at the potential of −0.63 V vs NHE). When

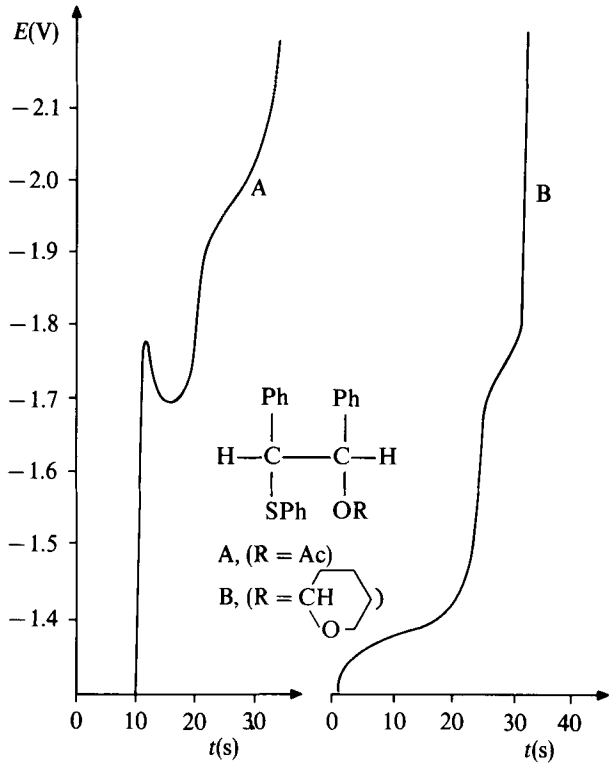
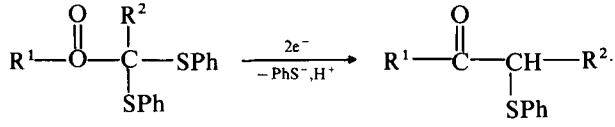
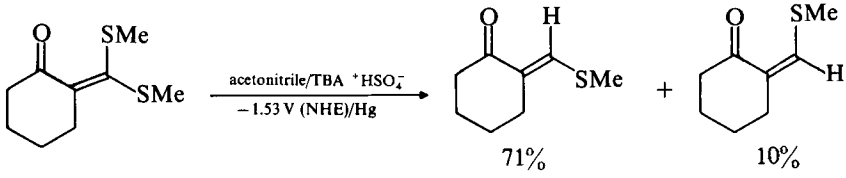


FIGURE 4. Chronopotentiometric curves for 2.5×10^{-3} M solutions. Constant current: $I = 7\,\mu A\,mm^{-2}$. Hanging mercury electrode. Electrolyte: DMF 0.1 M Et_4NClO_4. Reference electrode: Ag/AgI 0.1 M. From Reference 36



SCHEME 10



SCHEME 11

sufficiently activated, the cathodic reduction of ketene dithioacetals was shown to be feasible[40] (Scheme 11), then exhibiting the cathodic cleavage of only one C—S bond.

B. Oxidation

The oxidation of organic sulfides is now quite well documented[30]. When achieved in aqueous solutions, the oxidation proceeds in two successive two-electron steps affording first the sulfoxide and then the sulfone (equation 17). Thus, the oxidation of diphenyl

$$R^1SR^2 \xrightarrow[H_2O/-2H^+]{-2e^-} R^1SOR^2 \xrightarrow[H_2O/-2H^+]{-2e^-} R^1SO_2R^2 \qquad (17)$$

sulfide in perchloric acid at +1.30 V vs saturated calomel electrode leads almost quantitatively to the corresponding sulfoxide. Under such experimental conditions, the oxidation in two steps is rather general and does not depend—in principle—on groups R^1 and R^2 (aliphatic or/and aromatic). The effect of the medium was studied in the course of the oxidation of aryl methyl sulfides[41]. When sufficiently dry, weakly nucleophilic solvents are used for carrying out the organic sulfide oxidation, the nature of the process is fundamentally changed, affording at a platinum anode dimeric sulfonium salts (equations 18–20). The mechanism of this sulfonium salt formation had been

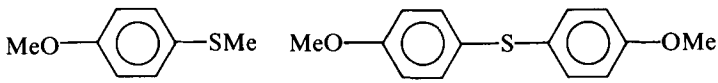
$$2\,MeSMe \xrightarrow[-H^+]{-2e^-} MeSCH_2\overset{+}{S}(Me)Me,\ ClO_4^- \qquad (18)$$
(acetonitrile/$NaClO_4$)

$$2\,PhSPh \xrightarrow[-H^+]{-2e^-} PhH_2\overset{+}{S}-C_6H_4-SPh,\ ClO_4^- \qquad (19)$$
(acetonitrile/$LiClO_4$)

$$2ArSR \xrightarrow[-H^+]{-2e^-} ArR\overset{+}{S}-Ar-SR,\ BF_4^- \qquad (20)$$

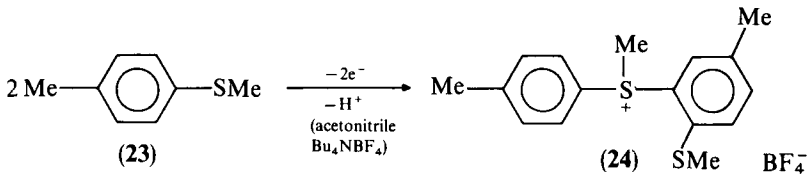
discussed in a previous review[30]. In the case of aryl sulfides, all the proposed pathways claimed that a radical cation was the necessary intermediary.

Electrogenerated radical cations from **21** and **22** were found[42] from voltammetric

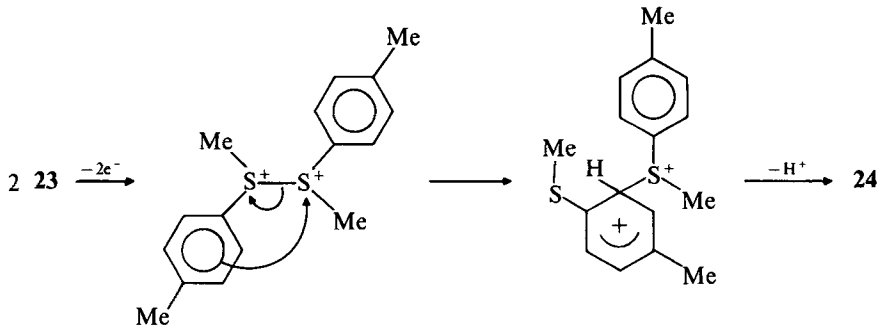


(21) **(22)**

studies to be of unexpectedly high stability. Although the *para* position on the phenyl ring is now occupied, it was found that the electrophilic substitution may alternatively take place on other free positions (equation 21). The structure of **24** (established by X-ray



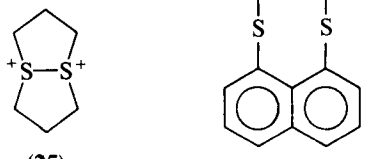
(23) **(24)** (21)
(acetonitrile Bu_4NBF_4)



SCHEME 12

analysis)[42] contributes to the assumption of the transient formation of a dicationic dimer involving each of the sulfur atoms (Scheme 12).

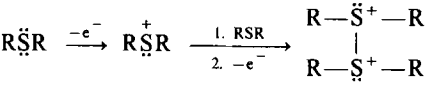
A dicationic salt **25** from the chemical oxidation of 1,5-dithiooctane could be easily obtained[43], however compound **26** is oxidized irreversibly[44] according to a two-electron



(25)

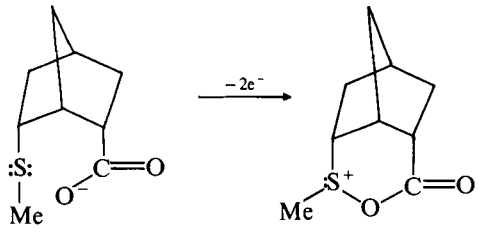
(26)

step (+0.70 V vs Ag/Ag^+) which does not lead to a similar intermediate but to the monosulfoxide, presumably because of the use of a relatively wet acetonitrile as solvent. Indeed, when the electrolyses are carried out in extremely well dried solvents like acetonitrile, it was shown[45] very recently that the anodic oxidation of aliphatic sulfides proceeds globally under such experimental conditions via a one-electron step only. Voltammetric analysis (a one-electron oxidation peak with an associated reduction step fitting well the dimer formation) allows one to propose the scheme in equation 22.



(22)

The ease of the electrochemical oxidation of some dialkyl sulfides was established[46] to depend on the neighboring presence of electron-rich groups (e.g. carboxylate or hydroxyl). Thus, the study of the anodic behavior of variously 2-substituted 6-(methylthio) bicyclo [2.2.1] heptanes strongly suggests the formation of the cationic intermediate **28** from the *endo-endo* sulfide **27** (Scheme 13). The oxidation of **27** was achieved in the presence of ^{18}O-labelled water with incorporation of the label into the oxygen atoms of both the sulfoxide and carboxylate moieties of the final product.



(27) (28)

SCHEME 13

When oxidized in the presence of an excess of the parent arene derivative, diaryl sulfides were shown[47] to afford directly the corresponding sulfonium ions: This reaction

$$\mathrm{Ar{-}S{-}Ar + Ar'H \xrightarrow[-H^+]{-2e^-} Ar{-}\overset{+}{S}(Ar'){-}Ar}$$

has been described in the case Ar = Ar' = *p*-An, leading to the trianisylsulfonium cation. The kinetics of this reaction have been obtained[47].

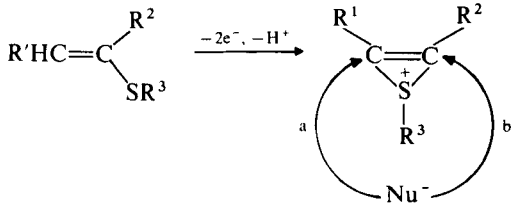
The anodic reactivity of 2,2,2-trifluoroethyl sulfides in the presence of nucleophiles (MeO^- and AcO^-) was studied very recently and allows[48] the preparation of highly useful trifluoromethylated building blocks (Scheme 14). This activation reaction was also

$$\mathrm{CF_3CH_2SAr \xrightarrow[-H^+/-e^-]{-e^-} [CF_3\overset{+}{C}HSAr] \longleftrightarrow [CF_3CH{=}\overset{+}{S}Ar]}$$

$$\downarrow \mathrm{MeO^-}$$

$$\mathrm{CF_3CH(OMe)SAr}$$

SCHEME 14



$$\xrightarrow[Nu^- = OH^-]{a} R^1{-}CO{-}CHR^2SR^3$$

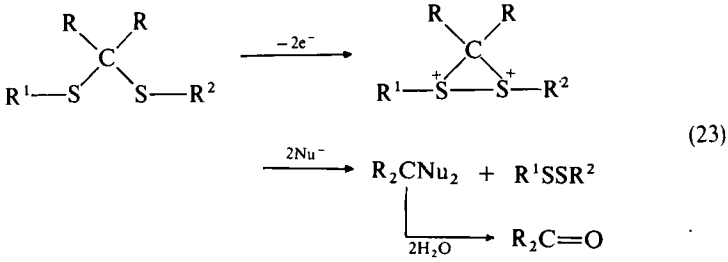
$$\xrightarrow[Nu^- = OH^-]{b} R^1{-}CHSR^3{-}COR^2$$

SCHEME 15

used in the presence of other nucleophiles; thus, the anodic monofluorination of halogenoalkyl phenyl sulfides was reported[49].

The particular aspects of the anodic oxidation of vinylic sulfides were also pointed out[124]. It has been suggested that a bridged sulfonium ion could be formed and decomposed by nucleophiles according two distinct routes (Scheme 15).

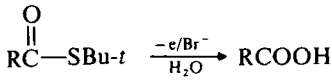
Surprisingly, 1,3-dithiones were found[50] to behave anodically in a rather unexpected way (equation 23). This reaction was found[51,52] to be extremely convenient for carrying



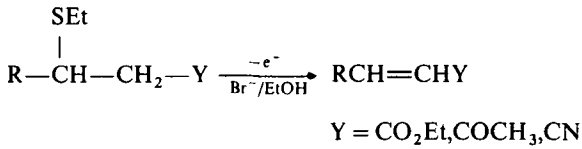
(23)

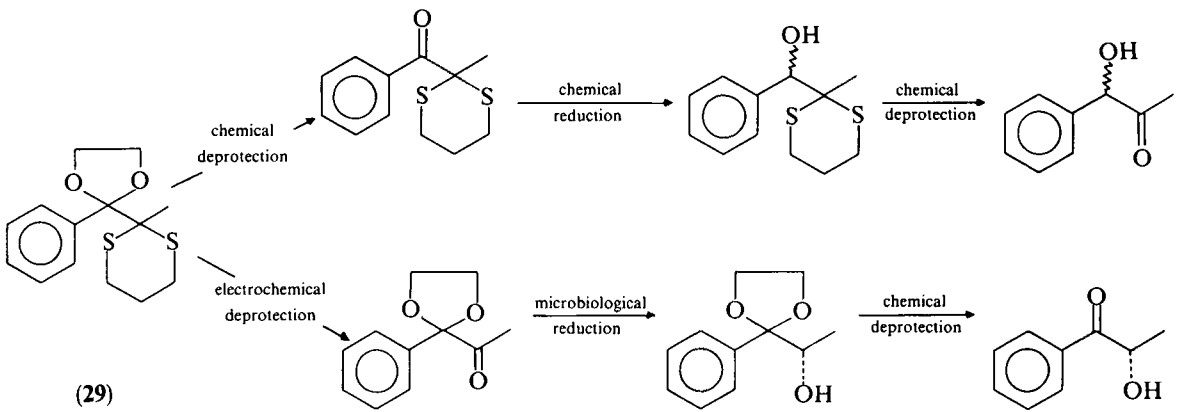
out mild deprotection of carbonyl compounds in wet acetonitrile. Conditions to complete such a reaction by indirect means[53,54] (using an organic oxidizing species like triarylamine radical cation constantly regenerated at the anode) were found. In the case where R^1 and R^2 are aromatic, the nature of the oxidation was discussed and seems to obey[52] an EC-type mechanism: the electron transfer is followed by a fast cleavage reaction. This anodic deprotection reaction is now well documented[55] as, for example, in the effective deprotection of sugars[56] and the elegant preparation of acylsilanes[57]. Additionally, a very interesting work by Mousset and Veschambre and coworkers[58] has demonstrated the reciprocal interest of chemical and electrochemical deprotections exemplified by Scheme 16 (chosen test molecule: **29**) allowing the selective formation of two regioselective ketols according to the route followed.

Electrochemical oxidation of *S-t*-butyl thiolates (deprotection of carboxylic acids) was performed in neutral conditions in an undivided cell equipped with platinum electrodes[59]. However, the current efficiency was found to be rather low. The anodic reaction



conducted indirectly in the presence of bromide or chloride salts affords the corresponding carboxylic acids in high yields. Other kinds of anodic cleavage of C—S bonds may be performed[60] easily from Michael-type thiol adducts on strongly activated unsaturated double bonds.




chemical
deprotection
chemical
reduction
chemical
deprotection
electrochemical
deprotection
microbiological
reduction
chemical
deprotection
(29)

SCHEME 16

III. THIOLS AND SULFUR–SULFUR BRIDGES

Thiols and thiolates are readily oxidized electrochemically to the corresponding disulfides (equation 24). The oxidation peak of thiophenol at a platinum anode in aqueous

$$2\ \mathrm{RSH} \underset{2e^-,2H^+}{\overset{-2e^-,-2H^+}{\rightleftharpoons}} \mathrm{RS{-}SR} \tag{24}$$

methanolic solution was found[61] to depend on pH. The variation peak[67] potential upon pH exhibits a slope of 60 mV/pH. The oxidation of thiols at a mercury anode is complicated[62] by the involvement of mercury in the oxidation process (equation 25).

$$2\ \mathrm{RSH} + \mathrm{Hg} \longrightarrow (\mathrm{RS})_2\mathrm{Hg} + 2\mathrm{H}^+ + 2\mathrm{e}^- \tag{25}$$

Many studies do concern the cathodic reduction of disulfides which appears to be a very clean and convenient source of thiolate ions or thiols depending on pH (however, it is worth recalling that thiolates are often readily oxidized by air). The kinetics, chemical reversibility and stability of the reagents involved at different electrode materials were studied[63] (see, e.g. Figure 5).

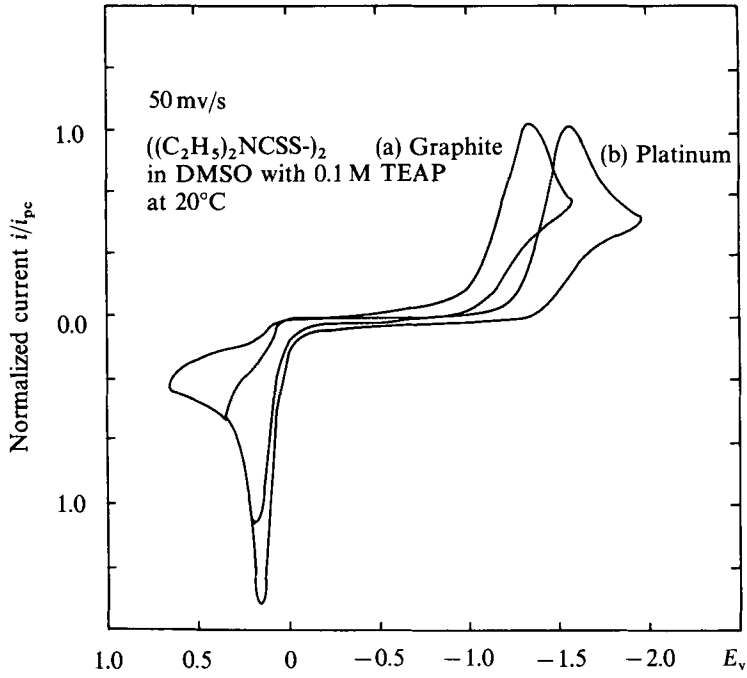
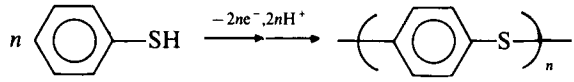


FIGURE 5. Voltammetric response for a thiolate/SS bridge conversion (case of tetraethythiuram disulfide, TETD). Electrode materials are specified in the figure. Electrolyte: DMSO containing Et_4NClO_4 (TEAP). Temperature: 20 °C. Potentials are referred to $Ag/AgCl/Cl^-$ electrode. Initial scan directions are reducing. Reproduced by permission of the Electrochemical Society form Reference 63

It has been emphasized that microscopic reversibility of those redox processes makes possible (in principle) the construction of electrode materials for rechargeable batteries based on the organic disulfide-thiol couple. In the case of thiolates, the mechanism of coupling was pointed out[64] and the redox potential of the reaction

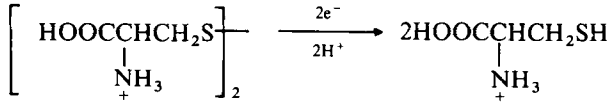
$$RS-SR^{\cdot-} + 2H^+ + e^- \rightleftharpoons 2RSH$$

was established in aqueous media for several R's. Experimental conditions for the anodic polymerization of thiophenol (in dry nitromethane with added high amounts of trifluoroacetic acid) were found[65]. This reaction (equation 26) was claimed to be a convenient route for the formation of pure poly(*p*-phenylene sulfide).



(26)

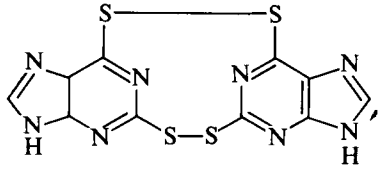
The electrochemical formation of cystein **31** can be performed on an industrial scale[66] directly by cathodic scission of cystine **30** in sulfuric acid (equation 27). Tests of



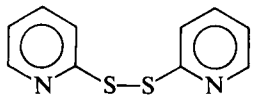
(27)

(30) **(31)**

production based on 300–500 kg per day were successful. Other studies on the formation and the cleavage of S—S bridges are quite numerous in the literature. Thus, for example, purine-2,6-dithiol produced **32a**[67] at a pyrolytic graphite electrode and pyridinethiols yielded[68] compound **32b**.



(32a)



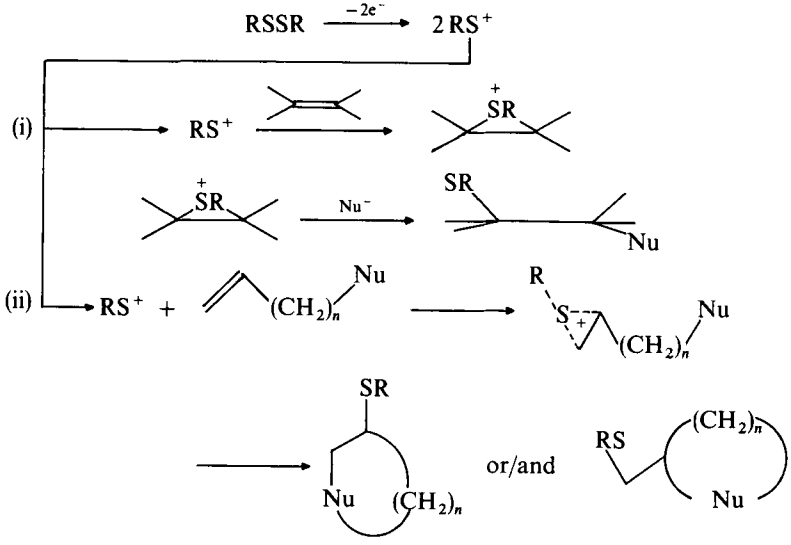
(32b)

The reduction of the diverse S-oxides of diphenyl disulphides [PhS(O)SPh, $PhSO_2SPh$, $PhSO_2S(O)Ph$ and $PhSO_2SO_2Ph$] was also investigated[69] in aqueous solution. The reduction of disulfides in the presence of oxygen when conducted in dry DMF leads[70] to the corresponding sulfinate in good yield. A mechanism based on the electron exchange between thiolate and dioxygen is reproduced in Scheme 17.

Diphenyl disulfide was reported[71] to be cleaved anodically with the formation of a 'PhS^+' transient. This reaction appears to be quite general and applicable to most disulfides. The oxidative cleavage can be performed by direct or indirect means. Such anodically produced electrophilic intermediates can react with double bonds[72] to lead to addition or they may initiate cyclization[73] involving structures such as alkenols and alkenoic acids (Scheme 18).

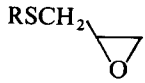
$$RSSR \xrightarrow{2e^-} 2RS^-$$
$$RS^- + O_2 \rightleftharpoons RS^{\cdot} + O_2^{\cdot -}$$
$$RS^{\cdot} + O_2^{\cdot -} \longrightarrow RSO_2^-$$
$$2RS^{\cdot} \longrightarrow RSSR$$

SCHEME 17

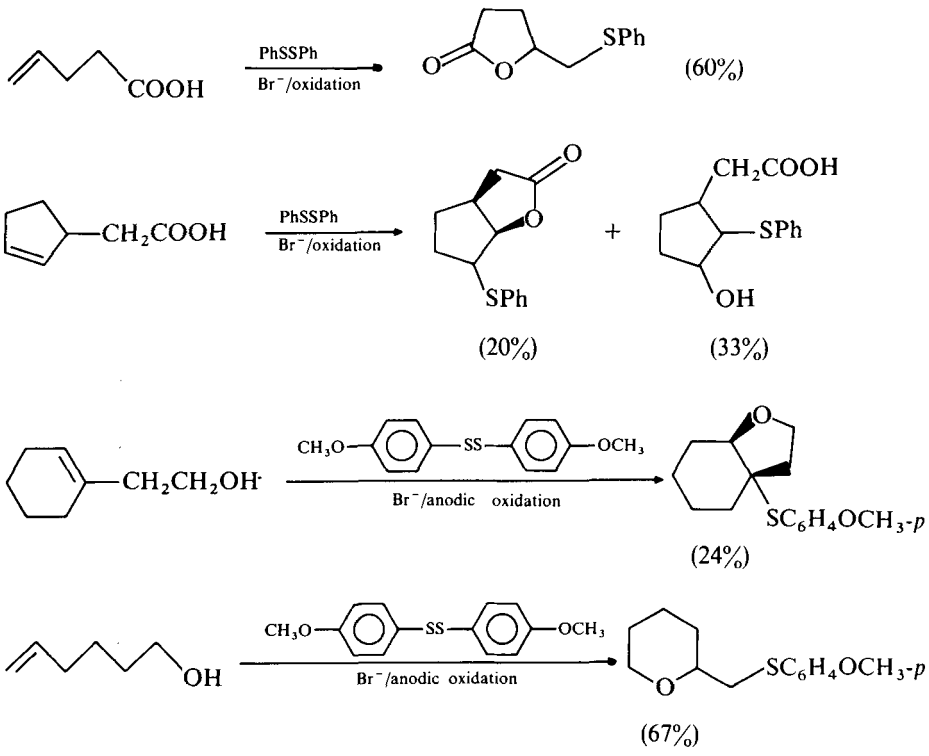


SCHEME 18

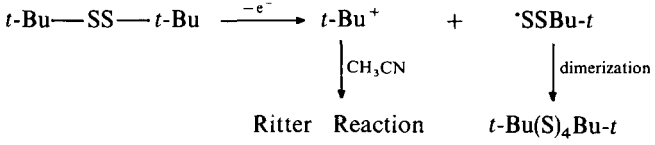
This reaction was facilitated[73] in an indirect way (with Br^- as a mediator) because of the very positive oxidation potential of the disulfide (Scheme 19). Additionally, specific electrochemical reactions concerning both thiols and thiolates were also reported. Thus the 'reduction' of thiols at a platinum cathode in an aprotic solvent (e.g. acetonitrile) gives rise to the corresponding thiolate usable *in situ* as a nucleophile[74]. In this manner, the electrochemical alkylsulfenylation of epichlorhydrin[75] can also be achieved (R = Bu, n-C_8H_{17}, n-$C_{10}H_{21}$).



Mercaptans and n-alkane thiols possess the property to be strongly absorbed at gold, silver and platinum electrodes leading[76] to a specific 'coating' of these electrodes and also allowing the building of self-assembled mixed-monolayers and that of artificial membranes by incorporation of a hydrophobic mediator into the absorbed layer[77].



SCHEME 19



SCHEME 20

Lastly, phenyl thiolates of weak electroactivity are known to react as soft nucleophiles with electrogenerated electrophilic radicals. The reactivity is the basis of cathodically activated $S_{RN}1$ reactions. However, the symmetrical cleavage involving the sulfur–sulfur bond is not always observed[78]. Thus di-*t*-butyl disulfide was shown to cleave into *t*-butyl cation (Scheme 20).

IV. SULFONES

If most sulfones are known to react with chemical reducing reagents like dissolved metals and amalgams, their ability to react via electron transfer (heterogeneously by means of

a cathodically polarized electrode or homogeneously by means of anions or anion radicals possessing sufficient reducing power) should depend on the level of their respective LUMO. In other words, the first charge transfer may occur more or less easily within an accessible range of potential [up to -3 V vs Saturated Calomel Electrode (SCE), this potential value being about the most reducing potential reached since there is no electrolyte–solvent couple electrochemically stable beyond this value] only if the sulfonyl group is directly connected to an unsaturated system (e.g. an aromatic moiety). Obviously, the redox potential range necessary to observe electron transfer(s) onto most sulfones is, however, located within a range where both proton and water are reduced. Accordingly, the use of aprotic (or weakly protic) organic solvents appears in most cases to be absolutely necessary.

The conditions of the electrochemical reactivity of sulfones (electron transfer, cleavage, redox catalysis, occurrence of acidic proton, action of electrogenerated bases in unbuffered media, cathodic elimination, etc.) were fully discussed in a previous review[79] and therefore are not evoked here. Let us, however, recall the cleavage mechanism of aromatic sulfones according to the nature of substituents (electron withdrawing or donating) on the aromatic system.

$$\mathrm{ArSO_2R} \xrightleftharpoons{e^-} [\mathrm{ArSO_2R}]^{\cdot -} \tag{28}$$

$$[\mathrm{ArSO_2R}]^{\cdot -} \xrightarrow{k_c^1} \mathrm{Ar^{\cdot} + RSO_2^-} \tag{29}$$

$$[\mathrm{ArSO_2R}]^{\cdot -} \xrightarrow{k_c^2} \mathrm{R^{\cdot} + ArSO_2^-} \tag{30}$$

$$\begin{matrix}\mathrm{Ar^{\cdot}}\\ \mathrm{R^{\cdot}}\end{matrix} + [\mathrm{ArSO_2R}]^{\cdot -} \longrightarrow \begin{matrix}\mathrm{Ar^-}\\ \mathrm{R^-}\end{matrix} + \mathrm{ArSO_2R} \tag{31}$$

$$\text{or} \begin{cases} \mathrm{Ar^-\ and\ R^-} \xrightarrow{\text{proton source}} \mathrm{ArH\ and\ RH} & (32) \\ \mathrm{Ar^{\cdot}\ or\ R^{\cdot}} \xrightarrow[\mathrm{XH}]{\text{H-donor solvent}} \mathrm{ArH\ and\ RH + X^{\cdot}} & (33) \end{cases}$$

$$\mathrm{X^{\cdot} + [ArSO_2R]^{\cdot -}} \longrightarrow \mathrm{X^- + ArSO_2R} \tag{34}$$

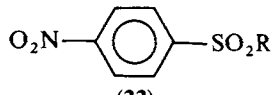
The above scheme underlines the passage through an anion radical as an obligatory transient. The lifetime of this intermediate depends on the nature of substituents present on the Ar group. One may assume that with electron-withdrawing substituents, the formation of the anion radical should correspond to the occupation of the LUMO (π^* level) and the cleavage reaction mainly affords Ar$^{\cdot}$ radicals.

Concomitantly, such anion radicals as intermediates may present a certain stability. On the other hand, with electron-donating substituents on the Ar group, the lifetime of anion radicals was found to be much shorter ($k_c^1 \ll k_c^2$) and the first charge transfer could generally fit a $\pi \rightarrow \sigma^*$ like transition. Here, the regioselectivity of the observed scission reaction was found to be fundamentally changed and appears to be a source of R$^{\cdot}$ radical. The fate of radicals of both kind, whatever the nature of the cleavage reaction, depends on both the reducing capability of the medium (heterogeneous when k_c^1 or/and k_c^2 are extremely large, allowing the formation of a radical at the electrode surface, or homogeneous when diffusion permits more stable anion radicals to cleave in solution) and the H-donor character of the solvent used or electrolyte towards those transient free radicals. The scheme above summarizes the mode of cleavage of aryl alkyl

sulfones in general, which then corresponds to a two-electron reaction according to an E-C Disproportionation mechanism since the second electron transfer takes place in solution (in cases where k_c^1 or $k_c^1 \ll 10^{-6}\,s^{-1}$). Values of E° (redox potential of the first charge transfer) and E_p (peak potential in voltammetry for the overall conversion $ArSO_2R \rightarrow RH$ or ArH) may depend on a number of parameters, especially on the energy level of the LUMO and kinetic factors. However, it can be said that the $ArSO_2$ group is in most cases not a very good 'electrophore' (moiety of the molecule which determines to a large extent the level of the relevant LUMO) and accordingly values E° and E_p (of different significance but found to be very near) correspond to that of rather reducing potentials [say within a range of -2.2 V when Ar = Ph to -1.8 V when Ar is a polyaromatic system (all values referred to SCE)].

A. Cathodic Cleavage of Monosulfones

The aromatic sulfones **33–35** exhibit moderately or very stable anion radicals and then the $\pi \rightarrow \pi^*$ transition to the LUMO is confirmed. With such systems favoring the



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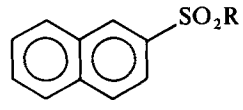

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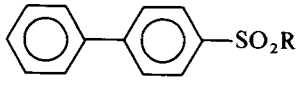

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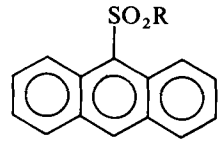


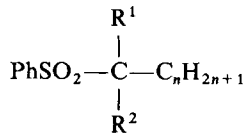
(36)

cleavage of Ar—S bonds, the regioselectivity of scission can be easily checked by the observation of voltammetries in nonaqueous media in the presence small amounts of proton donors where the two main steps are:

$$ArSO_2R \xrightarrow[2H^+\ (\text{proton source})]{2e^-} ArH \quad \text{(irreversible first peak)}$$

$$ArH \xrightarrow{e^-} ArH^{\cdot -} \quad \text{(reversible second peak)}$$

However, sulfones **36** (R = alkyl, Ph) behave abnormally owing to the occurrence of a fast reversible dimerization process probably through the radical anion coupling in Scheme 21. The cathodic cleavage of allylic and propargylic aryl sulfones demonstrated[125] the ability to form the corresponding free radical able to be trapped by acceptors or to dimerize.



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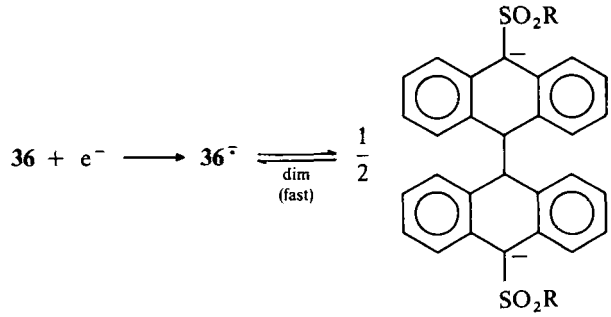
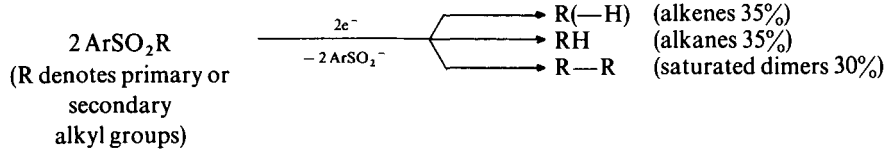


SCHEME 21



SCHEME 22

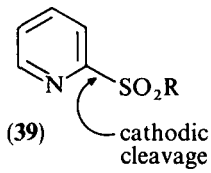
The behavior of long-chain sulfones **37** ($n \geqslant 7$) was also studied[81]. Thus media of very low acidity, unexpected coulometric balances demonstrate a global consumption of one mole of electron per mole of substrate: the two main reasons for this are (i) the occurrence of a dimerization process and (ii) the β-elimination provoked by electrogenerated bases at the cathode interface (Scheme 22). Therefore, the cleavage of the C—S bond has two concomitant sources: the classical electrochemical cleavage producing one equivalent of a strong base per each electron pair transferred leading to β-elimination on the nonreduced substrate either in the reaction layer or in the catholyte. The specific behavior of long-chain sulfones (formation of dimers R—R) could be due to the amphilic nature of substrates, strongly adsorbed and then possibly cleaved in the heterogeneous phase. Nucleophilic displacements by R^- anions at the starting sulfone appear unlikely as a source of dimer, since sulfones possessing secondary R groups lead also to a similar amount of R—R dimers.

Diaromatic sulfones **38** were also studied and do exhibit rather stable anion radicals. They can be regarded as a facile way to produce both Ar$^\bullet$ and Ar'$^\bullet$ radicals. Such aryl

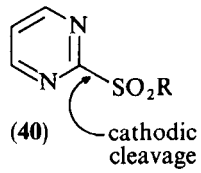
$ArSO_2Ar'$

(38)

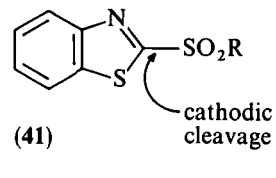
radicals (for addition to unsaturated systems or to spin markers) were also produced[82] from the monosulfones **39–41**. The electrochemical method was also reported to be a



(39)



(40)

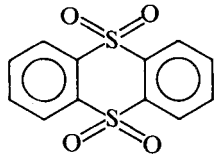


(41)

facile route to the corresponding alkyl sulfinate especially from **41** (this reaction was carried out with primary $R = C_8$, C_{10}, C_{12} or C_{18}), the formation of which was followed continuously by means of selective extraction using a two-phase system.

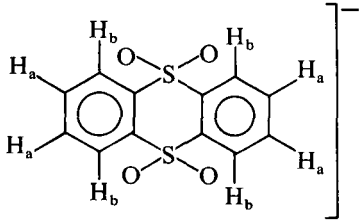
B. Disulfones

9,9,10,10-Thianthrene tetraoxide **42** has been studied electrochemically[83] and was found to afford both surprisingly stable radical anions and dianions. The ESR spectrum of the anion radical of **42** obtained by *in situ* electrolysis in DMF containing tetraalkylammonium



(**42**)

salts exhibits (Figure 6) only a quintet, easily interpreted by the splitting of protons *a*. On the other hand, for protons *b* the splitting constant is extremely small. Therefore, the antibonding orbital of the anion relative to each aromatic ring corresponds[126] to an antisymmetric one. Moreover, the low coupling constants found experimentally fit very well an equal delocalization of the charge between the two aromatic nuclei.



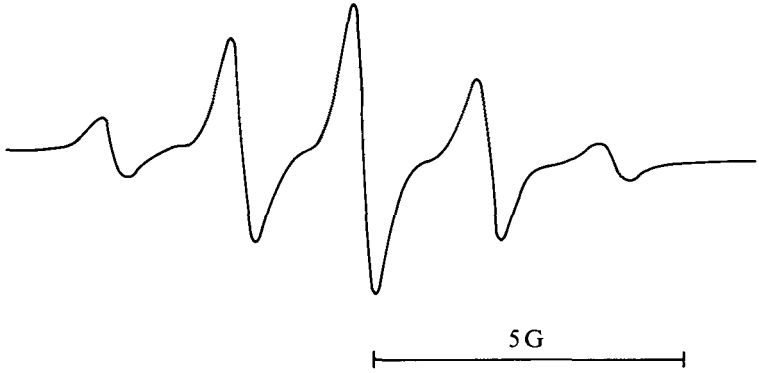


FIGURE 6. ESR spectrum of the **42** anion obtained under electrolysis (DMF–Bu_4NBF_4 0.1 M). Pt grid. Current density 10 $\mu A\,cm^{-2}$

The capability of the dianion of **42** to be used as a reducing species was demonstrated[83] in cyclic voltametry in the presence of aromatic halides ArX. Kinetic data concerning the values of k constants at room temperature are available.

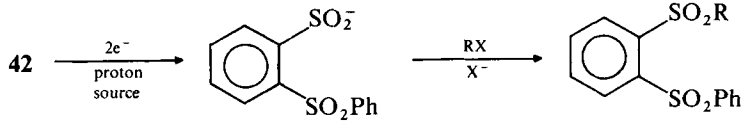
$$\mathbf{42} \underset{}{\overset{e^-}{\rightleftharpoons}} \mathbf{42}^{\cdot-} \overset{e^-}{\rightleftharpoons} \mathbf{42}^{=}$$

$$\mathbf{42}^{=} + \mathrm{ArX} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathbf{42}^{\cdot-} + \mathrm{ArX}^{\cdot-}$$

$$\mathrm{ArX}^{\cdot-} \xrightarrow{k_c} \mathrm{Ar}^{\cdot} + \mathrm{X}^-$$

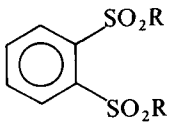
A comparison of the reducing power for both anion radicals and dianions of similar redox potentials was made. Electron exchange kinetic values of the **42** dianion were found to be about 10 times lower those than of the corresponding anion radicals, which can be explained by an increase in the reorganization energy in the course of the homogeneous electron transfer.

The cleavage reaction of **42** under cathodic means was also studied[84], and the formation of an open sulfinate was demonstrated. The addition of primary aliphatic halides RX at the end of the electrolysis allows facile formation of a new series of disulfones **43** in high yields.

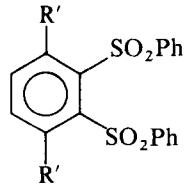


(43)

The behavior of *ortho*-bis(alkylsulfonyl) and (arylsulfonyl) benzenes **44** appears worthwhile to be described in some detail. First of all, let us describe the nice electrocatalytic reaction found by Novi and collaborators[85] with **45** where R′ = Me, in weakly H-donor solvents (e.g. DMSO) and in the presence of a strong base such as tetrabutylammonium acetate. The reactivity of **45** was fully explained by the catalytic cycle in Scheme 23 when only an activation electron transfer takes place at the cathode. When side reactions such as reduction of the free radical and transfer of a hydrogen atom also occur, the overall electricity consumption necessary for the formation of the monosulfone **46** is very low (0.14 mole of electron per mole of **45**).

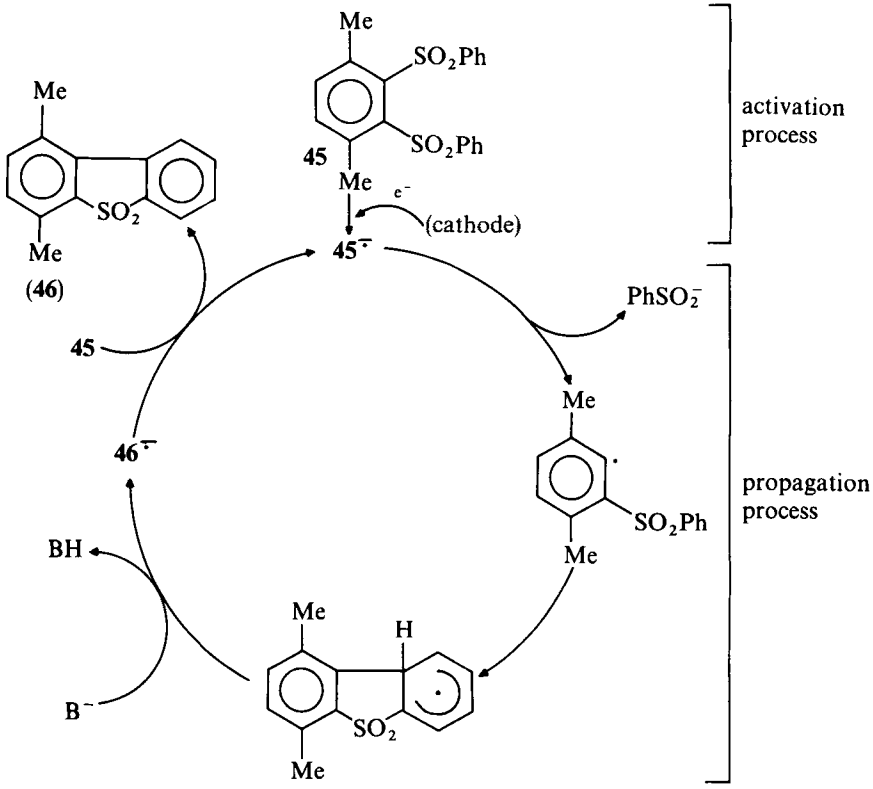


(44)

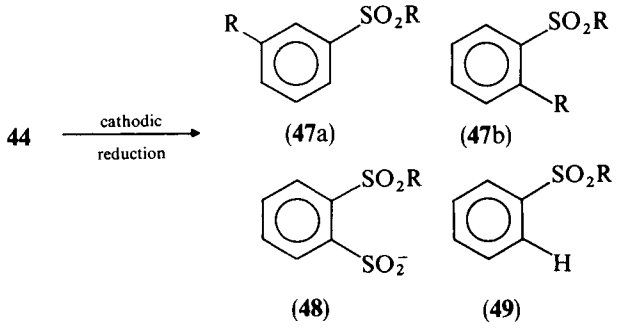


(45)

Differences in the cathodic behavior between the series **44** (R = Ph) and series **44** (R = alkyl) are dramatic. The latter, when reduced in an aprotic solvent for a wide range of primary R substituents affords[86] the product distribution shown in Scheme 24. The total yield experimentally reported for **47a** + **47b** was found to be equal to that of **48**. The disappearance of **44** anion radical was shown to correspond to a bimolecular reaction



SCHEME 23



SCHEME 24

TABLE 1. Potentiostatic electrolyses for compounds **44**[a]

Substrate **44** with R =	Fixed potential E (V)	Electricity Consumption ($F\,mol^{-1}$)	Experimental conditions	Isolated products (%)			
				47a	**47b**	**48**	**49**
Me	−1.32	1.42	aprotic medium	traces	0	75	10
Et	−1.18	1.34	aprotic medium	33	2	30	13
		1.12	presence of $PhSNBu_4^b$	42	traces	—	0
		1.45	presence of phenol[c]	22	2	28	28
n-Bu	−1.21	1.31	aprotic medium	32	2	34	11
		1.10	presence of $AcONBu_4^d$	44	traces	—	0
n-Oct	−1.22	1.44	aprotic medium	30	0	35	18
i-Pr	−1.25	1.48	aprotic medium	17	traces	53	12

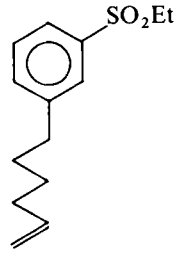
[a]Solvent: DMF. Electrolyte: Bu_4NBF_4 0.1 M. Cathode: stirred mercury pool of area 10 cm^2, Divided cell. Reference system: Ag/AgI/I^- 0.1 M.
[b]excess of nucleophile: 20 times.
[c]excess of proton donor: 4 molar equivalents.
[d]excess of base: 6 molar equivalents.

(kinetics studied by UV, ESR or voltammetry) except with R = Me and/or secondary alkyl groups for which classical monomolecular-type cleavages were found. Accordingly, the latter afford high yields of **48** (see Table 1).

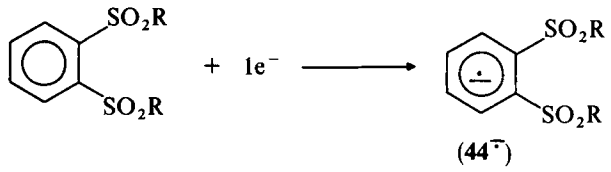
It was established that the reactivity of the **44** anion radical should fit an S_N2-like reaction between this species and the substrate. Kinetic constants for bimolecular reactions were found to be of the order of $50\,M^{-1}\,s^{-1}$ (e.g. R = *n*-Bu) while cleavage rate of the anion radical is about $0.4\,s^{-1}$ (when R = Me). The ratio between these two kinetic constants implies that substrate concentration may strongly determine the overall rate and therefore the nature of the reaction.

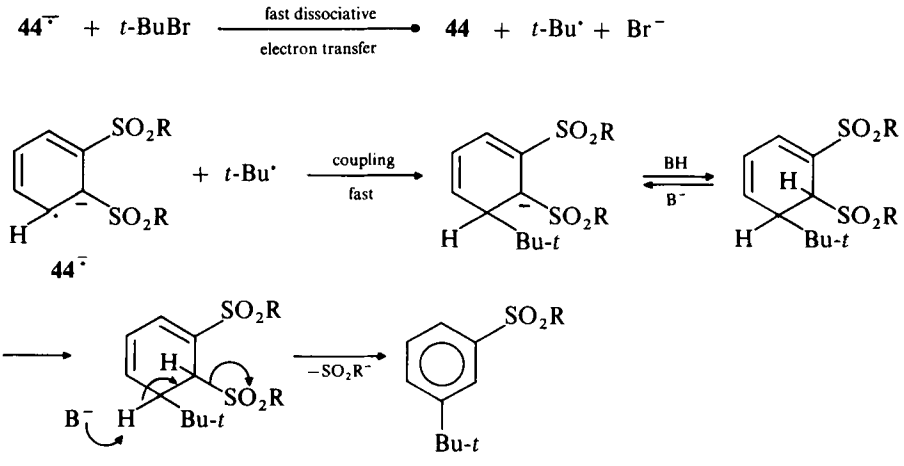
Similarly, disulfones **44** were also reduced in the presence of electrophiles other than the starting substrate. With primary alkyl halides RX in excess (and especially when X = I or Br), very high yields of substituted compounds **47** were obtained. The mechanism in Scheme 25 may account for the alkylated compound formation, supposed *a priori* to be based on a coupling reaction.

Surprisingly, the use of radical chemical scavengers does not decrease the yield of alkylated compounds. Moreover, when RX is now a radical probe such as hexenyl bromide, one should expect competition of the attachment of two radicals (Scheme 26), since $k_{cyclization}$ is known to be very high. Surprisingly, the mixed reduction of **44** (R = Et) and hexenyl bromide in twenty-fold concentration excess leads to **50** with an isolated yield

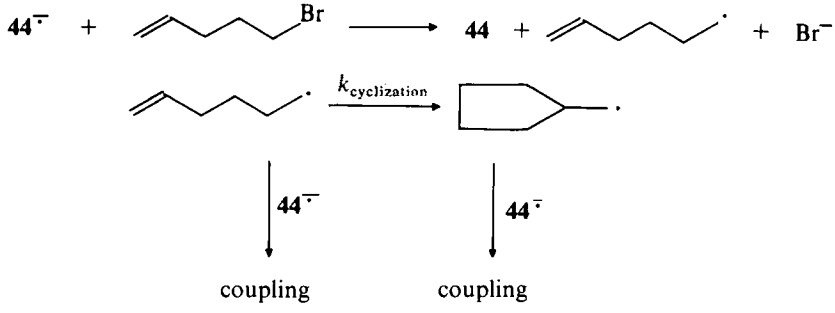


(50)





SCHEME 25



SCHEME 26

of 60% and in the product mixture no compound possessing a cyclopentenyl moiety was found. Consequently, it can be expected that the alkylation occurs fast inside a solvent cage (sc).

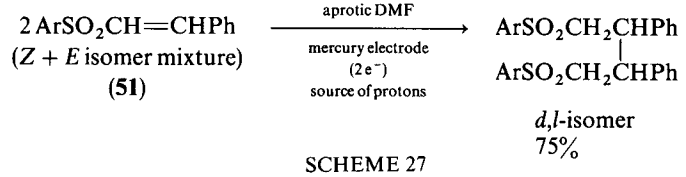
$$44^{\cdot-} + RX \longrightarrow [44, R^{\cdot}, X^{-}]_{sc} \longrightarrow [44\text{—}R]^{\cdot} + X^{-}$$

$$[44\text{—}R]^{\cdot} \xrightarrow{-H^{\cdot}} 50$$

C. α,β-Ethylenic Sulfones

The electrochemical behavior of olefins activated by a sulfonyl group is totally different from that of α,β-ethylenic ketones or nitriles. With the former series there is practically no case of dimerization or saturation, probably for structural reasons but also because the reduction of most sulfones cannot be completed in aqueous or in acidic media.

The example in Scheme 27 is an exceptional one[87]. Aromatic ethylenic sulfones **51** (with Ar = Ph or *p*-Tol) were found to lead rather selectively to the corresponding *d,l*



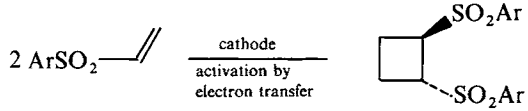
SCHEME 27

δ-disulfones. However, in an unexpected manner, the cathodic reactivity of other ethylenic sulfones **52** (R = H or alkyl) when studied in aprotic organic solvents revealed the existence of electrocatalytic cyclodimerizations or additions. Thus, with R = H, sulfones **52** afford the corresponding cyclodimers often in fairly high yields.

$$ArSO_2CH{=}CHR$$

(52)

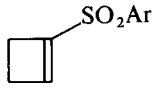
Cyclodimers **53** have not been described so far. Their formation by electron transfer activation at a mercury or platinum cathode requires a very low electricity consumption (0.1 to 0.2 mole of electron per mole of **52**). Attempts to produce cyclodimers **53** by chemical reducing reagents acting by electron transfer (e.g. dissolved metal in THF) have



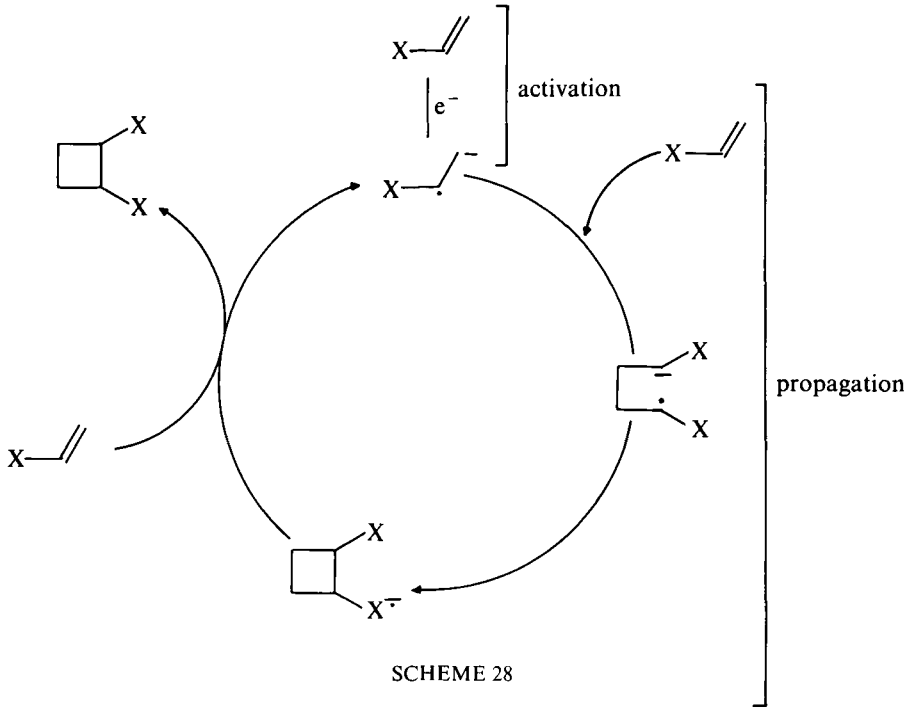
(52, R = H) **(53)**

trans isomer
(52–95%)

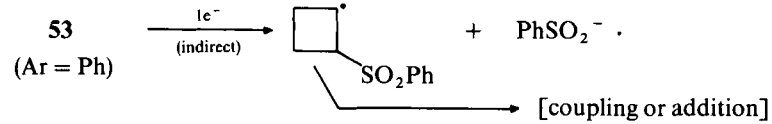
failed so far. The formation of **53** can be understood through a catalytic cycle (see Scheme 28; X represents the arysulfonyl moiety) based on the thermodynamic inequality $E^\circ_{52} > E^\circ_{53}$ which appears consistent with voltammetric data. Best yields are obtained when the activation reaction is conducted in an indirect manner (e.g. by means of an electro-chemically produced anion radical mediator. It is worth noting that **53** is strongly sensitive to the basicity of the medium and therefore small amounts of **54** can be isolated.



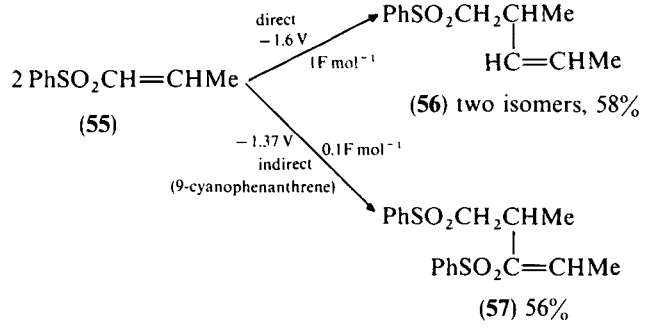
(54)



SCHEME 28



Cyclodimers **53** (Ar = Ph) can be regarded as good synthons[87] in cyclobutane chemistry since cleavage may provide the corresponding free radical, which in turn may be easily trapped or coupled. Until now, the cyclodimerization reaction could only be achieved

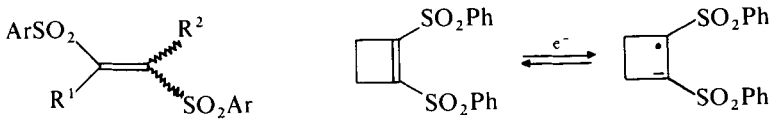


SCHEME 29

in the vinylic series. However, when R ≠ H, the reactivity is differently oriented . In this case the addition is still electrocatalytic, but the product distribution depends on the electroactivity of the adduct. In Scheme 29, the product is readily reduced, but it is protected when indirect activation is achieved. The difference in electricity consumption lies only in the cathodic cleavage of one of the C—S bonds.

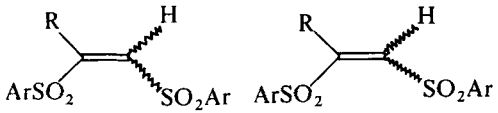
D. Ethylenic Disulfones

Sulfones possessing the general structure **58** exhibit fairly stable anion radicals. For example, the half-lifetime of the anion radical of **59**: is surprisingly long and the reactivity of the double bond (except for facile saturation in the presence of an efficient proton donor) toward alkyl halides and other electrophiles was found[80] to be very low. The ESR spectrum of **59**˙ obtained under electrolysis at room temperature (Figure 7) exhibits an alternating linewidth effect, implying probably the localization[126] of the electron between the two phenylsulfonyl groups here not considered as equivalent.



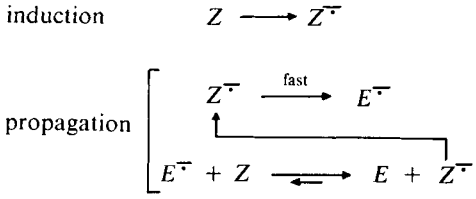
(58) (59) (59˙⁻)

The isomerizations of geometrical isomers of **58** series by cathodic induction were also achieved[88]. This reaction is of interest since the synthesis of *Z* and *E* isomers may proceed according to quite different procedures. Below is examplified the $Z \rightarrow E$ conversion by cathodic means of isomers **60** and **61**, conveniently performed in aprotic media in order to prevent protonation of transient anion radicals.



(60) (61)

In this series, *Z* isomers are less stable and the thermodynamic unequality $E^\circ_Z < E^\circ_E$ renders possible the isomerization with very high or even quantitative (when R = Ph) yields. The occurrence of such $Z \rightarrow E$ transformations can be easily detected in voltammetry where it is a characteristic feature in the course of the first and second sweeps as exhibited in Figure 8. The *Z* anion radical reduced is first transformed fast into an *E* anion radical, making feasible a chain reaction starting and propagating at the cathode interface.



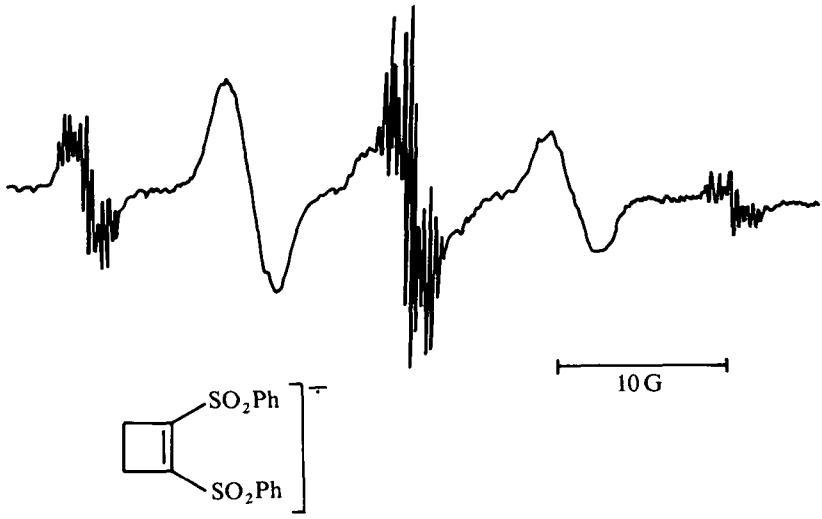


FIGURE 7. Unexpected ESR response of **59** anion obtained under electrolysis exhibiting an alternating linewidth effect. Electrolyte: DMF + Bu_4NBF_4 0.1 M. Platinum grid. Current density: 10 $\mu A\,cm^{-2}$

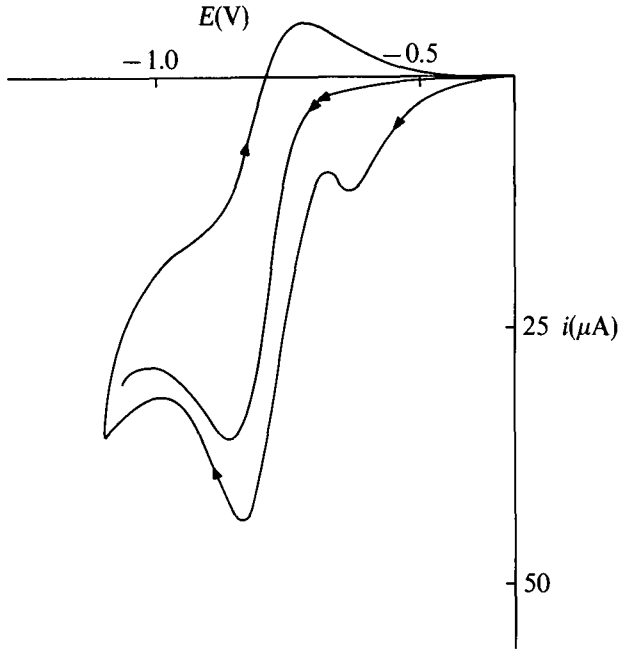
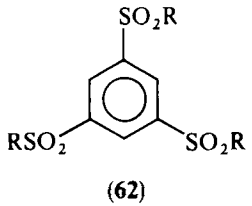


FIGURE 8. Cyclic voltammetries (first and second sweeps) of compound **61** (R and Ar = Ph). Concentration: 2.7×10^{-3} M. Sweep rate: 0.1 $V\,s^{-1}$. Electrolyte: DMF containing Bu_4NBF_4 0.1 M. Potentials are referred to Ag/AgI/I^-: 0.1 M system. Pt microcathole

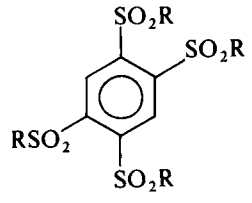
Similar transformations were also attempted on simpler **60** and **61** isomers (e.g. R = H). However, transient anion radicals involved in the isomerization process are then obviously less stable. Consequently, a drop in the transformation yields of the order of 40% was observed. The other compounds are cleavage products as excepted for such substrates for which $\pi \rightarrow O^*$ like transitions are more expectable.

E. Other Aromatic Polysulfones

The cathodic reductions of trisulfones and tetrasulfones, **62** and **63**, respectively, were also studied. However, their behaviors are quite different: thus **62** (R = Et) was found[89]

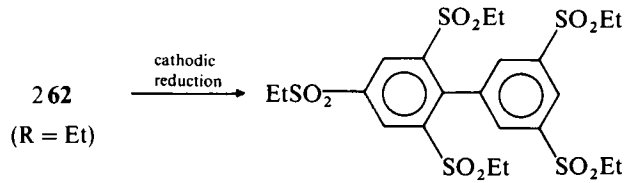


(62)



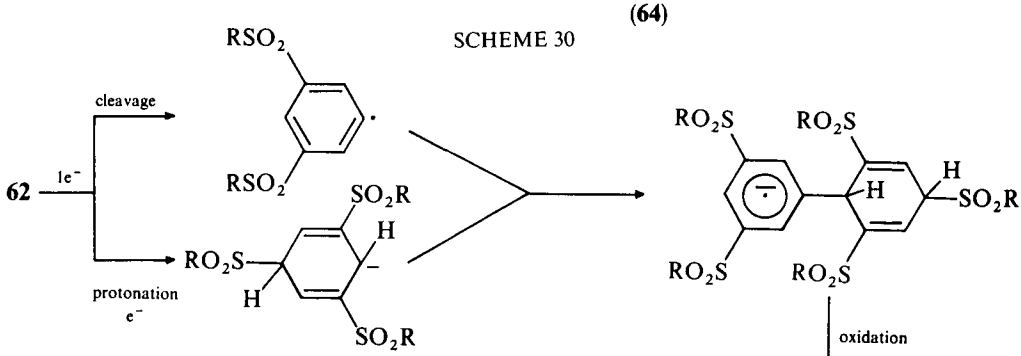
(63)

to be reduced in aprotic medium with major formation of the unexpected coupling product **64** (Scheme 30). It seems (but was not yet fully demonstrated) that the production of **64** would be facilitated by the concomitant formation of both a σ aryl radical from **62** and a nucleophile obtained from the dihydro reduction of the phenyl ring, leading to a $S_{RN}1$-type reaction. The nature of the associated and mandatory oxidation processes and their location cannot be for the moment, completely determined. Other sulfones (R = CF_3) were also studied[90], again involving the formation of dimers (Scheme 31).



(64)

SCHEME 30



SCHEME 31

64

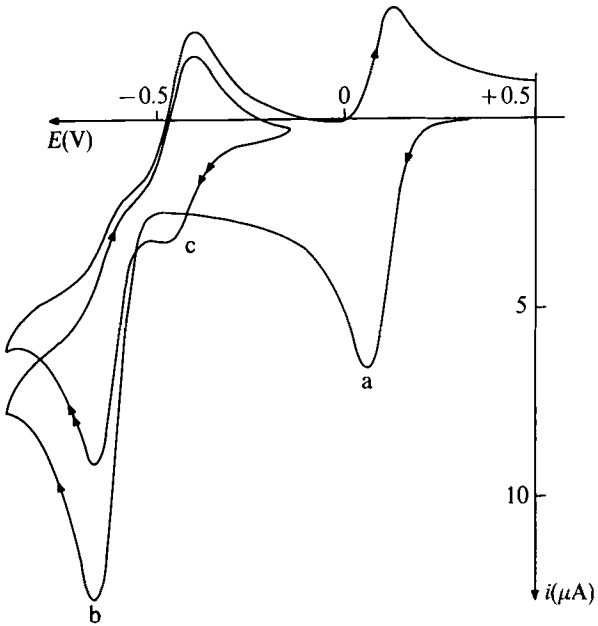
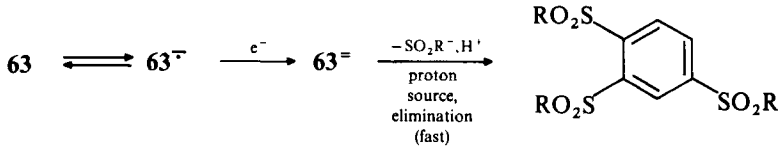


FIGURE 9. Cathodic behavior of tetrasulfone **63** (R = Ph). Voltammetry in DMF/Bu_4NBF_4 0.1 M at a stationary platinum microelectrode. Sweep rate: 100 mV s^{-1}. Reference electrode: Ag/AgI/I^- 0.1 M. Steps (a) and (b) correspond respectively to the formation of the anion radical and the dianion of **63**. The latter is readily cleaved into the related trisulfone, the redox response of which appears as (c)

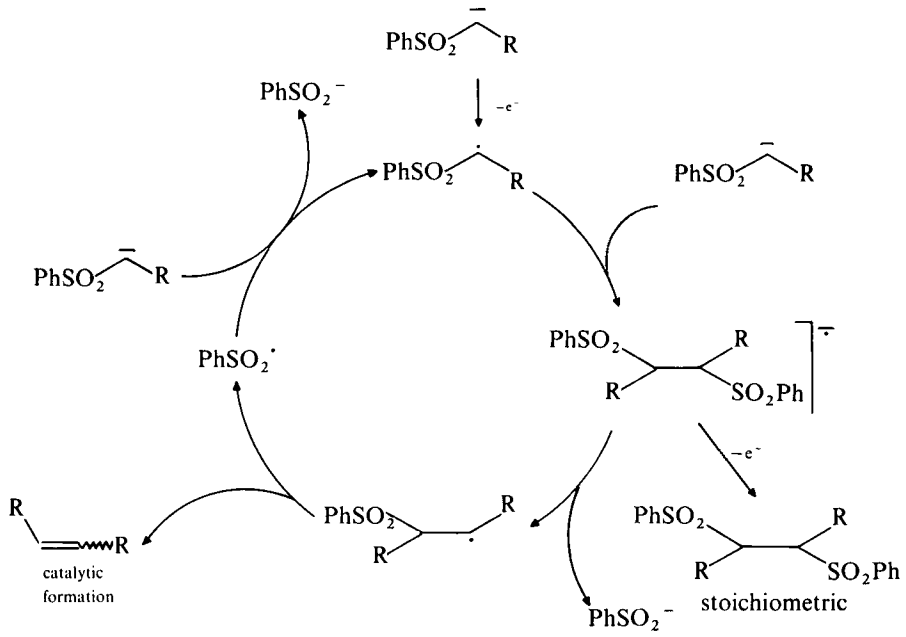
The formation of dihydro compounds from tetrasulfones **63** (Figure 9) and their elimination to yield the corresponding trisulfones can be demonstrated in an elegant manner by cyclic voltammetry. The standard potential values for the **63** series are extremely high, especially in the case where R = Ph. Therefore tetrasulfones **63** are among the compounds most easily reduced cathodically[89]. Anion radicals, as expected, are extremely stable and one has to reach the potential corresponding to the formation of the dianion to get the cleaved form.



(65)

F. Oxidation of Sulfone Anions

Anions of sulfones can be easily oxidized either chemically (CuX_2 or FeX_3) or electrochemically. Examples of dimer formation are available in the recent literature. The activity of sulfone anions in the presence of an oxidant or a positively polarized electrode was very recently described[91] by Amatore's group (Scheme 32).



SCHEME 32

The reactivity of the transient free radical (dimerization or olefin formation) has been discussed in terms of the relative amounts of oxidation (being either stoichiometric or catalytic).

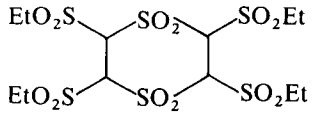
The coupling products of polysulfone anions submitted to anodic oxidation in other respects were also isolated[92].

$$RSO_2CH_2SO_2R \underset{BH}{\overset{B^-}{\rightleftharpoons}} RSO_2\bar{C}HSO_2R$$

$$\xrightarrow{e^-} RSO_2\dot{C}HSO_2R \overset{dim}{\rightleftharpoons} 1/2 \begin{array}{l} RSO_2CHSO_2R \\ | \\ RSO_2CHSO_2R \end{array}$$

The coupling reaction was found to be reversible (with reverse formation of the free radical upon temperature increase). More complex coupling reactions affording polysulfones such as **66** were also described[92].

$$2\,EtSO_2CH_2SO_2CH_2SO_2Et \xrightarrow[\substack{(Na)\\ \text{anodic}\\ \text{oxidation}\\ -4e^-}]{MeOH/LiClO_4}$$



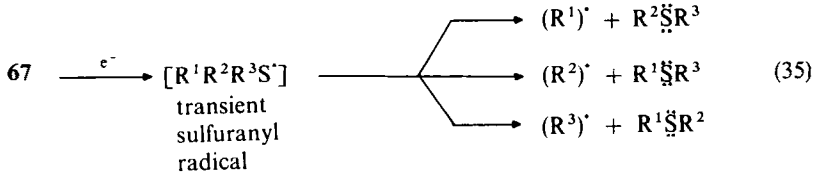
(66)

V. SULFONIUM IONS

The cathodic cleavage of onium salts, such as ammonium, phosphonium, sulfonium and sulfoxonium salt was extensively studied, especially by Horner[93] in its organic aspect. Here, we will focus on the behavior of sulfonium ions which *all* present[94] a cathodic step. Some of them can be easily reduced in aqueous media. Their fairly good solubility (both in aqueous and organic media) allows them also to be regarded as electrolytes and therefore their cathodic reactivity will eventually influence the product distribution. The first charge transfer to **67**-type salts could be understood in most of the cases (when R^1, R^2 and R^3 are aliphatic) as a dissociative one, and the transition can correspond to a

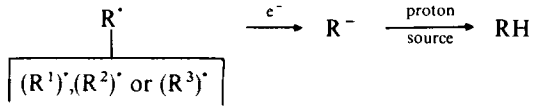
(67)

$\pi \rightarrow O^*$ process (equation 35). The fragmentation should depend on the capability of each radical formed to be stabilized or not. Leaving-group propensities could be determined[95] chemically (e.g. in one-electron reduction by means of potassium metal) and the following order was established: benzyl > secondary > primary > methyl > phenyl.

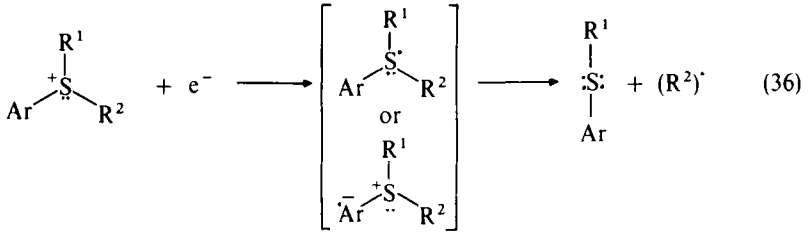


(35)

In the presence of an excess of reducing species, radicals $(R^1)^\cdot$, $(R^2)^\cdot$ and/or $R)^\cdot$ are usually reduced very fast and, owing to the dissociative character of the relevant electron transfer leading to their formation, the mechanism is strongly expected to be ECE (two heterogeneous electron transfers E associated with an extremely fast chemical reaction, which is the decomposition[96] of the transient sulfuranyl radical at room temperature).



On the other hand, by introducing into the structure a group possessing an intrinsically low LUMO (symbolized in equation 36 as Ar), transition to the π^* level can be considered (e.g. in equation 36, where R^2 is the favored leaving radical). Some examples are given in Table 2 showing voltammetric results for cases[97] where Ar = 1-naphthyl in the



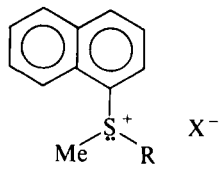
(36)

TABLE 2. Peak potentials (at a stationary plantinum microcathode) obtained with sulfonium salts **68**[a]

	Compound **68**		
	R	X	E_p (V)
68a	CH_3	CF_3SO_3	−1.51
68b	$CH(CH_3)_2$	BF_4	−1.49
68c	$H_2CC_6H_5$	BF_4	−2.23
68d	$H_2CC_6H_4CN$	BF_4	−0.92
68e	$H_2CCOC_6H_5$	CF_3SO_3	−0.74
68f	$H_2CC(C_6H_5)=C(CN)_2$	CF_3SO_3	−0.17

[a]Concentration: 10×10^{-4} M. Electrolyte: acetonitrile containing 0.1 M tetrabutylammonium tetrafluoroborate. Reference electrode: Saturated Calomel Electrode.

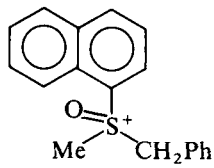
sulfonium series **68**. The huge potential shift between **68a** and **68f** is probably due to a large difference in cleavage kinetics, obviously favoring formation of highly stabilized radicals.



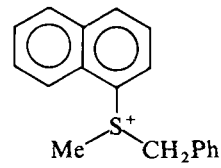
(**68**)

Approaches on the relative levels of σ^* and π^* of the LUMO and HOMO energies were made[98], using AM1 calculations with different Ar groups in the sulfonium compounds **69**. Thus it was found[98] that electrochemical and photochemical data, fluorescence quantum yields and also excited singlet state lifetimes, strongly indicate the crossover between σ^* and π^* LUMO states when strongly stabilized aryl groups such as naphthacene are involved. It is foreseeable that choosing a much less good leaving group R should strongly favor the $\pi \rightarrow \pi^*$ transition.

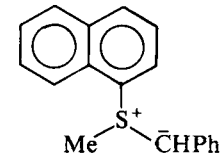
Lastly, let us emphasize the large difference of reducibility (measured in peak potentials vs SCE) between the sulfoxonium, the sulfonium and the corresponding ylide groups shown below[98].



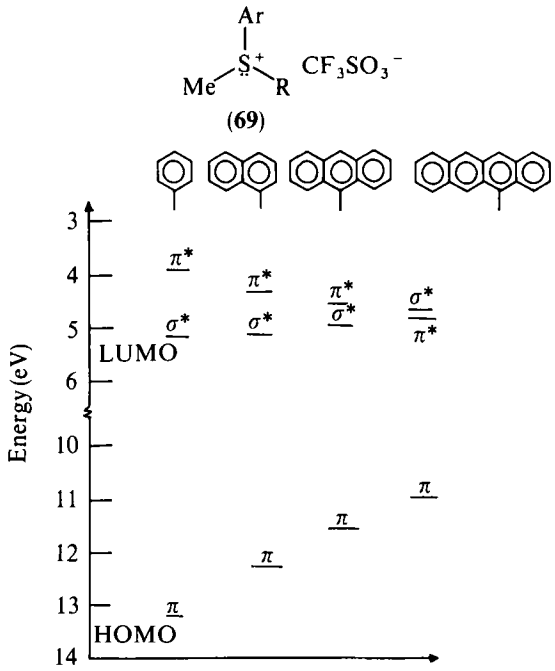
−0.79 V



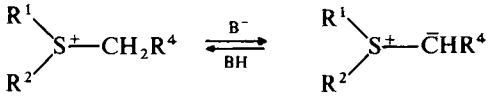
−1.23 V



−1.74 V



The cathodic behavior of sulfonium salts in organic solvents rendered basic by the addition of strong nonelectroactive bases in these media can be dramatically changed (equation 37). As a matter of fact, the electroactivity of sulfonium ions in the presence of a base is considerably shifted towards more reducing potentials because of the formation of the corresponding ylide **70**. The cathodic behavior of **67** studied in nonbasic media does not have to be the same as that of the ylide **70**. In the course of electrolyses conducted in nonbuffered media, one has to consider the acidity of the sulfonium groups



(37)

(67) **(70)**

which can give rise to the formation of the ylide. Conclusions—e.g. electric yield in potentiostic (at controlled potential) or product distribution in intentiostatic (imposed intensity) electrolyses—can be totally changed. In order to avoid side reactions depicted in equations 38 and 39, the addition of a proton donor, the pK_a of which is near to that of the starting sulfonium compound, can be helpful.

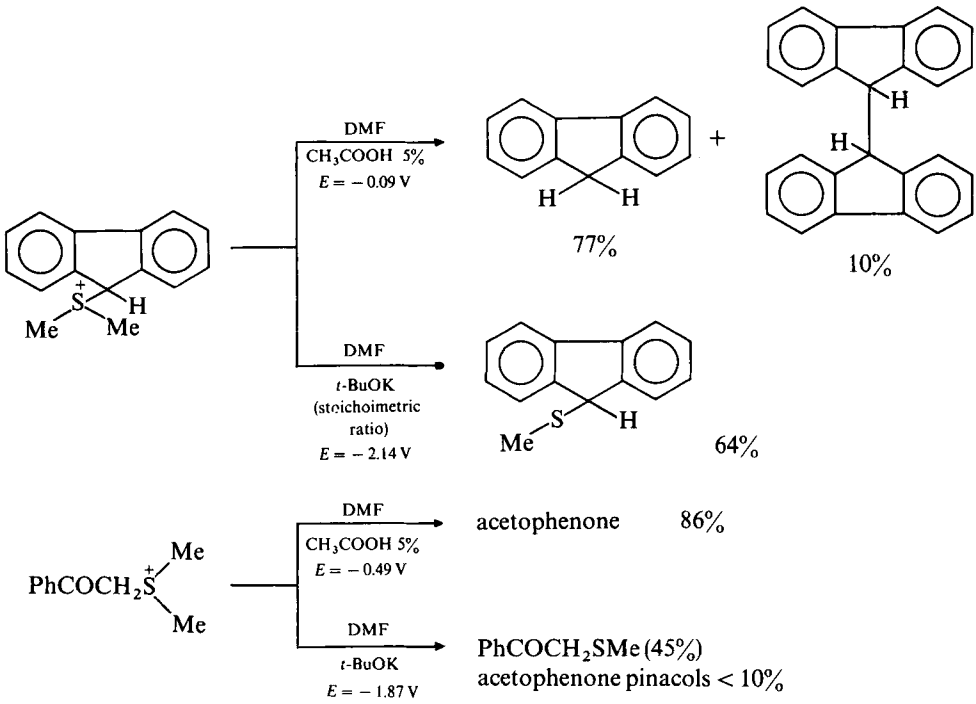
$$\mathbf{67} \xrightarrow{2e} (R^1)^- + R^2S{-}CH_2R^4 \tag{38}$$

$$(R^1)^- + \mathbf{67} \rightleftharpoons (R^1)H + \begin{matrix} R^1 \\ \diagdown \\ \overset{+}{S} \\ \diagup \\ R^2 \end{matrix}{-}\bar{C}HR^4 \tag{39}$$

In the frequent case where the ylide **70** is not electroactive at the potential at which **67** is cleaved and the acid–base equilibrium involving the sulfonium groups lies strongly towards the right side, the global (and generally observed), reaction can be written as in equation 40.

$$2\,\mathbf{67} \xrightarrow{2e^-} (R^1)H + \mathbf{70} + R^2SCH_2R^4 \qquad (40)$$

The electrochemical reaction is apparently monoelectronic with 50% of the substrate generally recovered after the work-up. There is practically no study available on the cathodic behavior of sulfonium ylides for at least two reasons: (i) the very reducing potentials which have to be reached to make the electron transfer onto **70** achievable, and (ii) the choice of a base which determines the use of a suitable electrode material (e.g. with *t*-BuOK and *n*-BuLi, the ease of amalgam formation on mercury electrodes necessitates the use of glassy carbon cathodes). The two examples given in Scheme 33 outline the dramatic change observed[99] by addition of a strong base.

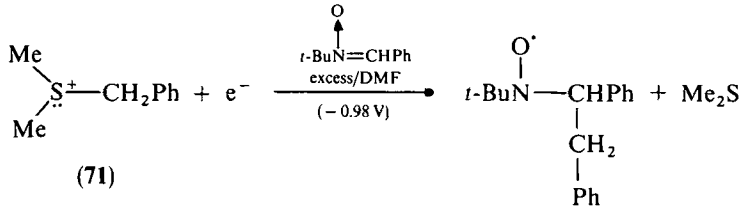


SCHEME 33

Nevertheless, owing to the high reducing potentials necessary for their cleavage, sulfonium cations can be considered as a very convenient source of free radicals. For this process, the standard potential of the conversion of the free radical produced by the scission $R^{\bullet} \rightarrow R^-$ has to be smaller than the reduction potential of **67**. Therefore, electrochemically formed radicals can further undergo addition, coupling or spin-trapping reactions.

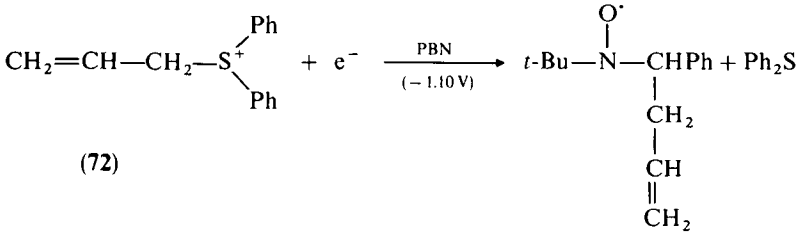
A facile way to foresee the mode of cleavage and what C—S bond is preferentially broken in the course of the chemical reaction associated with the charge transfer, is to use spin markers[100] which lead after addition of electrogenerated free radicals, to stabilized labeled paramagnetic species often easily analyzed by means of ESR spectroscopy.

For example, the dimethylbenzylsulfonium compound **71** reduced in the presence of an excess of *t*-butylphenylnitrone (BPN) affords the formation according to a one-electron process of the corresponding stable nitroxide (characteristic six-line ESR response) after addition of a benzyl radical (Scheme 34). These trapping reactions are effective provided



(71)

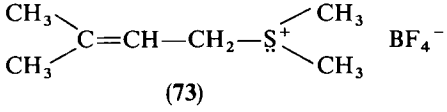
$a_N = 14.57$ G
$a_H = 2.44$ G



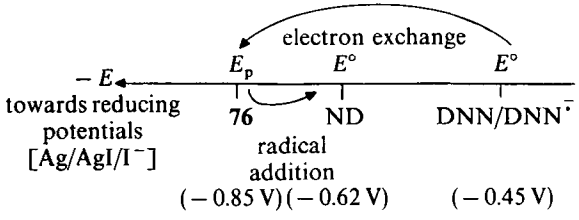
(72)

$a_N = 14.57$ G
$a_H = 2.44$ G

SCHEME 34



(73)



SCHEME 35

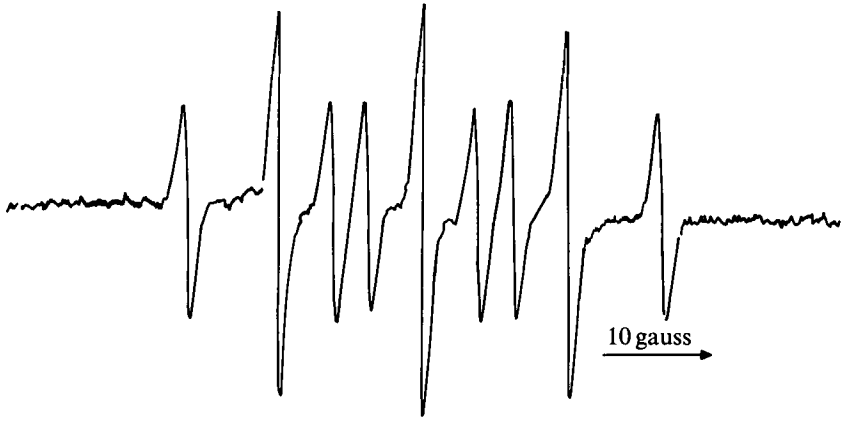
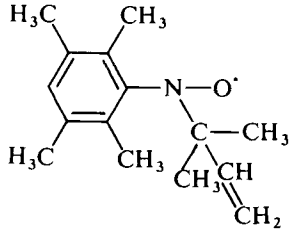


FIGURE 10. ESR of the radical adduct with nitrosodurene obtained from the cathodic fragmentation of the sulfonium compound **73** ($a_N = 13.73$ G and $a_H = 8.80$ G). Case of an indirect reduction by 1,8-dinitronaphthalene electrogenerated anion radical (from Reference 100)

the electrolyzed sulfonium cations are *more* electroactive than BPN. In cases where this condition is not fulfilled, one should consider the use of a mediator, the radical anion of which does not react with the spin marker. The case of **72** in the presence of the spin trap (nitrosodurene ND) indirectly reduced by the anion radical of 1,8-dinitronaphthalene (DDN) is shown in Scheme 35). Thus, the produced nitroxide was demonstrated to be the one obtained from **73** and corresponding to the trapping of the dimethylallyl radical (Figure 10).



The expected strong instability of the transient sulfuranyl radical formed after charge transfer onto starting onium cation **67** allows one to consider[101] sulfonium compounds as candidates to perform redox catalysis reactions, allowing in this manner cleavage (and therefore free radical formation) in solution. Far from the electrode, the rate of reduction of these free radicals is diffusion controlled, but other very fast reactions (coupling, addition, spin trapping) may also take place in the bulk. Equations 41 – 48 show the indirect reduction of **67** (R_3S^+) by means of the anion radical of the mediator A, provided the inequality $E^\circ_A < E^\circ_{67}$ is fulfilled. The nature of the observed reactions [principally understood as a competition between the reduction of R$^\cdot$ radical (reaction 45) and the obtainment of the alkyldihydro form ARH (reaction 46)] appears to depend on the rate of the electron transfer. Let us take as an example the mixed electrolysis of trimethylsulfonium tetrafluoroborate (reduction potential $E = -1.76$ V) in the presence of anthracene or of benzophenone.

cathode interface

$$A \underset{\text{(electrolyte } M^+ X^-)}{\overset{e^-}{\rightleftharpoons}} (A^{\cdot -}, M^+) \quad (41)$$

solution

$$(A^{\cdot -}, M^+) + R_3S^+ \rightleftharpoons (A^{\cdot -}, R_3S^+)\ \text{diffusion} \quad (42)$$

$$(A^{\cdot -}, R_3S^+) \rightleftharpoons \begin{matrix}(A, R_3S^{\cdot}) \\ \text{or} \\ (A, R_2S, R^{\cdot})\end{matrix}\ \text{activation} \quad (43)$$

$$(A, R_2S^{\cdot}) \rightleftharpoons A + R_2S + R^{\cdot}\ \text{diffusion} \quad (44)$$

$$R^{\cdot} + A^{\cdot -} \xrightarrow[\text{transfer}]{\text{electron}} R^- + A \quad (45)$$

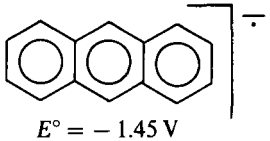
or

$$R^{\cdot} + A^{\cdot -} \xrightarrow{\text{coupling}} AR^- \xrightarrow{\text{proton source}} ARH \quad (46)$$

$$R^{\cdot} + HX \longrightarrow RH + X^{\cdot} \quad (47)$$

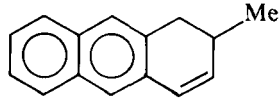
$$R^{\cdot} \longrightarrow \text{coupling or disproportionation} \quad (48)$$

Reaction 49 in Scheme 36 affords the expected alkyldihydro anthracene and therefore fits 'perturbed' redox catalysis where the key step is the coupling of a methyl radical and an anthrancene anion radical. On the other hand, when the potential gap between $A^{\cdot -}$ formation and R_3S^+ reduction is made much larger, the rate of the homogeneous electron transfer is expected to be very slow and the sulfonium cation acts preferentially as a proton donor: in the example given in reaction 50, the carbonyl group of benzophenone is then two-electron reduced, contributing to the ylide formation which then leads to a specific reactivity with the carbonyl group.

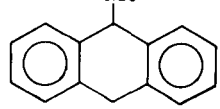


$E^\circ = -1.45$ V

$\xrightarrow[\text{DMF}]{Me_3S^+}$

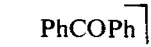


40%



60% (49)

while



$E^\circ = -1.25$ V

$\xrightarrow[\text{DMF}]{Me_3S^+}$

benzhydrol 50%

1,1-diphenyl ethanediol 50% (50)

SCHEME 36

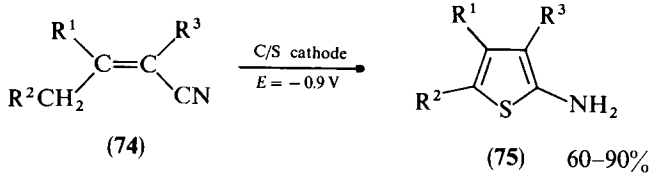
Similarly, t-Bu$\overset{+}{\underset{\cdot\cdot}{S}}Me_2$ ($E = -1.33$ V) was found to be an efficient t-butylation reagent. However, sulfoxonium salts are[99] too acidic to give anything other than dihydro forms.

VI. THE CARBON–SULFUR ELECTRODE

The use of sacrificial carbon–sulfur electrodes (generally made from a 1:2 molten mixture of graphite powder and sulfur) allows the easy activation (anodic or cathodic) of sulfur even in organic solvents in which this element is not soluble. Therefore[102,103], electrophilic species S_y^{2+} may be readily produced by anodic polarization ($E > -1.6$ V/SCE) while, on the contrary, nucleophilic entities S_x^{2-} are formed when sulfur–carbon electrode is cathodically polarized ($E < -0.6$ V/SCE).

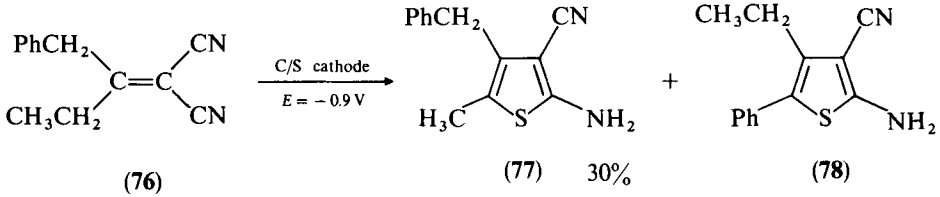
A. Cathodic Activation

Ylidene nitriles **74** with R^1 and R^2 = alkyl groups and with R^3 being an electron-withdrawing group (CN, CO_2R, COPh, etc.) can be converted[104] at the sulfur/carbon cathode into 2-aminothiophenes **75** often in good yield (Scheme 37). With ylidene nitriles bearing two activated methylene groups like **76**, two different aminothiophenes are obtained (Scheme 38).



(74) (75) 60–90%

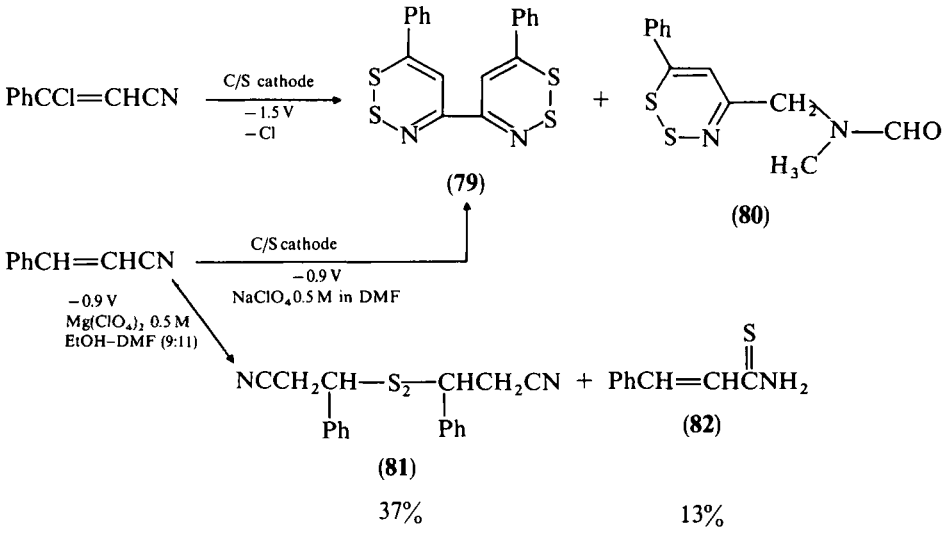
SCHEME 37



(76) (77) 30% (78)

SCHEME 38

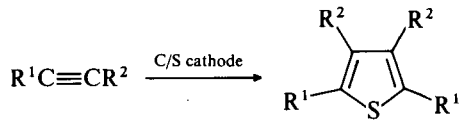
Substrates bearing potential leaving groups were also widely studied[105–107]. The nucleophile formation (obtained either from the cathodic cleavage of organic substrates or from reduction of the C–S electrode) can be easily monitored by fixing the applied potential. These reactions are rarely selective and a wide palette of sulfur organic compounds can be prepared, but each only in moderate yields. Sometimes, S—S bridges can be included with or without involving a DMF moiety (here used as a solvent); see Scheme 39.



SCHEME 39

Thus, the bicyclic product **79** (6,6'-diphenyl-4,4-di-1,2,3-dithiazine) can be obtained either from 3-chloro-3-phenylpropenenitrile in moderate yield (44%) at a rather reducing potential or directly from cinnamonitrile in much higher yield (75%). Note the formation of amide **80** and also the dramatic orientation change (obtainment of compounds **81** and **82**) in the presence of magnesium salt and proton donor added to DMF.

Alkynes were also reported[108] to react cathodically at the C/S cathode and to produce tetrasubstituted thiophenes **83** in fairly high yields.



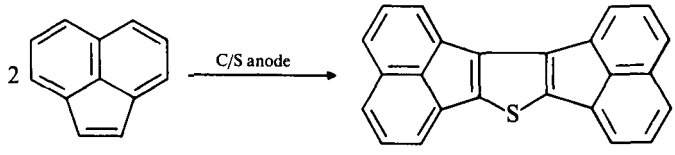
(83)

$R^1C=CR_2$		Isolated product **83** (%)
R^1	R^2	
H	Ph	no reaction
H	CO_2Et	10
Ph	CHO	82
Ph	CO_2Me	85
Ph	CN	80
CO_2Me	CO_2Me	32

B. Anodic Activation

The formation of electrophilic species like S_2^{2+} and S^{2+} can be expected[109] through direct oxidation of the S/C anode at rather oxidizing potentials. Electrophilic

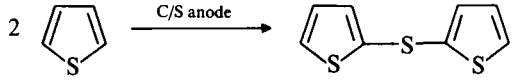
substitutions or/and additions will occur after the electrolysis. Thus, acenaphtylene leads at room temperature to the corresponding thiophene **84** (Scheme 40). Many other examples of electrophilic substitution drawn from very recent work [108–112] are now available. With thiophenes and furans, C—S bridges are always obtained (Scheme 41).



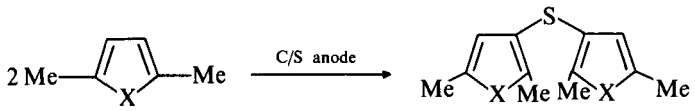
70%

(84)

SCHEME 40



(85) 30%



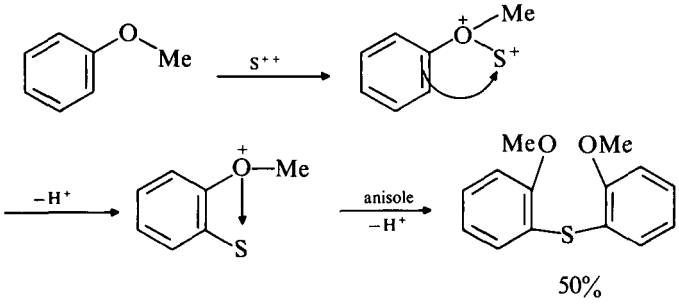
X = O or S

(86) X = O 92%

X = S 73%

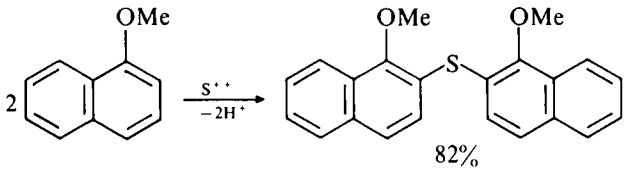
SCHEME 41

The action of S/C anode was also shown to be of high interest with aromatic ethers and phenols. The regioselectivity of the substitution can be explained by the basicity of the ether function (Scheme 42). With phenols, the reaction was found to be less selective (Scheme 43).

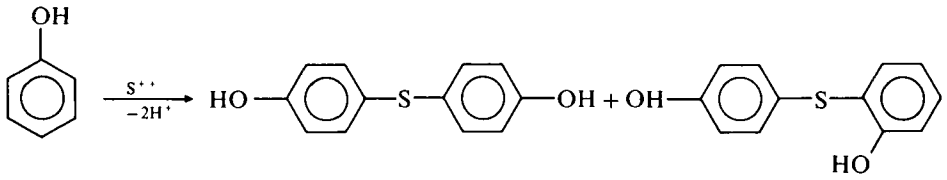


50%

SCHEME 42



while

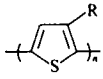
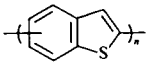
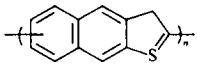
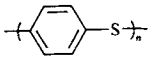
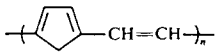
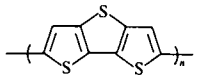
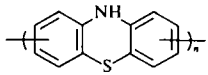


SCHEME 43

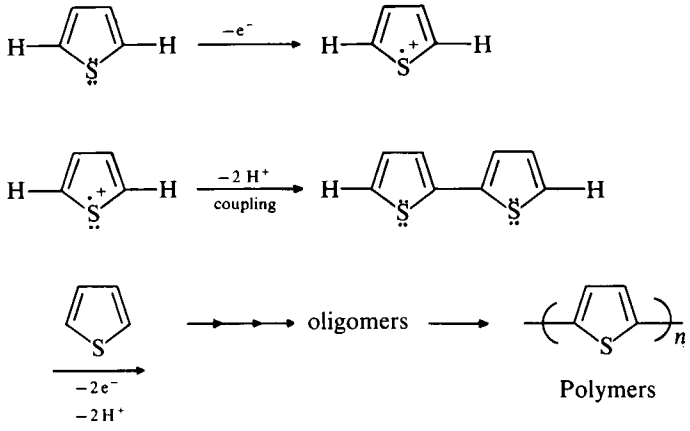
VII. POLYMERIZATION OF SULFUR-CONTAINING AROMATIC MOLECULES

Aromatic systems are well known to afford the formation dimers, oligomers and polymers by anodic means, mostly in poorly nucleophilic media[113]. In some cases (see Table 3) insoluble but electrically conducting deposits grow at the anode surface. Such materials are directly obtained in their p-doped state and their conductivity is

TABLE 3. Sulfur-containing conducting polymers

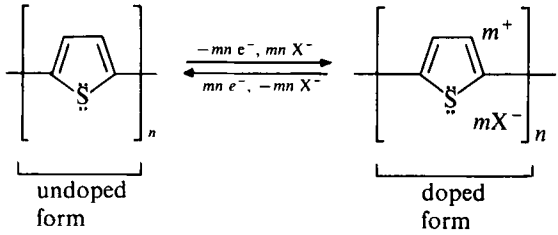
Entry	Monomeric unit formula	Polymer name	Reference
1		Polythiophene (R = Me, functionalized chain, etc.)	114
2		Poly(benzo[*b*]thiophene)	115
3		Poly(naphtho[2,3-*c*]thiophene)	116
4		Polythiophenol	117
5		Poly(2,5-thienylenevinylene)	118
6		Poly[dithieno-3,2-*b*: 2′,3′-*d*) thiophene	119
7		Poly(phenothiazine)	120
8		Poly(sulfur nitride)	121

the condition for their constant growing in thicker and thicker layers. Depending on the electronic structure of the monomer and the conditions of the reaction, as well as on the nature of the electrolyte anion considered here as a dopant, great changes in the conductivity of the film can be observed. With most of the electrodeposited polymers, this electronic conductivity is of the order of $0.1\,S\,cm^{-1}$ to $100\,S\,cm^{-1}$. Molecular weights are generally extremely large. The anodic polymerization process written below for the case of thiophene consumes 2 moles of electrons per mole of



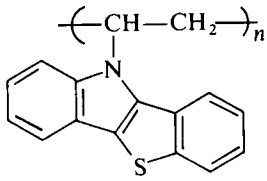
SCHEME 44

substrate (Scheme 44). Since the redox potential of the polymer is generally smaller than that of the monomer, the polymer is *directly* obtained in its oxidized form, i.e. in its doped

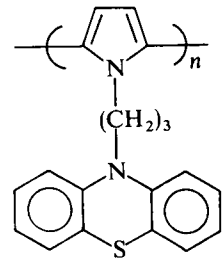


conductive form where m represents the doping rate of the polymer, often of the order of 0.2 to 0.4 electron hole or positive charge-per monomer unit. Table 3 shows some electroactive polymers containing sulfur and generally anodically prepared. In the series, the most versatile materials are made from thiophenes often substituted in the 3-position. R in entry no. 1 in Table 3 can be functionalized (e.g. the thiophene moiety may bear a chiral center, a polyether chain, a basic or an acidic function, etc.).

Other kinds of polymers can possess organic moieties with at least one sulfur atom. Those polymers exhibit particulars caused by the presence of redox centers, possibly in addition to the intrinsic conductivity of the main polymeric chain. For example, poly(*N*-vinylthionaphthene-indole) **87** can be chemically produced[122] by polymerization of the vinyl group. The product is considered as a redox polymer with redox centers attached to a nonconducting polyvinyl chain.

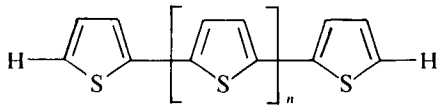


(87)



(88)

On the other hand, the poly(pyrrole-phenothiazine) **88** is anodically[123] formed by pyrrole polymerization. This conducting polypyrrole chain possesses phenothiazine redox centers: two reversible one-electron steps occur in oxidation at less oxidizing potentials than the redox potential of the main polymeric chain. Additionally formation of radical cations and dications (analogous to polarons and bipolarons) on isolated thiophene oligomers **89** (with $1 \leqslant n \leqslant 6$) was carried out[127].



(89)

VIII. ACKNOWLEDGMENTS

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CHAPTER 11

Syntheses and uses of isotopically labelled compounds with sulphur-containing functional groups

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ABBREVIATIONS*

AIBN	α,α-azobisisobutyronitrile
BBB	blood brain barrier
Bn	benzyl
BOC	*N*-*t*-butoxycarbonyl
CNS	central nervous system

*See also abbreviations on the preliminary pages of this volume.

DDC	dicyclohexylcarbodiimide
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone
DIBAH	diisobutylaluminium hydride
DMS	dimethyl sulphide
DBN	1,5-diazabicyclo[4.3.0]non-5-ene
Dyglyme	dimethoxyethane
EOB	end of bombardment
FAB-MS	fast atom bombardment–mass spectrometry
GLC-MS	gas liquid chromatography–mass spectrometry
HPLC	high performance liquid chromatography
ID-GC-MS	isotope dilution–gas chromatography–mass spectrometry
Iodogen	1,3,4,6-tetrachloro-3α,6α-diphenylglycouril
KIE	kinetic isotope effect
Kryptofix 222	2,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane
LSC	liquid scintillation counting
MIBK	methyl isobutyl ketone
NCA	non-carrier added
PBP	penicillin binding protein
PET	positron emission tomography
Pipsyl chloride	4-iodobenzenesulphonyl chloride
PMB	*p*-methoxybenzyl
PTC	phase transfer catalysis
Py	pyridine
RR	Raman resonance
RT	room temperature
TATT	triaminetrithiol
TBAF	tetrabutylammonium fluoride
TBDPS	*t*-butyldiphenylsilazane
TEATT	tetraaminetrithiol
TFA	trifluoroacetic acid
TMSCl	Chlorotrimethylsilane
TLC	thin layer chromatography
TS	transition state
TSC	thiosemicarbazone

I. INTRODUCTION

Sulphur-containing organic compounds play an important role in life processes and are constituents of numerous drugs. Their isotopically labelled analogues have been used to trace the pathways of the molecules with sulphur in functional groups in the course of their transformations in living organisms, and to identify their metabolites. The industrial desulphuration of petroleum is also an ever-actual task in environmental sciences facing the disastrous problem of acid rain. Several steps in the synthetic schemes applied for production of isotopically labelled compounds have been found to be attractive for fundamental physico-chemical studies and have been investigated recently with hydrogen kinetic isotope effect (KIE) methods. Suggestions concerning the relevant structures of transition states have been made. Solvolytic reactions have been the most frequent objects of such studies contributing greatly to the domain of physical organic chemistry. Deuterium and tritium KIE studies will stimulate the corresponding heavy isotope effect investigations which are less frequent. Unfortunately, the majority of kinetic deuterium isotope effect studies have been carried out at a single temperature (the most accessible one for spectroscopic observations) and the number of conclusions which can

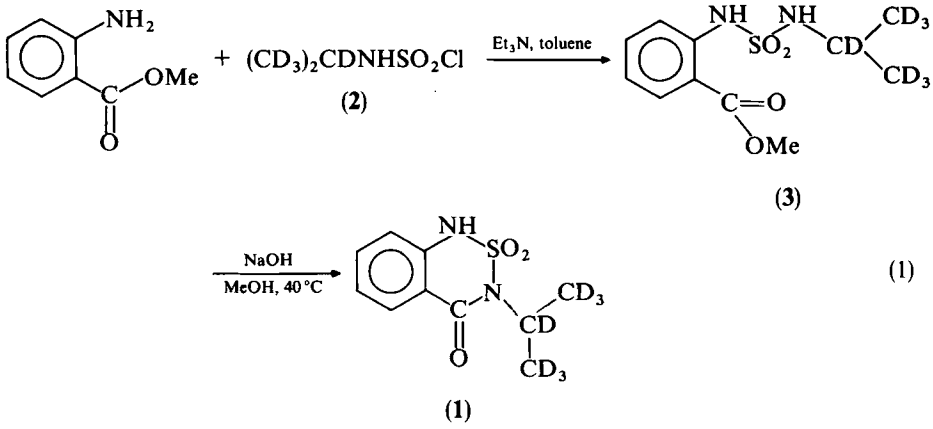
be drawn is rather limited. Nevertheless, these are important first approaches to the investigation of the rate-determining reaction steps and some recent studies are presented in Section V. The development of modern isotope separation technologies will result in the increase of tracer and isotope effect studies, and a brief review of physical researches related to sulphur chemistry is therefore given in this chapter too.

II. SYNTHESIS OF COMPOUNDS LABELLED WITH STABLE ISOTOPES

A. Synthesis of Deuterium and Carbon-13 Labelled Compounds

1. Synthesis of [D_7]-bentazone

3-[D_7]-isopropylbenzo-2-thia-1,3-diazinon-(4)-2,2-dioxide, **1**, the deuteriated internal standard, is needed for quantitative determination by isotope dilution–gas chromatography–mass spectrometry (ID–GC–MS) of bentazone. This herbicide, not easily biodegradable and found in rain water[1] and drinking water[2], has been synthesized[3] as shown in equation 1 from methyl anthranilate with sulphamoyl chloride **2**[4] via the intermediate sulphonamide **3**, in an isotopic purity of 95 atom%.



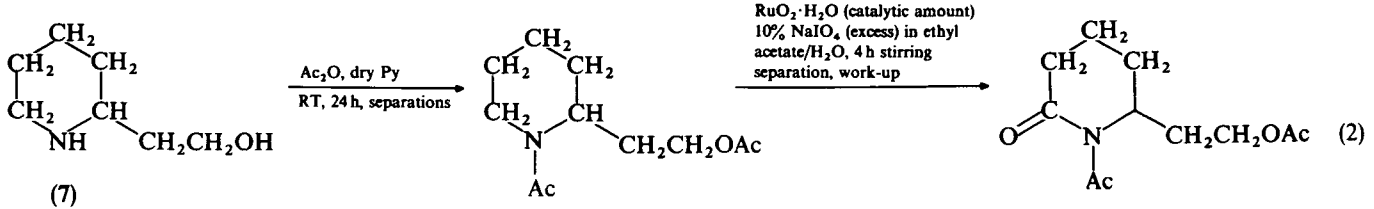
(1)

2. Synthesis of dideuteriated [±]-thioridazine

This phenothiazine-type antipsychotic agent (**4**) has been synthesized[5] in a seven-step procedure (equations 2 and 3). The 2-(2-hydroxyethyl)-1-methyl[6,6-$^2H_2$]piperidine (**5**) has been obtained[5–8] by ruthenium tetroxide oxidation of the *N*,*O*-diacetylated derivative (**6**) of aminoalcohol (**7**) and subsequent lithium aluminium deuteride reduction of *O*-acetylated 2-(2-hydroxyethyl)-6-piperidinone **8**. **4** has been produced in at least 76% yield by treatment of **5** with thionyl chloride and *N*-alkylation of 2-methylthio-10*H*-phenothiazine with the obtained 2-(2-chloroethyl)-1-methyl[6,6-$^2H_2$]piperidine[8], and applied for metabolic and pharmacokinetic studies.

3. Synthesis of L-[4,4-$^2H_2$] and D,L-[3,3,4,4-$^2H_4$]methionine

L-[4,4-$^2H_2$]methionine **9** and D,L-[3,3,4,4-$^2H_4$]methionine **10** have been synthesized in 40% and 26% overall yields, respectively[9,10], as shown in equations 4 and 5. The deuteriated compounds **9** and **10** as well as [3,3-$^2H_2$] and [2,3,3-$^2H_3$]methionine synthesized

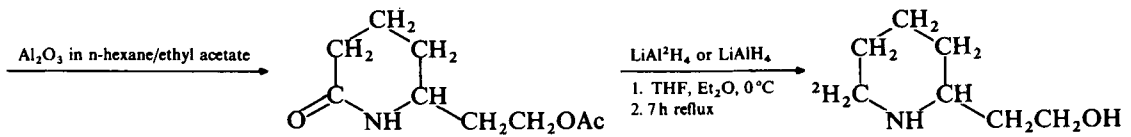


(7)

(6) 90% yield

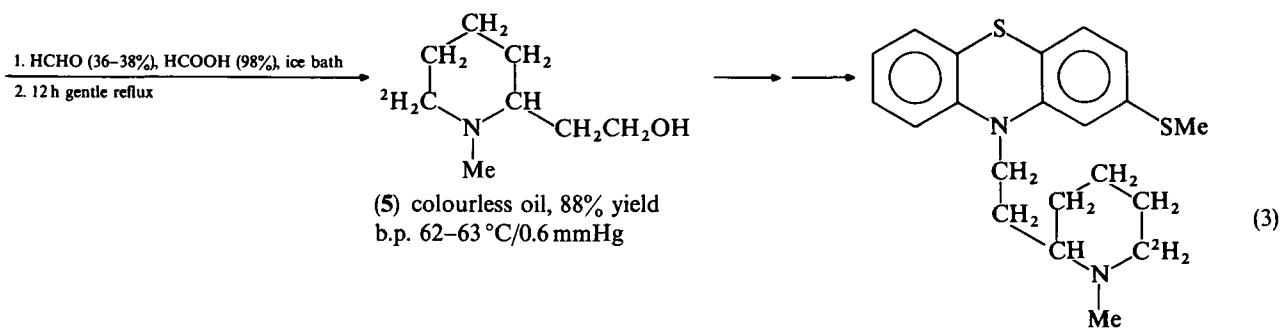
87% yield, pale yellow
liquid b.p. 120–122 °C/0.02 mmHg

(2)



(8) 76% yield, m.p. 77–78 °C

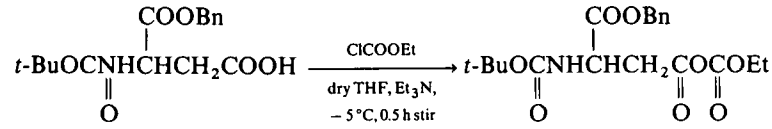
(7)–$^2H_2$ m.p. 36–38 °C

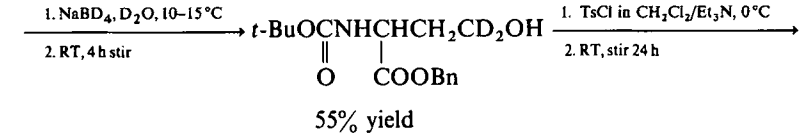


(5) colourless oil, 88% yield
b.p. 62–63 °C/0.6 mmHg

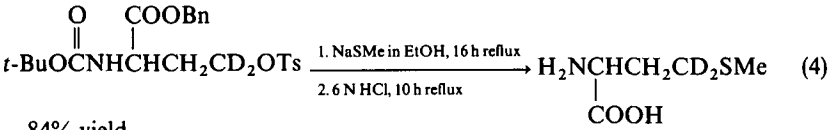
(3)

(4)



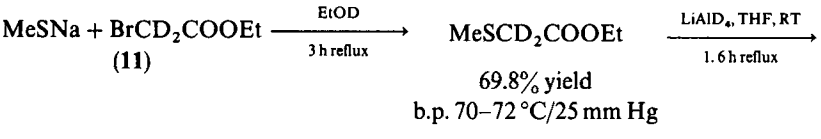


55% yield

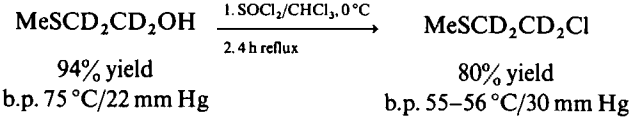


84% yield

(9) 69.5% yield
m.p. 275–277 °C

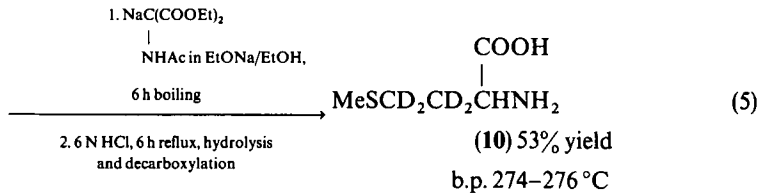


69.8% yield
b.p. 70–72 °C/25 mm Hg



94% yield
b.p. 75 °C/22 mm Hg

80% yield
b.p. 55–56 °C/30 mm Hg

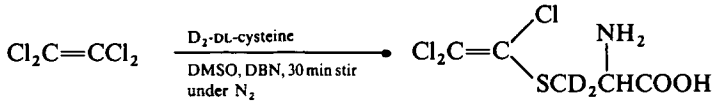


(10) 53% yield
b.p. 274–276 °C

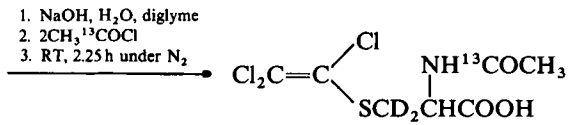
previously[11] have been utilized to study the biosynthesis of 1-aminocyclopropane-1-carboxylic acid and of L-azetidine-2-carboxylic acid[12] and to study the ^{1}H and ^{13}C NMR of various methionine derivatives.

4. Synthesis of deuterium and carbon-13 labelled analogues of the cysteine and N-acetylcysteine conjugates of tetrachloroethylene

S-(1,2,2-Trichlorovinyl)-DL-cysteine-3,3-$^{2}H_2$, **12**, has been prepared[13] from tetrachloroethylene and DL-cysteine-3,3-$^{2}H_2$ (equation 6a). The ^{13}C-*N*-acetyl-*S*-(1,2,2-trichloro-

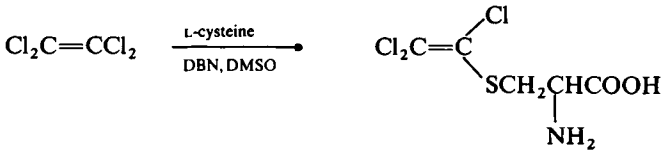


(12) 60% yield
m.p. 148–149 °C

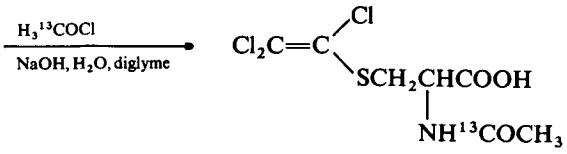


(6a)

(14) 47% yield, tan solid,
m.p. 158–159 °C, 97% purity



(13)
m.p. 153.5–155.5 °C



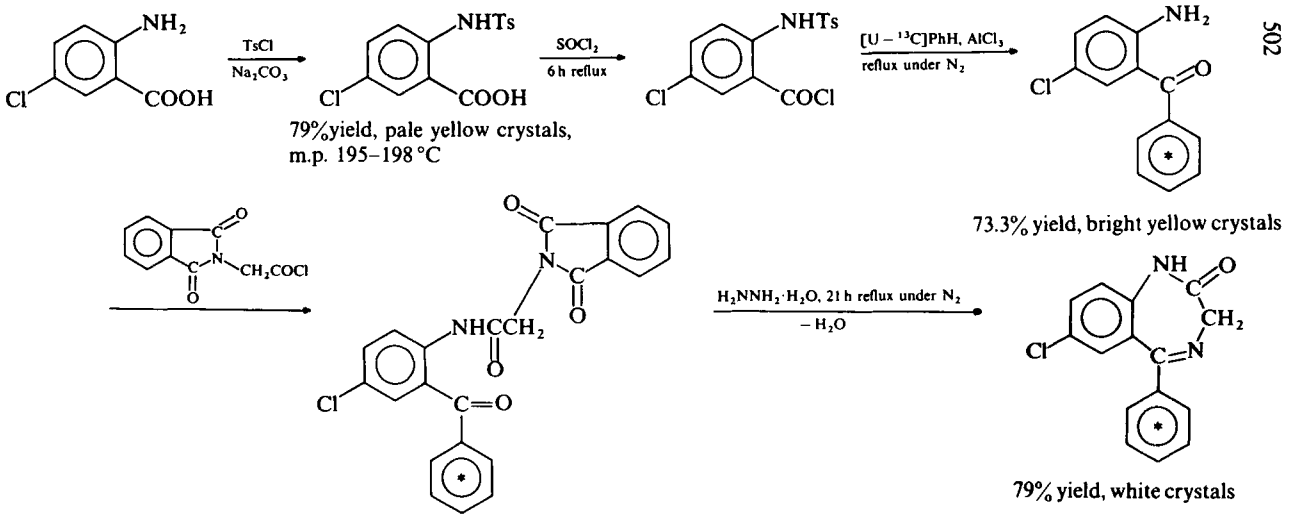
(15) 63% yield, light tan solid,
m.p. 155–156 °C, 97% purity via ^{13}C NMR

(6b)

vinyl)cysteine compounds **14** and **15** have been prepared[14] via acetylation of the deuteriated and unlabelled cysteine conjugates **13** with ^{13}C-acetyl chloride (equations 6a and 6b). Both compounds **14** and **15** have been applied for quantitative mass spectral determinations of the cysteine and *N*-acetylcysteine metabolites of tetrachloroethylene in rat and in mice[15–20].

5. Synthesis of adinazolam mesylate multiply labelled with carbon-13 and deuterium

The title compound **16** labelled with stable isotopes, a triazolobenzodiazepine possessing anxiolytic and antidepressant activity[21–23], has been synthesized[24] (equation 7) for conducting bioavailability studies. The double-labelled **16b** has been prepared for use as an internal standard.



(7)

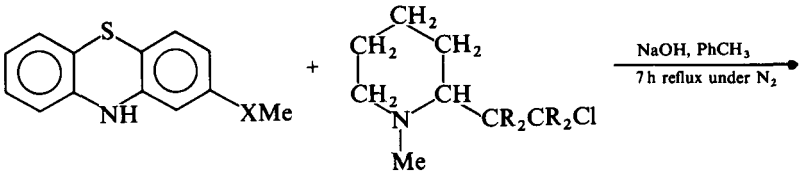
(16a) R = ^{1}H, 16% overall yield based on [$^{13}C_6$] benzene

(16b) R = ^{2}H, 22% overall yield based on [$^{13}C_6$] benzene and 87.9% yield based on *N,N*-di[$^{2}H_3$]methyl-aminoacetyl hydrazine m.p. 241–243 °C

• = [U-^{13}C] = labelled uniformly with ^{13}C (> 99% enrichment) in the unsubstituted phenyl ring. The double-labelled **16b** has been prepared for use as an internal standard.

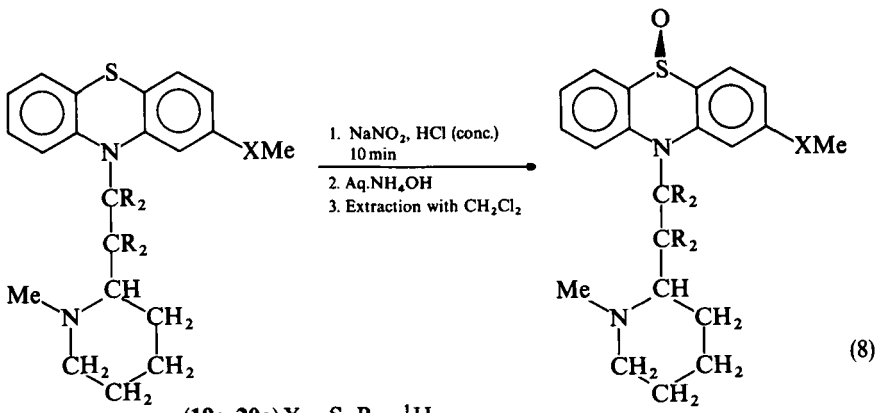
6. Synthesis of deuterium-labelled mesoridazine and sulphoridazine

Four deuterium atoms have been introduced[25] into the ethyl group of the *N*-10 side chain of these *S*-oxidative metabolites of thiorizadine (antipsichotic drugs[7]) for metabolic and pharmacokinetic studies and to establish the true internal standards for their GLC-MS assays[25] (equation 8). *N*-10 alkylation of **17b** or of **17c** with 2-(2-chloro[1,1,2,2-$^2H_4$]ethyl)-1-methylpiperidine **18b** produced [1,1,2,2-$^2H_4$]-labelled mesoridazine **19d** and sulphoridazine **19f** in good yields. Selective ring sulphur oxidation of these compounds with nitrous acid resulted in tetradeuteriated analogues of the 5-sulphoxide metabolites of thioridazine, mesoridazine and sulphoridazine, **20a–f**.



(17a) X = S
(17b) X = SO
(17c) X = SO_2

(18a) R = H
(18b) R = ^2H

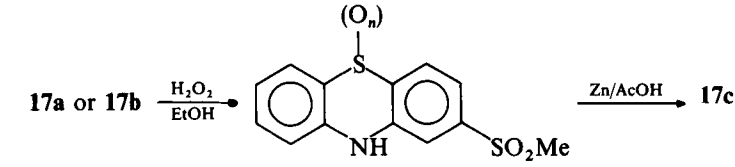


(8)

(19) **(19a, 20a)** X = S, R = ^1H (77% yield) **(20)**

(19b, 20b) X = S, R = ^2H (thiorizadine)[7]
(19c, 20c) X = SO, R = ^1H (mesoridazine)
(19d, 20d) X = SO, R = ^2H (mesoridazine)
(19e, 20e) X = SO_2, R = ^1H
(19f, 20f) X = SO_2, R = ^2H (sulphoridazine)

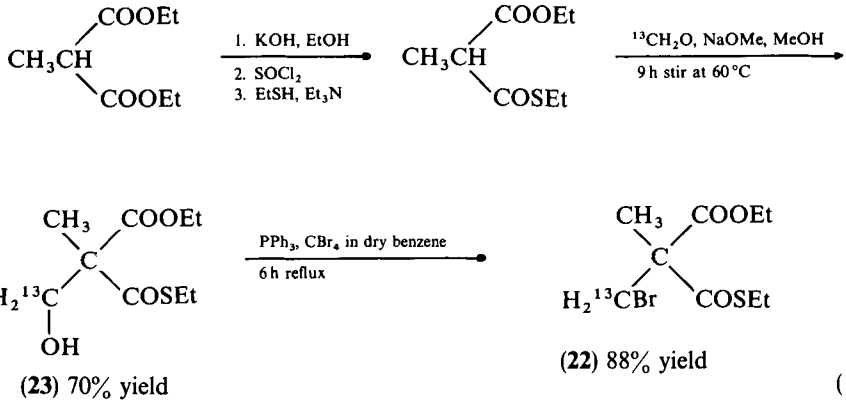
17a or **17b** with 30% hydrogen peroxide yielded a mixture of the phenothiazine ring *S*-oxidation products **21a** and **21b** which, reduced with zinc-acetic acid, gave the sulphone **17c** (equation 9).



(21a) $n = 1$
(21b) $n = 2$ (9)

7. Synthesis of O,S-diethyl 2-(bromomethyl-^{13}C)-2-methylthiomalonate

This compound **22** has been prepared[26] from *O,S*-diethyl methylthiomalonate and paraformaldehyde-^{13}C and treating the intermediate **23** with triphenylphosphine and carbon tetrabromide[27] (equation 10). This new procedure is more efficient and more direct than the previous one[28] based on condensation of dibromomethane with the carbanion derived from the methylmalonate ester. **22** has been required for a mechanistic model study of coenzyme B_{12}-dependent mutase reactions by means of a ^{13}C-NMR technique.[26]

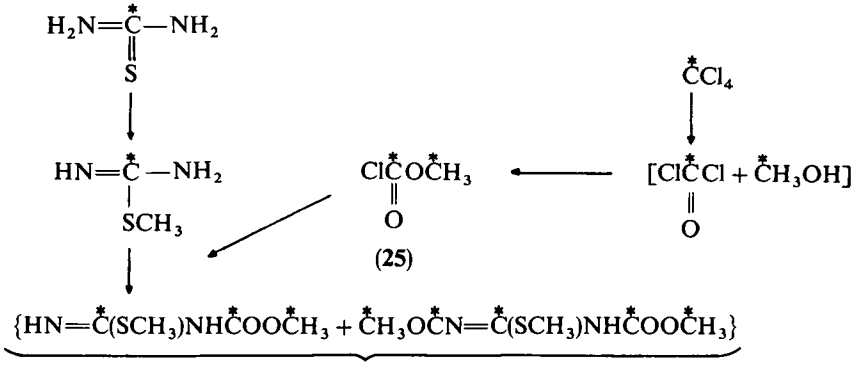


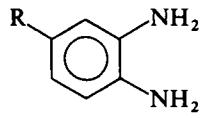
(23) 70% yield

(22) 88% yield (10)

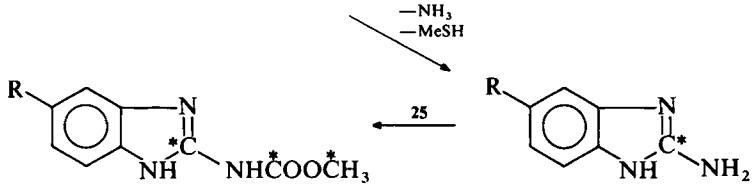
8. Synthesis of multi-^{13}C-labelled 5-substituted methyl N-(1H-benzimidazol-2-yl) carbamates

Eight methyl *N*-(1*H*-benzimidazol-2-yl) carbamates **24a–h** with various $R_{(5)}$-substituents have been ^{13}C-labelled[29] at $C_{(2)}$ and at the carbonyl and methoxy carbons according to equation 11. The three labelled positions have been chosen since they are at or near the site involved in binding to tubidin[30,31] which performs a variety of vital functions in the cell. The intermediate *S*-methyl (isothiourea-^{13}C) and methyl-^{13}C-chloroformate-^{13}C have been prepared respectively by methylation of thiourea-^{13}C with dimethyl sulphate[32] and by reaction of methanol-^{13}C with phosgene-^{13}C, generated from ^{13}C-carbon tetrachloride[33].





(11)



(**24a**) R = PhCO
(**24b**) R = n-C_3H_7O
(**24c**) R = n-C_3H_7S
(**24d**) R = PhS
(**24e**) R = n-C_4H_9
(**24f**) R = PhCH(OH)
(**24g**) R = PhSO
(**24h**) R = n-C_3H_7SO

9. *Synthesis of ^{13}C- and ^{14}C-labelled dithiopyr*

The ^{13}C- and ^{14}C-labelled title compound, 2-(difluoromethyl)-4-(2-methylpropyl)-6-(trifluoromethyl)-3,5-pyridinedicarbothioic acid *S,S*-dimethyl ester, **26**-^{14}C or **26**-^{13}C, is a herbicide used for weed control in transplanted rice and turf. It has been obtained[34,35] as shown in equation 12 starting from [1-^{14}C]isovaleraldehyde. **26**–^{13}C has been prepared similarly with 44% overall yield. Its chemical purity was 98.6% (by GLC); ^{13}C isotope enrichment was 99 atom % by GLC-MS analysis.

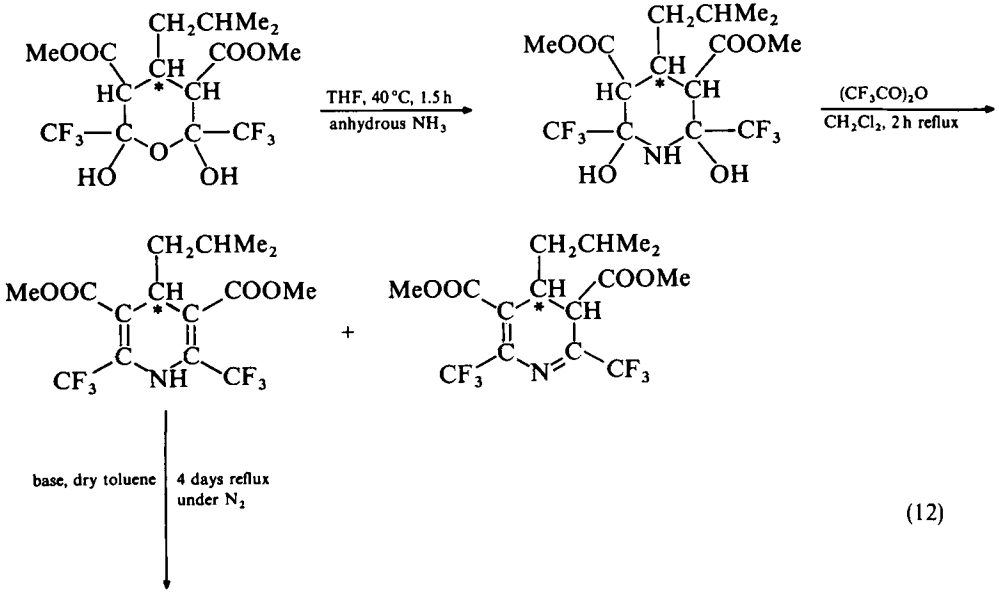
10. *Synthesis of ^{13}C and ^{14}C doubly labelled CP-73,850 (zopolrestat)*

The title compound **27**, 3,4-dihydro-4-oxo-3{[5-(trifluoromethyl)-2-^{14}C-benzothiazolyl]-methyl}-1-phthalazineacetic acid and its ^{13}C analogue, a potent *in vivo* aldose reductase inhibitor[36], have been synthesized[37,38] as shown in equation 13. Compound **27** has been used for metabolism and pharmacokinetic studies related to tissues susceptible to diabetic complications[38,39].

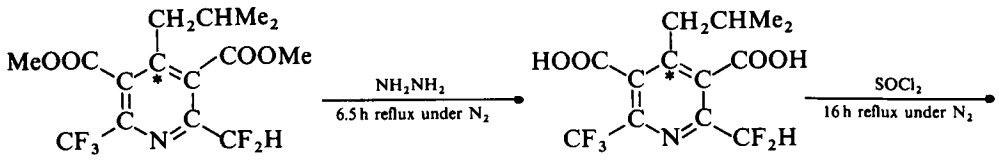
$$CH_3CH(Me)CH_2\overset{*}{C}HO + CF_3\overset{O}{\overset{\|}{C}}CH_2COOMe \xrightarrow[24\,h\ reflux]{Piperidine,\ CH_2Cl_2}$$

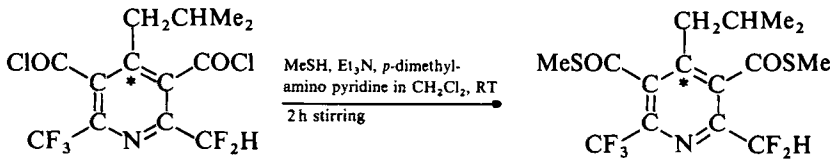
(2231 mCi, specific activity 29.8 mCi mmol^{-1})

*C = ^{14}C



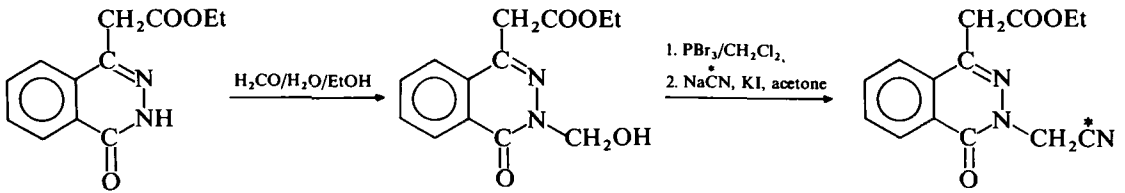
(12)





colourless oil

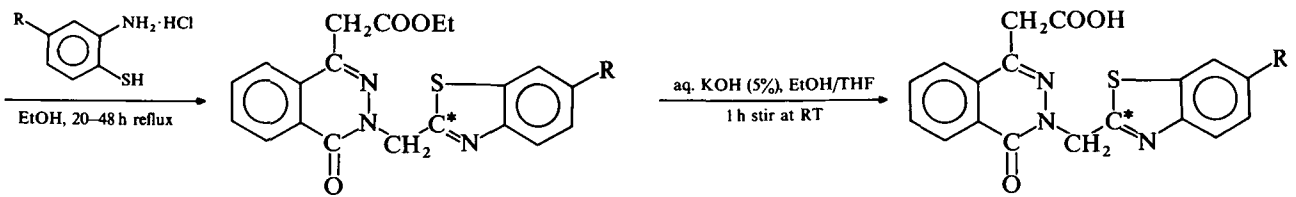
(**26**) 88% yield, solid, 99.8% purity
specific activity 29.24 mCi mmol^{-1}



(28a) 72% yield

$\overset{*}{C} = {}^{13}C$, 75% yield
$\overset{*}{C} = {}^{14}C$, 95.1% radiochemical purity

(13)



(29a) R = CF_3; $\overset{*}{C} = {}^{13}C$, m.p. 135–136 °C
(29b) R = CF_3; $\overset{*}{C} = {}^{14}C$
(29c) R = F; $\overset{*}{C} = {}^{14}C$

(27a) R = CF_3; $\overset{*}{C} = {}^{13}C$
(27b) R = CF_3; $\overset{*}{C} = {}^{14}C$
m.p. 196 °C, radiochemical purity 99.3%, specific activity 25.1 μCi mg^{-1}
(27c) R = F; $\overset{*}{C} = {}^{14}C$,
m.p. 218–219 °C, radiochemical purity 97.9%, specific activity 25.1 μCi mg^{-1}

B. Synthesis of ^{18}O- and ^{34}S-Labelled Compounds

1. Synthesis of [^{18}O]thionyl chloride

The [^{18}O]thionyl chloride has been obtained[40] during a study of the stereochemical course of chemical and enzyme catalysed sulphuryl transfer reactions[41,42].

In the present method of conversion of $S^{18}O_2$ to $S^{18}OCl_2$ 1,4-bis-(trichloromethyl)-benzene in the presence of a catalytic amount of ferric chloride has been used as the chlorinating agent. The S=O stretching frequencies of $S^{16}OCl_2$ and $S^{18}OCl_2$ (in CCl_4) are 1238 cm^{-1} and 1192 cm^{-1}, respectively (cf ν 1339 cm^{-1} for SOF_2 vs ν 1285 cm^{-1} for $S^{18}OF_2$)[43].

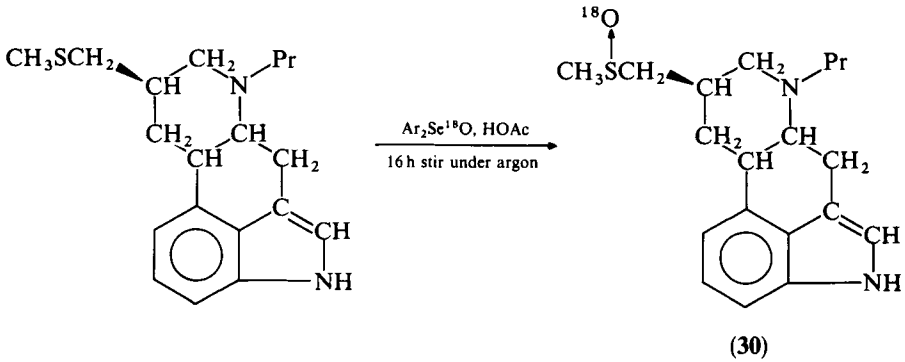
2. Synthesis of [^{18}O]sulphoxides

$Me_2S^{18}O$ (69% [^{18}O] enrichment), $(C_6H_5CH_2)_2S^{18}O$ (68.8% [^{18}O] enrichment), 4-MeC_6H_4S[^{18}O]Me (69% [^{18}O] enrichment) and $Ph_2S^{18}O$ (69.1% [^{18}O] enrichment) have been prepared[44] by two-phase bromine oxidation of the corresponding sulphides dissolved in CH_2Cl_2 stirred with a solution of [^{18}O]water (enriched to 69.6%) in pyridine at room temperature for 15 min (or 6 h in the case of less reactive diphenyl sulphide); see equation 14. Less [^{18}O] enrichment has been observed in previous methods[45,46]. [^{18}O] DMSO has been applied for stereospecific conversion of P-chiral dialkyl hydrogen phosphorothioates into the corresponding dialkyl [^{18}O]phosphates[47].

$$R^1SR^2 \xrightarrow[H_2{}^{18}O/Py]{Br_2 \text{ in } CH_2Cl_2} R^1S(=\,{}^{18}O)R^2 \qquad (14)$$

3. Synthesis of 8β-{methylsulphinyl-[^{18}O]-methyl}-6-propylergoline

The title compound **30** has been synthesized[48] by the reaction of 8β-(methylthiomethyl)-6-propylergoline (pergolide) with the mild and selective oxidizing agent bis-(4-methoxyphenyl)-selenium [^{18}O]-oxide, **31** (equation 15). The low 52.6% incorporation of ^{18}O (as determined by FAB-MS) into **30** is probably caused by ^{18}O exchange between ^{18}O-sulphoxides and acetic acid[49,50]. **31**, highly enriched in ^{18}O (93%), has been obtained from the dibromoselenide by reaction with labelled sodium hydroxide (equation 16).



(30) (15)

$$p\text{-AnSeBr}_2 + \text{Na}^{18}\text{OH} \xrightarrow{H_2{}^{18}O} p\text{-AnSe}^{18}\text{O} \quad (16)$$
(31)

4. Synthesis of D,L-[^{34}S]cysteine hydrochloride

Racemic [^{34}S]cysteine, needed for investigation of the role of cysteine in food systems, has been synthesized[51] by Michael addition of [^{34}S]thioacetic acid to α-acetamidoacrylic acid followed by hydrolysis of the *N,S*-diacetyl [^{34}S]cysteine obtained (equation 17). L-[^{34}S]cysteine (and radioactive cysteine also) were obtained previously[52,53] in low yield from ^{34}S with benzylmagnesium chloride, adding to L-β-chloroalanine and reduction of the intermediate *S*-benzylcysteine with sodium in ammonia.

$$\begin{array}{l} CH_2{=}CCOOH \\ \quad | \\ \quad NHAc \end{array} + Ac^{34}SH \xrightarrow[90\,^\circ C,\,10\,min + 12\,h]{\text{anhydrous DMF}} \begin{array}{l} Ac^{34}SCH_2CHCOOH \\ \qquad\quad | \\ \qquad\quad NHAc \end{array}$$

70% yield
m.p. 116–118 °C

$$\xrightarrow[5\,h\,reflux\,under\,Ar]{20\%\,HCl} \begin{array}{l} H^{34}SCH_2CHCOOH \\ \qquad\quad | \\ \qquad\quad NH_2\cdot HCl \end{array} \quad (17)$$

93% yield m.p. 139–141 °C

III. SYNTHESIS OF TRITIUM, CARBON-14, SULPHUR-35 LABELLED COMPOUNDS AND MULTILABELLED COMPOUNDS

A. Synthesis of Tritium-labelled Compounds

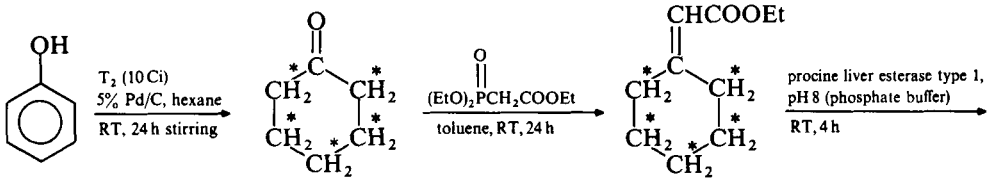
1. Synthesis of tritiated β-(S-benzylmercapto)-β,β-cyclopentamethylene propionic acid

This compound (**32**), a vital component in the synthesis of several arginine vasopressin antagonists[54,55], has been tritium labelled in the cyclohexyl ring[56] for investigation of its metabolism and ultimate fate *in vivo*, by reduction of phenol with tritium gas followed by Wadsworth–Emmons reaction[57] of the tritiated cyclohexanone (equation 18). The radiochemical purity of **32** (over 92%) was sufficient for direct use in solid-phase peptide synthesis[58].

An alternate synthetic route (equation 19) has been rejected since it leads to production of tritiated cyclopentamethylene propionic acid **34** as the major product (80–100% yield).

2. Synthesis of polyunsaturated glyceryl alkyl ethers tritiated at $C_{(2)}$

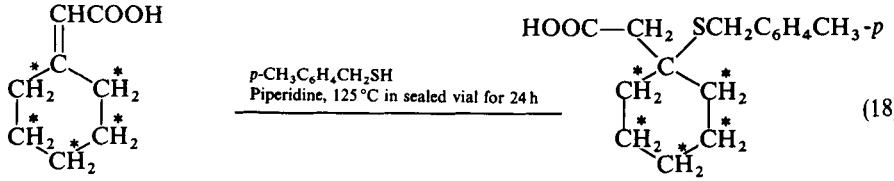
Long-chain alkenyl ethers of glycerol, structurally related to the corresponding esters[50], can be efficiently introduced into lipoproteins[60]. They have been tritium labelled at the $C_{(2)}$ position[61,62] as shown in equation 20. The resulting tritium-labelled 1,3-di-*cis*-9′-octadecenyloxy-2-propanol-[2-^{3}H] **37** has been converted to the trialkyl ethers (**38** and **39**) using *cis*-9-octadecenyloxy methanesulphonate and 9,11-octadecadienyl methanesulphonate, respectively.



H*—tritium label

(33)

27% overall yield
2.75 Ci, 99.3% radiochemical purity

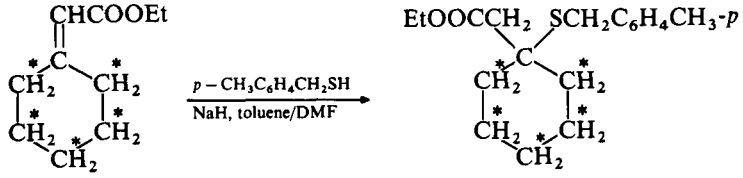


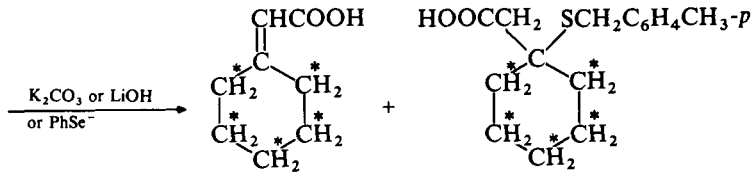
(18)

(34)

81% radiochemical yield
85% radiochemical purity

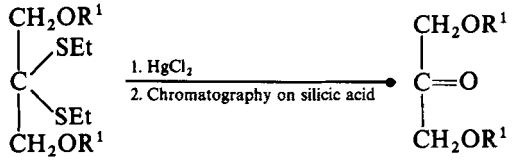
(32) 80% yield
50% radiochemical yield,
specific activity 96.9 ± 2.3 Ci mmol^{-1}





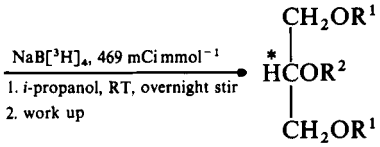
(34) (32)

(19)

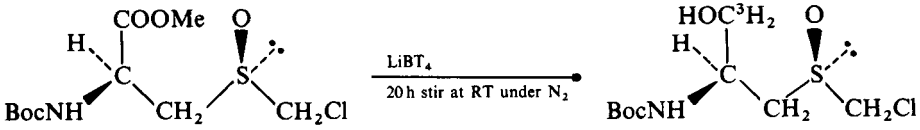


(35) (36)

(20)

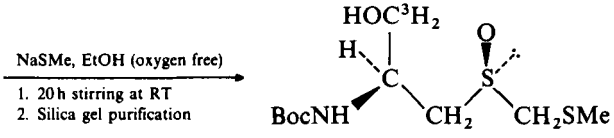


(37) R^2 = H (0.74 mCi, specific activity 118 mCi mmol^{-1}, 98.4% purity)
(38) R^2 = *cis*-9-octadecenyl (98.4% pure)
(39) R^2 = *cis*, *cis*-9,11-octadecadienyl (99% pure)

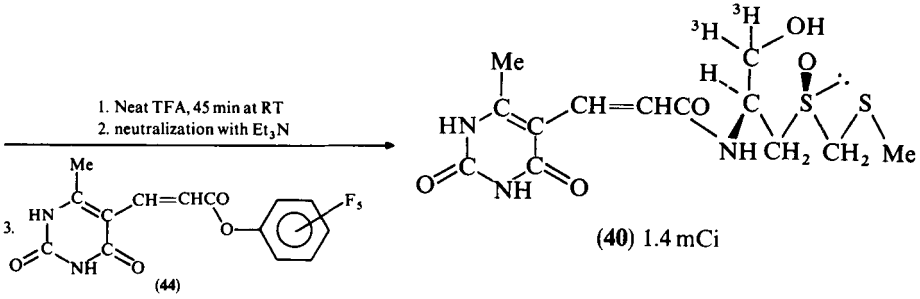


(41) (42)

(263 mCi, crude product)
24.6 mCi after purification on silica gel



(43)



(40) 1.4 mCi

(21)

The product **39** did not exhibit the absorption near 230 nm associated with a conjugated double-bond system[63].

3. *Synthesis of tritium-labelled sparsomycin*

The optically active tritium-labelled title compound **40**, an anticancer agent on the ribosomal level, affecting protein biosynthesis[64], which was used in biochemical studies previously[65,66], has been prepared[67,68] as shown in equation 21. ^{3}H-NMR analysis[60] of **40** pointed to a ratio of mono- over ditritiated compound of approximately 2:1. The pilot ^{3}H-NMR studies have been carried out with tritiated sparsomycine of much lower specific activity (0.3 Ci mmol^{-1}; 11 GBq mmol^{-1}) synthesized using commercially available sodium borotritide. The pharmacokinetic behaviour of [^{3}H]-**40** in mice and interaction of [^{3}H]-**40** with peptidyl transferase are under investigation.

4. *Synthesis of tritium-labelled 1S,2S-(−)-trans-2-isothiocyanato-N-methyl-N-[2-(1-pyrrolidinyl)-cyclohexyl]benzeneacetamide*

The optically pure title compound **45** is a site-directed irreversible drug, containing a reactive electrophilic functional group able to form a covalent bond with the kappa opioid receptor to which the drug is bound and thus allowing its identification and purification[70–72]. It has been synthesized[73] by dibromination of optically pure 1*S*,2*S*-(−)-*trans*-2-amino-*N*-methyl-*N*-[2-(1-pyrrolidinyl)cyclohexyl]benzeneacetamide **46** followed by catalytic tritiation of dibromide-(−)-**47** and transformation of the obtained tritium-labelled (−)-**48** into **45** by treatment with thiophosgene (equation 22).

5. *Synthesis of ^{3}H-labelled levamisole*

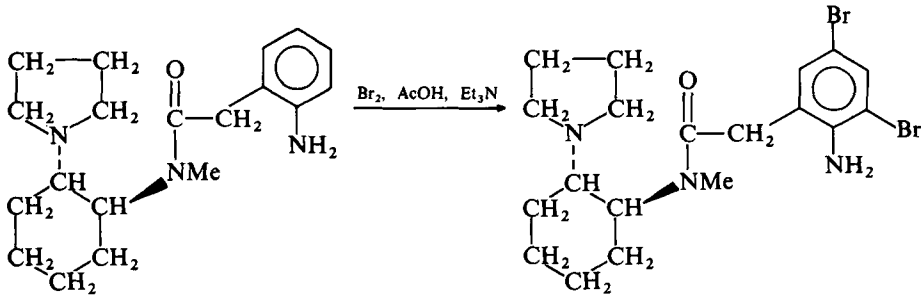
Levamisole **49**, the *levo* isomer and the more active form of the anthelmintic *d,l*-tetramisole[74], is active against most of the nematodes of animals and man[75]. It has been tritium labelled[76] in the stable $C_{(2)}$-position of the phenyl group (equation 23) for immunological studies[77]. The racemate **50** has been resolved by successive salt formation with (*S*)-(−) and (*R*)-(+) tartaric acid. The final product **49** contained 99.9% HPLC pure ^{3}H-levamisole monohydrochloride (62.7 mCi, radiochemical yield 33.7%) and had a specific activity of 10.8 Ci mmol^{-1} (44.8 mCi mg^{-1}) and a $[\alpha]_D^{20}$ of −138.8° (conc. = 0.934% in methanol)[74].

6. *Synthesis of tritium-labelled 4-fluoro-1-[1-(2-thienyl)]cyclohexylpiperidine ([^{3}H]-FTCP,* **54***)*

This compound was needed for autoradiographic studies of the mammalian brain, analogously to the PET studies with the corresponding [^{18}F] derivative prepared previously[78]. It has been synthesized[79] as shown in equation 24 with the reaction sequence **55** → **56** → **57** → **58** → **59** → **54**. The radiochemical yield of **54** was 1.2% only (25.6 mCi, specific activity 14.0 Ci mmol^{-1}) probably due to the presence of thiophene.

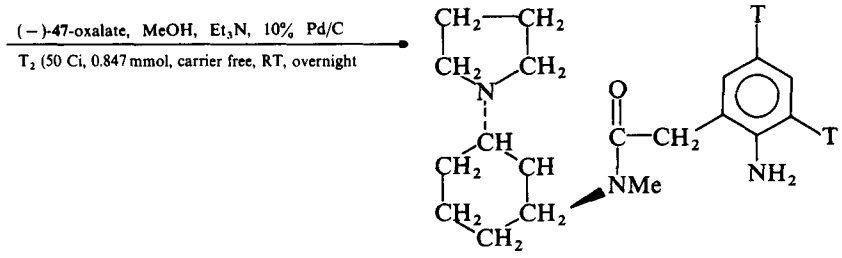
7. *Synthesis of (3,4-[^{3}H]cyclohexyl)-N-{1-(2-benzo[b]thienyl)cyclohexyl}piperidine ([^{3}H]-***60***)*

The title compound, [^{3}H]-**60**, is a selective probe for the dopamine–reuptake complex (an important CNS binding site with which cocaine is known to interact). It has been synthesized[80] in 7 steps starting with readily available cyclohexane-1,4-dione monoethylene ketal and benzo[*b*]thiophene (equation 25). Tritium label has been introduced



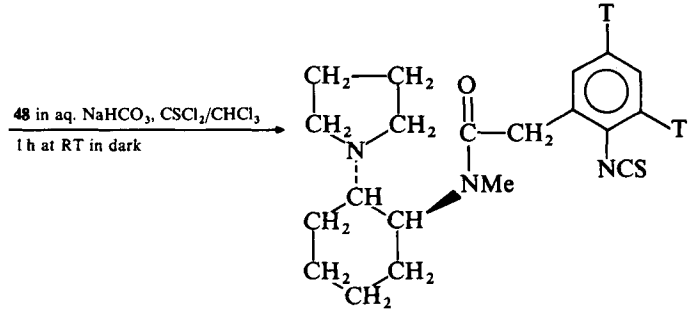
(−)-(**46**) (1.03 mmol)

(−)-(**47**) colourless oil, 57% yield;
(−)-**47**-oxalate salt, m.p. 203–204 °C



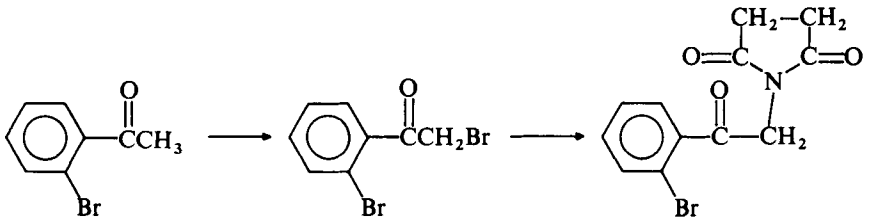
[^{3}H]-(**48**)

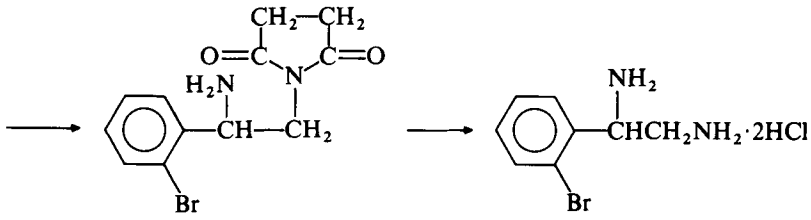
14% radiochemical yield based on
47-oxalate, specific activity 31.2 Ci mmol^{-1}



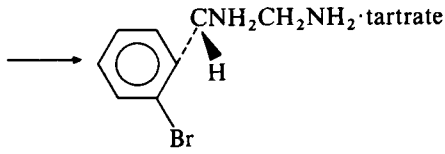
[^{3}H]-(−)-(**45**), 13.3% yield (6.66 mCi),
radiochemical purity > 99%

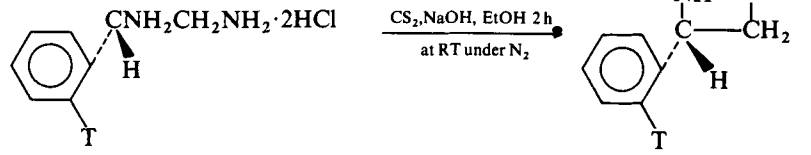
(22)





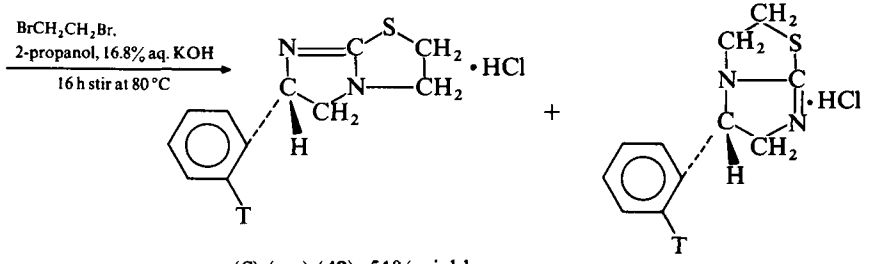
rac-(**50**)





(*S*)-(+)-(**52**), 641 mCi

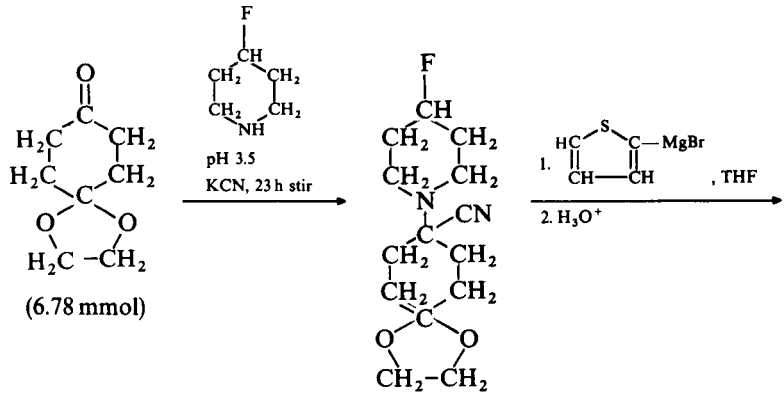
(*S*)-(+)-(**53**), 99% yield



(*S*)-(−)-(**49**), 51% yield

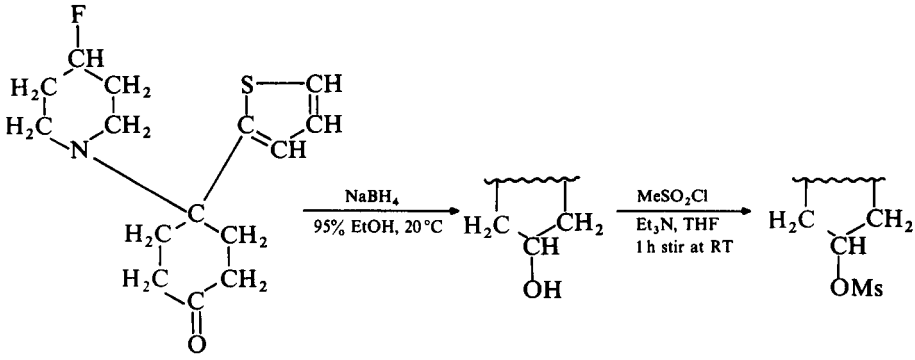
(*S*)-(**49a**) (49% yield according to HPLC)

(23)

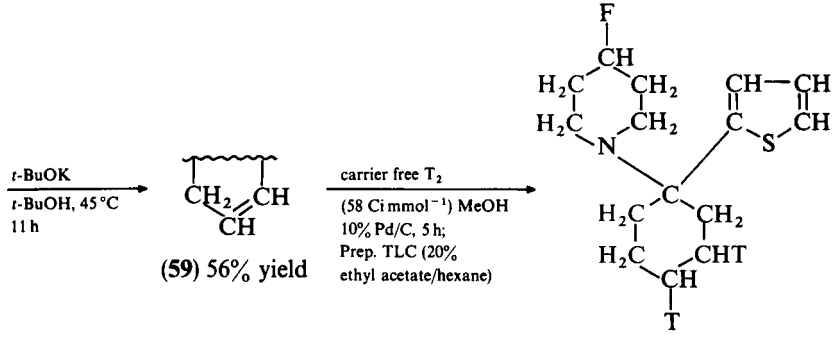


(6.78 mmol)

(**55**) 93% yield, m.p. 106 °C



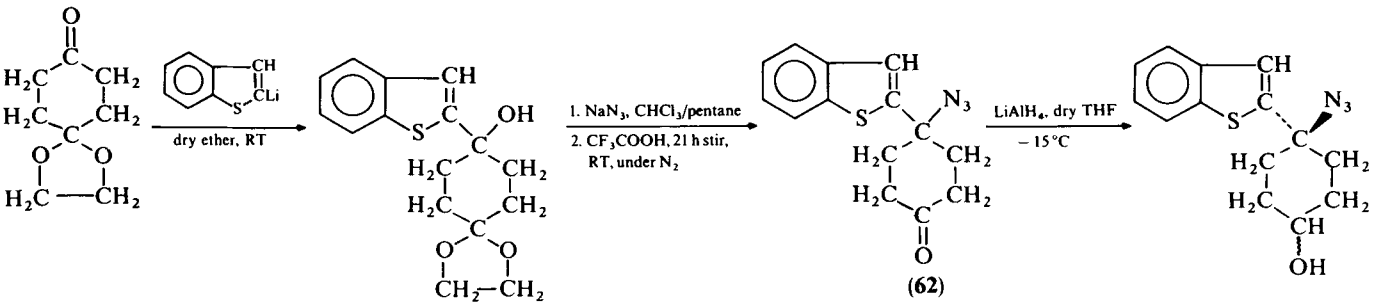
(**56**) 36% yield, m.p. 81–83 °C (**57**) 87% yield (**58**) 96% yield



(**59**) 56% yield

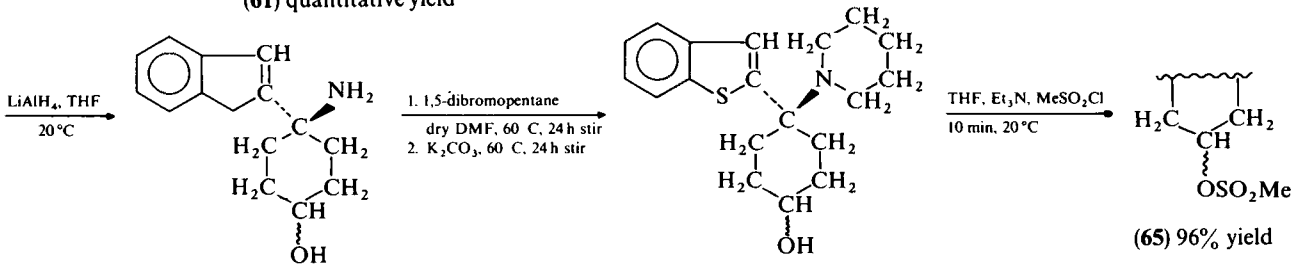
(**54**) 99% radiochemical purity

(24)



(**61**) quantitative yield

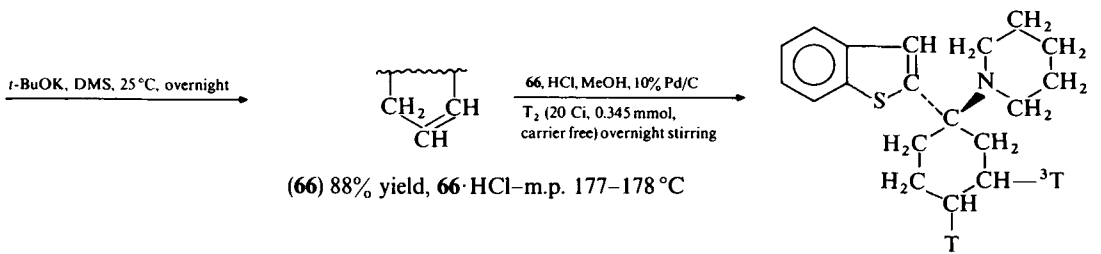
(**62**)



(**63**) 90% overall yield from **61**

(**64**) 83% yield

(**65**) 96% yield



(**66**) 88% yield, **66**·HCl–m.p. 177–178 °C

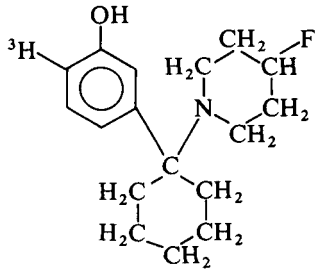
[^{3}H]-(**60**) 7.3% yield (255 mCi), radiochemical purity > 99.5%

(25)

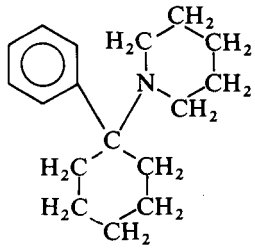
in the final step into the 3- and 4-positions of the cyclohexyl ring by catalytic tritiation of *N*-{4-(2-benzo[*b*]thienyl)cyclohexenyl}piperidine **66** to give [^{3}H]-60 in 73% yield, with a specific activity of 29.8 Ci mmol^{-1} (51.9% isotopic incorporation).

8. Synthesis of [^{3}H]-4-fluoro-1-[1-(3-hydroxyphenyl)cyclohexyl]piperidine

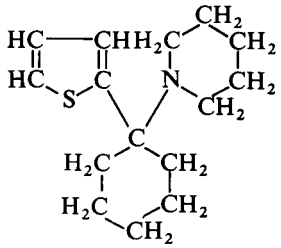
The title compound, [^{3}H]-FOH-PCP **67**, has been synthesized[81,82] as shown in equation 26 to investigate the regional distribution of the binding sites in brain and mode of action of phencyclidine [1-(1-phenylcyclohexyl)piperidine, **68**–PCP], an anaesthetic agent for human use causing bizarre dissociative effects[83,84] in patients after their emergence from the anaesthesia.



(**67**) [^{3}H]-FOH-PCP



(**68**) -PCP

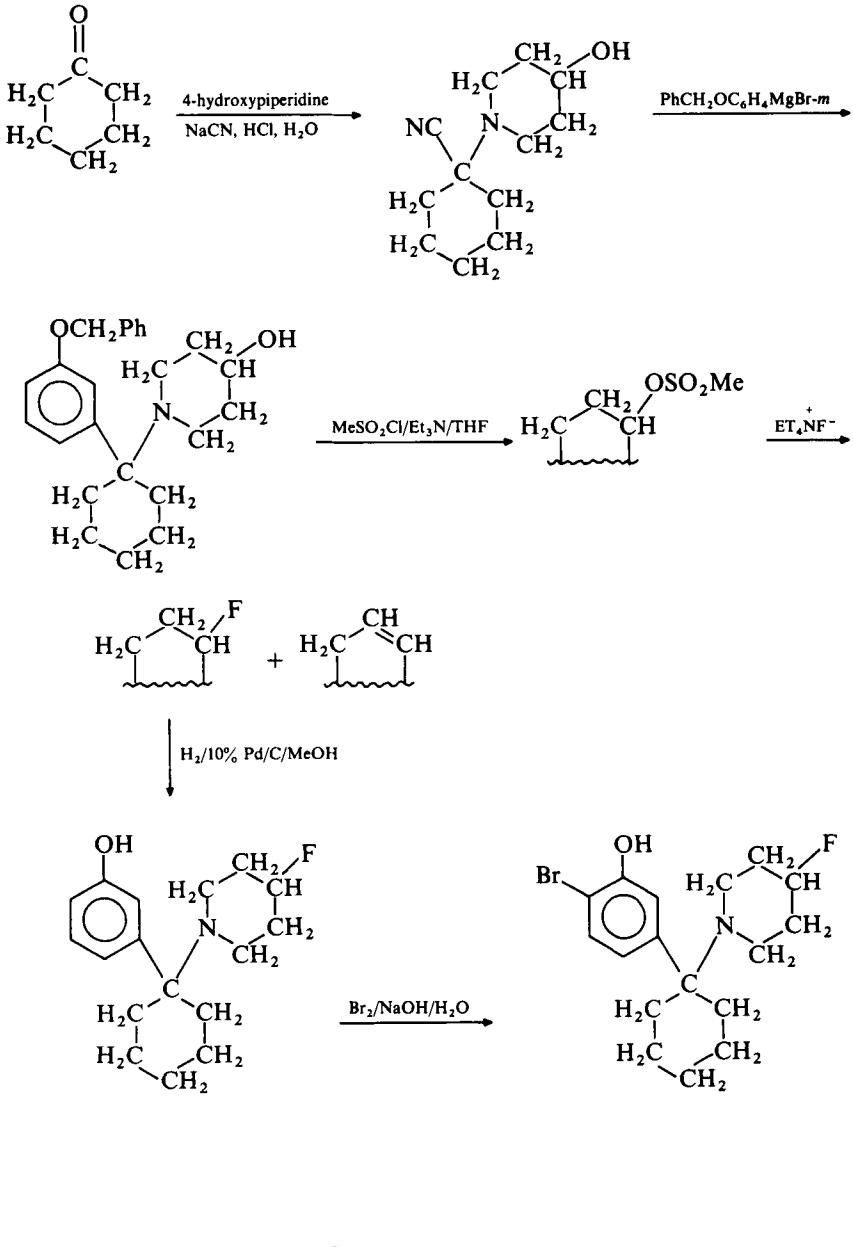


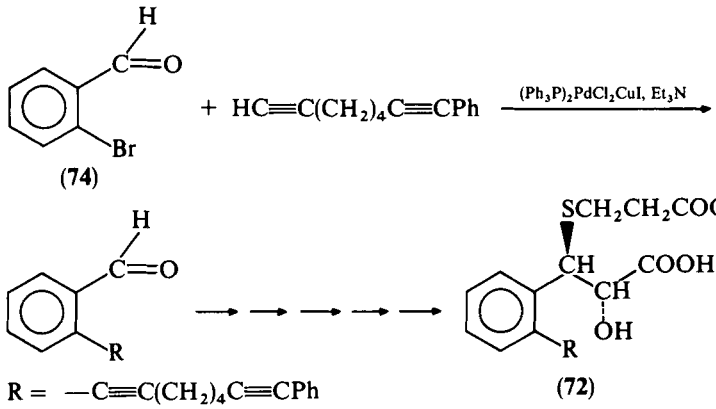
(**69**) -TCP

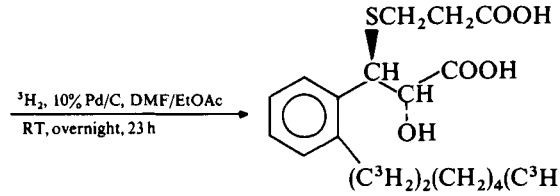
Displacement of [^{3}H]TCP, **69** by FOH-PCP and related PCP receptor ligands in rat brain membranes has been investigated[86].

9. Synthesis of tritium-labelled leukotriene antagonist SK&F 104353

Tritium-labelled (2*S*, 3*R*)-3-[(2-carboxyethyl)thio]-3-{2-(8-phenyl[^{3}H]octyl)phenyl}-2-hydroxypropionic acid (SK&F 104353, **70**) and methyl *erythro*-3-[(2-carbomethoxyethyl)-thio]-3-{2-(8-[^{3}H]-phenyloctyl)-phenyl}-2-hydroxypropionate **71** with high specific activity have been prepared[87] by catalytic tritiation of the corresponding unsaturated and halogenated precursors **72** (equation 27) and **73** (equation 28) synthesized from the corresponding benzaldehydes **74** and **75**. The halogenated substrate provided the dimethyl ester derivative with specific activity of 55 Ci mmol^{-1} while the unsaturated

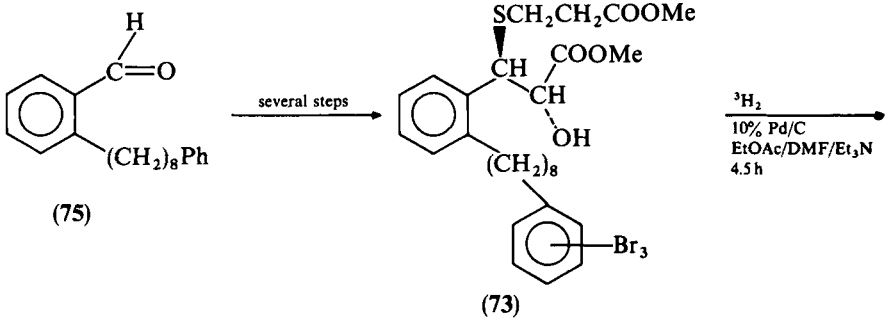

4-hydroxypiperidine
NaCN, HCl, H2O
PhCH2OC6H4MgBr-m
MeSO2Cl/Et3N/THF
ET4NF-
H2/10% Pd/C/MeOH
Br2/NaOH/H2O
3H2/Et3N/MeOH
10% Pd/C, 1 h
[3H]-(67)
specific activity 23 Ci mmol-1
99.5% radiochemical purity85
8.84 radiochemical yield85
(26)

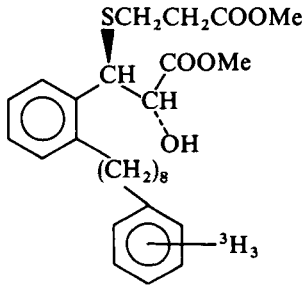




(27)

(70) 4.5 Ci, radiochemical purity > 97%
specific activity 138 Ci mmol^{-1}





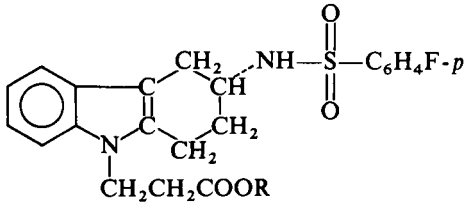
(28)

(71) 1490 mCi in benzene solution, rediochemical purity > 97%

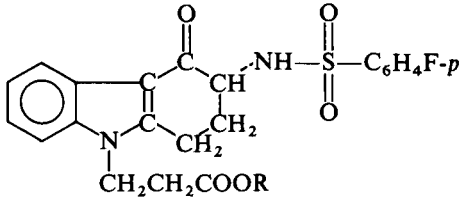
precursor produced directly [^{3}H]SK&F 104353 (**70**). To minimize the decomposition **70** was dissolved in degassed ethanol and stored at −80 °C under argon atmosphere.

10. Synthesis of (3R)-3-(4-fluorophenylsulfonamido)-1,2,3,4-tetrahydro-9-[4-^{3}H] carbazolepropionic acid

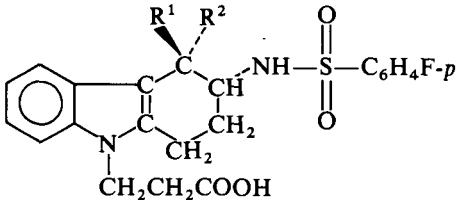
The title compound, {[^{3}H]BAY u 3405} **76**, a thromboxane A_2-receptor/antagonist, required for receptor binding studies, has been tritium labelled[88] as shown in equation 29.



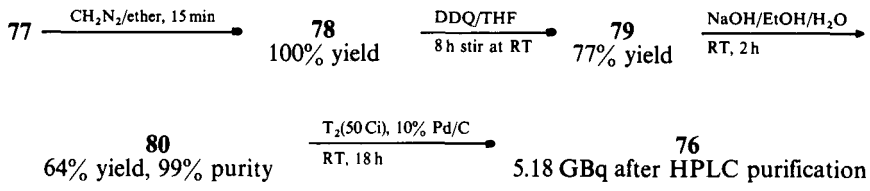
(**77**) R = H
(**78**) R = Me



(**79**) R = Me, m.p. 208 °C (dec.)
(**80**) R = H



(**76**) $R^1 = {}^1H$, $R^2 = {}^3H$
$R^1 = {}^3H$, $R^2 = {}^1H$



(29)

The specific activity of **76** is equal to 7.9 Ci mmol^{-1} (292.3 GBq mmol^{-1}). This value is very low in comparison with the specific activity of 58.2 Ci mmol^{-1} (2.15 TBq mmol^{-1}) theoretically possible, and is caused by dilution of the tritium with the labile hydrogens of the sulphonamide and carboxyl groups and with moisture present in solvent.

11. Radiochemical synthesis of tritium-labelled aromatic onium salts of oxygen, sulphur, selenium and tellurium

Aromatic onium derivatives have found a wide chemical and technical application[89,90]. Chemical synthesis of isotopically multilabelled metal-organic compounds is a many-step

process sometimes difficult or impossible to carry out. Nuclear-chemical one-step synthesis yielding phenyl onium derivatives with maximum specific activity has been used successfully in such cases[91]. It involves the ion–molecular interactions of phenyl cations, produced in β-decay of benzene multilabelled with tritium, with diphenyl derivatives of oxygen, sulphur, selenium and tellurium (equation 30). Besides compound **81**, tritium-labelled substrate $[^3H]Ph_2M$ **82** and tritium-labelled **83** were also produced (equation 31 and 32).

$$C_6{}^3H_6 \xrightarrow{\beta^-} C_6{}^3H_5^+ \xrightarrow{Ph_2M} [C_6{}^3H_5(Ph)_2M]^+ \xrightarrow{BF_4^-} [C_6{}^3H_5(Ph)_2M]^+ BF_4^- \quad (30)$$

(**81**)

$$[C_6{}^3H_5(Ph)_2M]^+ \xrightarrow[-C_6H_5^+]{\text{fragmentation}} C_6{}^3H_5(Ph)M \quad (31)$$

(**82**)

$$C_6{}^3H_5^+ + 2C_6H_6 \longrightarrow C_6{}^3H_5{-}C_6H_5 + C_6H_6H^+ \quad (32)$$

(**83**)

The labelled products have been produced by keeping the mixture consisting of $C_6{}^3H_6$, $(Ph)_2M$ and KBF_4 in ampoules sealed under vacuum for preset times. The radiochemical syntheses have been carried out at $-196\,°C$ and at $25\,°C$ to investigate the effect of the liquid and solid states on the yield of labelled products. The percentage yields of labelled produced salts and of labelled substrates in solid and liquid phases increase in the order O < S < Se < Te, as shown in Table 1.

The low yield of triphenyl oxonium cations correlates well with the low donor activity of oxygen in comparison with those of the heavier elements (S, Se and Te) of the VIa group[92]. Triphenyloxonium cations are thermally and chemically more stable than phenyl cations of S, Se and Te.

12. Synthesis of tritium-labelled dialkyldithiophosphates

Tritium-labelled [^{3}H]dialkyldithiophosphates have been found to be promising organic analytical reagents[94] for radiochromatographic determination of 10^{-12}–10^{-13} quantities of elements (Cd, Pb, Hg, Cu) particularly in environmental studies. They have been synthesized[93] by heterogeneous catalytic exchange of the nickel and palladium salts of dialkyldithiophosphates with tritium gas in the presence of 5% Pd/$BaSO_4$, 10% Pd/C [or $(PhP)_3Rh(I)Cl$], by catalytic hydrogenation of unsaturated precursors and in reactions of previously synthesized tritium-labelled alcohols with P_2S_5. The last method gave the [^{3}H]-labelled analytical reagents with the highest specific activities (equal to 4400 GBq mol^{-1}). The analytical applicability of the tritiated reagents obtained has been

TABLE 1. Product and substrate yields in $C_6{}^3H_6$–$(Ph)_2M$–KBF_4 systems

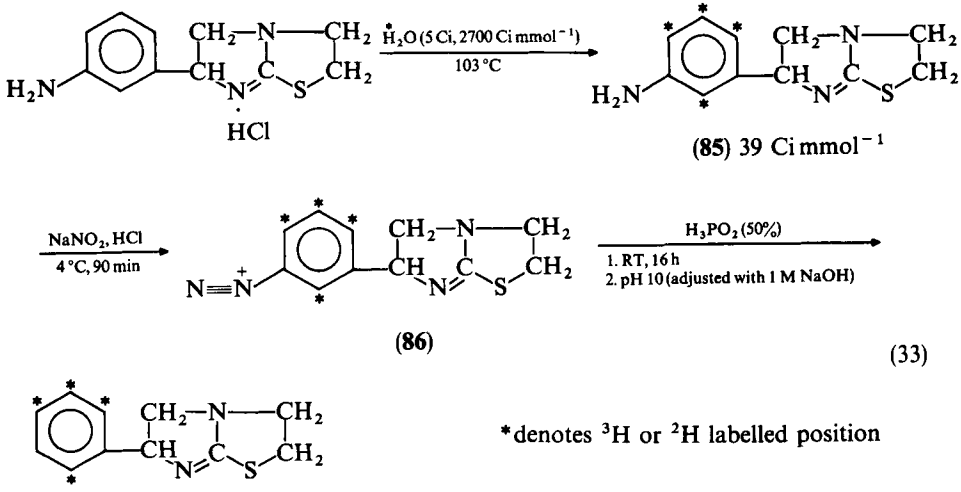
	Product yield (%)		Substrate yield (%)	
M	solid phase	liquid phase	solid phase	liquid phase
O	5.2	5.4	2.7	2.4
S	12.9	14.4	10.2	13.1
Se	21.6	18.9	21.2	42.6
Te	42.7	33.2	33.9	52.6

demonstrated by showing the very well resolved radiochromatogram of the solution containing 10^{-9} mol of [^{3}H]di-n-propyldithiophosphates of cadmium, lead, mercury and copper[93].

B. Synthesis of Compounds Multilabelled with Hydrogen Isotopes and Heavy Atom Isotopes

1. Synthesis of deuterium- and tritium-labelled m-aminolevamisole (MAL) and levamisole (LEV)

[^{3}H]LEV **84**, a widely used anti-parasitic agent, and its more active analogue [^{3}H]*m*-aminolevamisole (MAL) **85**, have been prepared[95] by tritiation of MAL·HCl in [^{3}H]$_2$O and subsequent diazotization followed by deamination (equation 33). Both products have been purified by preparative HPLC. Deuteriations of **85** and **84** were carried out previously[96] and, from these, optimal conditions for tritiation of **84** and **85** have been deduced.

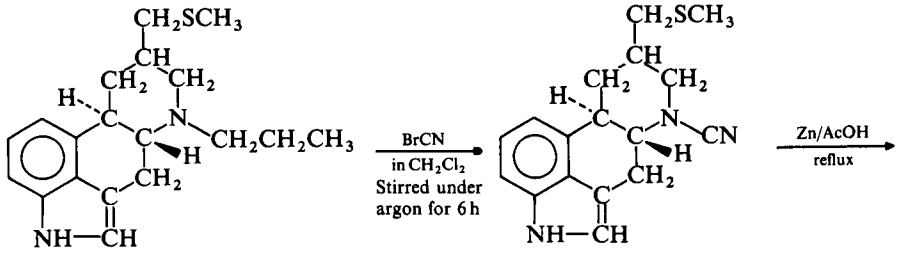


(84) 15% radiochemical yield, purity > 90%
37 Ci mmol^{-1}

The extent of labelling with tritium was less than with deuterium under the same experimental conditions. This has been explained by the loss of tritium by self-radiolysis of **84** and **86** and by radiolysis during storage. No loss of deuterium or deamination of [^{2}H]MAL was found by mass spectral analysis. The exchange method of labelling of **85** and **84** lacks the specificity of dehalogenation but it is simple, yields products of higher specific activity which is essential in the measurement of binding to the LEV receptor of parasitic nematodes and avoids complex syntheses[76].

2. Synthesis of [^{2}H]-, [^{3}H]- and [^{14}C]-labelled 8β-[(methylthio)methyl]-6-propylergoline mesylate (pergolide mesylate)

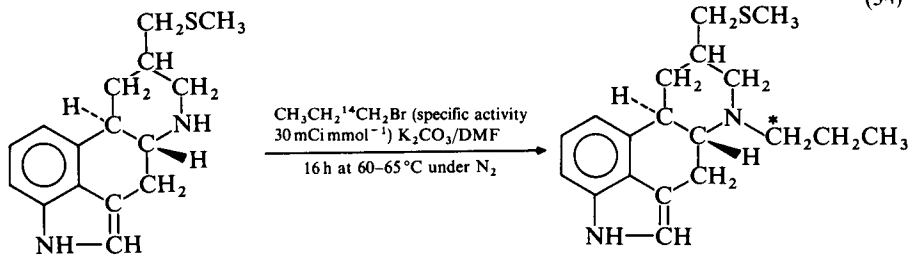
*a. Pergolides **87a**, **87b** and **88*** labelled with deuterium, tritium and carbon-14 in the N^6-propyl group are needed to study the utility of pergolide mesylate in the treatment



(**87**) as MsOH salt

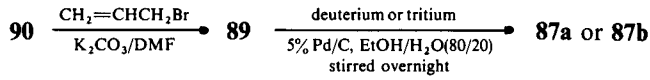
88% yield

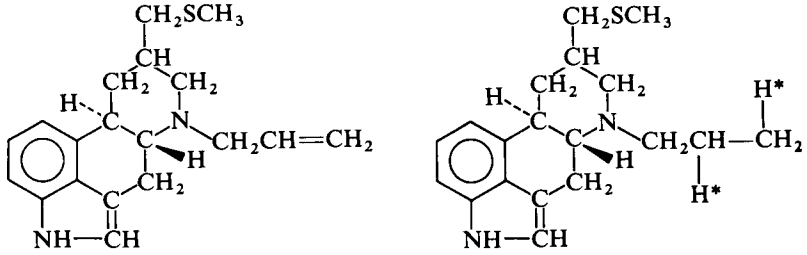
(34)



(**90**) 67% yield

(**88**) as MsOH salt
specific activity 28.23 mCi mmol^{-1},
radiochemical purity > 97%





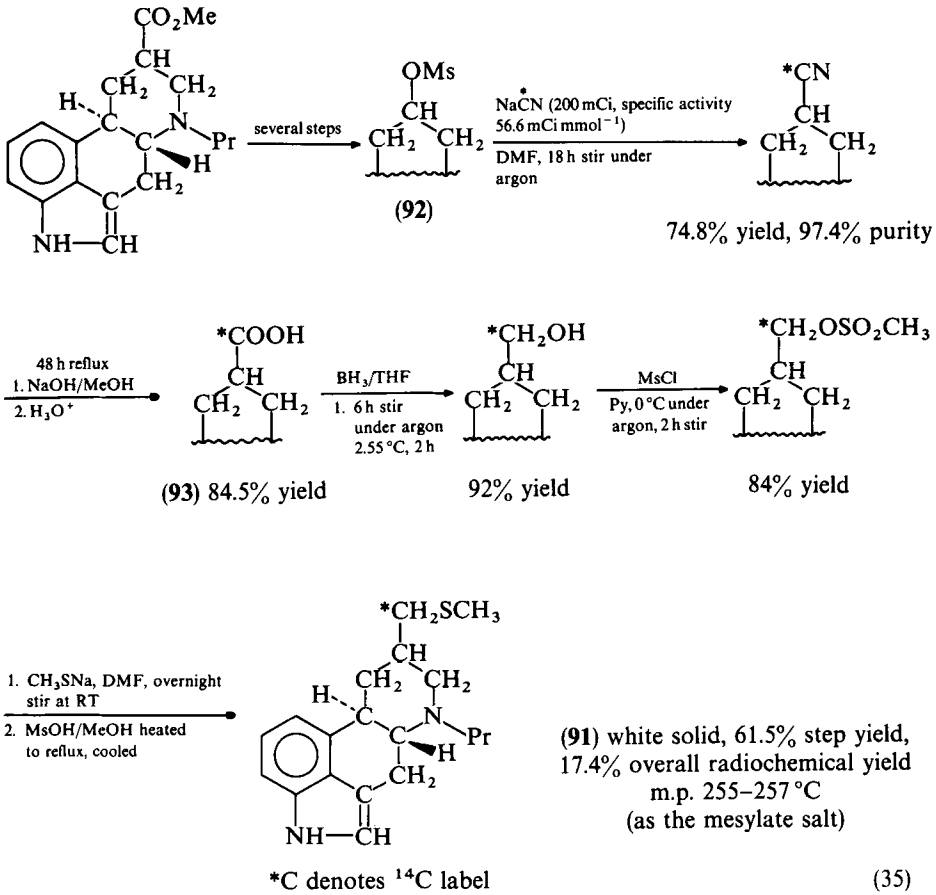
(**89**) as MsOH salt

(**87a**) H* denotes ^{2}H label
(**87b**) H* denotes ^{3}H label

of Parkinson's disease and prolactine-release related disorders[97]. The first two have been synthesized[98] (equation 34) by the palladium-catalysed tritiation or deuteriation of the 6-allyl derivative **89** and the latter by reaction of 8β-[(methylthio)methyl]ergoline] **90** with 1-[^{14}C]-1-propyl bromide[98]. Both NMR and MS showed the incomplete deuteriation of **87a** caused by deuterium exchange with the non-deuteriated solvent at the surface of the catalyst[99]. The specific activity of **87b** after removing the labile tritium

in methanol and purification by preparative TLC was 25.2 Ci mmol^{-1} (61.5 mCi mg^{-1}) and the radiochemical purity was 98%.

b. Pergolide mesylate ***91*** radiolabelled in the 17-position with carbon-14 has been prepared in the reaction of 8β-mesyloxy-6-propylergoline **92** with [^{14}C]sodium cyanide followed by base hydrolysis of the nitrile obtained and conversion of the 8β-carboxy-6-propylergoline-[^{14}C] (**93**) to pergolide mesylate **91** via a four-step sequence (equation 35). The product **91**-8β-[(methylthio)methyl]-6-propylergoline-17-[^{14}C]mesylate had a specific activity of 6.44 mCi mmol^{-4} and a radiochemical purity of 97.7–99.3% as determined by TLC (autoradiography).



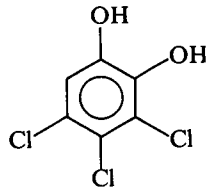
(35)

3. Synthesis of radiolabelled alkyl aryl ethers and sulphides in phase-transfer two-phase systems

For toxicological studies[100,101], *O*- and *S*-methyl or ethyl-substituted phenols and thiols, labelled with ^{3}H or ^{14}C in the alkyl group, have been synthesized[102] in a two-phase

system with PTC at room temperature, using ^{3}H- or ^{14}C-labelled methyl iodide and ethyl iodide, catalytic amounts of tetrabutylammonium hydrogen sulphate (TBA), a molar amount of base (NaOH) and appropriate amounts of phenol or thiol. The products have been isolated by TLC in isotope yields ranging from 38% to 100%.

3,4,5-Trichlorocatechol **94** reacting with ^{14}C-MeI (1 mCi, specific activity 2.4 mCi mmol^{-1}) in the presence of TBA and NaOH in a two-phase $PhCH_3$ and water suspension produced 3,4,5-trichloroguaiacol (55% yield), 4,5,6-trichloroguaiacol (34% yield) and 3,4,5-trichloroveratol. Similar reaction of **94** with ^{3}H-MeI gave tritium-labelled 3,4,5-trichloroguaiacol (31%), 4,5,6-trichloroguaiacol (25%) and 3,4,5-trichloroveratrol (4%).



(94)

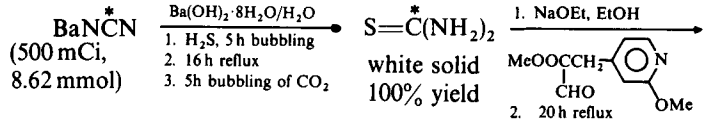
In a CH_2Cl_2/H_2O two-phase system in the presence of TBA and NaOH using [^{14}C]MeI, [1-^{14}C]EtI or [^{3}H]MeI as alkylating agents and with various phenols and thiols as substrates, the following ^{14}C- and ^{3}H-labelled products have been obtained: methylthio-2,5-dichlorobenzene (57%), methylthio-2,6-dichlorobenzene (70%), methylthio-2,4,5-trichlorobenzene (95%), methylthio-pentachlorobenzene (100%), 4-methylthio-2,2',5,5'-tetrachlorobiphenyl (76%), 4-ethylthio-2,2',5,5'-tetrachlorobiphenyl (66%), 4,4'-bis(methylthio)-2,2',5,5'-tetrachlorobiphenyl (38%) and 2-methylthio-4-bromoacetophenone (65%), in the last case using 4-bromophenacyl-thiol as the substrate.

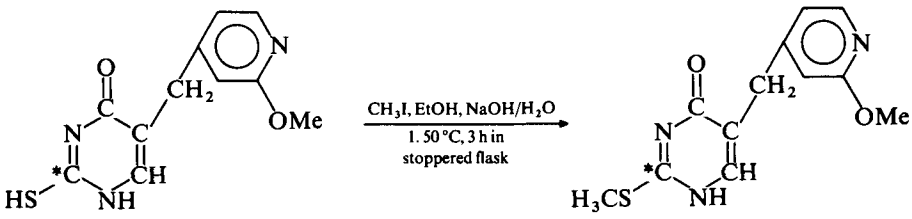
The above alkyl aryl sulphides have been oxidized to the corresponding sulphones with H_2O_2 in acetic acid[103]. The following sulphones have been obtained: [^{14}C]methylsulphonyl-2,5-dichlorobenzene, [^{14}C]methylsulphonyl-2,6-dichlorobenzene, [^{14}C]methylsulphonyl-2,4,5-trichlorobenzene, [^{3}H]- and [^{14}C]methylsulphonyl-pentachlorobenzene, 4-[^{14}C]methyl- and 4-[1-^{14}C]ethylsulphonyl-2,2',5,5'-tetrachlorobiphenyl and 4,4'-bis-[^{3}H]methylsulphonyl-2,2',5,5'-tetrachlorobiphenyl. These ^{14}C- and ^{3}H-labelled sulphides and sulphones have been prepared for autoradiographic studies of their uptake, distribution and elimination.

4. Synthesis of ^{14}C- and ^{3}H-labelled donetidine and its trihydrochloride

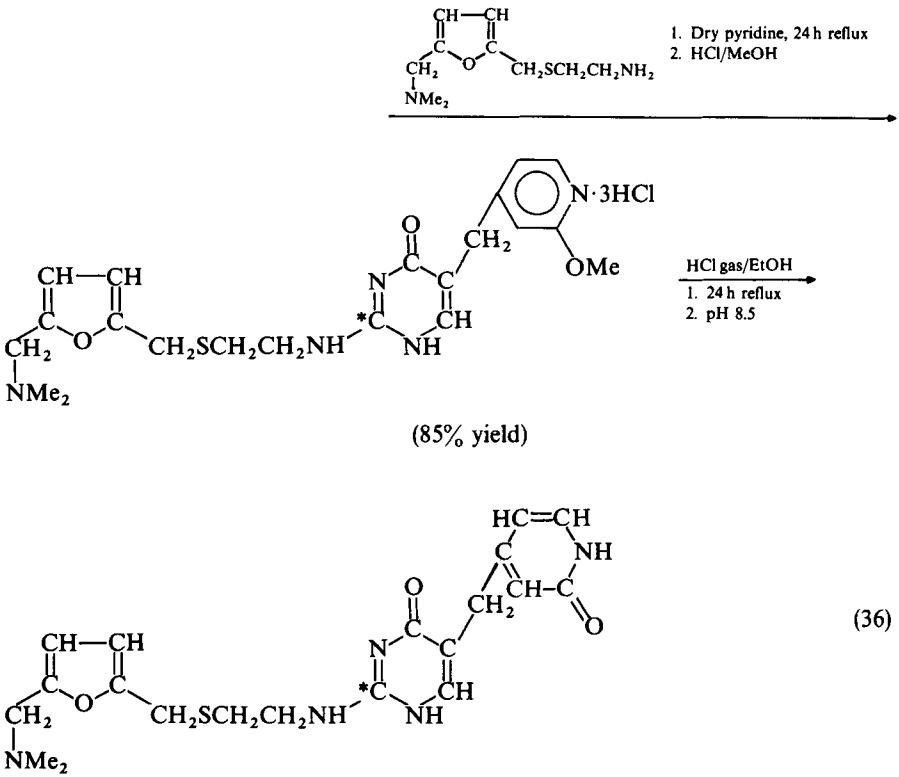
^{14}C-labelled donetidine **95** (free base) needed for pharmacokinetic studies in healthy humans and ^{14}C- and ^{3}H-donetidine trihydrochloride (**96, 97**), a highly potent inhibitor of histamine-stimulated acid secretion in both animals and man[104], have been synthesized[105] as shown in equations 36, 37 and 38.

a. 2-[2-(2-N,N-Dimethylaminomethyl-5-furanylmethylthio)ethylamino]-5-(6-hydroxy-4-picolyl)-[2-^{14}C]-4-pyrimidone ***95***, ^{14}C-labelled in $C_{(2)}$ position of the pyrimidone ring, has been obtained in a five-stage synthesis (equation 36) starting from barium[^{14}C] cyanamide.





pale, yellow solid (65% yield) pale, yellow solid (80% yield)

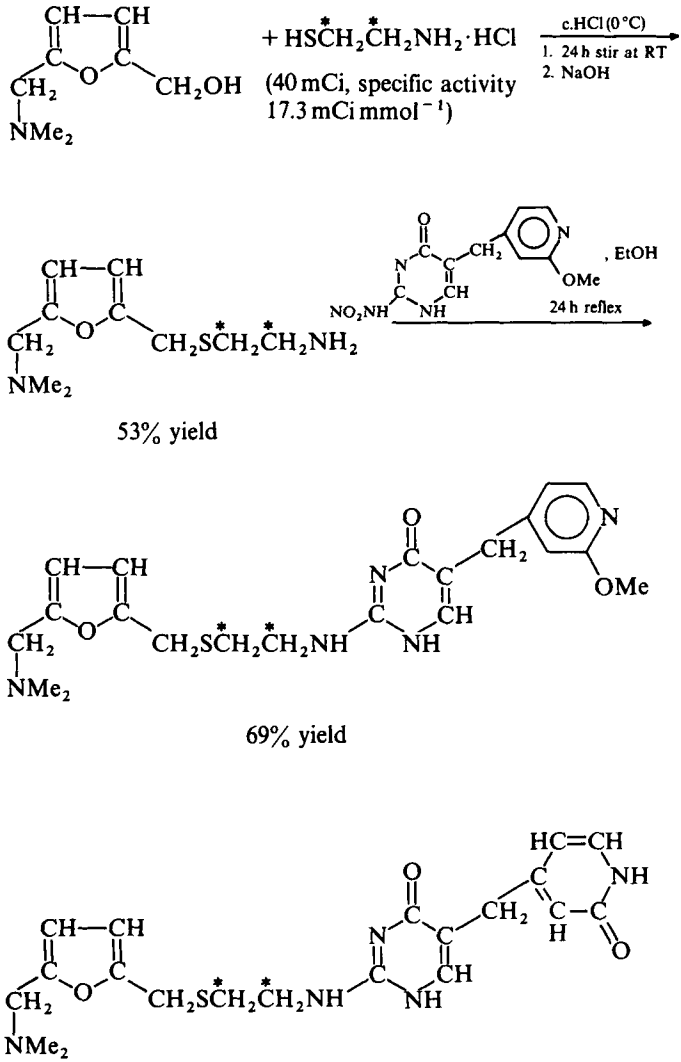


(85% yield)

(36)

(95) red oil (59% yield) → yellow oil after HPLC → buff solid (45.1 mCi, 20% yield), radiochemical purity of 99%; overall radiochemical yield of 9%, specific activity 57.8 mCi mmol^{-1}

b. $^{14}C_2$-*donetidine trihydrochloride* ***96***, labelled in both methylenes of the aminoethyltio moiety, has been obtained starting from [1,2-$^{14}C_2$]-cysteamine hydrochloride in 18% overall radiochemical yield at a specific activity of 15.4 mCi mmol^{-1} (equation 37).

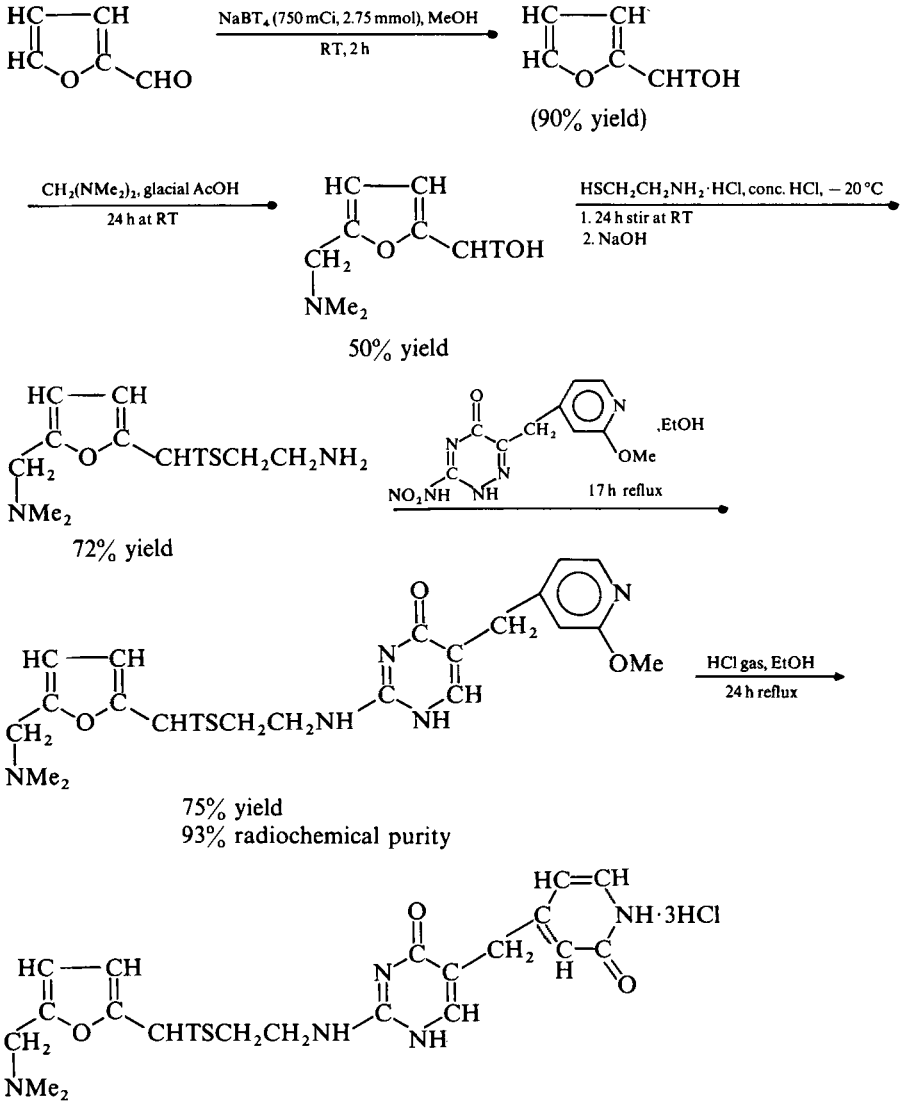


(37)

(**96**) 55% step yield, specific activity of 15 mCi mmol^{-1}, 97.3% radiochemical purity

$^{*}C$ denotes ^{14}C

c. ^{3}*H-donetidine trihydrochloride* ***97***, labelled with tritium in the methylene of the furanylmethylthio moiety, has been obtained in a five-stage synthesis (equation 38) starting from sodium boro[^{3}H]-hydride in 1% overall radiochemical yield at a specific activity of 33.7 mCi mmol^{-1}.

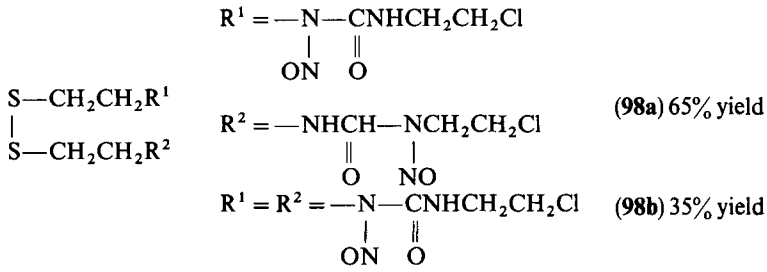


(38)

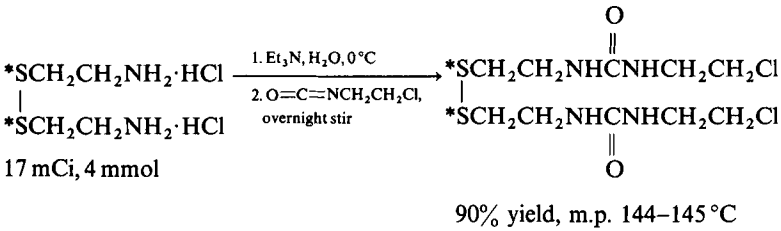
T denotes tritium

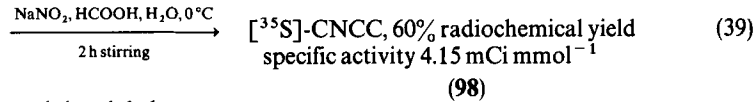
5. Synthesis of ^{35}S-, ^{14}C- and ^{3}H-labelled CNCC

The title compound, di-[2-chloroethyl)-2-*N*-nitroso-*N*-carbamoyl]-*N,N*-cystamine, **98a** and **98b**, has been ^{35}S-, ^{14}C- and ^{3}H-labelled on the two sulphur atoms of the cystamine group, on the urea carbonyl and on the position 1 of the 2-chloroethyl group for metabolic study *in vivo* of CNCC (equation 39 and 40).



a. ^{35}S*-labelled CNCC* has been prepared[106] as shown in equation 39. The product **98** has been isolated by HPLC using aprotic solvents in view of the instability of **98** in protic ones.

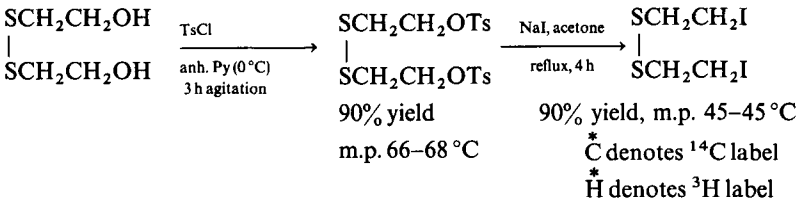




(39)

*S denotes sulphur label

b. ^{14}C*- and* ^{3}H*-labelled CNCC* have been prepared as shown by equation 40.



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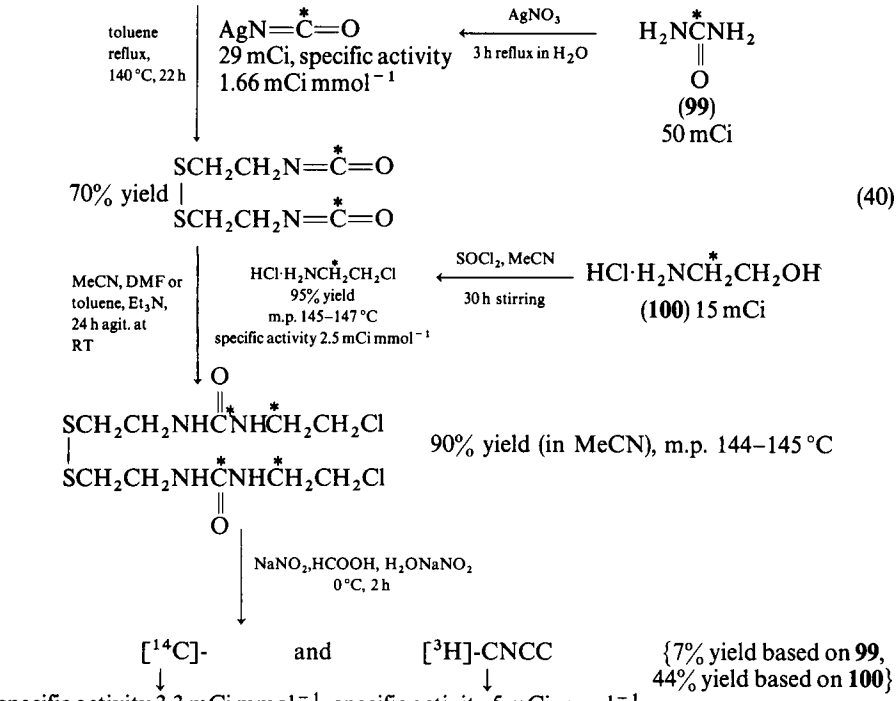
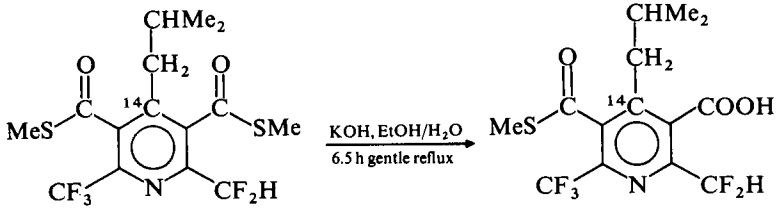


(40)

C. Synthesis and Applications of Carbon-14 Labelled Compounds

1. Synthesis of ^{14}C-labelled monoacidic metabolites of dithiopyr

Two isomeric monocarboxylic acid derivatives of dithiopyr **101**, an experimental herbicide used for weed control, have been synthesized recently[107] for metabolism studies. 2-(Difluoromethyl)-4-(2-methylpropyl)-5-[(methylthio)carbonyl]-6-(trifluoro-methyl)-3-pyridine[4-^{14}C]-carboxylic acid **102** has been obtained[107] by selective potassium hydroxide hydrolysis of ^{14}C-labelled dithiopyr **101** (equation 41).



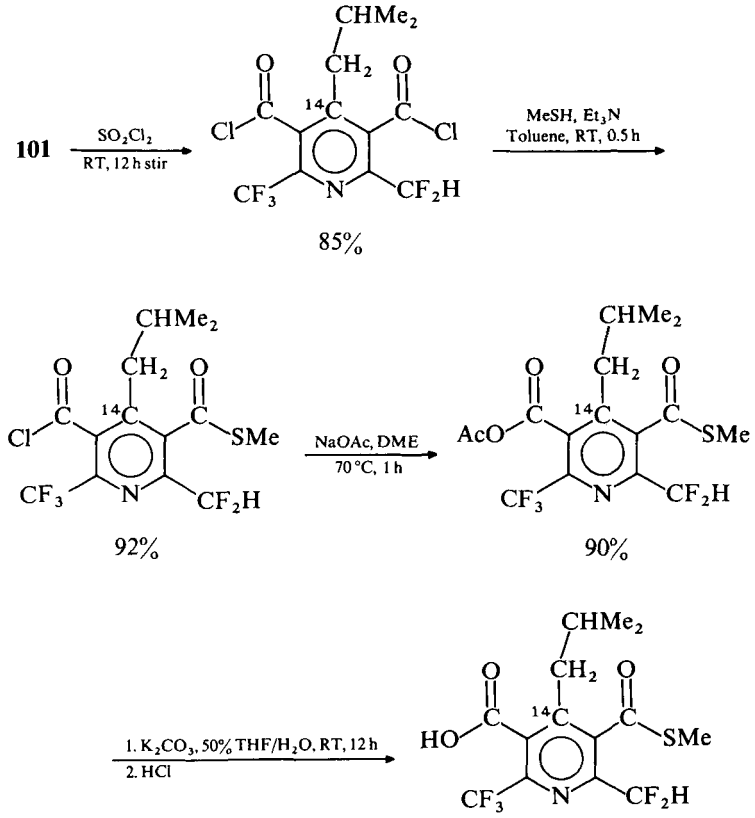
(101)
specific activity 29.2 mCi mmol⁻¹
0.066 mmol

(102)
58% yield
99% chemical purity
specific activity 29.1 mCi mmol⁻¹

(41)

The different reactivities of the two thioester groups have been explained by formation of hydrogen bonding between the hydrogen of the $—CHF_2$ group and the thioester carbonyl group at the $C_{(3)}$ of the pyridine ring, which renders the carbonyl more susceptible to nucleophilic attack[108,109].

The isomeric monoacid 6-(difluoromethyl)-4-(2-methylpropyl)-5-[(methylthio)carbonyl]-2-(trifluoromethyl)-3-pyridine[4-^{14}C]carboxylic acid (**103**) has been prepared in 43% overall yield as shown in equation 42. ^{14}C-labelled dithiopyr has been synthesized previously[34].

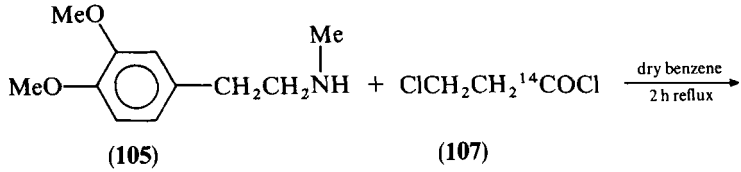


(103)

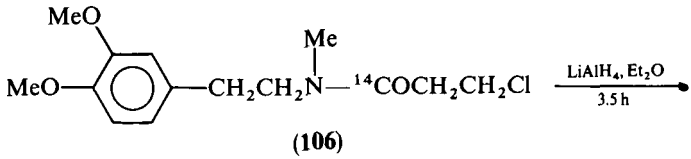
99% radiochemical purity (HPLC/LSC analysis)
specific activity 29.2 mCi mmol^{-1}

2. Synthesis of 1-{4-[3-(N-methyl N-[3,4-dimethoxy β-phenethyl]amino) [3-^{14}C]-propyloxy]benzenesulphonyl}-2-isopropyl indolizine

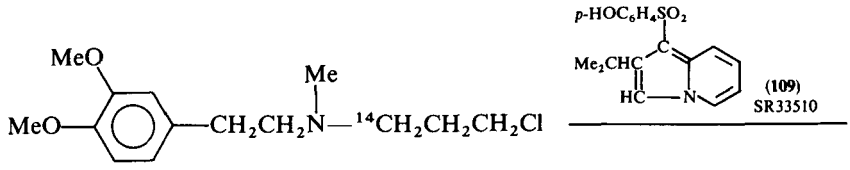
The title compound, [^{14}C]SR 33557, **104**, showing calcium channel blocking activity and of potential use in the treatment of cardiovascular pathologies[110], has been ^{14}C



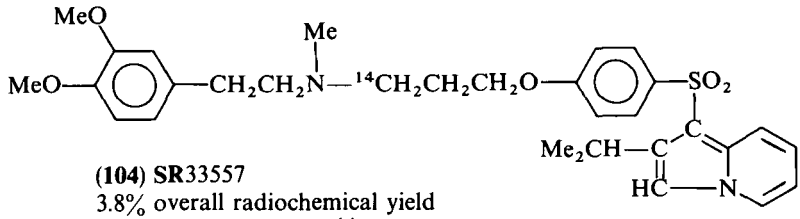
(105) (107)



(106)



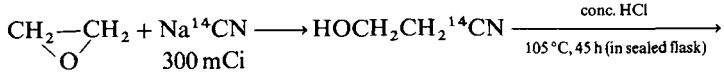
(108) 58% yield

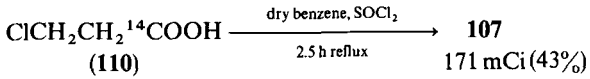


(104) **SR**33557
3.8% overall radiochemical yield
starting from sodium [^{14}C] cyanide

(43)

labelled for pharmacokinetic studies[111] according to equation 43. 3-Chloro[1-^{14}C]propionyl chloride **107** has been prepared[112], as shown in equation 44.





(44)

3. Synthesis of sodium 2-mercapto-[^{14}C]ethanesulphonate

The title compound, MESNA **111**, used mainly for eliminating urotoxic effects of the metabolite (acrolein) of cytostatics of cyclophosphamide type, and oxidized quickly in blood to sodium 2,2-dithio-bis-ethanesulphonate (DIMESNA, $t_{1/2} = 16.5$ min), has been synthesized[113] from [1-^{14}C]ethanol (equation 45).

$$CH_3{}^{14}CH_2OH \xrightarrow[350\,^\circ C \text{ in pyrolytic reactor}]{Al_2O_3} CH_2{=}{}^{14}CH_2 \xrightarrow{Br_2/CCl_4}$$
(5.5 mCi)

$$BrCH_2{}^{14}CH_2Br \xrightarrow[120\,^\circ C,\,4\,h\ reflux]{Na_2SO_3/EtOH} Br(\overset{*}{C}H_2)_2SO_3Na \xrightarrow[3\,h\ boiling]{(NH_2)_2CS/H_2O}$$
(2.12 mCi)

$$SH_2NCS(\overset{*}{C}H_2)_2SO_3H \xrightarrow[\text{2. Neutralization to pH 6.6 with 4\% aq. NaOH}]{NH_3\,(conc.)\ \text{1. 50 °C under argon}} HS(\overset{*}{C}H_2)_2SO_3Na \qquad (45)$$

(112)

232 μCi

m.p. 269 °C (dec)

(111)

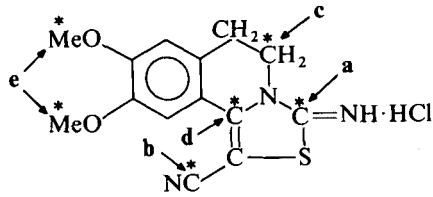
131 μCi

specific activity

0.083 μCi mmol^{-1}

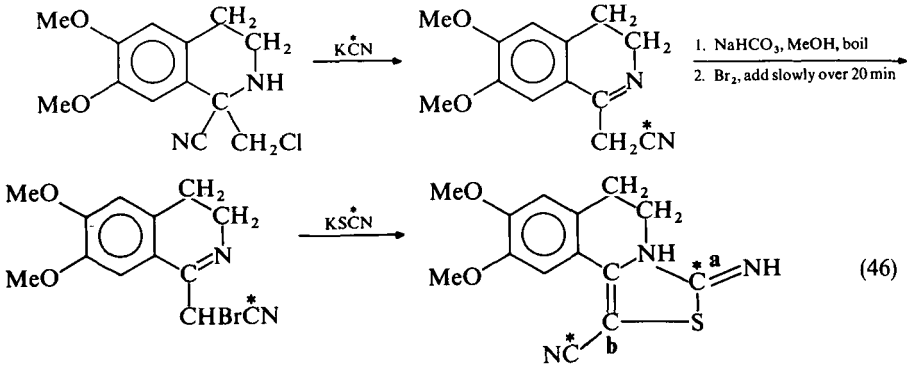
4. Synthesis of ^{14}C-labelled 1-cyano-3-imino-8,9-dimethoxy-3,4,5,6-tetrahydro-thiazolo[4,3-a]isoquinoline hydrochloride

This compound **113**, a potent coronary dilatator increasing circulation in the ischemic area, has been labelled[114] with ^{14}C in the various positions **a**, **b**, **c**, **d** and **e** as shown in structure **113** and in equations 46–48, using KS^{14}CN, K^{14}CN, homoveratrylamine[1-^{14}C]



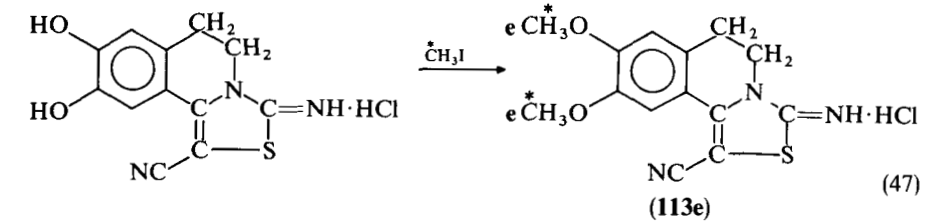
(113)

and cyanoacetic[1-^{14}C] acid as labelled starting materials. The compound **113a** was obtained with the best radiochemical yield using KS^{14}CN as starting material, but the easy degradation of the thiazole ring during the metabolism made it unsuitable for pharmacokinetic studies. The cyanoacetic acid [1-^{14}C] used in equation 48 has been prepared[115,116] in 83% yield from sodium acetate [1-^{14}C] (143 mCi) and KCN via bromoacetic[1-^{14}C]acid.

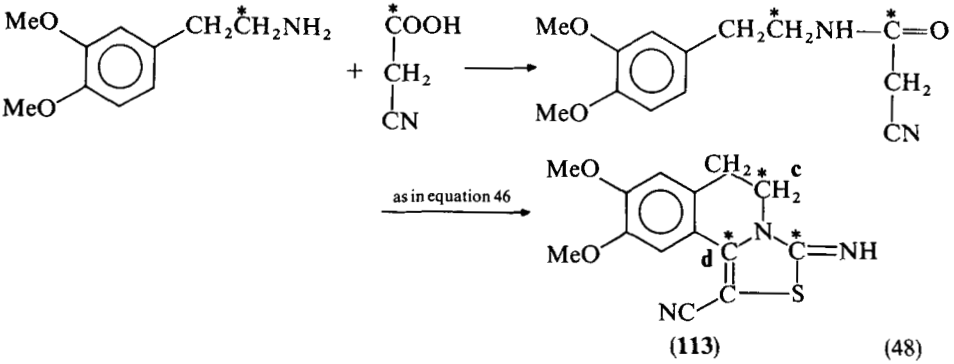


66% yield of a compound **a**
24.7% yield of compound **b**

(46)



(113e) (47)

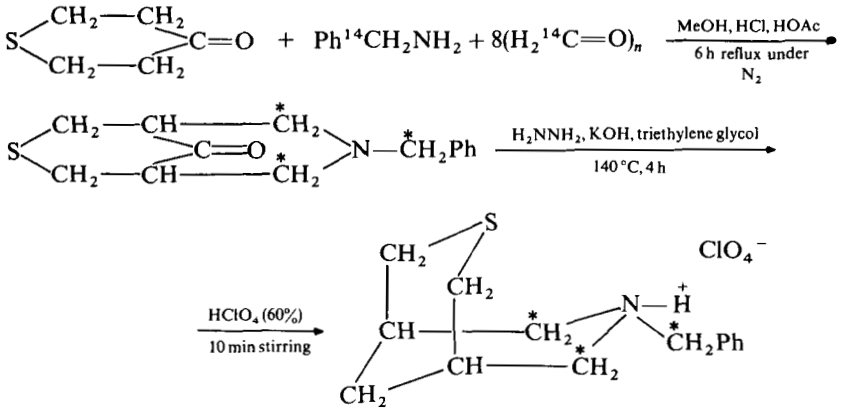


(113) (48)

6% yield of compound **c**
100% yield of compound **d**

5. Synthesis of 7-benzyl-7-aza-3-thiabicyclo[3.3.1]nonane hydroperchlorate-6,8,10-$^{14}C_3$

This compound, **114**, possessing antiarrhythmic activity[117,118], has been synthesized[119] and used in metabolic studies in animals[120], employing commercially available 4-thianone and two labelled starting materials, benzylamine[7-^{14}C] and paraformaldehyde[$^{14}CH_2$] (equation 49). The crude amine obtained by Wolff–Kishner reduction of the carbonyl oxygen was converted immediately to the hydroperchlorate **114**.

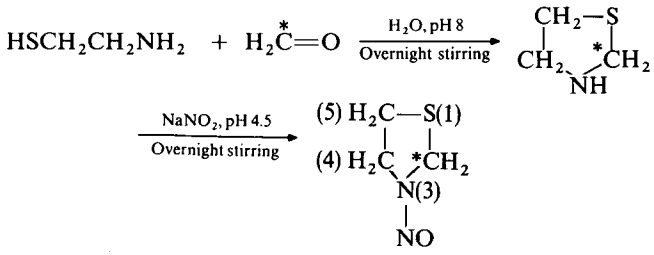


(114) (49)

m.p. 154.5–155 °C

6. *Synthesis of 2-^{14}C-N-nitrosothiazolidine*

N-Nitrosothiazolidine **115** is found in many smoke-cured meats[121]. It has been ^{14}C-labelled[122] at the $C_{(2)}$ position (equation 50) for pharmacokinetic and metabolic studies since the electron-withdrawing influence of N and S atoms would tend to make this position accessible for biooxidation.

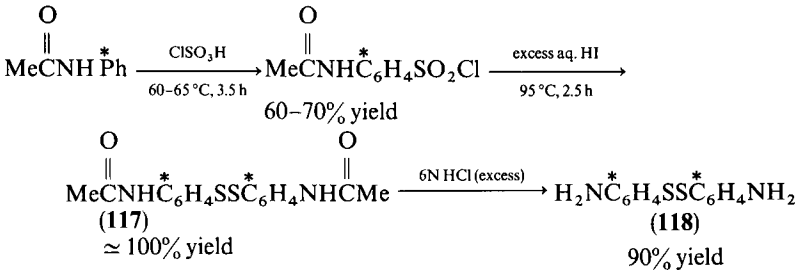


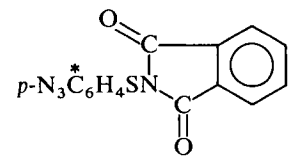
(50)

(**115**, yellow oil), specific activity 41.55 μCi mmol^{-1},
30.7% overall yield, 99.4% radiochemical purity

7. *Synthesis of ring-labelled 3-[(4-azidophenyl)dithio]propionic acid[^{14}C]*

The title compound, [^{14}C]APDP **116**, a cleavable, heterobifunctional photolabelling reagent[123,124], needed for membrane-labelling experiments (in biomembrane structure, intermacromolecular interaction and photoinduced crosslinking investigations), has been synthesized[125] by chlorosulphonation of uniformly ring-labelled acetanilide[^{14}C] followed by reductive dimerization of the product to 4-acetamidophenyl disulphide **117**. Hydrolysis of **117** and diazotization of **118** produced 4-azidophenyl disulphide **119**, which has been converted to **116** via *N*-(4-azidophenylthio)phthalimide (**120**); see equation 51. The position of the ^{14}C label on the ring allows transfer of radioactivity from the macromolecule of interest to biological targets.



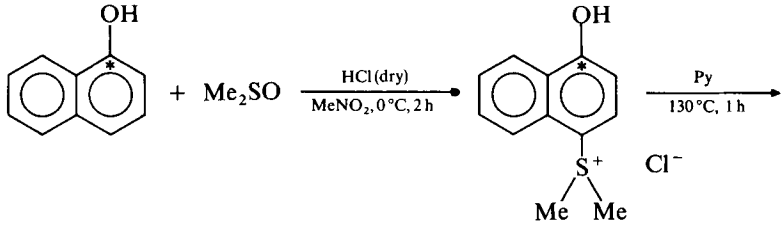


$\xrightarrow[\text{benzene, smooth reaction}]{HSCH_2CH_2COOH}$ p-$N_3C_6H_4SSCH_2CH_2COOH$ (51)

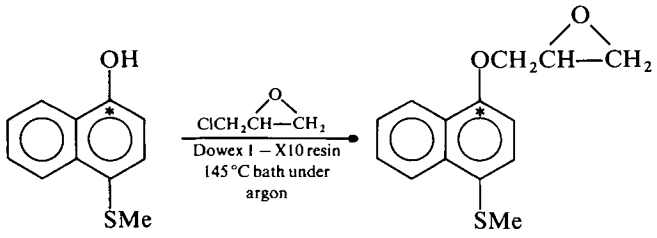
(**116**) *ca* 75% yield
specific activity 27 mCi mmol^{-1}
C_6H_4, Ph = uniformly ^{14}C-labelling ring

8. Synthesis of ^{14}C-labelled 4'-methylthiopropranolol (MTP)

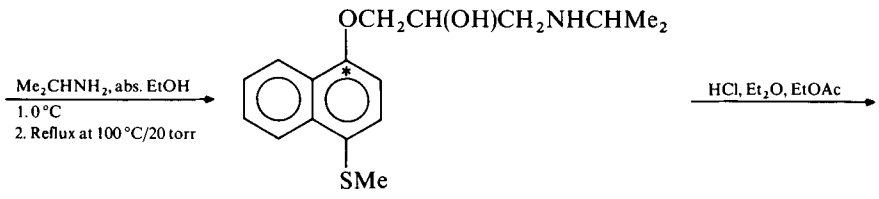
The title compound, MTP **121**, identified in urine as a hydrolysis product of an unidentified metabolite of the antihypertensive drug propranolol, has been labelled[126] with carbon-14 in the 1-position of the naphthalene starting with 1-naphthol[1-^{14}C] (equation 52). Its specific activity was found to be 11.68 mCi mmol^{-1}.



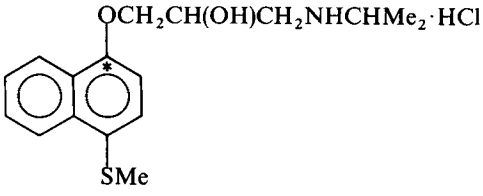
87.9% yield



86.8% yield 86.7% yield



86% yield (crude), 32% yield pure, after six recrystal. from isooctane/*i*-BuCOMe

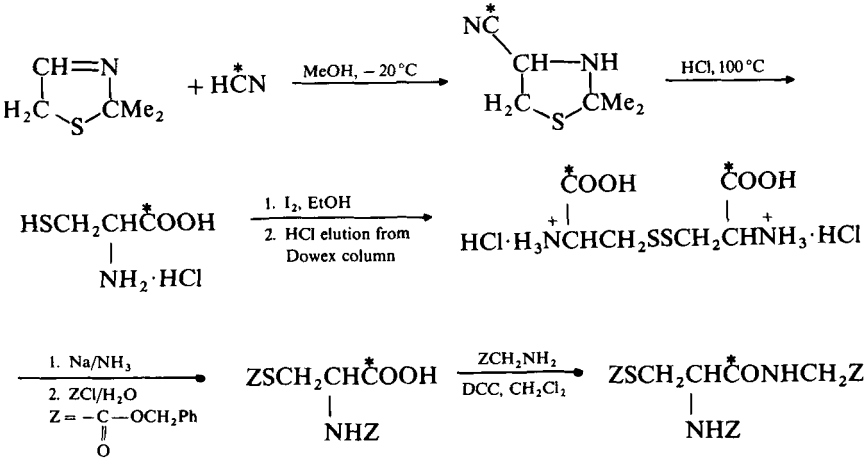


(52)

(121) MTP·HCl, 100% step yield, 18.76 mCi, 98.9% radiochemical purity specific activity 11.68 mCi mmol^{-1}

*9. Synthesis of N-[N-L-γ-glutamyl-L-cysteinyl-(carbonyl-^{14}C)]glycine (glutathione-^{14}C) and synthesis of [cys-^{14}CO]-(5S,6R)-LTC$_4$ (**127**)*

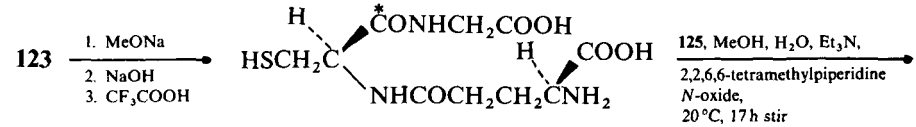
These peptidolipids, possessing high biological activities like contraction of smooth muscles or vasodialtion[127], are very active mediators involved in immediate hypersensitivity reactions and asthma-related diseases[128]. They have been prepared[129] as shown in equations 53 and 54, starting with NaCN[^{14}C] and 2,2,-dimethylthiazoline.



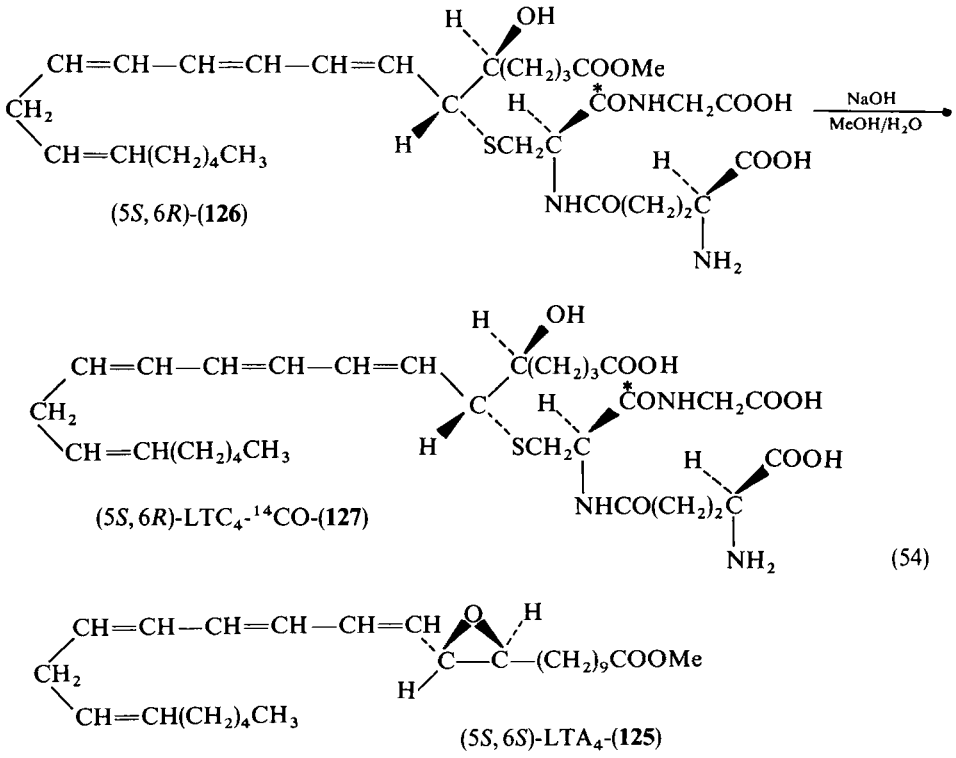
(D, L)-(**122**), 9.1 mCi
specific activity 50 mCi mmol^{-1}

(L, L)-(**123**), 9.6 mCi
specific activity 50 mCi mmol^{-1}, 20% yield

(53)

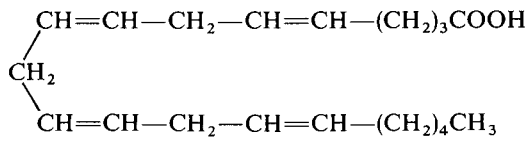


(**124**) (L, L)-glutathione-^{14}CO



(54)

The peptido-leukotriene (5*S*,6*R*)-LTC_4 **127** and other peptide leukotrienes are produced in natural conditions by stereo- and enantiospecific enzymatic oxidation of arachidonic acid **128** by 5-lipoxygenase through the intermediate unstable allyl epoxide



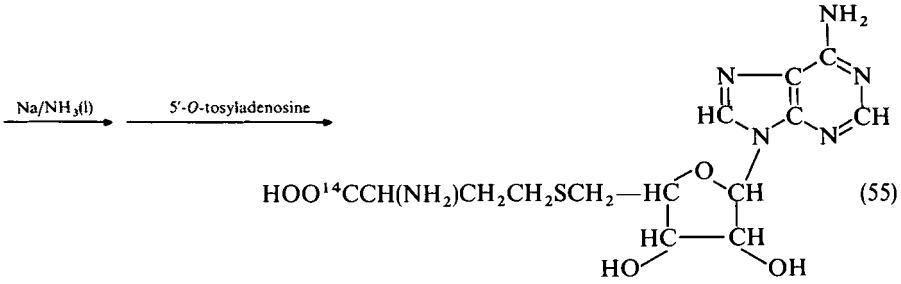
(128)

125. Glutathione-^{35}S and [Glu-U-^{14}C]glutathione have been synthesized previously[130]. Tritium labelling of the lipophilic part of LTA_4 and related LTE_4 metabolites are described also[131,132].

10. Synthesis of S-adenosyl-L-[1-^{14}C]-homocysteine

The title compound **129**, a by-product of methyl transfer reactions of biological importance[133], has been prepared[134] from commercially available L-[1-^{14}C]-methionine, by conversion of the latter to *S*-benzyl-L-[1-^{14}C]-homocysteine, which in turn with 5'-*O*-tosyladenosine gave **129** (equation 55).

$$MeSCH_2CH_2CH(NH_2)^{14}COOH \xrightarrow[24\text{ h reflux}]{BnCl,\ HCl\ (conc.)} PhCH_2SCH_2CH_2CH(NH_2)^{14}COOH$$
(23.5 mCi)



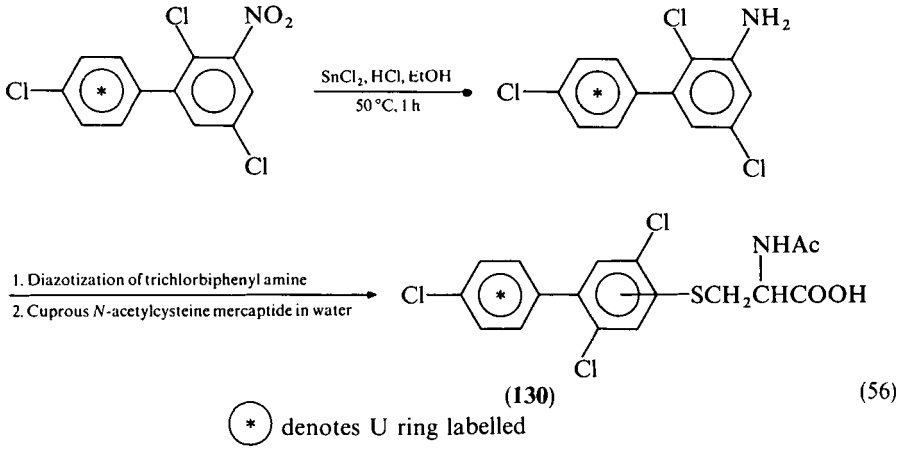
(55)

(**129**) 99% radiochemically pure; specific activity 31.9 μCi mg^{-1}, total activity 1.72 mCi

11. Synthesis of 2,4',5-trichloro[^{14}C]biphenyl mercapturic acid

The title compound, triCB **130**, has been ^{14}C-labelled[134] according to equation 56, in order to prove that it is the precursor of methyl sulphide and methyl sulphone metabolites of triCB which accumulate in lung bronchial mucosa[136,137].

$$p\text{-}ClC_6H_4NH_2[U\text{-}^{14}C] + 2,5\text{-}Cl_2C_6H_3NO_2 \xrightarrow[120\,^\circ C,\ 3\text{ h}]{AcOH,\ 3\text{-methylbutyl nitrite}}$$
377 MBq
specific activity 178 MBq·mmol^{-1}

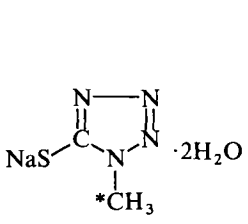


(**130**) (56)

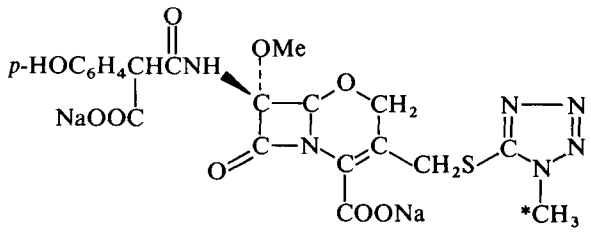
(*) denotes U ring labelled

12. Synthesis of 1-[^{14}C]methyl-1H-tetrazole-5-thiol ([^{14}C]NMT) and (NMTT[^{14}C]; latamoxef)

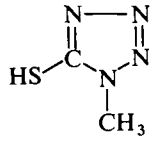
Sodium 1-[^{14}C]methyl-1-*H*-tetrazole-5-thiolate (**131**) and [^{14}C]latamoxef disodium salt **132** have been synthesized[138] to conduct *in vivo* metabolic studies of the thiol **133** liberated from the parent unlabelled antibiotic latamoxef, widely used therapeutically



(131)

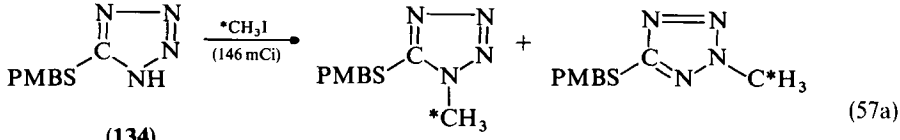


(132)

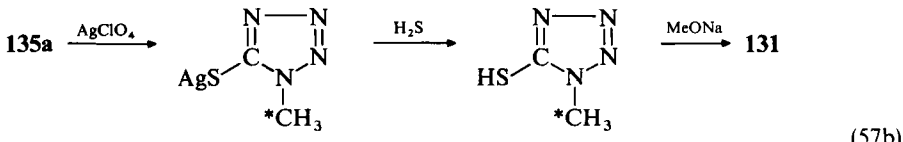


(133)

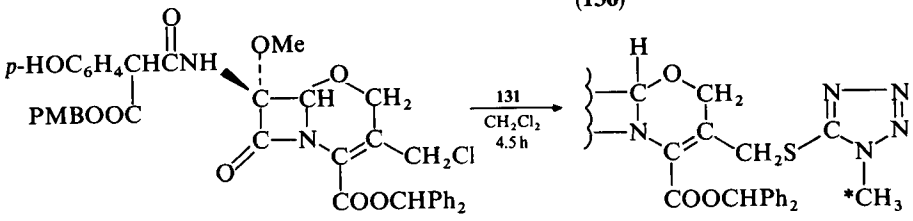
as a representative third-generation β-lactam antibiotic[139]. **131** has been obtained in 26% overall radiochemical yield as shown in equations 57a and 57b involving methylation of the *p*-methoxybenzyl (PMB) thio ether **134** with [^{14}C]methyl iodide, deprotection of thio ether **135a** with silver perchlorate and treatment of the thiol **136** with MeONa. **132** has been obtained by coupling of the thiolate **131** with the 3-chloromethyl oxacephem derivative **137** and deprotection of the [^{14}C]latamoxef diester **138** with $AlCl_3$ in anisole (equation 58).



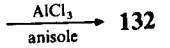
(134) (135a) (57a)



(136) (57b)



(137) (138) m.p. 102–104 °C
90.4% radiochemical yield

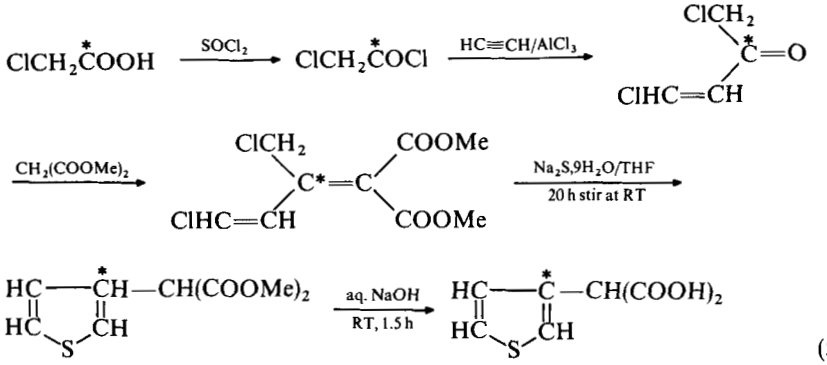


(58)

94% yield from **138**, specific activity 12.1 mCi mmol^{-1}

13. Synthesis of [thienyl-3-^{14}C]temocillin

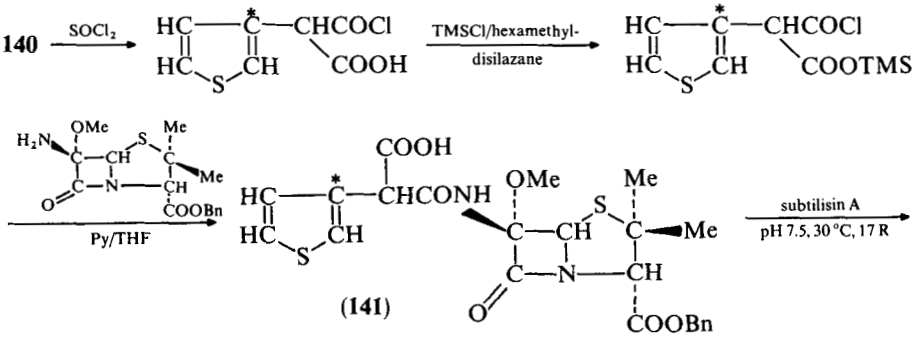
The ^{14}C-labelled novel penicillin antibiotic[140], **139**, has been prepared[141] for metabolic studies from [1-^{14}C]chloroacetic acid via 3-[3-^{14}C]thienylmalonic acid **140** (equations 59 and 60).



(59)

(140) 13.0 *mCi*

(13% radiochemical yield; radiochemical purity > 97%)



C* denotes ^{14}C label

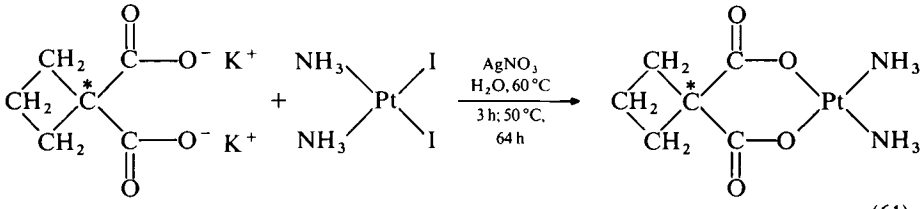
(139) (60)

radiochemical purity ≃ 89%

Removal of the benzyl protecting group in **141** has been effected by enzymatic hydrolysis using subtilisin A. The overall radiochemical yield of **139** from **140** was 13%.

14. Synthesis of cis-diamino{1,1-[1-^{14}C]cyclobutanedicarbonyloxy(2)-0,0} platinum(II)

This cisplatin derivative **142**, showing antitumor activity and less toxic than the parent compound cisplatin, has been obtained[142] by condensing of *cis*-diaminodiiodoplatinum (**144**) with 1,1-[1-^{14}C]cyclobutanedicarboxylic acid dipotassium salt in the presence of silver nitrate (equation 61).

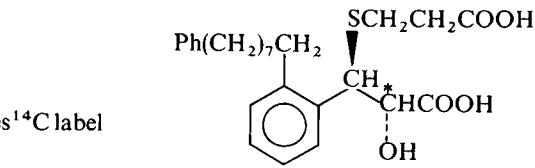


(**143**) (**144**) (**142**) (61)

radiochemical purity 99.2%,
specific activity 3.1 μCi mg^{-1}

15. Synthesis of carbon-14 labelled leukotriene antagonist

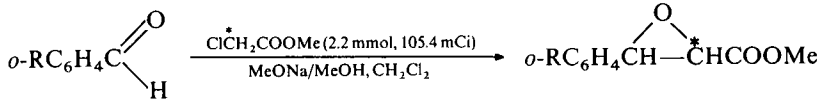
The enantiomerically pure (2*S*, 3*R*)-3-[(2-carboxyethyl)thio]-3-[2-(8-phenyloctyl)-phenyl]-2-hydroxy[2-^{14}C]propionic acid (**145**), a novel high-affinity leukotriene receptor antagonist of potential therapeutic utility in disease states such as bronchial asthma[149], has been synthesized[144] from methyl chloro[2-^{14}C]acetate as shown in equation 62.



$\overset{*}{C}$ denotes ^{14}C label

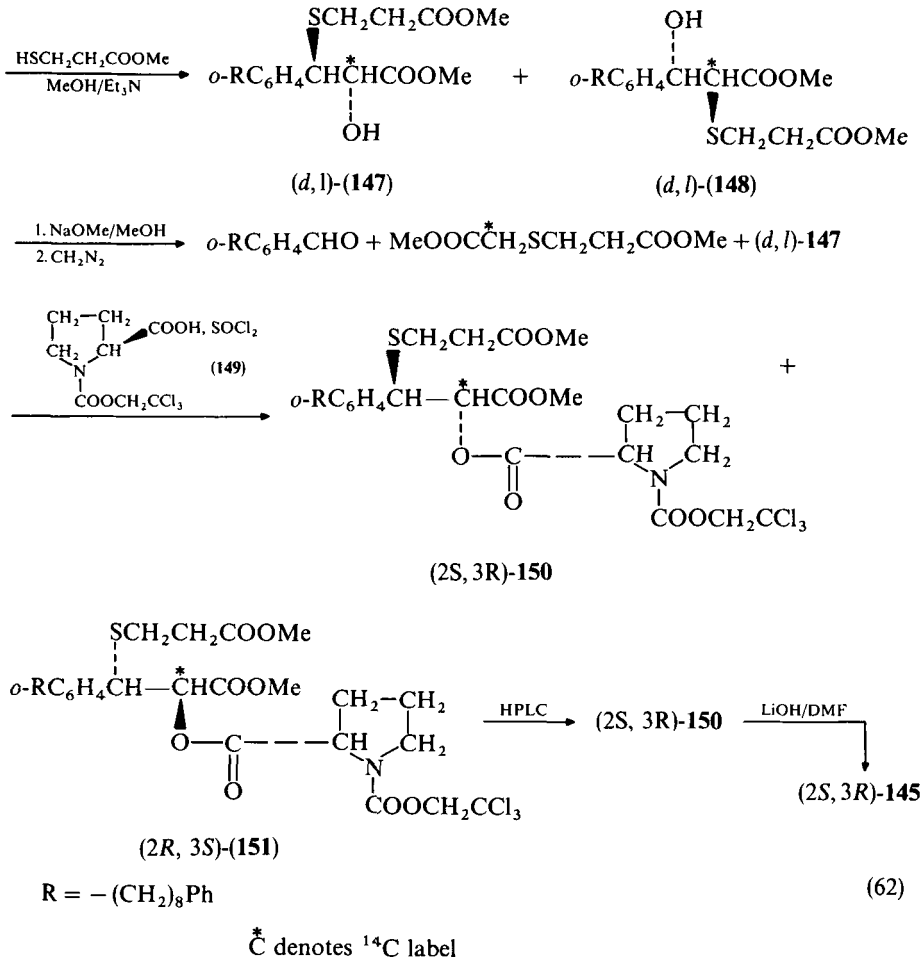
(2*S*, 3*R*)-(**145**) {[^{14}C]SK&F 104353}

This involved the *trans*-epoxide ester **146** labelled at $C_{(2)}$ as the key intermediate, separation of the two regioisomers **147** and **148** by retroaldol cleavage with NaOMe/MeOH, treatment of the post-reaction mixture with CH_2N_2 to regenerate the methyl ester **147** and its isolation by chromatography. Optical resolution has been achieved by derivatizing the racemic **147** with the (*S*)-proline derivative **149** followed by HPLC separation of the diastereomers to provide enantiomers **150** and **151** in a combined 47% yield. **150** has been subsequently hydrolysed to yield **145** (36%), with radiochemical purity higher than 98%. The total activity of **145** was 5.4 mCi, the specific activity being 16.1 mCi mmol^{-1} (5% overall radiochemical yield from methyl chloro[2-^{14}C acetate). **145** stored in EtOH solution under argon at − 80 °C was radiochemically stable for 19 months.



(*d*, *l*)-(**146**)

(*continued*)

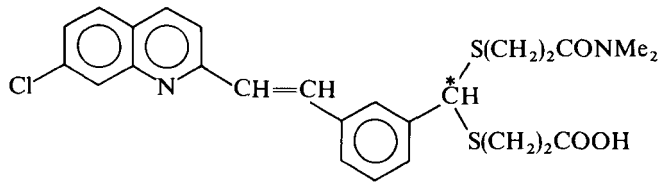


$R = -(CH_2)_8Ph$ (62)

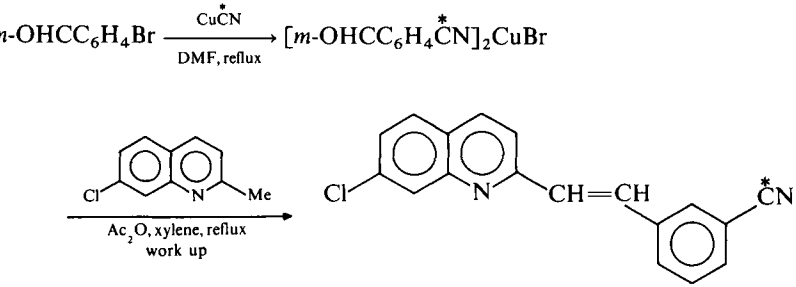
$\overset{*}{C}$ denotes ^{14}C label

16. Synthesis of carbon-14 labelled LTD_4 antagonist MK-571

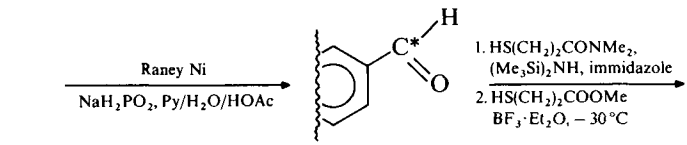
This new cysteinyl leukotriene **152** involved in the etiology of human bronchial asthma[145,146] has been synthesized[147] as shown in equation 63. Condensation of 3-[^{14}C]cyanobenzaldehyde with 7 chloroquinaldine followed by reduction of nitrile **153**



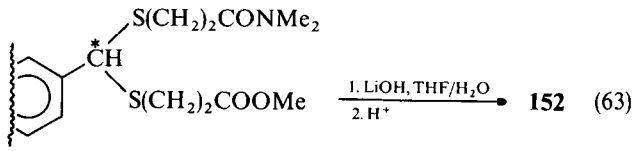
(**152**) [^{14}C]MK-571



(153)



(154)

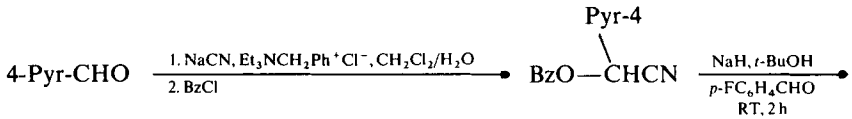


(155)

provided [^{14}C]aldehyde **154** which in the first step gave the crude O-silylated hemithioacetal, and in the second yielded **155**. Subsequent ester hydrolysis afforded [^{14}C]MK-571 in 14% overall radiochemical yield with specific activity 12.3 mCi mmol^{-1} and 97% radiochemical purity. Rapid purification, protection from light and storage at -55 °C was necessary since **152** decomposed easily.

*17. Synthesis of carbon-14 labelled 6-(4-fluorophenyl)-5-(4-pyridyl)-2,3-dihydroimidazo[2,1-b]thiazole (SK&F 86002; **156**)*

156, a useful non-steroidal anti-inflammatory and immunomodulatory agent[148], has been triply labelled[149] with carbon-14 as shown in equation 64 involving the condensation of an asymmetric bezoin **157** with thiourea, followed by alkylation of **158** and separation of two products **156a** and **156b** by flash chromatography. The use of 1,2-dibromo[$^{14}C_2$]ethane greatly increases the overall radiochemical yields.



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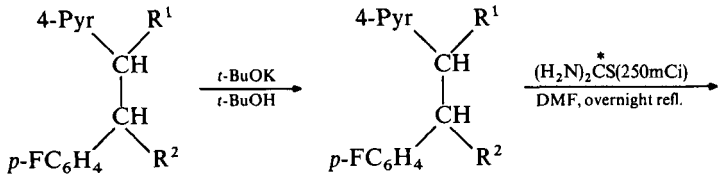
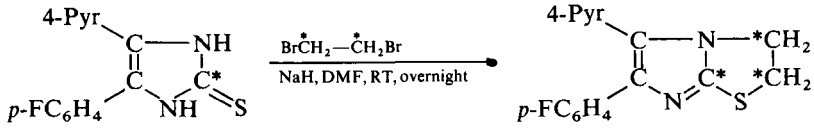
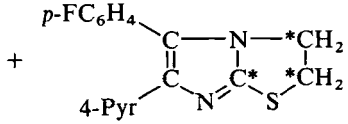


(**a**) $R^1 = (=O)$; $R^2 = (-OBz)$ (**157a**) $= (=O)$; $R^2 = (-OH)$
(**b**) $R^1 = (-OBz)$; (H) $R^2 = (=O)$ (**157b**)$R^1 = (-OH)$; $R^2 = (=O)$



(**158**) (**156a**)



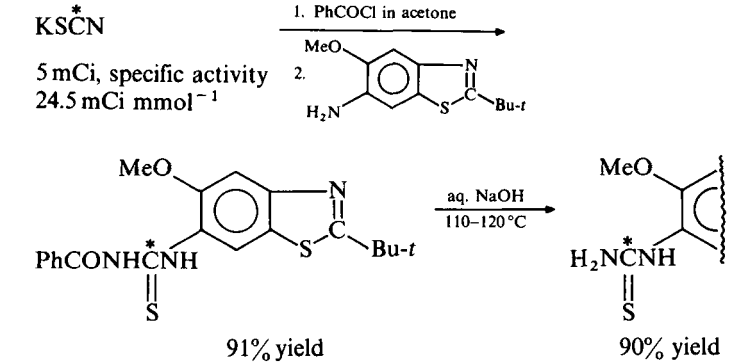
(64)

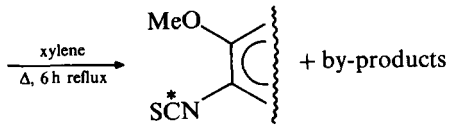
(**156b**)

156a; 14% radiochemical yield crude and 0.7% pure, based on [^{14}C]thiourea.
156b; 40% radiochemical yield crude (65 mCi) and 10% pure, based on 1,2-dibromo[$^{14}C_2$]ethane.
The radiochemical purity of **156** was 99.4%, the specific activity was 12.4 mCi mmol^{-1}.

18. Synthesis of S-(2-carboxyethyl)-N-(2-t-butyl-5-methoxy-benzthiazol-6-yl)-[^{14}C]dithiocarbamate

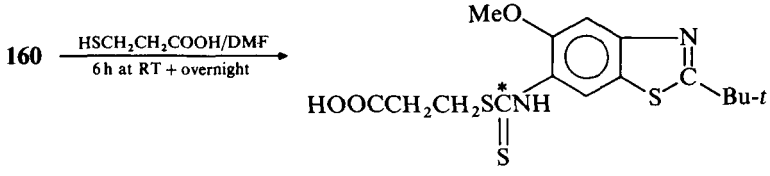
This experimental antifilarial pre-drug **159** (CGP 20376 or CGI 16483) exhibiting potent micro- and macro-filaricidal activity in rodents, cattle and in man[150] has been ^{14}C-labelled on the dithiocarbamoyl carbon atom in the side chain of the ring system[150] (equation 65).





(65a)

(**160**) CGP 20308



(65b)

(**159**)

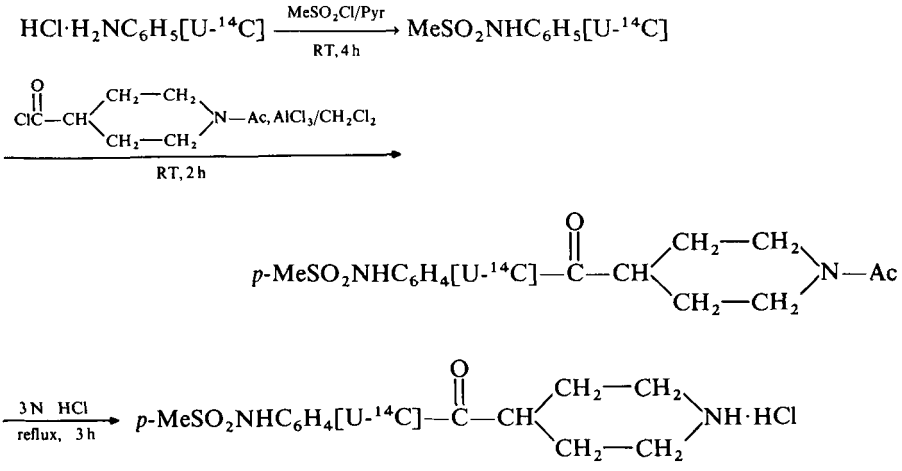
61%; radiochemical purity > 98%
specific activity 2.35 m Ci mmol^{-1}

The overall radiochemical yield starting from potassium [^{14}C]thiocyanate was 45%. All intermediate compounds have been tested by reversed isotope dilution analysis with authentic synthetic compounds (RDIA).

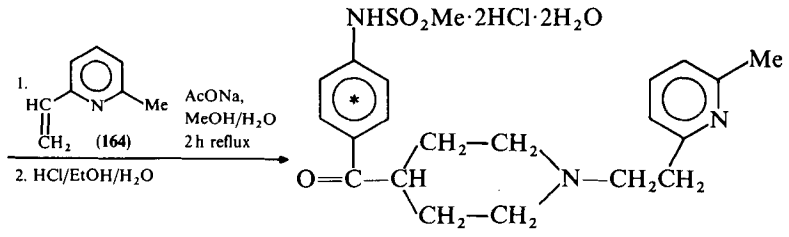
159 dissociated rapidly at physiological pH into its biologically active isothiocyanate precursor **160**, indicating that it might behave as a pro-drug.

19. Synthesis of [phenyl-^{14}C]4',4-piperidyl[carbonyl]-methanesulphonanilides

These ^{14}C-labelled antiarrhythmic agents E-4031 **161** and **162** of potential utility for prevention of ventricular tachycardia and ventricular fibrillation that may be causes of sudden death[151,152] have been synthesized[153] as outlined in equations 66a and 66b. The products **161** and **162** have been prepared by reacting the key intermediate **163** with 6-methyl-2-vinylpyridine **164** or (and) with 4-(3-chloropropyl)pyridine hydrochloride **165**,

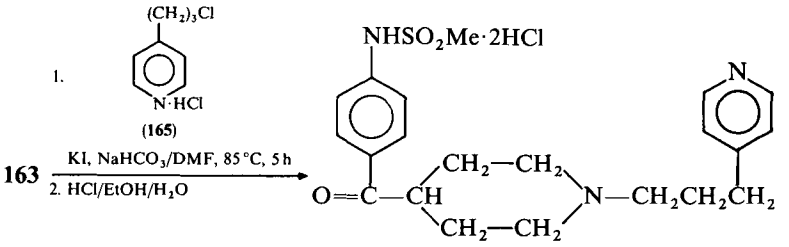


(**163**)



(66a)

(161)



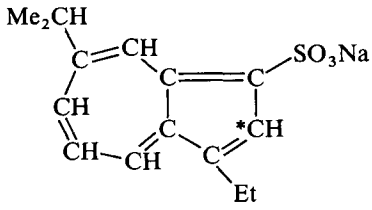
(66b)

(162) m.p. ~230 °C

respectively. ^{14}C-Labelled E-4031, **161**, and its pyridylpropyl analogue **162** were $98 \pm 0.1\%$ and $100 \pm 1\%$ radiochemically pure and both had specific activity equal to $112\,\text{mCi mmol}^{-1}$.

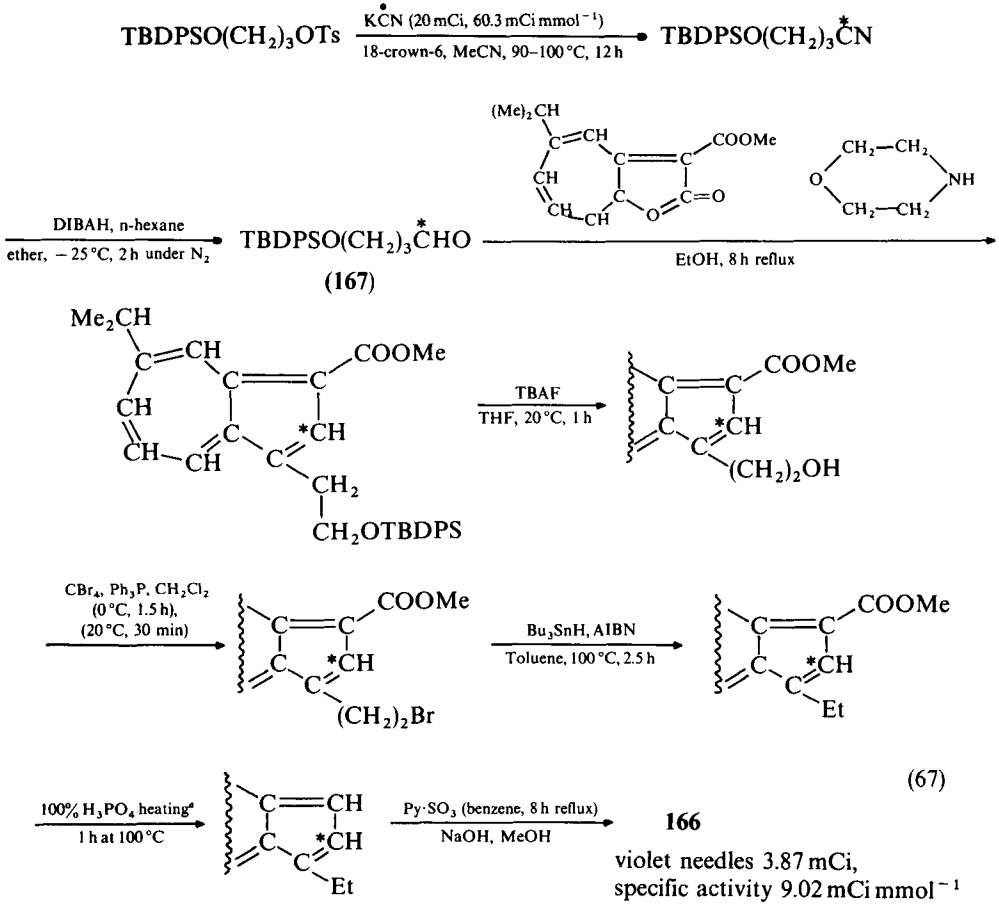
*20. Synthesis of sodium 3-ethyl-7-isopropyl-[2-^{14}C]-azulene-1-sulphonate (**166**)*

This compound is chemically more stable and shows more potent anti-inflammatory and anti-ulcerous activity than other alkylazulene derivatives[154]. It has been



(166)

^{14}C-labelled[155] at the 2-position in the azulene ring for the study of metabolism in the preclinical stage, using potassium[^{14}C]cyanide as shown in equation 67.

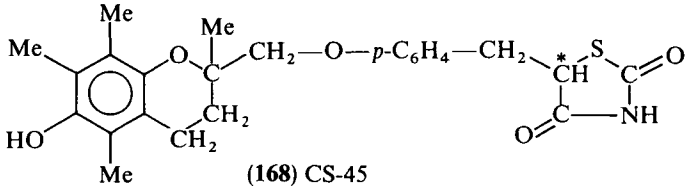


(67)

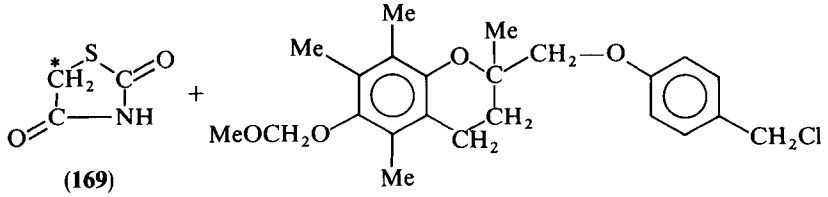
[a]Lactic acid undergoes decarbonylation in 100% H_3PO_4[155a]

21. Synthesis of (±)-5-[4-(6-hydroxy-2,5,7,8-tetramethylchroman-2-ylmethoxy]-5-^{14}C-thiazolidine-2,4-dione (^{14}C-Labelled CS-045)

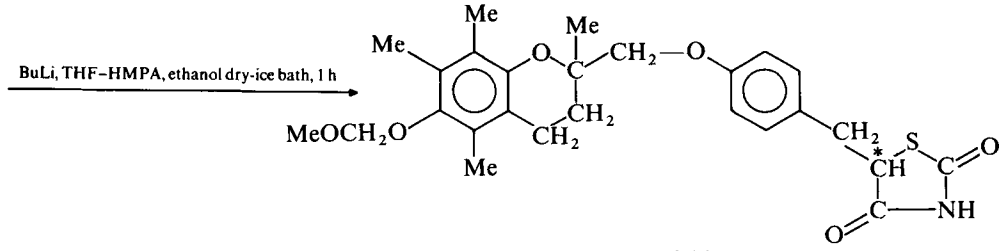
This new oral antidiabetic agent **168**, effective in insulin-resistant diabetic animal models[156,157], has been labelled with carbon-14 at the 5-position of the thiazolidine ring[158,159] by condensing [5-^{14}C]thiazolidine-2-4-dione **169** with 4-(6-methoxymethoxy-2,5,7,8-tetramethylchroman-2-ylmethoxy)benzyl chloride **170** (equation 68).



(168) CS-45

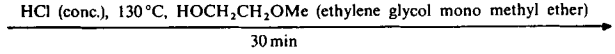


(169) (170)



yellow oil, 57% yield

(68)



168

pale yellow oil

After recrystallization from benzene; specific activity 703.4 kBq mg^{-1} after dilution with cold CS-045

D. Synthesis of Sulphur-35 Labelled Compounds

1. Synthesis of dimethyl [^{35}S]sulphide

Dimethyl sulphide is detected in wines, beers, foods, plants, algae, soils and in the environment in general[160,161]. It has been ^{35}S-labelled in high yield[162] by contacting hydrogen-[^{35}S]sulphide with methanol over an activated γ-Al_2O_3/1% SiO_2 catalyst (equation 69). Specific activity of **171** has been of the order of 1 mCi mmol^{-1}, but it could be increased by increasing the specific activity of the $H_2S[^{35}S]$ which is available up to 200 mCi mmol^{-1}.

[^{35}S]-Labelled **171** is produced also[169] for use in preparation of metallorganic compounds of high purity, needed in microelectronics[164], by direct exchange between commercial $Na_2[^{35}S]$ and Me_2S in the presence of water (equation 70). It has been suggested[163] that the rate of ^{35}S-exchange is determined by solvation and dissociation of Me_2S and formation of hydrogen bonding between —SH groups and sulphur of Na_2S.

$$2\,MeOH + H_2{}^{35}S \xrightarrow[360 \pm 5\,^{\circ}C]{\text{catalyst}} Me_2{}^{35}S + H_2O + \text{by-products} \qquad (69)$$

(171)

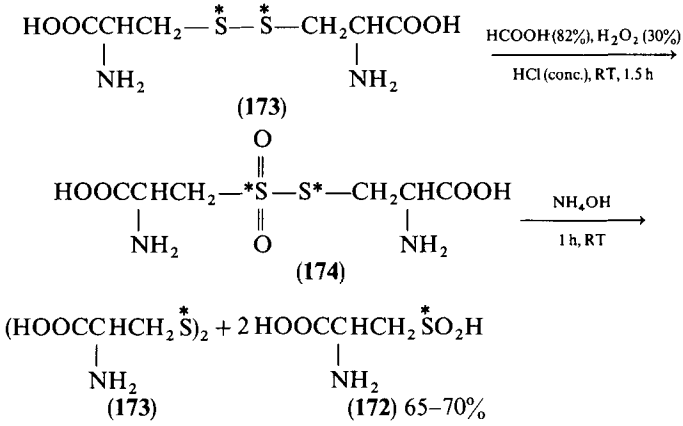
By-products: $CH_3{}^{35}SH$, Me_2O, CO, H_2 and CH_4

$$\underset{(0.0142\,g,\,400\,MBq)}{Na_2[^{35}S]} + \underset{(10\,cm^3)}{Me_2S} \xrightarrow[25\,^{\circ}C,\,80\,h\,\text{in sealed ampoule; 97\%}]{H_2O,(0.5\,cm^3)} Na_2S + \mathbf{171} \qquad (70)$$

In a similar manner [^{125m}Te]Me_2 and [^{75}Se]Me_2 have been obtained[165] by isotope exchange process taking place in M^*-I_2-$M(CH_3)_2$ systems through the formation of the unstable $M(CH_3)_2(MI_2)$ complex. They were applied for determination of Te and Se contaminants at the 10^{-5}–10^{-6} mass% level in methylated compounds of Ga, Al, Sb and of other metals used in the electronics industry.

2. *Synthesis of L-[^{35}S]cysteine sulphinic acid*

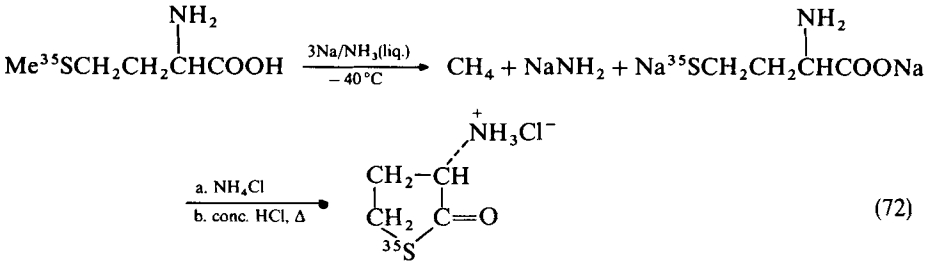
The synthesis of L-[^{35}S]cysteine sulphinic acid[166] (**172**) needed for study of cysteine sulphinic acid decarboxylase (converting **172** to hypotaurine and carbon dioxide in the mammalian brain[167]) has been redesigned[168] to a microscale (1–5 mg) synthesis (equation 71). The L-[^{35}S]cystine **173** has been first converted into the thiosulphonate intermediate **174**, which in turn yielded **172** and the starting L-cystine in a 2 to 1 molar ratio. The recovered **173** has been re-used. The product **172** has been separated from L-[^{35}S]cysteic acid, cystine and other by-products by TLC.



(71)

3. *Synthesis of L-[^{35}S]homocysteine thiolactone hydrochloride (**175**)*

175, an important metabolite involved in the methionine, cysteine and methylation metabolism[169], has been synthesized[170] by demethylation of L-[^{35}S]methionine followed by lactonization (equation 72).



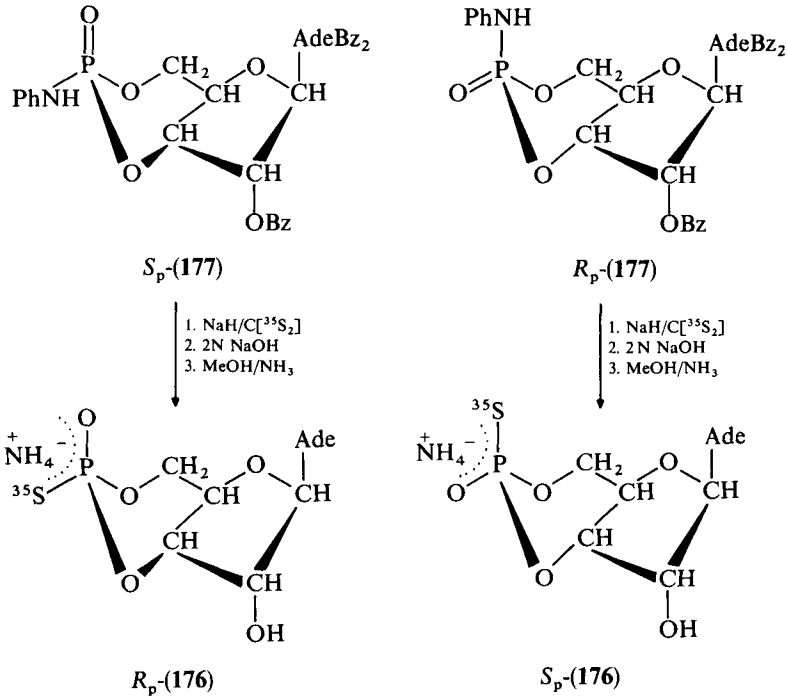
(72)

(**175**) (nearly quantitative cyclization)
specific activity 8.5 Ci mol^{-1}

The lactonization has been carried out in an inert atmosphere to prevent the oxidative dimerization of homocysteine to homocystine. **175** has been recovered by passing the methanol solution of the reaction mixture through a SEP-PAK alumina cartridge[171]. Methionine is held strongly by the alumina through its carboxyl group and is not eluted, contrary to the fast elution of **175**.

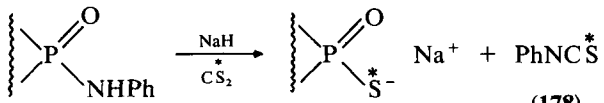
4. Stereospecific synthesis of cyclic adenosine 3′, 5′-R_p and S_p-phosphoro[^{35}S]thioates

The R_p- and S_p-diastereoisomers of [^{35}S]cAMPS (**176**) have been synthesized[172] as shown in equation 73, for studies of the role of **176** in the regulation of cellular mechanism, by treatment of both diastereoisomers of the tribenzoyladenosine phosphoranilidate derivatives **177** with sodium hydride and then with carbon [^{35}S]disulphide and



70% yield, radiochemical purity 99.2%,
radiochemical yield = 15%;
specific activity 8.4 MBq mmol^{-1} (73)

subsequent removal of the protective groups. A second radioactive product, PhNC[^{35}S] (**178**), has been produced also[173] (equation 74).

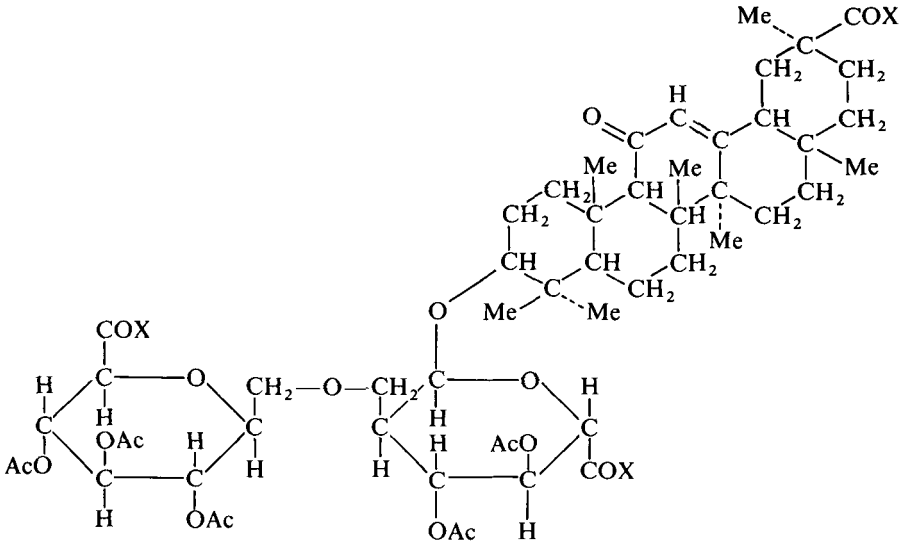


(74)

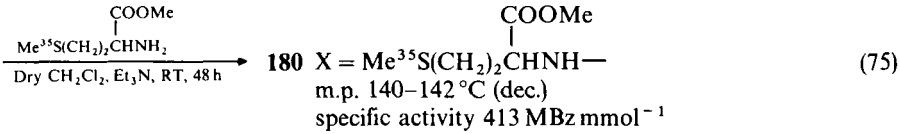
(179)

5. Synthesis of sulphur-35 labelled glycopeptide of glycyrrizinic acid with methionine

This glycopeptide **180** has been obtained[174,175] for pharmacokinetic studies by reaction of pentaacetylglycirrizinyl trichloride **180** (X = Cl) prepared in two steps from the corresponding unprotected acid, with [^{35}S]methionine methyl ester (equation 75).



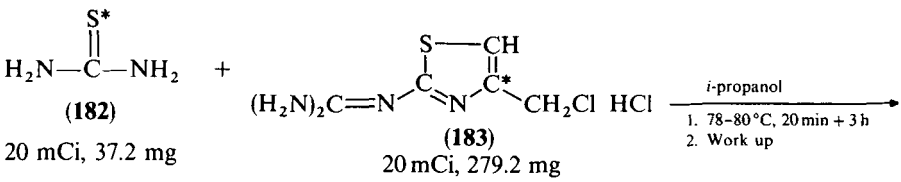
(**180**) X = Cl; m.p. 107 – 110 °C
specific activity 460 MBq mmol^{-1}

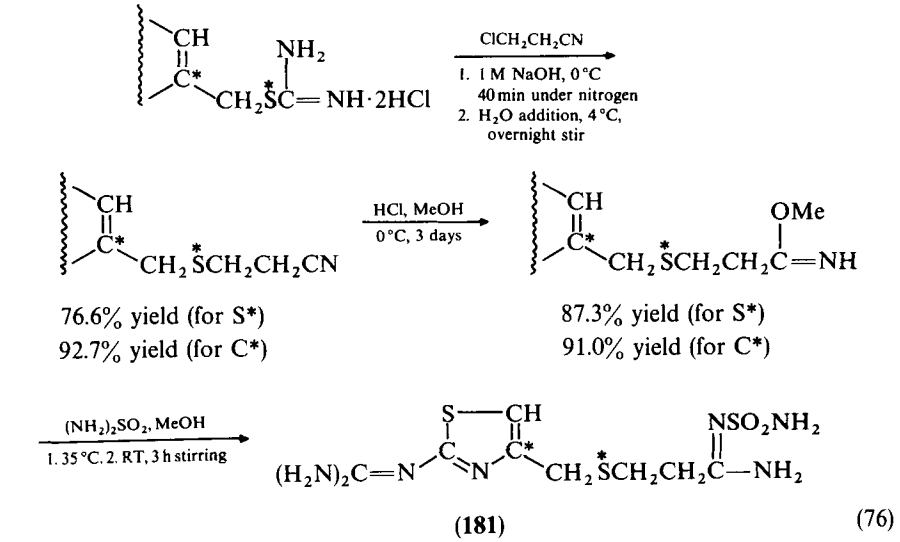


(75)

6. Synthesis of 3-{{[2-[(diaminomethylene)amino]-4-[4-^{14}C] thiazolyl]methyl} [^{35}S]thio}-N^2-sulphamoylpropionamidine

The title compound, famotidine **181**, a new potent histamine H_2 receptor antagonist[176], has been labelled with ^{35}S and with ^{14}C for metabolic studies[177] starting from the readily available [^{35}S]thiourea **182** and 4-chloromethyl-2-[(diaminomethylene)amino] [4-^{14}C]thiazole hydrochloride **183** (equation 76).



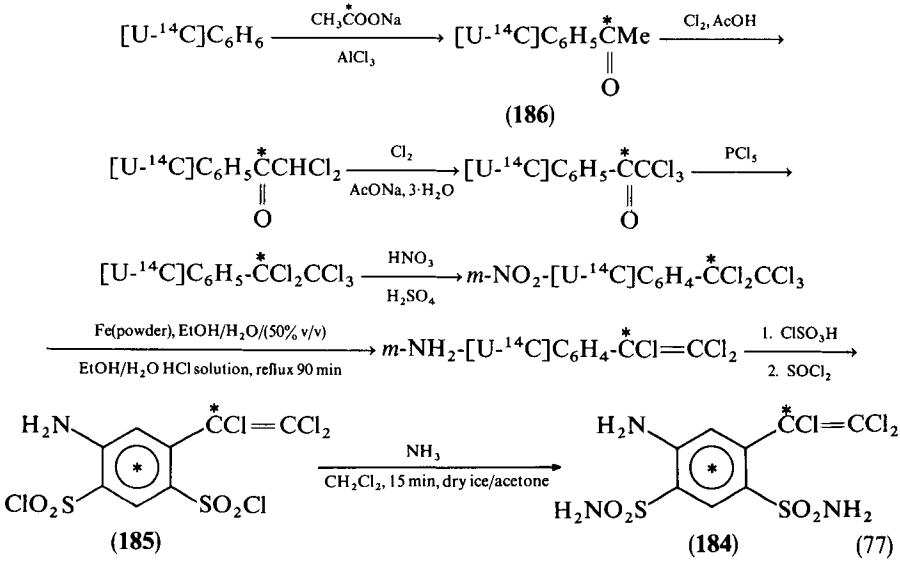


(181) (76)

(181a) 51.1% yield (for ^{35}S); specific activity 45.7 μCi mg^{-1}
(181b) 71.8% yield—total yield for ^{14}C; specific activity 47.6 μCi mg^{-1}

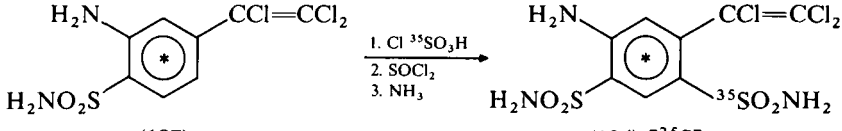
7. Synthesis of 4-amino-6-(trichloro[1-^{14}C]ethenyl)-1,3-[ring-U-^{14}C]benzenedi-[^{35}S]sulphonamide

[^{14}C]Clorsulon and [^{35}S]clorsulon (the drgus MK-0401, **184**, a new and potent fasciolide[178]), needed for residue and metabolism studies[179,180], have been synthesized in eight (equation 77) and three steps (equation 78), respectively[181].



(77)

The specific activity of 4-amino-6-trichloroethenyl-1,3-benzenedi[^{35}S]sulphonamide, **184**-[^{35}S], obtained in 49.1% yield based on the starting sulphonamide, was 28.8 mCi mmol^{-1}. The exchange between the sulphoamide group of the starting compound **187** with the $Cl^{35}SO_3H$ used is negligible and only one ^{35}S-enriched atom per molecule has been introduced into **184** in the course of the labelling procedures.



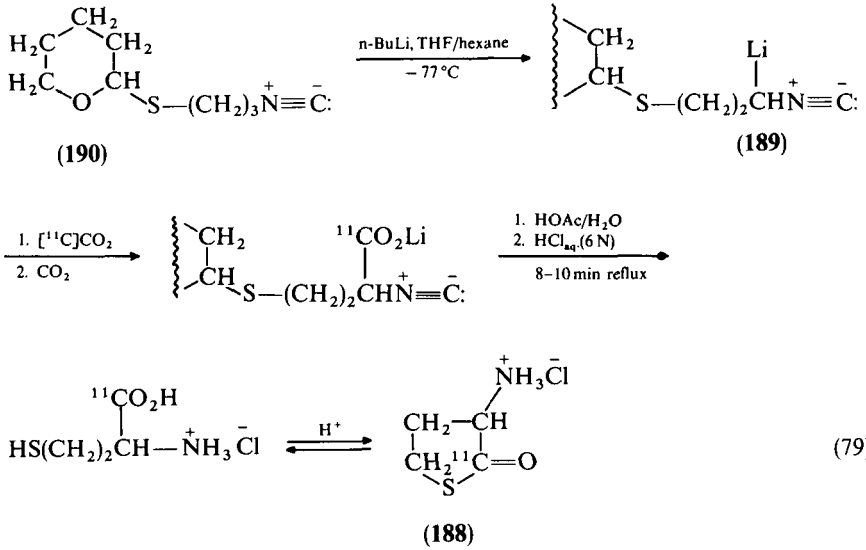
(**187**) (**184**)-[^{35}S] (78)

IV. SYNTHESIS OF PHARMACEUTICALS LABELLED WITH RADIOIMAGING AGENTS FOR *IN VIVO* SCANNING

A. Synthesis of Carbon-11 Labelled Compounds

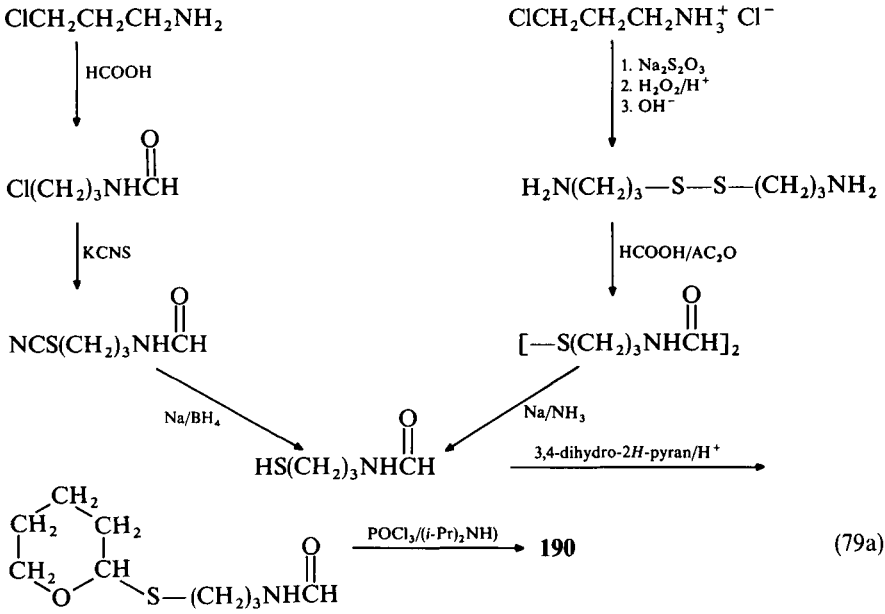
1. Synthesis of 1-[^{11}C]-D,L-homocysteine thiolactone

This compound, **188**, is a metabolic heart agent reacting with adenosine, which is increasingly produced in cardiac ischemia by dephosphorylation of adenine nucleotides and forming enzymatically *S*-adenosyl homocysteine (SAH)[182]. Thus, using ^{11}C-labelled homocysteine thiolactone, the local changes of free cardiac adenosine concentration have been determined in stenosed dog hearts[183–185]. The synthesis of **188** has been achieved[186] in 10–15% radiochemical yield by reaction of [^{11}C]CO_2 with α-lithiated *S*-(tetrahydropyran-2-yl)-3-thiopropylisonitrile **189** followed by deprotection of the mercapto group and lactonization of the resulting thioamino acid (equation 79).



(**188**) (79)

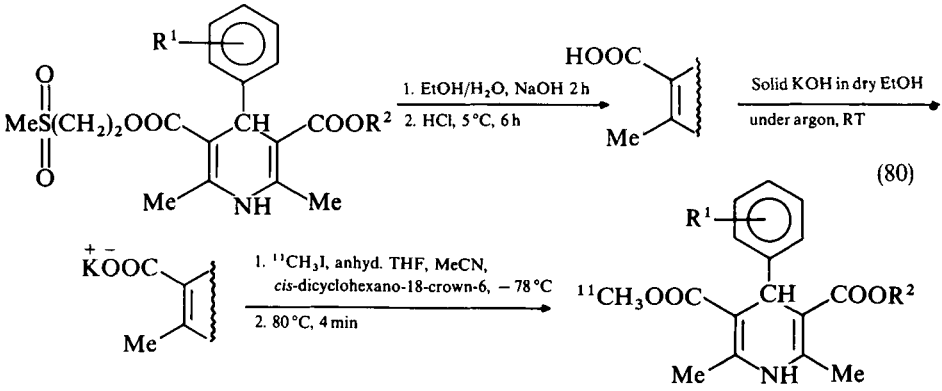
The precursor **190** has been prepared by two alternative pathways using in both 3-chloropropylamine as the starting material (equation 79a).



(79a)

2. Synthesis of carbon-11 calcium channel antagonists

Carbon-11 labelled 1,4-dihydropyridines[187,188] (^{11}C-nifedipine, ^{11}C-nisoldipine, ^{11}C-nitrendipine and ^{11}C-CF_3-nifedipine), **191–194** are calcium channel antagonists,



(80)

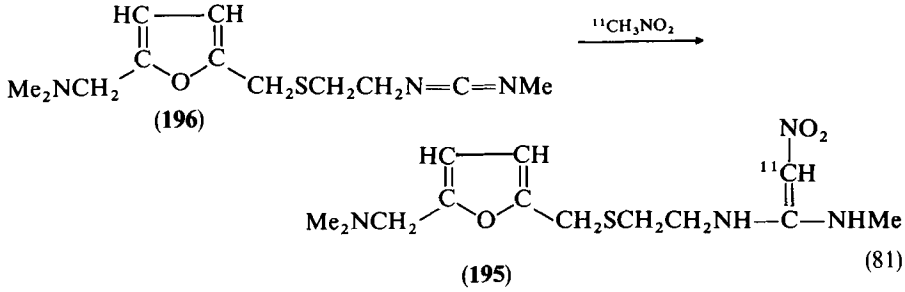
(**191**) $R^1 = o\text{-}NO_2$, $R^2 = Me$
(**192**) $R^1 = o\text{-}NO_2$, $R^2 = —CH_2CHMe_2$
(**193**) $R^1 = m\text{-}NO_2$, $R^2 = Et$
(**194**) $R^1 = o\text{-}CF_3$, $R^2 = Me$

specific activity 1.2×10^6 Ci mol^{-1}, radiochemical purity 99%

needed for the *in vivo* study of Ca^{2+} in smooth and cardiac muscle cells. They have been synthesized[189] by methylation with $^{11}CH_3I$ as shown in equation 80. ^{11}C was produced via the $^{14}N(p,\alpha)^{11}C$ nuclear reaction; the purity of $^{11}CH_3I$ was higher than 98% as checked by radio gas chromatography.

3. *Synthesis of [^{11}C]ranitidine*

Carbon-11 labelled ranitidine **195**, needed to visualize the H_2-receptors in the heart by PET, has been synthesized[190] by condensing [^{11}C]-nitromethane carbanion with the carbodiimide **196**[191] (equation 81). [^{11}C]nitromethane has been prepared[192] from [^{11}C]methyl iodide and sodium nitrite in DMF.

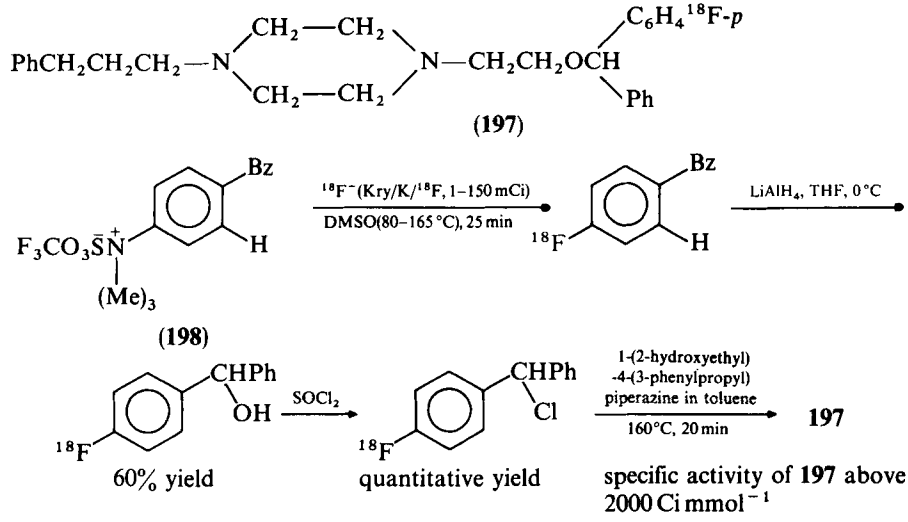


(81)

B. Synthesis of Fluorine-18 Labelled Compounds

1. *Improved synthesis of [^{18}F]GBR-13119*

This presynaptic dopamine uptake antagonist[193], 1-[2-{(4-[^{18}F]fluorophenyl) (phenyl)-methoxy}ethyl]-4-(3-phenylpropyl)piperazine, GBR-13119 (**197**), has been labelled with ^{18}F in the NCA form starting from 4-*N*,*N*,*N*-trimethylaniliniumphenylmethanone

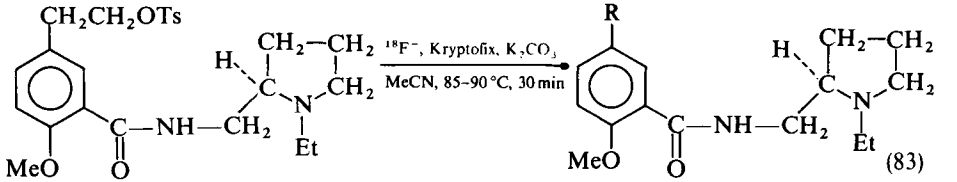


$Kry/K/^{18}F = Kryptofix\ 222/K_2CO_3/^{18}F^-$ (82)

trifluoromethanesulphonate **198** in > 98% radiochemical purity for human studies[194,195,196] (equation 82).

2. Radiosynthesis of (S)-N-[(1-ethyl-2-pyrrolidinyl)methyl]-5-(2[F-18]fluoroethyl)-2-methoxybenzamide

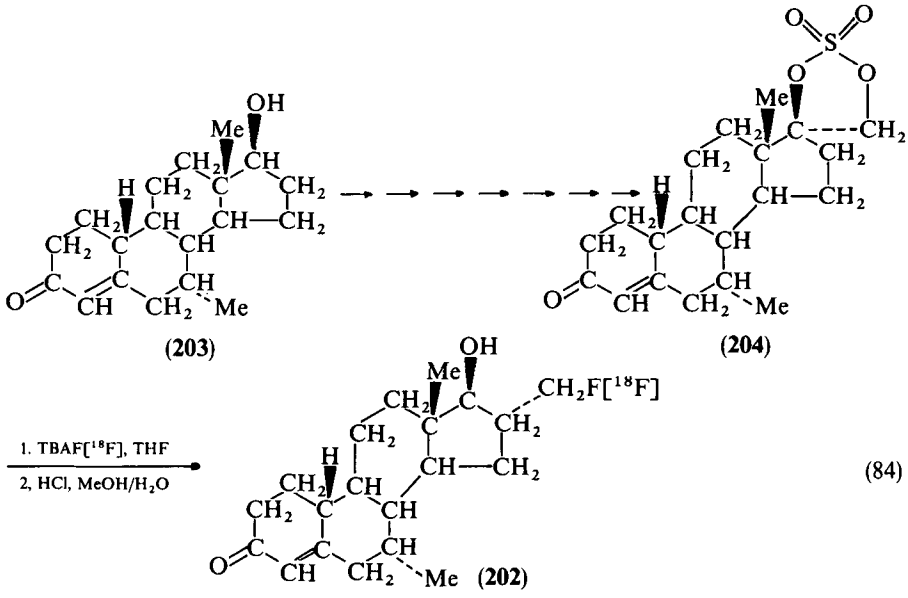
The title compound **199** is a new fluorine-18 labelled benzamide neuroleptic and potential PET radiotracer for dopamine D2 receptors in both primates and humans[197,198]. It has been obtained[199] in the reaction of ^{18}F-fluoride with the tosylate **200** in 10–25% yields (equation 83). The aminosulphonyl moiety of the clinically used antipsychotic sulpiride **201** has been replaced with fluoroalkyl group in order to avoid proximity of the fluorine atom to the pyrrolidine nitrogen and make this compound more lipophilic. Fluoroalkylation at the pyrrolidine nitrogen of raclopride, which is a substituted benzamide, lowers its affinity towards the D2 receptor and renders it incapable of being developed as a PET tracer[200].



(200) **(199)** R = $CH_2CH_2{}^{18}F$. **(201)** R = SO_2NH_2
specific activity 600–800 Ci mmol^{-1}

3. Synthesis of fluorine-18 labelled androgens

20-[^{18}F]fluoromibolerone **202**, needed for localization of prostatic tumors, has been synthesized[201] beginning with 7α-methyltestosteron **203** (equation 84). The radioactivity distribution of **202** (blood, bone muscle, spleen, lung, liver, fat, kidney, prostate) in rats

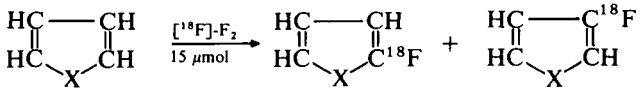


(203) **(204)** **(202)**

has been investigated also[201]. The prostate–muscle ratio was 12 at 4 h after the injection of a 100 μCi dose of **202** in 10% ethanol–saline to pretreated rats.

4. Synthesis of ^{18}F-labelled thiophene and N-methylpyrrole

2- and 3-[^{18}F]fluorothiophene and 2- and 3-[^{18}F]fluoro-*N*-methyl pyrrole have been synthesized[202] by the reaction of thiophene and *N*-methylpyrrole with molecular fluorine [^{18}F]-F_2 carried out in the dark at -63 °C in a 5×10^{-2} M solution in 2 ml of $CHCl_3$[203] (equation 85). The radionuclide used in synthesis was generated by the nuclear reaction ^{20}Ne(d,α)^{18}F with specific activity in the range 0.5–2.0 Ci mmol^{-1}.

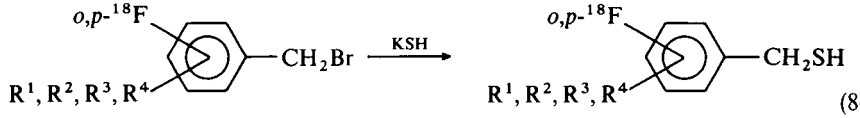


For X = N—Me	23% yield	+	73% + 4%	35 ± 3%
For X = S	53%		29% + 18%	11 ± 3%

(85)

5. Synthesis of aromatic [^{18}F]RSH compounds

Substituted [^{18}F]fluorobenzyl bromides were the key intermediates for NCA radiosynthesis of aromatic [^{18}F]RSH compounds[204], as shown in equation 86.

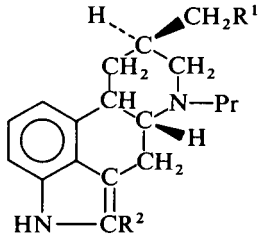


(86)

C. Synthesis of Compounds Radiolabelled with Iodine-125 and Selenium-75

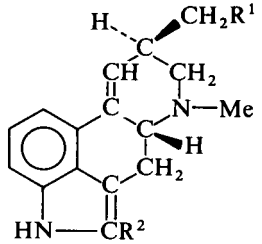
1. Synthesis of ergolines radiolabelled with ^{125}I and ^{75}Se

Several central nervous system diseases are associated with changes in the density of dopaminergic receptors[205–208]. A series of ergoline derivatives, analogues of pergolide



Pergolide (**205**)

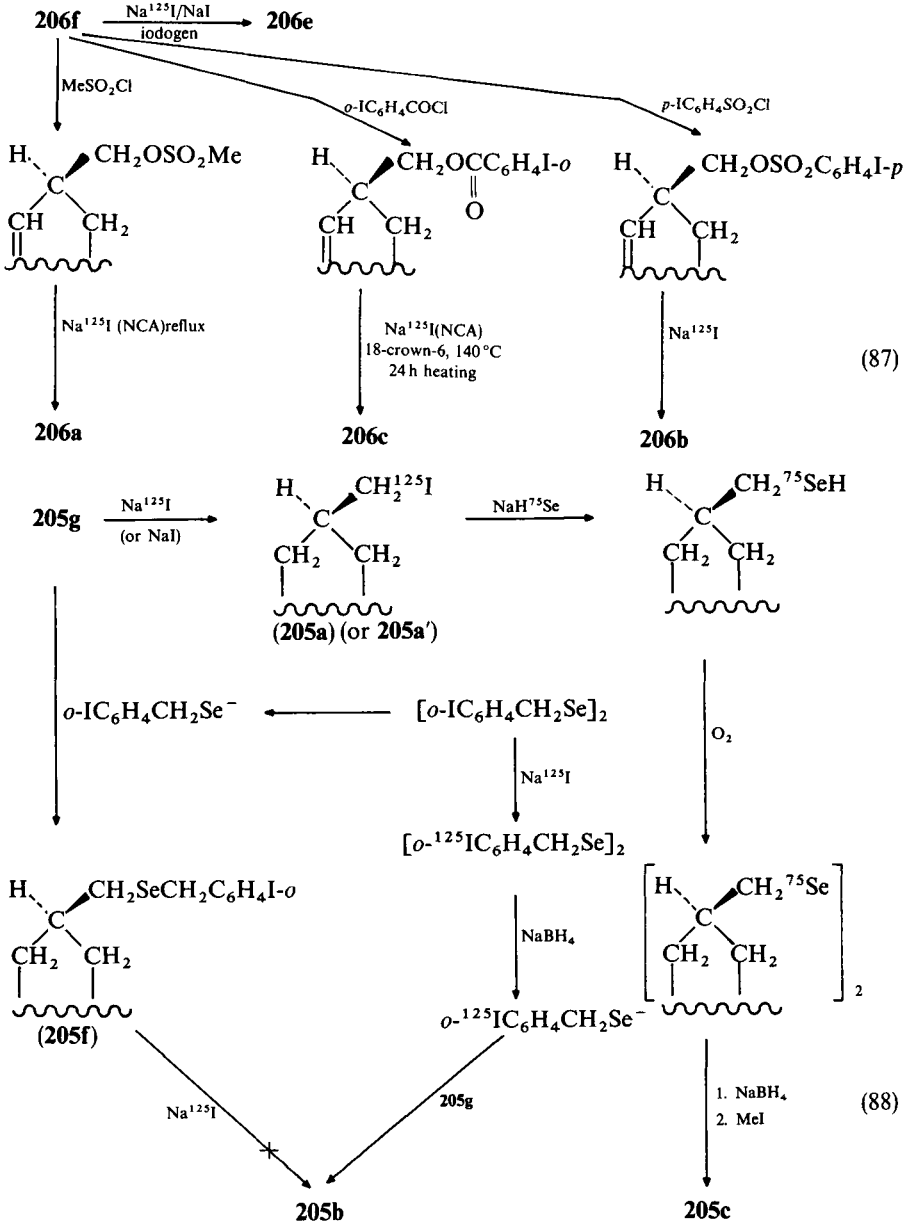
(a) $R^1 = {}^{125}I$; $R^2 = H$
(a') $R^1 = I$; $R^2 = H$
(b) $R^- = o$-^{125}I-iodobenzyl selenide; $R^2 = H$
(c) $R^1 = SMe$; $R^2 = {}^{125}I$
(d) $R^1 = OSO_2Me$; $R^2 = {}^{125}I$
(e) $R^1 = {}^{75}SeMe$; $R^2 = H$
(f) $R^1 = SMe$; $R^2 = H$
(g) $R^1 = OSO_2Me$; $R^2 = H$



Lysergol (**206**)

(a) $R^1 = {}^{125}I$; $R^2 = H$
(b) $R^1 = 4$-^{125}I-$C_6H_4SO_3$; $R^2 = H$
(c) $R^1 = 2$-^{125}I-$C_6H_4CO_2$; $R^2 = H$
(d) $R^1 = 4$-^{125}I-C_6H_4S; $R^2 = H$
(e) $R^1 = OH$; $R^2 = {}^{125}I$
(f) $R^1 = OH$; $R^2 = H$

205 and lysergol **206**, known to possess central dopaminergic receptor agonistic activity[208], have therefore been radiolabelled with ^{125}I or ^{75}Se either at the 17-position (attached to the 8β-methylene) or at the 2-position of the indole part of the ergoline moiety (as shown in equations 87 and 88) and evaluated for their ability to cross the BBB of rats for potential use as radiopharmaceuticals for imaging the brain[209].



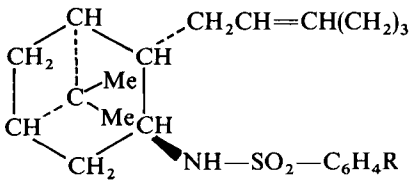
205a, **205a'**, **205b**, **205c** and **205f** have been prepared as shown schematically in equation 88. 8β-(Methyl[^{75}Se]seleno)-methyl-6-propylergoline **205e** has not been prepared by direct treatment of **205g** with methyl[^{75}Se]selenide in THF/EtOH as in the case of non-labelled **205e**, due to the volatility and danger of handling methylselenide-^{75}Se.

Extensive biodistribution studies have shown that pergolide **205e** and pergolide **205a** have the highest uptake in the brain, adrenal and heart with good organ-to-blood ratios.

A conclusion has been reached that analogues of pergolide labelled with ^{123}I (a superior imaging radionuclide, $T_{1/2} = 13.2$ h, $E_\gamma = 159$ keV [83.3%]) may yield a clinically useful brain imaging radiopharmaceutical[209].

2. Synthesis of [^{125}I]-I SAP

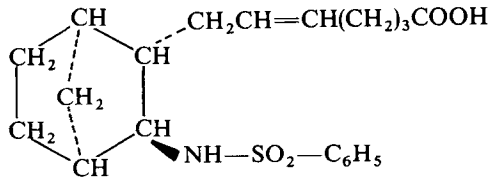
This compound, 7-[(2*R*, 2*S*, 3*S*, 5*R*)-6,6-dimethyl-3-(4-[^{125}I]-iodobenzenesulphonylamino)-bicyclo[3.1.1]hept-2-yl]-5(*Z*)-heptenoic acid, ^{125}I-SAP, **207**, is a high affinity thromboxane A_2 (TXA_2)/prostaglandin H_2 (PGH_2) receptor antagonist. It has been labelled[210] with ^{125}I($T_{1/2} = 60.14$ days, maximum specific activity 1.737×10^4 Ci g^{-1}) by electrophilic destannylation, which enables one to introduce the radiolabel in the last reaction step[211] under very mild conditions (equation 89). The bicyclic pinane nucleus has been chosen in preference to the norbornyl system [^{3}H]S-145 (**209**)[212,213] because the optically active



(207), ^{125}I-SAP, R = ^{125}I-*p*

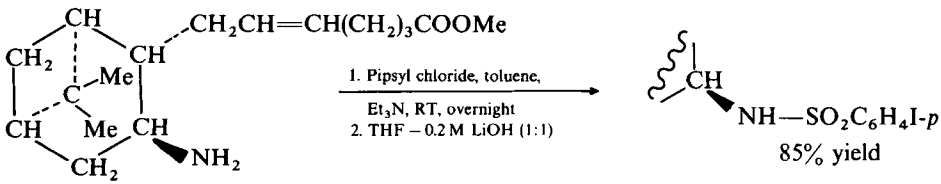
(208), R = 4-NH_2 or 3-NH_2

specific activity 2200 Ci mmol^{-1}



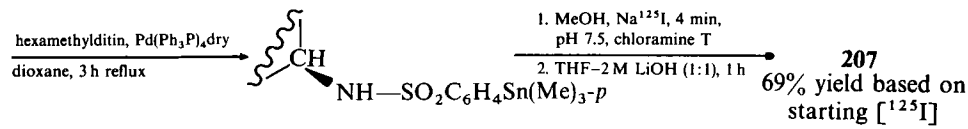
(209)

starting materials are readily available and result in enantiomerically pure analogues. It has been very difficult (very poor and highly variable yield) to substitute [^{125}I] for the amino group in **208** or to remove it by standard methods.



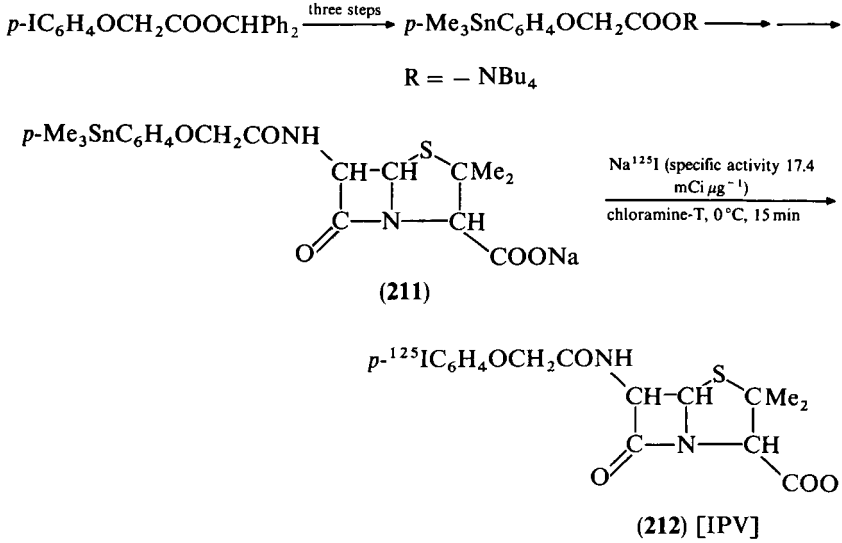
(210) (Reference 214)

(89)



3. Synthesis of p-[^{125}I]-penicillin V

High yield and site-specific radioiodination of *p*-(trimethylstannyl)penicillin V, **211**, with Na[^{125}I], using a modification of the chloramine T-method (equation 90), has been used[215] to synthesize the title compound IPV, **212**, an imaging agent with high specific activity, autoradiolytic stability and needing short radiographic exposure times for use in PBP (penicillin binding protein[216]) studies. At a specific activity of 37.5 Ci mmol^{-1} and a concentration of 28 μg ml^{-1} at 4 °C, the storage half-life of [^{125}I]IPV, as judged by microbiological analysis, is 21 days. 15–24 hours exposure time is required for autoradiography in a typical PBP experiment at this specific activity level. [^{125}I]IPV is a stable and useful reagent for rapid PBP assays, in place of [^{3}H]-penicillin G[217,218] or [^{14}C]-penicillin G[219,220]. The reaction has been terminated by adding an aqueous solution of sodium metabisulphite. The solution obtained has been stored at 4 °C and diluted as required for the PBP experiments.



(90)

The method of equation 90 can be applied to the synthesis of other labelled β-lactam antibiotics.

D. Synthesis of Compounds Labelled with Technetium-99m, Radioisotopes of Copper, Platinum-195m and Radioisotopes of Potential Use for *in vivo* Scanning

1. Synthesis of compounds radiolabelled with technetium-99m

a. Synthesis of tetraaminetrithiol (TEATT). TEATT has been prepared from tris(2-aminoethyl)amine as shown in equation 91 and used to synthesize a new technetium-99m labelled lipophilic brain and heart blood flow imaging agent[221]. Tc-99m labelling has been achieved in high yields by reducing ammonium pertechnetate with tin(II) chloride or tin(II) tartarate in the presence of TEATT or TATT (triaminetrithiol). The resulting complexes are highly lipophilic and have good *in vitro* stability.

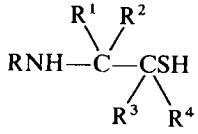
$$N(CH_2CH_2NH_2)_3 \xrightarrow[Et_3N]{PhCH_2SCMe_2COCl} N[CH_2CH_2NHC(=O)CMe_2SCH_2Ph]_3$$

$$\xrightarrow{BH_3,\,THF} N[CH_2CH_2NHCH_2CMe_2SCH_2Ph]_3 \xrightarrow{Na/liq.\,NH_3}$$

$$N[CH_2CH_2NHCH_2CMe_2SH]_3\ (TEATT) \qquad (91)$$

Oxidation of tin(II) to tin(IV) has occurred during the complexation process. Tin is coordinated to three nitrogen and three sulphur atoms in a distorted octahedral environment. Labelling for immunoscintigraphy of mercaptotriamides and dimercaptodiamides with technetium-99m has been accomplished[222].

b. Synthesis of technetium-99m complexes with di-ligand thiolamines. Complexes of technetium-99m with about 52 di-ligand thiolamines of the type **213** have been obtained and their biodistribution in mice and baboons studied[223]. Brain uptake has been found to be optimal when R = n-propyl. Brain uptake in mice was much lower when R = n-C_4H_9. Labelling with ^{99m}Tc has been carried out by reacting the aminothiol hydrochloride, with $SnCl_2$ and sodium [^{99m}Tc]pertechnetate (about 10 mCi of ^{99m}Tc] in saline.



(213)

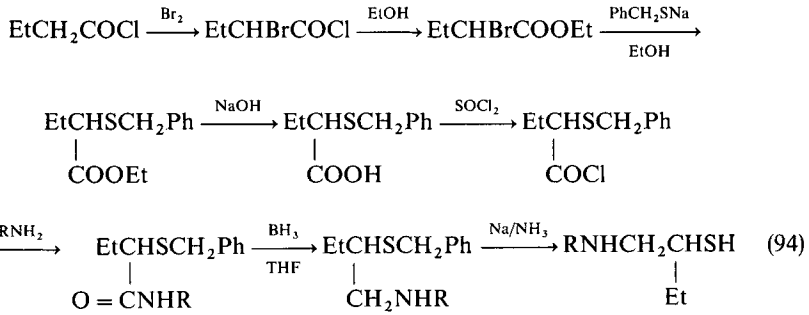
The thiolamines **213** have been synthesised by three methods illustrated by equations 92–94. ^1H, ^{31}P and ^{13}C NMR spectroscopy has been used to study the donor properties of the ligand donor atoms and the molecular conformations in In^{3+}, Ga^{3+}, Sn^{2+} and lanthanide complexes with various derivatives of mono- and polyaminoalkylacetic and phosphonic acids and aromatic iminodiacetic acids[224].

$$Me_2CHC(O)Me \xrightarrow{Br_2} Me_2CBrC(O)Me \xrightarrow[EtOH]{PhCH_2SNa}$$

$$Me_2C(Ac)CH_2Ph \xrightarrow[2.\ NaBH_4]{1.\ RNH_2} Me_2C(MeCHNHR)CH_2Ph \xrightarrow{Na/NH_3} RNHCHMeCMe_2SH \qquad (92)$$

$$Me_2CHCHO \xrightarrow{S_2Cl_2} Me_2C(CHO)—SS—CMe_2(CHO) \xrightarrow{RNH_2} Me_2C(RN{=}CH)—SS—CMe_2(HC{=}NR)$$

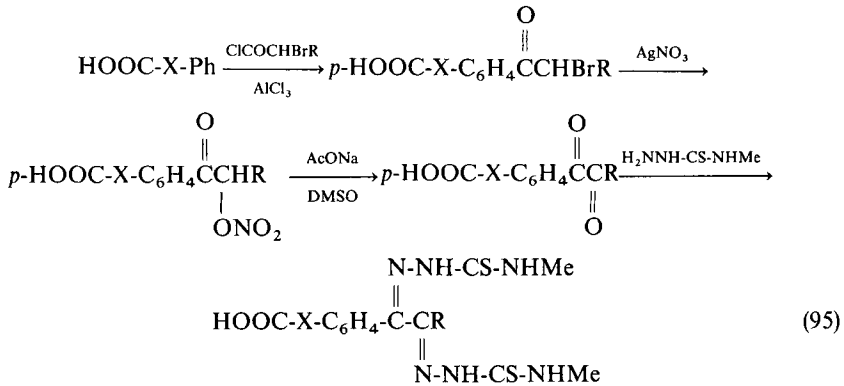
$$\xrightarrow{LiAlH_4} RNHCH_2CMe_2SH \qquad (93)$$



2. Radiolabelling of proteins with radioisotopes of copper using p-carboxyalkylphenylglyoxal bis-(4N-methylthiosemicarbazone) bifunctional chelates

Ga-68 ($T_{1/2}$ = 1.1 h, E_{β^+} = 1.89 MeV), Br-75 (1.6 h, 1.74 MeV), F-18(1.8 h, 0.64 MeV), Cu-61 (3.4 h, 1.20 MeV), Co-55 (17.5 h, 1.51 MeV), As-72 (26 h, 7.5 MeV), Zr-89 (78.4 h, 0.89 MeV) and Cu-64 ($T_{1/2}$ = 12.7 h, E_{β^+} = 0.65 MeV) (the last one produced in $^{63}Cu(n,\gamma)^{64}Cu$ and $^{64}Zn(n,p)^{64}Cu$ nuclear reactions) are potential positron-emitting radionuclides for protein radiolabelling. The single-photon emitting radionuclides such as technetium-99m, iodine-131 and iodine-132 attached directly to an amino acid residue of the protein are often easily detached from the antibody. In the case of radioisotopes of copper and indium, this simple method cannot be used and bifunctional chelate techniques are required for complexation of the radioisotope to the antibody.

Copper-64 has been found of use for labelling of tumor-specific antibodies for imaging by PET, since its relatively long physical half-life is compatible with the usual prolonged



(214)

X = CH_2; R = H
X = $(CH_2)_2$; R = Me
X = $(CH_2)_9$; R = Me
X = benzyl; R = Me

(Out of 52 compounds prepared the above four have been selected as examples).

period between administration and imaging (24 to 48 h) required to allow vascular clearance and tumor-specific uptake. Specific activities of 2 Ci mg^{-1} of Cu-64 are reached in 2.5×10^{15} n cm^{-2} s^{-1} thermal neutron flux. Copper-67 emitting, β-particles, $\langle\beta^{-1}\rangle = 142$ keV, $E_{max} = 0.576$ MeV, can be employed for the treatment of cancer[225,226,226a].

Numerous bis-(TSC) bifunctional ligands **214** have therefore been prepared[226] and evaluated for use in binding radioisotopes of copper to antibodies. They have been synthetized as shown in equation 95, avoiding the use of the highly toxic selenium dioxide for oxidation of the substituted acetophenones to 1,2-dicarbonyl compounds. The effects of the alkyl chain length 'X' and substitution R on the $C_{(2)}$ position for attaching radioisotopes of copper to proteins have been also studied[226]. After complexing ^{64}Cu or ^{67}Cu to the bis-TSC chelate, the acid moiety of the TSC chelate has been activated as the tetrafluorophenyl ester and this activated chelate has been attached to bovine serum albumin (equation 96).

$$\text{bis-thiosemicarbazone} \xrightarrow{\text{Cu(II)chloride}} \text{Copper–TSC complex} \xrightarrow{\text{tetrafluorophenol}} \text{Activated copper–TSC complex} \xrightarrow{\text{protein}} \text{Copper–TSC labelled protein} \tag{96}$$

3. Synthesis of ^{195m}Pt-labelled cis-diammine(1,1-cyclobutanedicarboxylate) platinum(II)

This second-generation anti-tumor drug (CBDCA), **215**, possesses a potency against ovarian cancers, similar to *cis*-diamminedichloroplatinum(II), but has greatly reduced emetic effect and virtually no nephrotoxicity at therapeutic doses. It has been ^{195m}Pt labelled by the new method outlined in equation 97 and used to investigate the formation of metabolic products in the plasma and their presence in the urine of rats[227]. Ag_2CBDCA has been prepared from 1,1-cyclobutanedicarboxylic acid with NaOH (pH 6.8) and then with $AgNO_3$. ^{195m}Pt ($T_{1/2} = 4.02$ days) has been produced in the ^{194}Pt(n, γ)^{195m}Pt nuclear reaction by irradiating ^{194}Pt (enriched to 95.06%) with neutrons for up to 96 hours at a flux of 2.0×10^{14} n s^{-1} cm^{-2}.

$$\overset{*}{K_2Pt}Cl_6 \xrightarrow[3\text{ h RT, } K_2CO_3\text{, RT}]{NH_2NH_2\cdot 2HCl \text{ at } -1\,^\circ C,\ 30\text{ min}} K_2\overset{*}{P}tCl_4 \xrightarrow{KI,\ 30\text{ min, RT}} K_2\overset{*}{P}tI_4 \xrightarrow[1\text{ h, RT}]{\text{conc. } NH_3}$$

$$cis\text{-}\overset{*}{P}t(NH_3)_2I_2 \xrightarrow[2\text{–}3\text{ h, RT in dark}]{0.95\text{ eq. mol. } Ag_2CBDCA} cis\text{-}\overset{*}{P}t(NH_3)_2(CBDCA) \tag{97}$$

(215)

48% overall yield

4. Synthesis of new radioisotopes of potential use for in vivo scanning

Some biologically essential elements, such as sulphur and phosphorus have no radioisotopes convenient for *in vivo* scanning. The isotopes ^{73}Se ($T_{1/2} = 7.1$ h, $E_{\beta^+} = 1.30$ MeV), ^{72}Se ($T_{1/2} = 8.5$ days, K, no β^+) and ^{72}As ($T_{1/2} = 26$ h, $E_{\beta^+} = 2.50$ MeV, 3.34 MeV) therefore drew the attention of radiochemists[228]. The nuclear reactions ^{79}Br(p, $\alpha \times$ n)^{72,73}Se and ^{75}As(p, xn)^{72,73}Se have been found useful when medium-energy protons (70 MeV) are available. Cu_3As_2 and KBr have been used as target materials. 100 mCi amounts of both nuclides have been achieved easily.

Iodine-124, a positron-emitting radionuclide (K, $E_{\beta^+} = 2.14\,\text{MeV}$, $1.53\,\text{MeV}$, $0.79\,\text{MeV}$), could be potentially useful for PET installations, which are far from an isotope production facility due to its relatively long (4.2 days) half-life. The ^{124}Te (d, 2n)^{124}I reaction using 91.7% enriched ^{124}Te target has been employed, but the production of ^{124}Te becomes cost-effective only if the ^{124}Te enriched target material can be recycled[229].

Positron-emitting 75 s $^{82}_{37}$Rb ($E_{\beta^+} = 3.15\,\text{MeV}$, $T_{1/2} = 1.2732\,\text{min}$) has recently found widespread interest in nuclear cardiology. The production of its parent nuclide 25.5 day ^{82}Sr (K-capture, no β^+) has therefore been elaborated[230,231]. RbCl target pellets ($2.75\,\text{g cm}^{-2}$) sealed into Al capsules have been bombarded with a 72-MeV cyclotron proton beam. The dissolved salt is isolated by column separation. Almost theoretical[232] yields have been reached in small test irradiations[233], ^{85}Rb(p, 4n)^{82}Sr.

Injector (II) cyclotron has also been used[234] for production of iodine-123 ($^{123}_{53}$I, $T_{1/2} = 13.2\,\text{h}$) and other longer-lived radioisotopes using high-current 72-MeV protons.

The yield of large-scale production of ^{75}Br ($E_{\beta^+} = 3.6\,\text{MeV}$, $3.1\,\text{MeV}$, $T_{1/2} = 1.7\,\text{h}$) has been improved[235] by irradiating with ^{3}He particles, not the target used in routine production[236,236a] but an As–Cu target containing 90% As.

V. GENERAL RADIOCHEMICAL, CHEMICAL AND PHYSICAL APPLICATIONS OF ISOTOPES

A. Radiochemical Applications

1. Chemical effects of the decay of sulphur-35 incorporated into butylthiol molecules

Previous studies[237–240] of the β^--disintegration of sulphur-35 in $^{14}C_2H_5{}^{35}SH$ and $^{14}C_2H_5{}^{35}SEt$ molecules have shown that more than 50% of the chlorine produced in the nuclear β-decay $^{35}S \xrightarrow{\beta^-} Cl$, is stabilized in the form of EtCl (equation 98). This

$$\left.\begin{array}{l} ^{14}C_2H_5{}^{35}SH \xrightarrow{\beta^-} [^{14}C_2H_5ClH]^+ \\ ^{14}C_2H_5{}^{35}SC_2H_5 \xrightarrow{\beta^-} [^{14}C_2H_5Cl\text{-}C_2H_5]^+ \end{array}\right\} \longrightarrow {}^{14}C_2H_5Cl \qquad (98)$$

means that the degree of excitation of molecular ions is insufficient for their fragmentation. The radiochemical investigation of the β^- disintegration of ^{35}S incorporated into molecules of primary and secondary butanethiols has been undertaken[241] to reveal how the stabilization of primary ions depends on the molecular structure. The butanethiols doubly labelled with both ^{35}S and ^{14}C, needed for analytical determination of products, have been synthesized[242,249] (equation 99). The final products C_4H_9SH-1(1,2-$^{14}C_2$) (1-mercapto[^{35}S]) and C_4H_9SH-2(1,2-$^{14}C_2$) (2-mercapto[^{35}S]) have been isolated by preparative gas chromatography[244]. The gas-phase decomposition of pure butanethiols or the same mixed with water vapour took place at 0.5 torr or 1 torr, respectively, in the dark at room temperature for 340–380 days, which were needed to obtain a required preset number of ^{35}S decays. The stable products formed, $^{14}C_4H_9Cl$-1 and $^{14}C_4H_9Cl$-2,

$$\left.\begin{array}{r} Ba^{14}CO_3 \longrightarrow Ba^{14}C_2 \longrightarrow {}^{14}C_2H_2 \longrightarrow {}^{14}C_2H_4 \longrightarrow {}^{14}C_4H_8 \\ ^{35}S \longrightarrow H_2{}^{35}S \end{array}\right\} \longrightarrow \left\{\begin{array}{l} ^{14}C_4H_9{}^{35}SH\text{-}1 \\ ^{14}C_4H_9{}^{35}SH\text{-}2 \end{array}\right. \qquad (99)$$

diluted with inactive butyl chloride, have been separated by gas chromatography and their radioactivity determined. The results have indicated that about 60% of the primary molecular ions are stabilized in the form of butyl chlorides. In the presence of water vapour the yield of butyl chlorides increased to about 90%. The structure of the butyl radical had no significant influence on the yields of butyl chlorides, $64.2 \pm 2.2\%$ and $63.2 \pm 2.3\%$ for n- and *s*-BuCl, respectively. The results have been interpreted[241] according to equations 100a and 100b, leading to BuCl-1 and BuCl-2 formation.

$$^{14}C_2H_5CH_2CH_2{}^{35}SH \xrightarrow{\beta^-} [^{14}C_2H_5CH_2CH_2ClH]^+$$

(216)

$$^{14}C_2H_5CHCH_3 \xrightarrow{\beta^-} \left[{}^{14}C_2H_5\underset{\displaystyle ClH}{\underset{|}{C}}HCH_3\right]^+ \qquad (100a)$$

$$\quad\;\; {}^{35}SH$$

(217)

The fate of the primary ions **216** and **217** depends on the degree of excitation at the time of their formation and the chemical and physical properties of the medium. The decomposition paths of primary **216** can be visualised as given in equation 100b. The

$$CH_3CH_2CH_2CH_2\overset{+}{C}lH \xrightarrow{a} [C_4H_9ClH]^+ \qquad (100b)$$

$$\xrightarrow{b} [C_4H_9Cl]^+ + H$$

$$\xrightarrow{c} C_4H_9Cl + H^+$$

$$\xrightarrow{d} C_4H_9^+ + HCl$$

$$\xrightarrow{e} C_4H_9^{\cdot} + [HCl]^+$$

$$\xrightarrow{f} \text{more than two fragments}$$

yields ($\approx 64\%$) of radioactive n-BuCl and *sec*-BuCl products indicate that the excitation of ions **216** and **217** is not sufficient to cause extensive destruction of these species (pathways e and d), which are stabilized in the form of butyl chlorides in encounters with vessel walls (equation 100c), or in gas-phase encounters with non-radioactive butanethiol carrier molecules (equation 100d). The increase in the yield of [^{14}C]butyl chlorides in the presence of water vapour is due to secondary ion–molecule charge transfer reaction (equation 100e). The maximum recoil energy of ^{35}Cl, E_0^{max}, equals

$$[^{14}C_4H_9ClH]^+ + M^- \longrightarrow {}^{14}C_4H_9ClHM \longrightarrow {}^{14}C_4H_9Cl + MH$$
$$[^{14}C_4H_9Cl]^+ + M^- \longrightarrow {}^{14}C_4H_9ClM \longrightarrow {}^{14}C_4H_9Cl + M \qquad (100c)$$

$$[^{14}C_4H_9ClH]^+ + C_4H_9SH \longrightarrow {}^{14}C_4H_9Cl + [C_4H_9SH_2]^+ \qquad (100d)$$

$$[^{14}C_4H_9ClH]^+ + H_2O \longrightarrow {}^{14}C_4H_9Cl + H_3O^+ \qquad (100e)$$

3.26 eV. Part of this energy, $E_d = E_0^{max}R/(M + R)$, where M is the mass of the recoil atom and R is the mass of the rest of the molecule, is 2.03 eV in the case of butyl chlorohydride. This value is lower than the bond energies $E_{(C-Cl)} = 2.63$ eV and $E_{(H-Cl)} = 4.41$ eV of the bonds to be split, but the sudden change in the charge of the nucleus ^{35}S from +16 to charge +17 of the newly formed nucleus ^{35}Cl is a second source of the electronic excitation of primary **216** and **217** ions, being of the order of 70 eV for the $^{35}S \xrightarrow{\beta^-} Cl$ transformation, resulting in the observed yield of butyl chlorides. The formation of ^{14}C-labelled butyl chlorides in the secondary reactions of hot Cl atoms with radioactive molecules of the medium is improbable because of the large (100-fold) excess of non-radioactive carrier.

2. Chemical effects of the decay of sulphur-35 incorporated into hexylthiol molecules

Under experimental conditions similar to those described in Section V.A.1, the chemical effects of the β-decay of ^{35}S, incorporated into primary and secondary n-hexanethiol, already labelled with ^{14}C, have been studied[245]. The doubly labelled hexanethiols **218** and **219** have been prepared[246,247] from hexene-1 and $H_2{}^{35}S$ as shown in equation 101. The hexanethiol isotopomers **218** and **219** have been separated and

$$Ba^{14}CO_3 \longrightarrow Ba^{14}C_2 \longrightarrow {}^{14}C_2H_4 \xrightarrow{Al(C_2H_5)_3}$$

$$Et\overset{*}{C}H_2\overset{*}{C}H_2\overset{*}{C}H{=}\overset{*}{C}H_2 \xrightarrow{H_2{}^{35}S} Et\overset{*}{C}H_2\overset{*}{C}H_2\overset{*}{C}H_2\overset{*}{C}H_2{}^{35}SH + Et\overset{*}{C}H_2\overset{*}{C}H_2\underset{{}^{35}SH}{\overset{*}{C}H}\overset{*}{C}H_3 \qquad (101)$$

(218) **(219)**

purified by preparative GLC. The final products of the transmutation studies, i.e. $*C_6H_{13}Cl$-1 and $*C_6H_{13}Cl$-2, have also been isolated by GLC and their radioactivity determined by a ratiometric method. About 60% of the primary molecular ions were stabilized in the form of hexyl chlorides. In the presence of water vapour the yield of hexyl chlorides increased to about 90%. Hexyl hydrochlorides **220** and **221** are the primary molecular ions formed in the transmutation of $[^{95}S]$hexanethiol molecules (equation 102). The excited molecular ions **220** and **221** can decompose into $[*C_6H_{13}Cl]^+ + H$, $*C_6H_{13}Cl + H^+$, $[C_6H_{13}]^+ + HCl$, $*C_6H_{13}^{\cdot} + [HCl]^+$ or undergo decompositions into more than two fragments. The results of radioactivity determinations indicate that $63.9 \pm 2.9\%$ and $61.4 \pm 2.3\%$ respectively of β-decays do not lead to a high enough excitation of **220** and **221** to cause their destruction. These are neutralized on

$$n\text{-}\overset{*}{C}_6H_{15}{}^{35}SH \xrightarrow{\beta^-} [n\text{-}\overset{*}{C}_6H_{13}{}^{35}ClH]^+$$

(220)

$$\overset{*}{C}_4H_9\underset{{}^{35}SH}{\overset{*}{C}H}\overset{*}{C}H_3 \xrightarrow{\beta^-} \left[\overset{*}{C}_4H_9\underset{{}^{35}ClH}{\overset{*}{C}H}\overset{*}{C}H_3\right]^+ \qquad (102)$$

(221)

the vessel walls (equation 103) or transfer a proton in an encounter with non-radioactive hexanethiol molecules (equation 104). Interactions of $[^{*}C_6H_{13}Cl]^+$ cations with $C_6H_{13}SH$ molecules or with the wall also yield stable ^{14}C-labelled hexyl chlorides.

$$[\text{n-}\overset{*}{C}_6H_{13}ClH]^+ + M^- \longrightarrow \overset{*}{C}_6H_{13}ClHM \longrightarrow \overset{*}{C}_6H_{13}Cl + MH \tag{103}$$

$$[\overset{*}{C}_6H_{13}ClH]^+ + C_6H_{13}SH \longrightarrow \overset{*}{C}_6H_{13}Cl + [C_6H_{13}SH_2]^+ \tag{104}$$

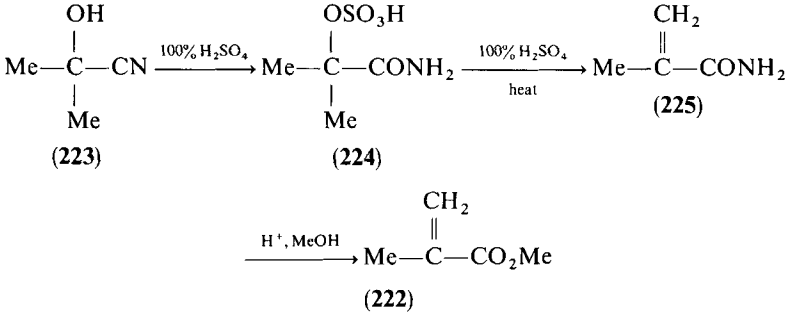
$$[\overset{*}{C}_6H_{13}ClH]^+ + H_2O \longrightarrow \overset{*}{C}_6H_{13}Cl + H_3O^+ \tag{105}$$

The increase in the yield of ^{14}C-labelled hexyl chlorides to $92.2 \pm 2.9\%$ and $90.8 \pm 2.4\%$ for $^{*}C_6H_{13}Cl$-1 and $^{*}C_6H_{13}Cl$-2 respectively is caused by an energetically favourable secondary reaction of water molecules with $[^{*}C_6H_{13}ClH]^+$ (equation 105). Water is an effective scavenger of protonated organic chlorides. The structure of hexanethiols has no substantial influence on the yield of hexyl chlorides. Increase in the carbon chain length from EtSH to BuSH caused the increase in the yield of the corresponding chlorides from 47% to 60%, but further increase in the chain to C_6 did not result in a similar increase in the yield, i.e. a plateau has been reached.

B. Chemical Applications

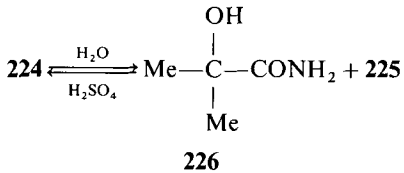
1. Deuterium isotope effect study of the mechanism of the formation of [$^2H_5$]methacrylamide from [$^2H_6$]2-methyl-2-sulphatopropionamide

The industrial production of methyl methacrylate **222**, proceeding according to equation 106, involves very fast conversion of 2-hydroxy-2-methylpropionitrile **223** in



(106)

100% sulphuric acid to **224** followed by slower elimination of sulphuric acid to give **225** and subsequent acid-catalysed methanolysis to produce the product **222**. By carrying out reaction 106 at low temperature (3 °C), pure crystalline samples of **225** and **226**



(107)

(equation 107) could be isolated[248]. The kinetics and the mechanism of H_2SO_4 elimination from **224** in 90–102% H_2SO_4 has been studied by multinuclear (^1H, ^2H, ^{13}C and ^{15}N) NMR. **226**-[$^2H_6$] and **224**-[$^2H_6$] have been synthesized as shown in equations 108a and 108b.

$$(CD_3)_2C{=}O \xrightarrow[-10\,^\circ C\,(base)]{HCN\,(0.2\,mol)} D_3C{-}\underset{\displaystyle CD_3}{\overset{\displaystyle OH}{\underset{|}{\overset{|}{C}}}}{-}CN \xrightarrow[2.\ Neutralization\ with\ CaO]{1.\ 98\%\ H_2SO_4,\ 5\,^\circ C,\ vigourous\ stirring}$$

(0.17 mol)

(223)

$$(CD_3)_2{-}\underset{\displaystyle CONH_2}{\overset{\displaystyle OH}{\underset{|}{\overset{|}{C}}}} \qquad 53\%\ yield \qquad (108a)$$

(226)-[$^2H_6$]

$$CD_3{-}\underset{\displaystyle CD_3}{\overset{\displaystyle OH}{\underset{|}{\overset{|}{C}}}}{-}CN \xrightarrow[5\,^\circ C,\ under\ N_2]{100\%\ H_2SO_4\ in\ MeNO_2} CD_3{-}\underset{\displaystyle CD_3}{\overset{\displaystyle OSO_3H}{\underset{|}{\overset{|}{C}}}}{-}CONH_2 \qquad (108b)$$

(224)-[$^2H_6$] 60% yield

Pseudo-first-order rate constants for the formation of **225** calculated from experiments carried out using a constant concentration of acid and constant initial substrate concentration (2.7% w/w) are presented in Table 2. These data give $E_{(Arrh)} = 118 \pm 10\,kJ\,mol^{-1}$ and $\Delta S^{\#} = 9 \pm 10\,J\,mol^{-1}\,K^{-1}$ in 98.5% H_2SO_4 and $E_{(Arrh)} = 109 \pm 10\,kJ\,mol^{-1}$ and $\Delta S^{\#} = -2 \pm 10\,J\,mol^{-1}\,K^{-1}$ in 100% H_2SO_4.

Deuterium kinetic isotope effects for the elimination carried out at 90 °C using a 5% solution of **226** or a 5% solution of hexadeuteriated **226** in various acid strengths, presented in Table 3, are consistent with a rate-determining C—H/C—D bond cleavage. No convincing correlation between k_H/k_D values and acid concentration in the 95–103% range has been found.

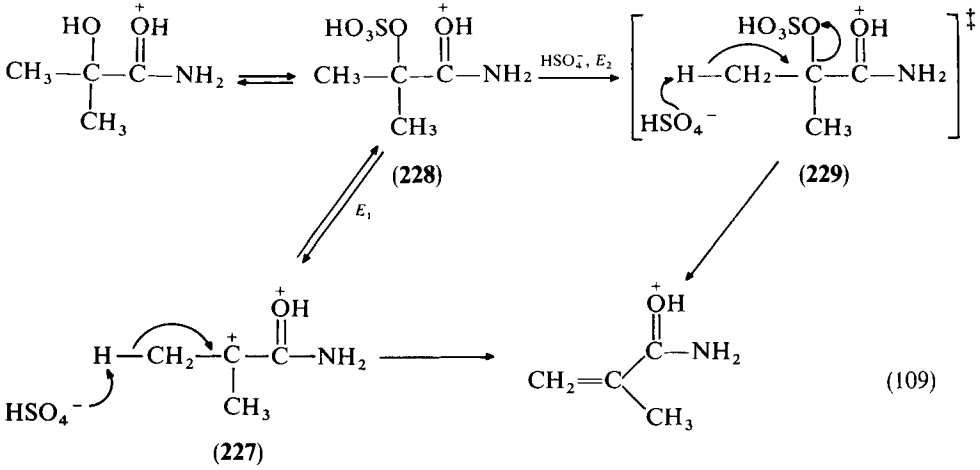
TABLE 2. Kinetic data for the formation of **225** at different temperatures and two acid strengths

	$k \times 10^4\,(s^{-1})$	
T(K)	98.5% H_2SO_4	100% H_2SO_4
343.0	0.82	1.5
348.0	1.62	2.3
353.0	2.33	5.0
358.0	4.33	7.0
363.0	8.67	14.6

TABLE 3. Kinetic deuterium isotope effects in the elimination leading to **223** at 90 °C for different sulphuric acid concentrations

% H_2SO_4	$k_H \times 10^4$ (s^{-1})	$k_D \times 10^4$ (s^{-1})	k_H/k_D
103	24.3	5.37	4.5 ± 0.1
100	13.1	2.54	5.2 ± 0.2
98	3.92	0.78	5.0 ± 0.1
95	1.48	0.35	4.2 ± 0.2

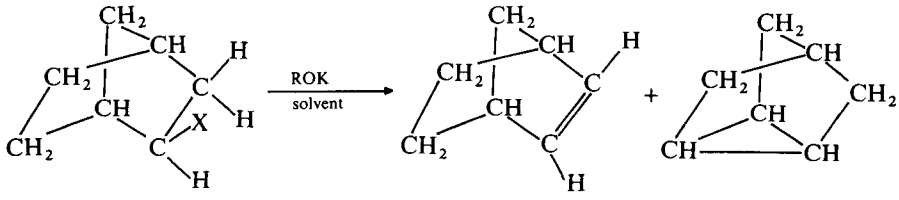
Additional studies concerning the dependence of k_{obs} for formation of **225** on the concentration of sulphuric acid employed and the corresponding plots of $\log k_{obs}$ vs acidity (H_0) for the elimination at 85 °C indicated[249-254] that only one monoprotonated form of **224** is reactive. The accumulated kinetic data resulted in the conclusion that the elimination is an E2 process occurring from the protonated substrate and involving the hydrogen sulphate anion as a base abstracting a methyl proton in the rate-determining step (equation 109). The earlier experiments[255] with ^{18}O-labelled **224** showed no loss of ^{18}O to the solvent. This eliminates the possibility of a pre-equilibrium step involving a doubly-charged intermediate **227** in the rate-determining step. The more likely E2 reaction path in which **228** reacts with a hydrogen sulphate anion in a concerted manner, as indicated in structure **229** (abstraction of the proton by the base proceeds synchronously with the formation of the double bond), should be corroborated by heavy atom (^{14}C, ^{18}O) kinetic isotope effect studies of this commercially important reaction[256].



(109)

2. Deuterium isotope effect in the base-promoted eliminations from exo-3-deuterio-exo-2-bicyclo[2.2.1]heptyl tosylate and chloride

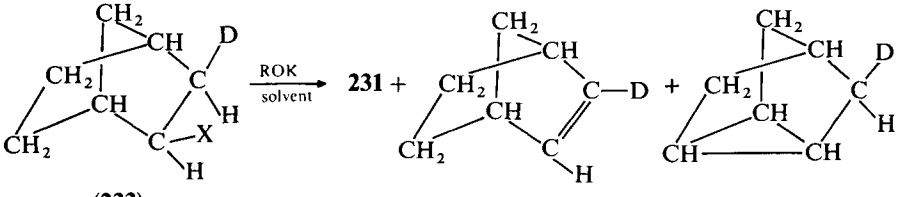
Exo-2-bicyclo[2.2.1]heptyl tosylate **230** reacting with potassium alkoxide bases in the presence of equimolar 18-crown-6 at 60 °C in triglyme yields two hydrocarbon products[257], bicyclo[2.2.1]hept-2-ene (**231**) and notricyclene (**232**) (equation 110). The relative proportion of **232** to **231** is very low (e.g. 0.21 to 99.79% with isopropoxide) but the amounts of **232** are precisely determined by GC and used for determination of $k_H/k_D \approx 2.2$ for *syn-exo* elimination.



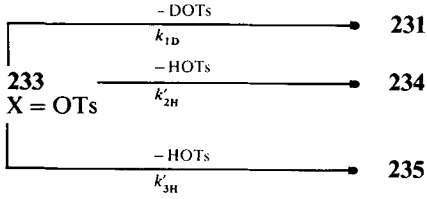
(230) (231) (232)

X = OTs or Cl (110)

Bimolecular *syn–exo* elimination from *exo*-3-deuterio-*exo*-2-bicyclo[2.2.1]heptyl tosylate **233** produces **231** and *anti-endo*-H elimination yields 2-deuterio-bicyclo[2.2.1]-hept-2-ene (**234**). The relative yields of *exo*-3-deuterionortricyclene **235** are approximately twice those for the eliminations from the non-deuteriated tosylate **230** (equations 111 and 111a).



(233) (234) (235) (111)

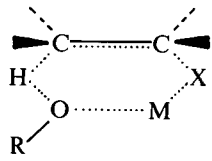


(111a)

The relative proportions of the hydrocarbon products using isopropoxide as a base are 86.03% (**231**), 13.51% (**234**) and 0.46% (**235**). k_H/k_D for *syn–exo* elimination were calculated from these values by using equation 112 derived by neglecting secondary deuterium isotope effects and assuming that all of the 1,2-elimination products result from *syn–exo* elimination. They are 2.2 with isopropoxide at 60 °C, 1.8 with *t*-butoxide at 60 °C in the presence of 18-crown-6 but 2.1 at 80 °C in the absence of 18-crown-6. These k_H/k_D values have been utilized to calculate a corrected percentage of *syn–exo* elimination (93.3%) and of (*syn–exo*)/(*anti–endo-H*) ratios (13.9 for the isopropoxide experiment). The larger amount of *exo*-3-deuterionortricyclene **235** from deuteriated tosylate **233** is due to retardation of the *syn–exo* bimolecular elimination process by a primary deuterium isotope effect.

The transition state **236** for *syn* elimination is stabilized by interaction with a metal

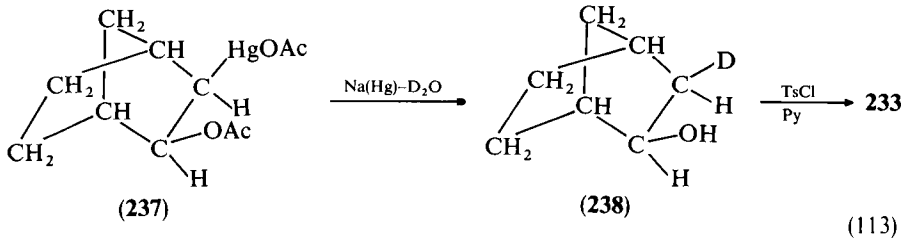
$$\frac{k_{1(H)}}{k_{1(D)}} = \frac{\%(\mathbf{235})\text{ from }\mathbf{233}}{\%(\mathbf{232})\text{ from }\mathbf{230}} \times \frac{\%(\mathbf{231})\text{ from }\mathbf{230}}{\%(\mathbf{231}+\mathbf{234})\text{ from }\mathbf{233}} \qquad (112)$$



(236)

M···OR associated pair. In the presence of 18-crown-6 ether this base association is disrupted and hence the relative proportion of *anti-endo-H* elimination product **234** is higher. The k_H/k_D value for the reaction of **233** with *t*-BuOK in triglyme in the absence of crown ethers has been determined by Kwart and coworkers[258].

The stereospecifically deuteriated tosylate **233** has been prepared by stereospecific *syn* addition[259] of mercuric acetate to bicyclo[2.2.1]hept-2-ene in acetic acid, and stereospecific reductive demercuration of the obtained acetoxymercurio acetate **237** with sodium amalgam in alkaline deuterium oxide. This provided the deuteriated alcohol **238** and was followed by conversion of the latter into deuteriated tosylate **233** (equation 113).



(237) (238) (113)

3. Deuterium isotope effect study of the reactions of N-(arylsulphonoxy)-N-alkylbenzylamines with MeONa–MeOH

The rate equation 114 of the regiospecific elimination reaction, producing only the corresponding benzylidenealkylamines, was found to be: $k_{obs} = k_0 + k_2[\text{MeONa}]$, where $k_0 = 0$ for $R^1 = Me$, indicating that it proceeds by competing solvolytic and base-promoted pathways[260]. The relative rates of elimination for the k_2 and k_0 pathways are 1, 0.67, 0.53, 0.35 and 0.27 for R^1 = Me, Et, *i*-Pr, *s*-Bu and *t*-Bu; and 1, 4.1, 5.1 and 8.7 for R^1 = Et, *i*-Pr, *s*-Bu and *t*-Bu, respectively.

$$PhCR^2_2N(OSO_2C_6H_4CF_3\text{-}m)R^1 + MeONa \xrightarrow{MeOH} PhCR^2{=}NR^1 \qquad (114)$$

R^2 = H or D

(237)	R^1 = Me	**(242)**	R^1 = Me
(238)	R^1 = Et	**(243)**	R^1 = Et
(239)	R^1 = *i*-Pr	**(244)**	R^1 = *i*-Pr
(240)	R^1 = *t*-Bu	**(245)**	R^1 = *t*-Bu
(241)	R^1 = *sec*-Bu	**(246)**	R^1 = *sec*-Bu

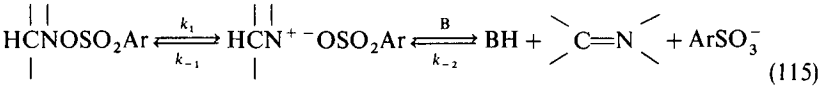
The results of kinetic and product studies and the k_H/k_D values listed in Table 4 revealed that the MeONa-promoted eliminations proceed by an E2 mechanism[260]; the reactions are second order and proceed through the reversible formation of the contact ion pair, followed by the rate-limiting deprotonation of the ion pair to the elimination

TABLE 4. Deuterium isotope effects for MeONa-promoted and solvolytic elimination from $PhCH_2N(OSO_2Ar)R^1$ in MeONa–MeOH[a]

Structure	k_{2H}/k_{2D}	k_{0H}/k_{0D}
237	3.6 ± 0.1	—
238	2.6 ± 0.1	2.0 ± 1.0
239	2.3 ± 0.1	1.3 ± 0.1
240	1.9 ± 0.1	2.2 ± 0.2

[a]Compounds **237–241** have been prepared *in situ* by reacting benzylalkylamines and arylsulphonyl peroxides[261] in EtOAc at $-78\,^{\circ}C$. Eliminations have been followed by monitoring the appearance of the absorption at the λ_{max} for **242–246**. Pseudo-first-order kinetic plots have been obtained.

product[262] (equation 115). The decrease in the k_H/k_D values for MeONa-promoted eliminations with bulkier alkyl substituents has been interpreted as resulting from a decrease in the extent of C—H bond cleavage, negative charge development at the β-carbon, increase in the N-leaving group bond rupture and the negative charge density on the leaving group oxygen atom in the imine-forming transition state. The transition-state structures for solvolytic and MeONa-promoted eliminations are similar with respect to the degree of 'C_β—H' and 'N_α—X' bond cleavage even though the mechanisms are different. A shift of the transition state toward E1-borderline is observed with an increase in the size of the alkyl group, owing to steric effects.

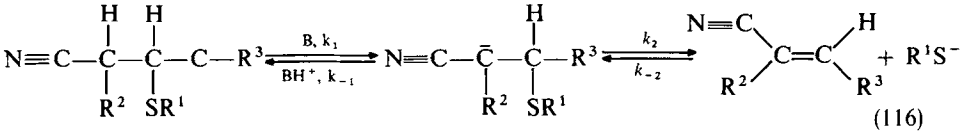


(115)

4. Deuterium exchange and isotope effect study of the addition and elimination reactions of β-cyano thioethers

The addition–elimination reactions presented in equation 116 of the β-cyano thioethers **247–249** with thiolate anions as the attacking and/or leaving groups have been

$N{\equiv}CCH_2CH_2SR$ (**247**) $N{\equiv}CCH(Cl)CH_2SR$ (**248**) $N{\equiv}CCH_2CH(CN)SR$ (**249**)



(116)

investigated[263,264] in 8.3% aqueous Me_2SO at $25\,^{\circ}C$. Deuterium exchanges in D_2O (8.3% Me_2SO-d_6) of protons β to the leaving group of the thiosalicylate adduct of acrylonitrile, **247a**, and of the methanethiol adduct of fumaronitrile **249a**, followed by NMR for 1–2.5 half-lives, have been found to be faster than elimination by factors of 5 and > 40, respectively. (These differences are larger than the factor of *ca* 2 that could arise from the difference in the basicity of OD^- in D_2O compared with OH^- in H_2O.)

$2\text{-}HO_2CC_6H_4SCH_2CH_2CN$ (247a) $CH_3SCH(CN)CH_2CN$ (249a)

The non-linear first-order kinetics for elimination from the thiophenol adduct of acrylonitrile and from the *p*-nitrophenol adduct of chloroacrylonitrile in D_2O also indicated[263] that proton exchange is faster than elimination.

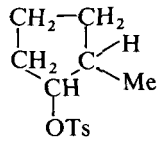
The kinetic solvent deuterium isotope effects k^{H_2O}/k^{D_2O} are 2.0 for the addition of thiosalicylate anion to form $2\text{-}HO_2CC_6H_4SCH(CN)CH_2CN$ and 1.1–1.2 for addition of β-mercaptoethanol and thioacetic acid anions to give $HOCH_2CH_2SCH_2CH_2CN$ and $CH_3COSCH_2CH_2CN$. The small values show that the addition step to form the carbanion is largely or entirely rate-limiting. The isotope effects of $k_H/k_D = 2$, 2.8 and 3.1 ± 0.6, respectively, for these reactions show that there is a significant isotope effect for proton transfer to the carbanion in a subsequent step. These results indicate that the additions proceed by reversal of the E1cB mechanism and involve initial thiol addition (k_{-2} in equation 116) which has little or no isotope effect, followed by protonation of a carbanion intermediate, which has a sufficient lifetime to discriminate between solvent protium or deuterium (k_{-1}).

The solvent KIE of 2.0 for the addition of thiosalicylate dianion to fumaronitrile indicates that the addition and protonation steps are both partly rate-limiting ($k_{-1} \sim k_{-2}$ in equation 116). The corresponding elimination reactions should proceed through the same carbanion intermediate in a stepwise E1cB mechanism (k_1 and k_2 in equation 116). The carbanion is protonated faster than it expels the nucleofuge. The value of the solvent KIE $k^{H_2O}/k^{D,2O} = 3.8$–4.0 for the addition of thionitrobenzoate dianion ($3\text{-}CO_2^-$, $4\text{-}NO_2)C_6H_3S^-$ to fumaronitrile, NCCH=CHCN, with rate-limiting protonation, and the primary KIE $k^H_{OH}/k^D_{OH} = 4.2$ for elimination of the thionitrobenzoate adduct of fumaronitrile catalysed by hydroxide in the reverse reaction are similar. Thus there should not be a large secondary solvent deuterium isotope effect for the addition of this thiol anion. Changing the pK_a of the leaving group facilitates its departure more than does proton removal from the β-carbon atom and thus the decrease in the k_{-1}/k_2 ratio changes the rate-limiting step from leaving group departure to proton removal. The nature of the carbanion intermediate, its transition state and the corresponding energy diagram have been discussed. The effect of the α-CN group is attributed to conjugation with the developing double bond in the TS for elimination[263a,b,c,d].

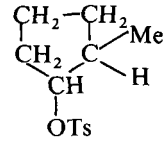
The problem of internal return and the lifetime of the carbanion intermediate in elimination reactions of β-cyanothioethers have also been discussed by Fishbein and Jencks[264]. The internal return competes with elimination of the leaving group as well as with diffusional equilibration of the abstracted proton and solvent protons. The olefin-forming eliminations proceed through a concerted E2 mechanism only when they cannot proceed through a stepwise mechanism because the carbanion has too short a lifetime to exist for several vibration frequencies. Free-energy diagrams illustrating the catalysis for elimination and exchange have also been presented. The E1cB elimination reaction of the C_6F_5SH adduct of fumaronitrile in 8.3% aqueous Me_2SO shows[264] strong buffer catalysis and primary deuterium isotope effects of $k_H/k_D = 4$–5.

5. *Deuterium isotope effects in solvolytic reactions*

a. Deuterium isotope effects in solvolysis of cis- and trans-2-methylcyclopentyl arenesulphonates. Continuing previous isotope studies[265–267], α-d and β-d kinetic isotope effects have been determined[268] in the solvolysis of *cis*- and *trans*-2-methylcyclopentyl arenesulphonates at 25 °C in different solvents ranging from 90% v/v aqueous ethanol to 90% aqueous 1,1,1,3,3,3-hexafluoro-2-propanol. The α-effect is

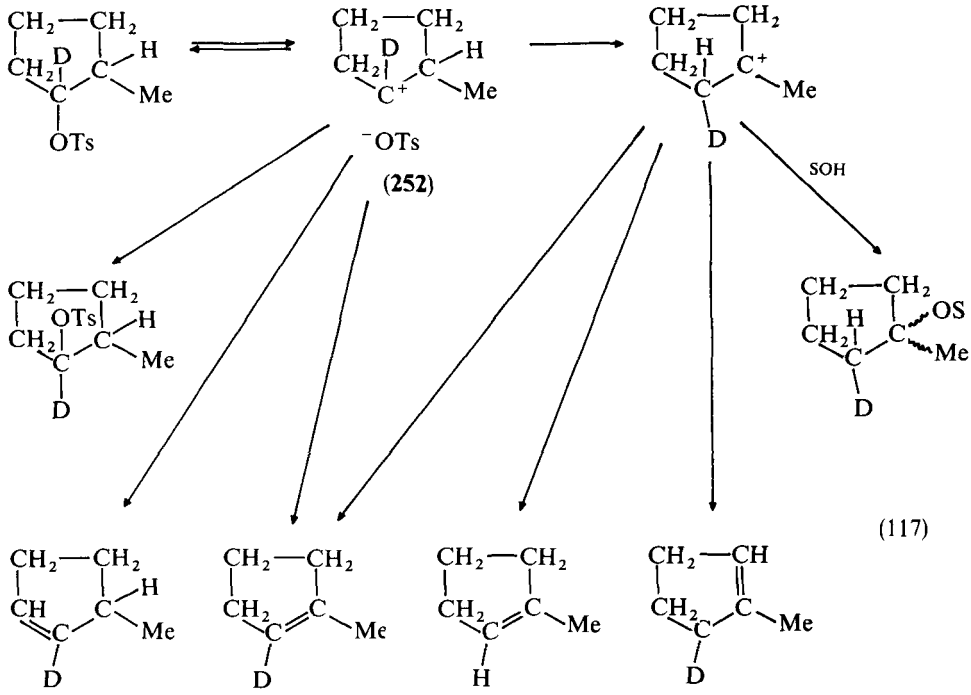


(250)



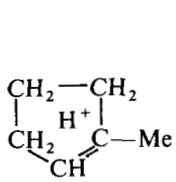
(251)

1.20–1.23 for both *cis*- and *trans*- isomers, indicating that in all solvents reversible ionization precedes the rate-determining step (equation 117). For *cis*-2-methylcyclopentyl tosylate **250**, the β-d effect of 1.904–2.304 indicates that hydride shift of the tertiary hydrogen occurs in the rate-determining step. The β-d effect for the *trans*-isomer **251** is never higher than 1.5 even in the most non-nucleophilic solvents, suggesting that only a small proportion of the product mixture is formed by rate-determining loss or migration of the β-hydrogen.



(117)

After reversible formation of the intimate ion pair **252**, most of the reaction proceeds by rate-determining hydrogen migration to convert the secondary cation into the more stable tertiary ion. In 70% v/v aqueous ethanol, substitution at the intimate ion pair **252** competes with rearrangement and slightly depresses the β-d effect, which is 1.904. The details of the proposed mechanisms have been quantitatively described with the aid of a steady-state analysis. The resonance structure **253** has been suggested to describe the TS of the hydrogen rearrangement and structure **254a** that of the methyl migration[268–269], with partial bond formation of the migrating methyl group, leading to **254**.



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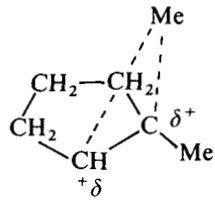
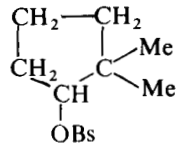


(254a)



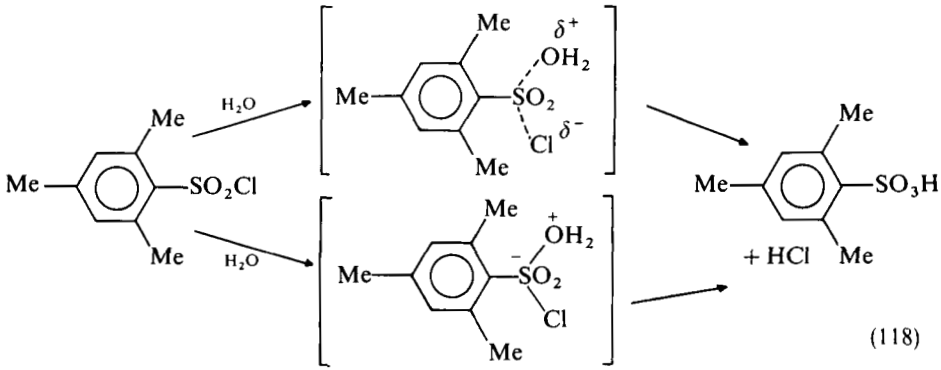
(254)

b. Solvolysis of 2,4,6-trimethylbenzenesulphonyl chloride. Deuterium solvent KIEs for solvolysis of 2,4,6-trimethylbenzenesulphonyl chloride, determined conductimetrically, have been found to be in methanol, and in water, both at 25 °C and interpreted[270] as

$$\frac{k_{SOH}}{k_{SOD}} = \frac{(1.02 \pm 0.01) \times 10^{-3}\ s^{-1}}{(6.08 \pm 0.01) \times 10^{-4}\ s^{-1}} = 1.68 \pm 0.02 \quad \text{(in methanol)}$$

$$\frac{k_{SOH}}{k_{SOD}} = \frac{(8.34 \pm 0.15) \times 10^{-2}}{(6.22 \pm 0.02) \times 10^{-2}} = 1.34 \pm 0.03 \quad \text{(in water)}$$

reflecting a dual reaction mechanism (equation 18). It has been proposed that the route favoured in less polar media is general-base catalysed, occurring possibly through an addition–elimination pathway.



(118)

6. Deuterium isotope effect study of the trifluoroacetylation of aryl vinyl sulphides

A kinetic and product ^{1}H-NMR study[271] of the trifluoroacetylation of aryl vinyl sulphides, ArSCH=CH_2, ArSCH=CD_2, *cis*-ArSCH=CHD and *trans*-ArSCH=CHD, by $(CF_3CO)_2O$ in the presence of pyridine-d_5 (equation 119) indicated that in this electrophilic substitution reaction a single-step concerted mechanism was involved (equation 120). The deuterium isotope effect, k_H/k_D, was found to be 2.5 ± 0.3 for the

$$\underset{\textbf{(255)}}{\text{ArSCH=CH}_2} \xrightarrow[CDCl_3, C_5D_5N, 35\,^\circ C]{(CF_3CO)_2O} \underset{\textbf{(256)}}{\text{ArSCH=CHCOCF}_3} \qquad (119)$$

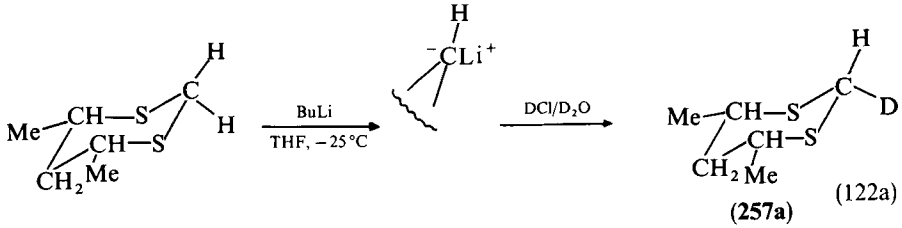
$$\textbf{255} \xrightarrow[-H^+]{CF_3CO^+} \textbf{256} \qquad (120)$$

trifluoroacetylation of **255**-2,2-d_2 (Ar = Ph)[272]. No primary deuterium isotope effect has been found in the trifluoroacetylation of aryl 2,2-d_2-vinyl ethers, proceeding probably as shown in equation 121. Vinyl ethers and vinyl sulphides are trifluoroacetylated by different mechanisms probably because the cationic intermediates $ArOCHCH_2COCF_3$ are stabilized more efficiently by 2p–2p overlap of the electron-deficient carbon atom and the 2p orbital of the adjacent oxygen atom and are stable, while cations $ArSCHCH_2COCF_3$ are stabilized less efficiently by 2p (carbon atom)–3p (orbital of the adjacent sulphur atom) overlap and hence vinyl sulphides cannot yield stable cationic intermediates.

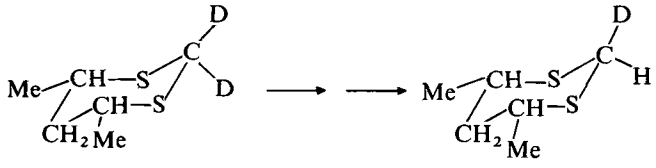
$$ArOCH{=}CH_2 \xrightarrow[\text{slow}]{CF_3CO^+} ArO\overset{+}{C}HCH_2COCF_3 \xrightarrow[\text{fast}]{-H^+} ArOCH{=}CHCOCF_3 \quad (121)$$

7. Negative ion reactions of 1,3-dithianes and 1,3-dithiane-1-oxides

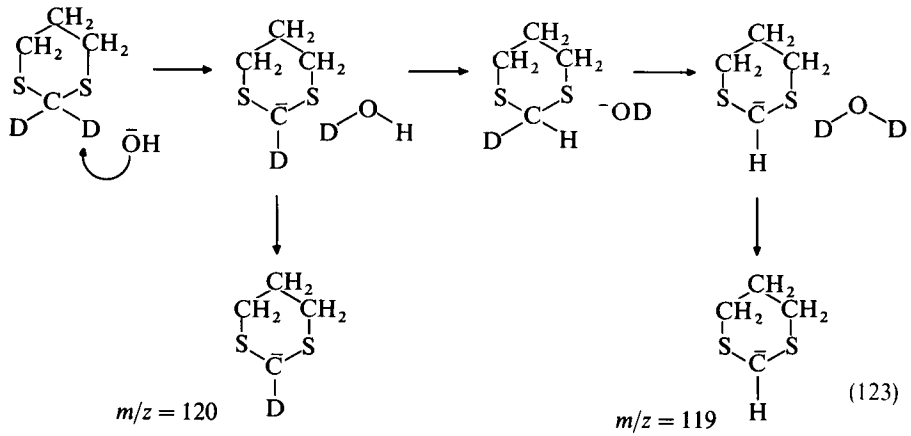
1,3-Dithianes and 1,3-dithiane-1-oxides have been labelled with deuterium at the $C_{(2)}$ position (equations 122a and 122b) and used to study the deprotonation of neutral molecules at $C_{(2)}$ with gaseous HO^-/DO^- ions[273] (equation 123). Similar treatment of the 2,2-dideutero analogue[274] **257b** gave the axial deuterium compound **257c**. The deuterium isotope effect k_H/k_D determined for the reaction of **257** with 'MeO^-' was 1.2 ± 0.1 and in the reaction with **e** (electrons) it was 1.3 ± 0.1. These gas-phase values are lower than the isotope effect of 2.5 determined in solution[275] and possibly indicate less C—H bond breaking in the transition state, but are in agreement with isotope effects observed in base-induced gas-phase eliminations of ethyl sulphide[276] and of cyclic thioethers[277]. The gas-phase elimination reactions of thioethers with OH^-, MeO^- and F^- exclusively proceed via an E2 mechanism, but with OH^- rapid exchange is observed within the reaction complex between the α-hydrogens of the sulphide and the hydroxide hydrogen prior to the E2 elimination. For the E2 eliminations the α- and β-deuterium isotope and leaving group effects have been determined as a function of the base strength[276] and the results were interpreted in terms of a variable E2 transition-state structure.



(257a) (122a)



(257b) (257c) (122b)



(123)

8. Deuterium isotope effect in the oxidation of aliphatic aldehydes, diols and α-hydroxyacids by sodium N-bromoarylsulphonamides in acid solution

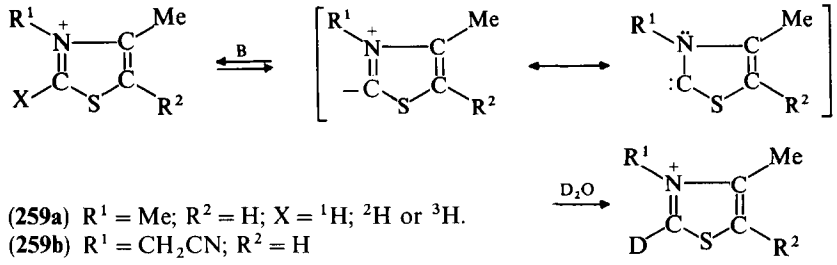
a. The oxidation of aldehydes[278], yielding the corresponding carboxylic acids, is first order with respect to each [oxidant], [aldehyde] and $[H^+]$. The primary KIE $k_H/k_D = 4.91 \pm 0.14$ and the solvent isotope effect $k_{H_2O}/k_{D_2O} = 0.43$ has been found in the oxidation of MeCHO at 298 K. If one assumes that the aldehydes react via hydrate forms, the rate of oxidation of formaldehyde compares favourably with the reactivities of other aldehydes. The rates of oxidation of the aldehyde hydrates correlated well with Taft's substituent constants, giving negative ρ values. A mechanism involving hydride transfer from aldehyde hydrate to oxidant has been proposed.

b. Oxidation of diols by sodium *N*-bromobenzenesulphonamide has also been studied[279]. The reaction is first order with respect to the diol and the oxidant. The oxidation of vicinal diols follows two mechanistic pathways, one acid-independent and the other acid-dependent. The oxidation of other diols shows a first-order dependence on hydrogen ion. No primary KIE has been found in the oxidation of [1,1,2,2-$^2H_4$]ethanediol. Solvent isotope effects for the diols ranged from 0.42 (3-methoxybutan-1-ol) to 2.24 (ethanediol). An acyclic mechanism involving the fission of the glycolic C—C bond has been proposed for the oxidation of vicinal diols. Other diols are oxidized by a hydride-transfer mechanism as are the monohydric alcohols[279]. These suggestions have not yet been corroborated with tracer and ^{14}C (and/or ^{13}C) isotope effect determinations.

c. Oxidation of α-hydroxyacids. No primary deuterium KIE has been observed[280] in the oxidation of lactic, glycolic, mandelic and 2-hydroxy-2-methylpropanoic acid by sodium *N*-bromobenzenesulphonamide (**258**). The reaction is first order in **258** and [substrate], is catalysed by hydrogen ions and yields the corresponding carbonyl compounds by oxidative decarboxylation. The dependence of the rate on acidity suggests that both $PhSO_2NHBr$ and its protonated form are reactive oxidants. The solvent isotope effect k_{H_2O}/k_{D_2O} is 3.99 at 303 K. Activation parameters for these oxidations and possible mechanisms have been presented[280].

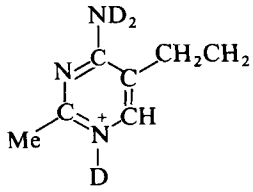
9. Thiazolium $C_{(2)}$-hydrogen exchanges

Experimental rate constants for $C_{(2)}$—H → D exchange and for $C_{(2)}$—D → H exchange from 3,4-dimethylthiazolium ion, **259a**, *N*(1′)-protonated thiamin, **259c** and



(124)

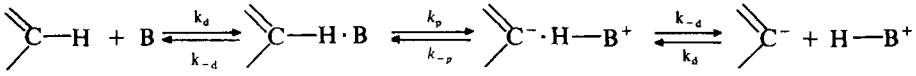
(**259a**) R^1 = Me; R^2 = H; X = ^{1}H; ^{2}H or ^{3}H.
(**259b**) R^1 = CH_2CN; R^2 = H

(**259c**) R^1 =  ; R^2 = CH_2CH_2OD (coenzyme thiamine)

(**259d**) R^1 = as above; R^2 = $CH_2CH_2OP_2O_6H_3$ (thiamin pyrophosphate)

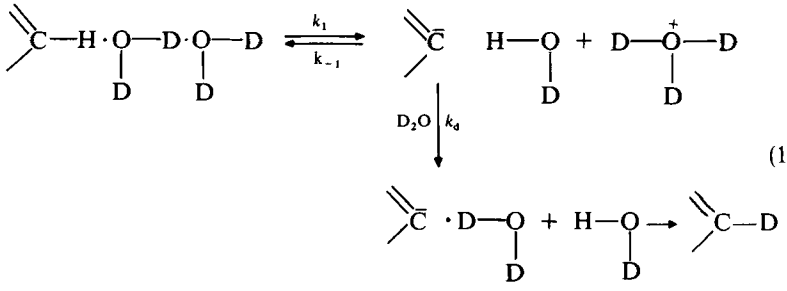
3-(cyanomethyl)-4-methylthiazolium ion (**259b**) have been determined by ^{1}H NMR in carboxylate and amine buffers at 30 °C in D_2O (or in H_2O) (equation 124). The detritiation rate constants for thiazolium $C_{(2)}$—T → D (or $C_{(2)}$—H → T in the case of (**259b**) have also been estimated by measuring the tritium content in the $C_{(2)}$-[^{3}H]thiazolium salts[281–283] at different exchange times.

The accumulated experimental results have been extensively discussed in terms of rate constants presented in equation 125. (The meanings of the various rate coefficients in



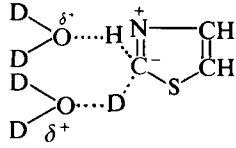
(125)

this equation are described in the original paper by M. Eigen, *Angew. Chem. Int. Ed. Engl.*, **3**, 1 (1964)). The role of internal return and of diffusion processes of species like TOH_2^+ or TOD_2^+ to thiazolium $C_{(2)}$ ylide in the $C_{(2)}$—H → T exchanges is stressed. Equation 126 has also been suggested as one of possible deuterium exchange pathways.



(126)

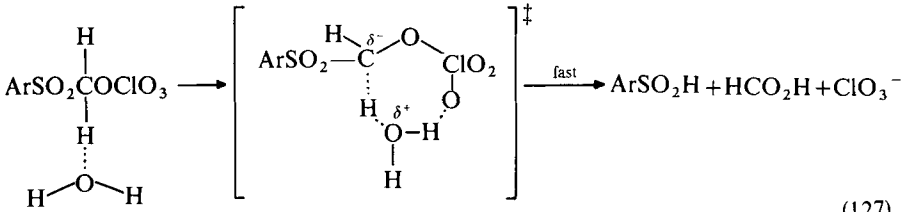
In this scheme the HOD molecule has to be replaced with D_2O molecule. Transient structures like **260** have also been proposed. A requirement for the removal of at least one water molecule from solvated HO^- or DO^- before the reaction is postulated. The rate constants for $C_{(2)}$—H → D exchange catalysed by deuterioxide ion increase with decreasing ionic strength. The mechanisms of thiazolium $C_{(2)}$-hydrogen exchanges have been studied in detail since several thiamin dependent enzymes catalyse aldol-type addition reactions between thiamin pyrophosphate **259d** and carbonyl compounds[284].



(260)

10. Kinetic isotope effect study of the mechanisms of hydrolysis

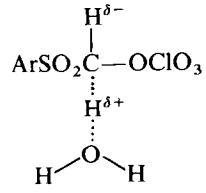
a. Study of the mechanism of the neutral hydrolysis of [(p-nitrophenyl)sulphonyl]methyl perchlorate. A large primary kinetic deuterium isotope effect, $k_H/k_D \approx 6$, indicated[285,286] that the hydrolysis of the covalent (arylsulphonyl)methyl perchlorate, **261**, which is first order in water and involves general base catalysis via rate-determining deprotonation at the α-sulphonyl carbon atom, proceeds through a symmetric transition state. Pseudo-first-order rate constants for hydrolysis of **261** in H_2O/D_2O mixtures at 25 °C are linearly dependent[286] on the atom fraction n of D in the solvent ($k_{obs} \times 10^3\ s^{-1} = 3.33$ ($n = 0$), 2.92 ($n = 0.18$), 2.60 ($n = 0.38$), 2.41 ($n = 0.57$), 2.05 ($n = 0.78$) and 1.79 ($n = 1$). This is consistent with a mechanism in which one water molecule in the transition state acts as a general base. The initial state preactivated by H-bonding to water is transformed into a cyclic transition state $TS_{(1)}$ in which one oxygen atom of the perchlorate group assists in the transfer of a proton from the carbon α to the sulphonyl to a H-bonded water.



($TS_{(1)}$) (127)

(261) Ar = p-$NO_2C_6H_4$

The OH group of water is removed from interaction with the medium in the rate-determining step (equation 127). The structure $TS_{(2)}$ has been rejected on the basis of the 'SWAG' procedure (Savage–Wood additivity of group interaction)[287].



$(TS_{(2)})$

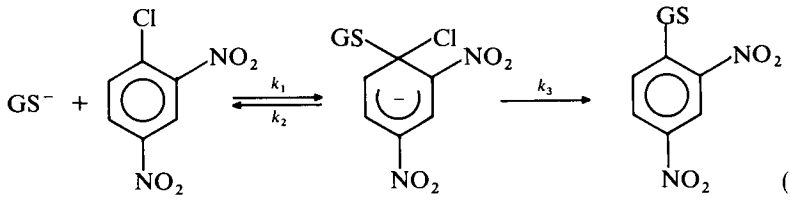
b. A solvent deuterium isotope effect of $k_{H_2O}/k_{D_2O} = 3.21$ has been found[288] in the *water-catalysed (spontaneous) hydrolysis of bis(p-nitrophenyl sulphite* in aqueous dioxane showing second-order dependence on water concentration. Several possible transition states for this reaction have been considered.

c. Activation parameters and deuterium solvent isotope effects found in *acid-catalysed hydrolysis and alcoholysis of 4-nitrophenyl N-acetylphenyliminosulphonate,* $PhSO(=NAc)\text{-}OC_6H_4NO_2\text{-}4$ carried out in aqueous (20% by volume) dioxane solutions of mineral acids, were consistent with a bimolecular (A2) mechanism[289].

d. Isotope effects of deuterium in position 2, salt effects and special salt effect *in the solvolysis of cis- and trans-2-arylcyclopentyl p-toluenesulphonates* in HCO_2H, AcOH and EtOH have been studied[290,291] and it has been found that all substrates show kinetic deuterium isotope effects $k_H/k_D > 1.15$. This suggested that the first step leads to the formation of an intimate ion-pair which then dissociates to a solvent separated ion-pair without participation of the H-atom at $C_{(2)}$. Solvent separated ion-pair formation is indicated also by the $LiClO_4$ special salt effect. Further studies[291] of the subsequent step in the solvolysis of a series of 1-deuteriated, 2-deuteriated and undeuteriated *cis*-2-arylcyclopentyl *p*-toluenesulphonates and comparison of the observed and calculated KIEs of $D\text{—}C_{(2)}$ allowed one to conclude that the steps following ionization have a preponderant effect on the total solvolysis rate[291].

e. Solvent KIEs on the reaction of *glutathione with 1-chloro-2,4-dinitrobenzene* **262** catalysed by rat liver *glutathione S-transferase* have been measured[292]. At pH (and pD) = 8.0 the isotope effects k_{H_2O}/k_{D_2O} ranged from 0.79 to 1.05 (equation 128). Solvent

$$GSH + H_2O \rightleftharpoons GS^- + H_3O^+$$

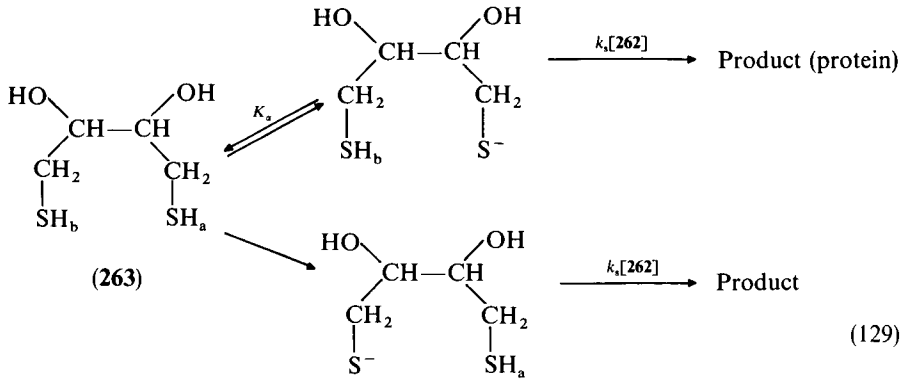


(128)

(262)

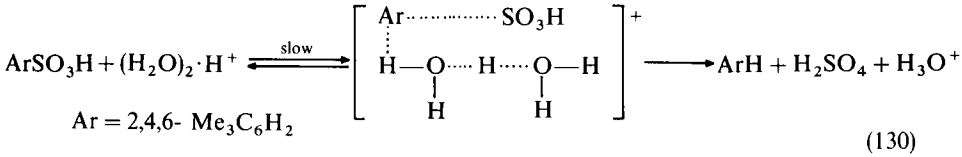
GSH = glutathione

isotope effects in non-enzymic reactions of glutathione or dithiothreitol **263**, with **262** (equation 129) of 0.84 and 0.87, have been observed[292] also and interpreted in terms of hydrogen-bond changes associated with the thiolate anion.



(129)

f. Deuterium isotope effect study of aromatic desulphuration in acidic media. Solvent D_2O–D_2SO_4 KIE has been applied[293,294] to determine the mechanism of aromatic desulphurative hydrolysis of mesitylenesulphonic acid in H_2SO_4, D_2SO_4 and H_3PO_4 at 25 °C which was classified as A–S_E2 (equation 130). The reaction rate is limited by the proton (deuteron) transfer. The k_H/k_D value of 2.8 ± 0.3 in much lower than the theoretical one for (O—H)/(O—D) bond rupture, indicating that in the transition state the proton (deuteron) is transferred to a large extent to the substrate to yield a σ-complex, $k_H/k_D = 0.4$ has been found in desulphuration of p-$MeC_6H_4SO_3H$ at 150 °C in H_2SO_4 and in D_2SO_4. This reverse deuterium isotope effect has not been given a full theoretical explanation although different activation energies for the processes carried out in D_2SO_4 and in H_2SO_4 have been postulated[293] as being responsible for inversion of the sign of the $\Delta \ln k (= \ln k_D - \ln k_H)$ value.



(130)

C. Brief Review of Deuterium Isotope Effect Studies of Compounds with Sulphur-containing Functional Groups

Acid-catalysed hydration of vinyl tosylates, benzoates and 1,1-ditosylates [CH_2=C(OX)R, where X = Bz, Ts] has been analysed[295] and it has been concluded that all the substrates react by the Ad_E2 mechanism of rate-limiting proton transfer to the double bond. The deuterium isotope after $k_{H^+}/k_{D^+} = 5.75$ found in the hydrolysis of $Me_3CCH{=}C(OTs)_2$ has been interpreted in terms of rate-limiting protonation of a substrate whose basic oxygens interact strongly with the acid solvent.

The kinetics of diazotization of 2-aminothiazole in aqueous sulphuric acid has been studied[296] and a solvent KIE for the diazotization in 72% D_2SO_4/D_2O, $k_H/k_D = 5.8 \pm 0.2$, has been determined. The accumulated data are consistent with a mechanism in which the 2-aminothiazole, protonated not at the NH_2 group but at the ring nitrogen, is attacked by the NO^+ ion.

The apparent molar volumes of sodium alkyl sulphates (Na dodecyl, dodecyl and tetradecyl sulphate) in normal and heavy water have been calculated[297] from densities measured in normal and in 99.85% heavy water at 25 °C. They are slightly but significantly different. Both the magnitude and direction of this isotope effect depend on alkyl chain length. The packing of the alkyl chains in the two media are different. The number of solvent molecules that penetrate into the micellar core per alkyl chain has been estimated.

The deuterium isotope effect has been used to estimate the transition state structure in the solvolysis of 2-chloroethyl methyl sulphide. Solvent influences in aqueous MeOH mixtures on initial and transition states have been studied and it has been concluded that charge development in the TS of this solvolysis is approximately 0.6 units of electronic charge[298].

Modification of the thiol SH group to thiocyanate at the active site of *Ascaris suum* NAD-malic enzyme resulted in change in the rate-determining steps for oxidative decarboxylation of L-malate. This was concluded[299] by observing the increase of deuterium isotope effects (on v_{max} and v_{max}/K_{malate} compared to the native enzyme), and the decrease in the ^{13}C isotope effect. The hydride transfer is becoming more rate-limiting.

Primary and secondary α-deuterium KIEs in the nucleophilic substitutions of benzyl and 1-phenylethyl benzenesulphonates with deuteriated aniline nucleophiles in acetonitrile at 30.0 °C have been determined[300] and the k_H/k_D values correlated with the possible structures of the transition states (four-centre one or typical S_N2).

KIEs for the reactions of 2-phenylethyl and 1-methyl-2-phenylethyl benzenesulphonates with deuteriated anilines in MeCN agree with the TS structures proposed on the basis of the sign and magnitude of the cross-interaction constants $\rho_{X,Z}$ between the substituents in the nucleophile (X) and the leaving group (Z). In the reactions of 2-phenylethyl derivatives all three reaction pathways, k_f, k_r and k_Δ, (i.e., the rate coefficients for the front-side attack for the reverse reaction and for the decomposition path, respectively) contributed competitively; the secondary KIEs observed with stronger nucleophiles changed into a primary KIE with four weaker nucleophiles, owing to the predominant contribution of the four-centre TS in the k_r path. In the 1-methyl-2-phenylethyl series, the k_r path played a major role, the contribution from the front-side nucleophilic attack, k_f, being negligible. In both reaction series, aryl participation was important for the p-CH_3O-substituted substrate[301].

No deuterium KIE has been observed[302] when carboxylic acids R^1COOH ($R^1 = C_5H_{11}$, $C_7H_{15}$and C_9H_{19}) have been condensed with aliphatic thiocyanates R^2SCN (R^2 = Me, cycloheptyl) in refluxing CF_3COOH or in CF_3COOD yielding R^1COSR^2 in 48–63%. This has been interpreted as evidence that protonation is not the rate-determining step. The yields of the intermediates, $R^1CONHCOSMe$, isolated in 32–37% yields under mild conditions, decrease with increasing size of R^1.

α- and β-Deuterium isotope effect studies of base-induced gas-phase E2 elimination reactions of diethyl sulphide have been carried out[309].

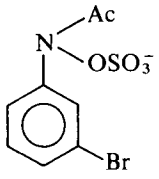
α-Deuterium isotope effect plots versus β values, representing the extent of the bond cleavage to the leaving group in the TS for a series of arenesulphonates in identical or similar solvents, have been used as mechanistic and TS probes in a study of the solvolysis of *endo*- and *exo*-2-norbornyl arenesulphonates[304].

The KIE $k_H/k_D = 4.3$ for β-H of $R^1C_6H_4S(O)CH_2CH_2C_6H_4R^2$ (R^1 = H, R^2 = 3-OMe, 4-Me, 3-Me, 4-Cl, 4-NO_2; R^1 = 4-Me, 3-Me, 4-Cl, 4-NO_2; R^2 = H) indicated that the pyrolysis of these substituted ethylphenyl sulphoxides proceeds via a nearly carbanion-like mechanism[305] in a five-membered cyclic TS. The activation enthalpy and entropy for $R^1 = R^2 = H$ have been found to be 110 kJ mol^{-1} and -45 J K^{-1} mol^{-1}, respectively.

S_N2 displacement in 2-(alkylthio)ethyl derivatives has been demonstrated[306] by studying the reaction mechanism of various 2-(alkylthio)ethyl and 2-(arylthio)ethyl derivatives with strong nucleophiles with the use of deuterium isotope effects.

An inverse secondary kinetic isotope effect of the disappearance of the S=O group during the reaction of thiobenzophenones with phenylallene ($PhCH{=}C{=}CH_2$, $PhCD{=}C{=}CH_2$ and $PhCD{=}C{=}CD_2$) is consistent with attack at C_β and indicates a change in hybridization at C_α and C_γ[307]. The deuterium isotope effect observed with $D_3COCH{=}C{=}CH_2$ compared with $MeOCH{=}C{=}CH_2$ represents a rotational isotope effect arising from the increase in mass on substitution of H by D[307].

Acid- and base-dependent hydrolysis of *N*-(sulphonatoxy)-3-bromoacetanilide **264** at 80 °C in the pH range 1.0–8.0 and by an uncatalysed path involving formation of *N*-(3-bromophenyl)hydroxylamine-*O*-sulphonate **265** has been studied in CD_3CN–D_2O by UV spectroscopic methods[308].



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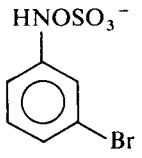


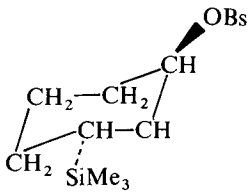
(265)

The solvent isotope effect using D_2O has been studied for oxidation of methionine by sodium *N*-bromobenzenesulphonamide in aqueous solution. Methionine sulphone is identified as the reaction product. Addition of the benzenesulphonamide reaction product retards the rate[309].

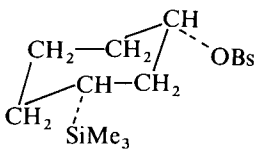
A very high β-deuterium KIEs, k_{CH_3}/k_{CD_3} of 2.13 at 60 °C, have been found in the solvolysis of 2-(3-chlorophenyl)-1,1,1-trifluoro-2-propyl tosylate and of its 2-aryl-2-propyl α-CD_3 analogue[310]. The effect decreased with increasing the electron-withdrawing ability of the substituent on the aromatic ring. The α-Me group contributes to the stabilization of the cationic centre in the TS.

Deuterium isotope effects upon solvolyses of alkyl sulphonates in DMSO have been discussed by Bowersox[311].

Large β-D isotope effects in the solvolysis of *trans*-3-(trimethylsilyl)cyclohexyl *p*-bromobenzenesulphonate **266** (yielding predominantly cyclohexene via H migration from $C_{(2)}$ and loss of the Me_3Si group), and small α- and β-deuterium isotope effects in the solvolysis of the *cis*-isomer **267** (giving bicyclo[3.1.0]hexane) have been determined and discussed by Shiner and coworkers[312].



(266)

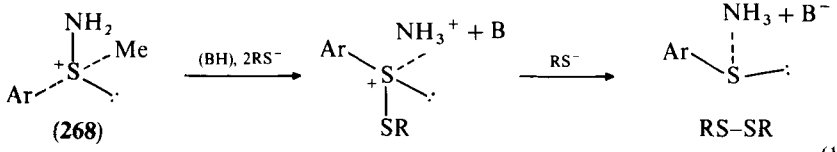


(267)

OBs = brosylate

The rate constants for proton transfer from the thiol groups in mercaptoacetal and 2-mercaptobenzoate to amines in aqueous solutions are by two orders of magnitude below the diffusion limit. The S—H···O hydrogen bond in 2-mercaptobenzoate is weak and has negligible effect on the rates of proton transfer. Deuterium solvent isotope effects on the equilibrium constants for the reaction of mercaptoacetate with four amines are in the range $K_{H_2O}/K_{D_2O} = 0.52–0.59$. Kinetic solvent isotope effects on the forward ($k_{f\,H_2O}/k_{f\,D_2D} = 2.4 \pm 0.4$) and reverse ($k_{r\,H_2O}/k_{r\,D_2O} = 4.3 \pm 0.7$) rate coefficients are large, but show no evidence for a maximum with changing the base strength of the amines over a limited range. The behaviour of thiols has been compared with the behaviour of O and N acids[313].

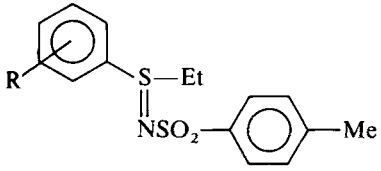
Kinetic study of the thiolate reduction of sulphilimine (**268**) salts $[XC_6H_4S(Me){:}NH_2]^+[2,4,6\text{-}Me_3C_6H_2SO_3]^-$ (where X = 4-MeO, 4-Me, H, 3-MeO, 4-halo, 3-Cl, 4-NO_2) by 2,4-$(O_2N)(S^-)C_6H_3CO_2H$ and 3-$(S^-)C_6H_4COOH$ has been carried out and the mechanism for this reaction in which S—S bond formation, S—N bond cleavage and proton transfer occur in a fully concerted TS has been proposed[314] (equation 131).



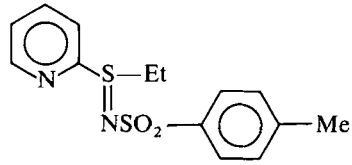
(131)

Solvent deuterium isotope effects for the proton catalysed reduction of *S*-phenyl- and *S*-(4-nitrophenyl)-substituted compounds by 3-nitro-5-thiobenzoic acid are $k_H/k_D = 7.62$ and 6.5, respectively. These unusually large effects suggest that a great deal of zero-point energy has been lost in the rate-limiting step. For the reduction of the same compounds with 3-thiobenzoic acid $k_H/k_D = 2.89$ and 1.66 have been found, respectively. They suggest a significant shift in TS structure on going to the more powerful nucleophile.

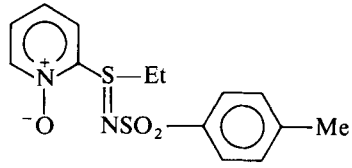
The effects of protic solvents, such as MeOH, on the pyrolysis of ethylaryltosylsulphimides **269** and their pyridine analogues **270** and **271** have been compared with those of C_6H_6 and 1,4-dioxane[315]. The rates for the pyrolysis of **269** in benzene, 1,4-dioxane and MeOH were 8.5:5.5:5.1 at 100 °C. The activation parameters of **269** in MeOH have been estimated to be $E_a = 115.1\ kJ\ mol^{-1}$ and $\Delta S^{\#} = -41.0\ J\ K^{-1} mol^{-1}$. The isotope effect in MeOH/MeOD was about 0.82, while for **270** and **271** it was near



(**269**) R = H, 4-Me, 4-OMe, 4-Cl, 4-NO_2, 3-Cl



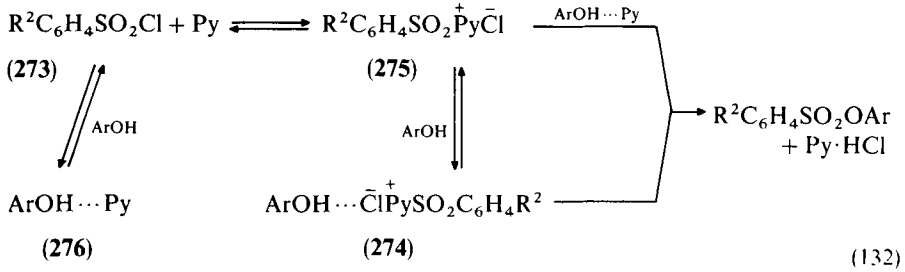
(**270**)



(**271**)

unity. The retardation by the protic solvent has been ascribed to the formation of a hydrogen bond between the solvent and the N atom of the sulphimide function of the substrate in the ground state.

An isotope effect $k_N^D/k_N^H = 1$ has been found in the sulphonylation[316] of $R^1C_6H_4OH$ or $R^1C_6H_4OD$ (R^1 = H) **272** by $R^2C_6H_4SO_2Cl$ (R^2 = 3-NO_2, 4-Br, 4-Cl, H, 4-Me, etc.), **273**, with β-picoline as catalyst and for the sulphonylation of **272** (R^1 = 4-MeO, 4-Me, 3-Me, H, 4-Br, 4-Cl) by **273** (R^2 = 4-Br) with 3,5-lutidine as catalyst. The nucleophilic mechanism of catalysis (equation 132) supported by lack of deuterium isotope effect has been discussed. The final products are formed either by decomposition of the complex **274** or by interaction of the intermediate **275** with complex **276**.



(132)

Nitrogen-15 KIEs in Menschutkin-type reactions of benzyl benzenesulphonates have been measured in acetone at 35 °C and the results have been discussed in connection with reactivity–selectivity relations[317].

D. Spectroscopic and Physical Applications

The IR and UV-visible spectra and some thermal analysis data for Cu(II) complexes and the H/D, CH_3/CD_3 and $^{63}Cu/^{65}Cu$ isotopes of planar dithiooxamides have been obtained and explained assuming planar S_2N_2 configurations around the Cu atom in a polymeric structure[318].

The Raman and IR spectra have been measured and a complete normal coordinate treatment for all the vibrations of *N*-(2-pyridyl)thioformamide and its N-deuteriated analogues has been carried out to assign correctly the recorded bands[319].

Extensive deuterium and oxygen-18 isotopic substitution studies[320], and normal coordinate calculations on all isotopomers, permitted one to assign 8 new IR absorptions (observed when Ar matrix samples at 12 K containing H_2S and SO_2 have been irradiated with a Hg–Xe arc lamp) to 8 vibrational modes of sulphinic acid (HSOOH)— a highly reactive molecule formed by H-atom addition to matrix-isolated SO_2 molecules.

The spectroscopic parameters of the vibrational states of $^{32}SO_2$ (021) and of $^{34}SO_2$ (200) have been obtained[321] from the analysis of some hyperweak adsorption bands of sulphur dioxide in the regions of 1055–2000 and 2200–2550 cm^{-1}.

^{34}S and ^{2}H isotopic shifts have been used[322] to assign absorption lines at 3539.8, 1309.2, 1097.2, 759.3 and (with less certainty) 1296.3 cm^{-1} to $HOSO_2$, a radical generated by the reaction of OH with SO_2 in a gaseous discharge-flow system at 300 K under 2–5 Torr of argon.

^{15}N-labelling experiments helped to assign correctly[323] the IR and Raman vibrational spectra of some sulphur nitrogen heterocycles, such as thiotrithiazyl chloride and chlorothiodithiazyl chloride and particularly of the compound $[S_4N_3]Cl$.

The vibrational assignment of *S*-methyldithizone based on 1,5-^{15}N- and 2,4-^{15}N-isotopic substitutions, as well as on D-substitutions of the methyl group, phenyl groups and N—H group has also been made[324].

Isotope effects on phosphorus-31 nuclear shielding in thiophosphites have been studied and it has been found that the ^{34}S isotope effect on the chemical shift of P(III) nuclei in $P(SR)_3$ esters, where R = Et, $(C_{12}H_{25})_n$ and Ph, is close to 20.6 ppb per P(III)—^{34}S bond; it is 3–4 times larger than for thiolo sulphur atoms in $S{=}P(SR)_3$ or $O{=}P(SR)_3$. Similar behaviour is noted for the $P(—S—)_3$ sites in P_4S_9 and P_4S_3 and for the downfield triplet of P_4S_8, which is assigned to the tri-coordinate P atoms of this sulphide. ^{13}C isotope effects are also reported for trialkyl(aryl)phosphorotrithioites and *S,S,S*-phosphorotrithioates[325].

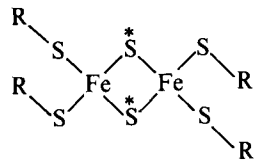
IR spectra of the ligands TDTH (tetradeuteriothiamin), THTHMP (tetrahydrothiamin monophosphate), THTHPP (tetrahydrothiamin pyrophosphate), their deuteriated (—ND_2, —OD) derivatives, their Pt^{2+} and Pd^{2+} complexes of formulas Pt(THTHMP)$_2$Cl$_2$, Pt(THTHMP)$_2$Cl$_2$·2HCl, Pd(THTHMP)$_2$Cl$_2$·2HCl, Pt(THTHPP)$_2$Cl$_2$, Pd(THTHPP)$_2$Cl$_2$·2HCl, etc, as well as their deuteriated (—ND_2,—OD) derivatives have been recorded[326] in the 250–4000 cm^{-1} region.

Microwave spectra from 26.5 to 39.0 GHz of *trimethylphosphine sulphide*, $(CH_3)_3P{=}^{32}S$ and three deuteriated species, $(CH_3)_2(CD_3)P{=}^{32}S$, $(CH_3)(CD_3)_2P{=}^{32}S$, $(CD_3)_3P{=}^{32}S$ and also $(CH_3)_3P{=}^{34}S$ have been measured[327] at ambient temperature, and the observed transitions have been assigned to the ground vibrational states for each molecule. Structural parameters have been obtained[327,328] including interatomic distances and bond angles. Raman spectra at ambient temperature have also been recorded for the solid states of all five isotopic species. Far-IR spectra of the d_6 and d_9 species have also been measured in Nujol mulls. Simple valence force-field calculations for $(CH_3)_3P{=}S$ and $(CD_3)_3P{=}S$ have been used to predict the frequencies for the fundamental modes of vibrations for the partially deuteriated species, $(CH_3)_2(CD_3)P{=}S$ and $(CH_3)(CD_3)_2P{=}S$. Reasonably good agreement has been obtained between the observed and calculated values. Observed vibrations in the Raman spectra of the polycrystalline, light and deuteriated species are in agreement with the calculated values of the isotopic shift factors for librations and intermolecular translational motions. The far-IR spectra of $(CH_3)_3P{=}S$ (ω = 98.75 and 55 cm^{-1}) and of $(CD_3)_3P{=}S$ (at 91.71 and 53 cm^{-1}) have also been recorded at room temperature and interpreted. The deuteriated species used have been obtained[327,329] by treating PCl_3, CH_3PCl_2 and $(CH_3)_2PCl$, respectively, with CD_3MgI, followed by reaction with sulphur, or in the case of $(CH_3)_3P{=}^{34}S$ using $(CH_3)_3P$ and isotopically pure ^{34}S.

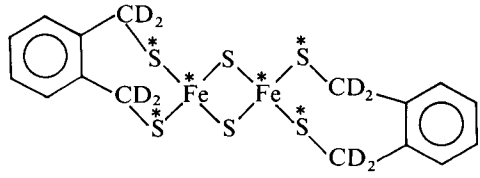
^{64,68}Zn and ^{2}H have been used[330] in a thorough vibrational analysis of the zinc halide dithiooxamides, $Zn(CH_3NHCSCSNHCH_3)X_2$ and $Zn[(CH_3)_2NCSCSN(CH_3)_2]X_2$ (X = Cl, Br and I).

Raman and IR vibrational spectra of tetramethylcyclobutane-1-one-3-thione (TMCBOT) and of its fully deuteriated derivative TMCBOT-d_{12} have been recorded[331] and a fairly complete set of vibrational frequencies and assignments for both molecules have been given.

Vibrational resonance Raman (RR) and IR spectra as well as normal-mode analysis have been reported[332] for complexes[333] of Fe_2S_2 proteins, as R_4N^+ salts: $(Et_4N)_2^+[Fe_2S_2(SMe)_4]^{2-}$, $[Pr_4N]_2^+[Fe_2S_2(SEt)_4]^{2-}$ and $[Et_4N]_2^+\{Fe_2S_2(S_2\text{-}o\text{-xyl})_2\}^{2-}$ (S_2-*o*-xyl = *o*-xylene-α,α'-dithiolate) and for their isotopomers with ^{34}S at the bridging positions (**277**) and for the xylenedithiolate complex **278** containing[334,335] ^{54}Fe ^{34}S at the terminal positions and ^{2}H at the methylene positions giving valuable isotope shift information. All eigth Fe—S stretching modes have been assigned. Due to coupling of Fe—S stretching with the S—C—C bending mode, the last one has been observed in the RR spectra. The frequencies and isotope shifts have been calculated using a



(277) R = Me, Et



$\overset{*}{S} = {}^{34}S$ (94% enriched) (278)

$\overset{*}{Fe} = {}^{54}Fe$ (97% enriched)

$Fe_2S_2(SEt)_4$ model with point-mass methyl and methylene groups and structural parameters of the *o*-xylenedithiolate complex[334]. The lowest-frequency Fe—S stretching mode, at about 275 cm^{-1}, is an IR-active out-of-phase breathing mode of the two linked FeS_4 tetrahedra, very sensitive to environmental asymmetry. A band of variable intensity at about 200 cm^{-1} is assigned to a mode involving mutual displacement of the Fe atoms (direct interaction of the Fe orbitals is suggested). RR bands in the 120–150 cm^{-1} region are assigned to S—Fe—S bending modes.

The effect of ^{18}O on the ^{31}P NMR chemical shifts for various salts of *O,O*-di-Et[^{18}O]-phosphorothioate in D_2O, 1,4-dioxane and MeCN have been determined[336] and compared with standard values for P—O bond orders. It has been concluded that the P—O bond orders in ion pairs are between 1.5 and 2.0. Ion pairing in organic solvents moderately decreases the P—O bond order by drawing fractional charge away from S and toward O.

S isotopes have been separated[337] in distillation columns at cryogenic temperatures under total reflux. The typical relative volatilities of $^{32}S/^{34}S$ are 1.0023 for H_2S, 0.9978 for SF_4, 0.9985 for SF_6, 1.0006 for COS and 1.0011 for CH_3SH. A $^{12}C/^{13}C$ volatility of 0.9982 was observed in COS. H_2S is considered as the best candidate for separation of sulphur isotopes by distillation. At present the existing distillation columns can produce 50 kg of ^{34}S at 15% enrichment per year, while smaller amounts of more highly enriched isotopes could also be produced.

The ^{34}S exchange equilibria between gaseous, SO_2 and its liquid SO_2 complexes with Bu_2O, anisole and pyridine have been studied at 279–290 K[338]. In the system 'SO_2–anisole·SO_2' the ^{34}S concentrates in the gas phase; in the case of 'SO_2–Bu_2O·SO_2' and 'SO_2–pyridine·SO_2' systems the ^{34}S isotope concentrates in the liquid phase. The observed ^{34}S enrichments are in agreement with theoretically calculated values[339].

Improved separation of the rare sulphur isotopes contained in $^{34}SF_6$ and $^{36}SF_6$ by infrared multiphoton dissociation at 140 K has been tested with CO_2 laser lines. For $^{33}SF_6$, further improvement of the selectivity would be desirable[340].

Isotopically selective two-step laser photodissociation of gaseous carbonyl sulphide, OCS, at 296–150 K has been used to enrich O and S isotopes[341]. A maximum enrichment factor of 4.89 ± 0.5 has been achieved at 150 K for enrichment of ^{18}O. The dependence of isotope enrichment on the densities of OCS, Xe diluent gas and C_2D_4 scavenger has been investigated also.

^{18}O-scrambling within the sulphonate during acetolysis of ^{18}O—^{13}C double labelled β-arylalkyl tosylates has been determined[342] by ^{13}C NMR tracer analysis based on ^{18}O-induced isotope shift and applied to study the ion-pair mechanism of this reaction.

The possibility of $^{32}S/^{34}S$ isotope separation by isotope selective multiphoton dissociation of SF_6 has been shown. The $^{32}SF_6$ adsorption peak disappeared completely and $^{34}SF_6$ was only left after 10 min irradiation with a high-power carbon dioxide lasers[343]. The ^{13}C separation worked also but was not reproducible[343].

A selectivity of > 10, useful for practical isotope separation, has been observed[344] at 0.25 to 0.5 mbar when SF_6 was dissociated by a CO_2 laser at the 1OP20 and 1OP32 lines. Both isotopes diffuse into the beam only after preheating to > 1000 K.

Enriched isotopes of S are becoming attractive for use as tracers in a variety of environmental and scientific experiments[348]. Many stages of separation are needed especially for ^{33}S and ^{36}S, which exist in low natural aboundance. Small amounts of highly enriched sulphur isotopes are provided by means of electromagnetic separation in calutrons. A two-stage process is planned to obtain large amounts of sulphur isotopes using gas centrifuges for pre-enrichment, followed by final enrichment in the calutrons. Thus conversion of enriched isotopes of sulphur from sulphur hexafluoride to a suitable compound for feed to the electromagnetic calutron separators is under study[345].

The sulphur oxidizing bacteria *Thiobacillus neapolitanus* produced cell carbon that was 24.6 to 25.1 mg/g lower in ^{13}C isotope abundance than the ambient source of carbon dioxide and bicarbonate. This ^{13}C isotope depletion was comparable to that found in organic material produced in deep-sea hydrothermal vent communities[346].

^{18}O, ^{32}S and ^{34}S isotope effects in sulphur monoxide molecules have been used in theoretical calculations of molecular parameters of SO isotope molecules[347].

VI. ACKNOWLEDGEMENTS

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CHAPTER 12

Soft metal ion-promoted reactions of organo-sulphur compounds

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I. INTRODUCTION

A few metal ions, especially Ag^+ and Hg^{2+}, have long been known to react readily with organo-sulphur compounds[1]. Often these reactions facilitate changes in the organo-sulphur compound that can also occur more slowly, either spontaneously or under catalysis by hydrogen acids. In a loose sense the metal ions catalyse such changes, but since the metal is frequently consumed as a covalent, and often insoluble, sulphide the processes are better described as metal ion-promoted. A typical example is the hydrolysis of thiolesters in aqueous solvents. This reaction occurs spontaneously, is (feebly) catalysed

Supplement S: The chemistry of sulphur-containing functional groups
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by hydrogen ions[2] (reaction 1) and is greatly accelerated by Hg^{2+} and Ag^{+} ions[3] (reaction 2). In reaction 2 the thiol is formed as a relatively insoluble metal derivative which must subsequently be decomposed if the free thiol is required. A variety of such metal ion-promoted reactions are known, and one of us reviewed[4] the literature relating to thiols, disulphides, thio-ethers, -acetals, -esters, -acids, -anhydrides and -amides in 1977. In these compounds the S atoms are divalent and can interact directly with the metal. Some of their metal ion-promoted reactions have been studied kinetically. In this chapter we treat our earlier review as a foundation. Some parts of the field have since been developed far more than others. Reactions of thiols and thioethers will be dealt with only briefly, and discussion throughout will concentrate on kinetic studies of mechanism. Most of this kinetic work is relatively recent; more is needed.

$$R^1COSR^2 + H_2O \xrightarrow{H_3O^+} R^1CO_2H + R^2SH \quad (1)$$

$$R^1COSR^2 + 2H_2O + Ag^+ \longrightarrow R^1CO_2H + R^2SAg + H_3O^+ \quad (2)$$

One difficulty frequently met in kinetic work is the low solubility of the metal sulphide product, since the presence of a precipitate can interfere with measurements, and can produce (unwanted) auto-catalytic effects. Homogeneous systems can, however, usually be obtained by the careful choice of conditions if UV spectroscopy is used to monitor the reactions, for with this technique the substrate concentration required will usually be very low. (Preparative-scale promotions are normally heterogeneous.) All the reactions reported involve soft (Class B) metal species and have heterolytic (Lewis acid–base) mechanisms.

In general[5] metal ion-catalysed reactions possess certain complications compared with hydrogen ion-catalysed reactions: with hard (Class A) metal ions chelating substrates are normally required, and with any metal ion its attachment to the substrate can induce the ionization of hydrogen atoms; the ionization of water (or other solvent) molecules solvating the ion is also possible. For these reasons metal ion-catalysed or -promoted reactions often display complex pH-dependencies. These complicating features tend to be minimal in soft metal ion-promoted reactions of organo-sulphur compounds, where the rather strong soft–soft interactions available mean that non-chelating substrates can be decomposed, and straightforward kinetic and mechanistic comparisons made with the same reactions when catalysed by hydrogen (Brönsted) acids. In practice catalysis by the proton (a hard acid) is relatively ineffective with S-substrates; that is one reason why the soft metal ion routes outlined in this chapter are important. This relative ineffectiveness means that in studies of the soft metal ion-promotion the contribution of hydrogen ion-catalysis can usually be ignored, and incidentally permits the promoted reactions to be studied at low pH values, conditions which minimize the dissociation of protons both from substrates and from water molecules coordinated to the metal ion.

II. REACTIONS OF THIOLS

Thiols readily form compounds (mercaptides) with metals. Mercaptides of soft metals (reactions 3 and 4) are poorly soluble. Sometimes more than one metal ion is engaged, and Ag^+ ions can lead to polymeric complexes[6]. Mercaptides can be useful in the isolation, identification and quantitative estimation of thiols[7]. They are normally stable but can decompose, especially on heating, to give mainly thioethers (e.g. reaction 5) with sometimes a disulphide or olefin (e.g. reactions 6 and 7). Mercaptide formation followed by reaction 5 or 7 constitutes a metal ion-promoted synthesis from the thiol. The detailed mechanisms of these, and of other similar, essentially heterogeneous processes are unknown.

$$2RSH + Hg(NO_3)_2 \longrightarrow (RS)_2Hg + 2HNO_3 \quad (3)$$

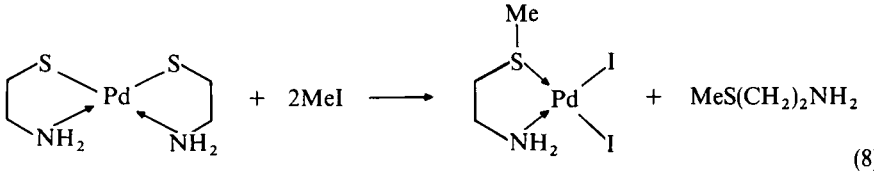
$$RSH + AgNO_3 \longrightarrow RSAg + HNO_3 \xrightarrow{AgNO_3} RSAg_2^+ + NO_3^- + HNO_3 \quad (4)$$

$$(MeS)_2Pb \xrightarrow{heat} Me_2S + PbS \quad (5)$$

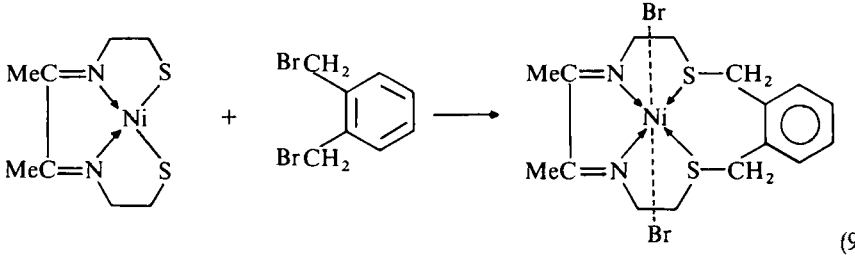
$$(EtS)_2Hg \xrightarrow{heat} EtS{-}SEt + Hg \quad (6)$$

$$(Me_3CS)_2Hg \xrightarrow{heat} Me_3CSH + Me_2C{=}CH_2 + HgS \quad (7)$$

The conversion of thiols into thioethers occurs more readily and cleanly when the mercaptide is treated with an alkyl or aryl halide, especially when the thiolate group is part of a chelate[8] (e.g. reactions 8 and 9). The reactions are conducted either in suspension or in solution in DMF, chloroform or alcohol. Studies under homogeneous conditions with different nickel complexes[8,9] suggest that the alkyl halide forms initially a 5-coordinated intermediate which then undergoes an intramolecular reaction (e.g. equation 10). The reaction of the second alkyl halide is found to be significantly faster



(8)



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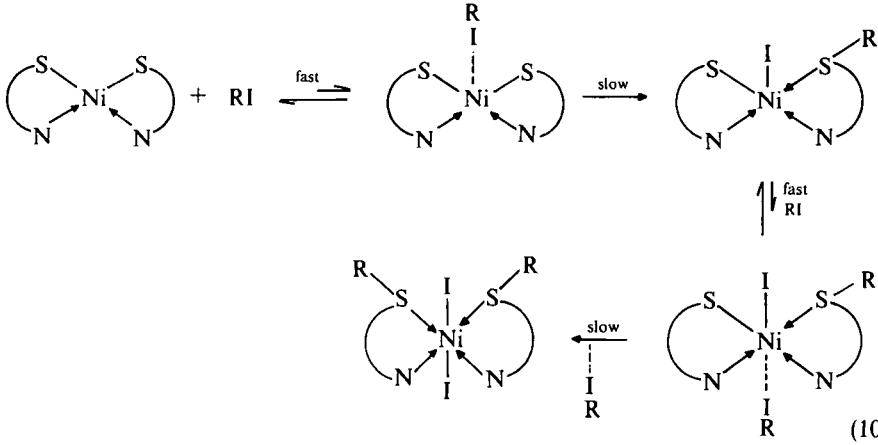
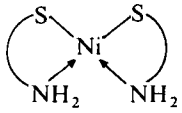


(10)

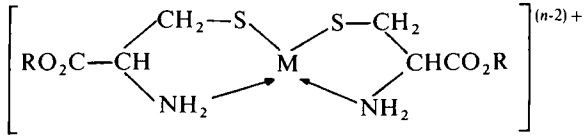
than that of the first, especially when the second step is wholly intramolecular as in reaction 9.

There has been little development in this area since[4] the 1970s, but chelates of β-aminothiols found convenient for thioether synthesis (reactions 8–10) have also been reported[10] to be useful in thiolester formation from such thiols and benzoyl halides (reaction 11). Very high yields of free β-aminothiolester are found with nickel complexes; Cu^{2+} is less effective. It is interesting and significant that acylation occurs at S rather than at N (but see Section V). There is as yet no mechanistic study.



$$+ \ 2PhCOCl \longrightarrow 2PhCOS(CH_2)_2NH_2 + NiCl_2 \quad (11)$$

The great stability of metal chelates involving thiolate ligands has consequences in many contexts. A further example[10] relevant to metal ion-promotion is the preferential coordination of cystein esters as in **1** (rather than via their ester groups) and the consequently relatively feeble catalysis by soft metal ions of the ester hydrolysis in aqueous solution. Other examples are given in Reference 4.



(1)

In promoting the reactions of thiols via mercaptide formation the role of the soft metal is not a straightforward diminution of the electron availability on S by the attachment of a positively charged species, as it is in catalysis by protons, and in most other examples of soft metal ion-promotion to be discussed; rather it involves the replacement of the more polarizing proton on S by the metal ion, when the S atom, although now bonded to the metal, becomes more accessible to attack by other electrophiles: it is a sort of indirect base catalysis brought about by induced ionization of the substrate. This role is analogous to that played by metal ions that accelerate hydrolyses of substrates in water by providing coordinated, but still nucleophilic, OH^- ions via the ionization of metal-bound water molecules[5]. In the examples given (e.g. reactions 10 and 11) the metal is probably sometimes able to activate both substrates, and convert an intermolecular reaction into a (more efficient) intramolecular process. None of these reactions is likely to be catalysed at all by protons. A final example from the older literature[11] involves the synthesis of sulphenamides from thiols (reaction 12).

$$R^1SH + AgNO_3 \longrightarrow R^1SAg + HNO_3 \xrightarrow{R^2_2NCl} R^1SNR^2_2 + AgCl + HNO_3 \quad (12)$$

III. REACTIONS OF THIOETHERS

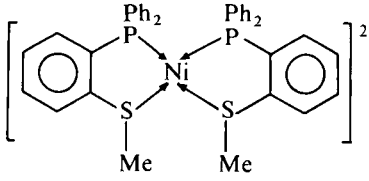
Most thioethers are stable towards attack by electrophiles. They are even less readily cleaved by hydrogen acids than are their O-analogues, and they form only stable addition compounds with more suitable electrophiles including soft metal ions (e.g. reaction 13). Carbon–sulphur bonds are thus difficult to break by electrophilic attack on S. It is found, however, that ethers R^1SR^2 in which R^1 is an aryl group, and R^2 is an alkyl

group having some stability as a carbocation, can be cleaved by soft metal species, especially under forcing conditions. Various lines of evidence[4] suggest that unimolecular cleavage of the C—S bond in the metal–ether complex is involved in the decomposition. For example, in reaction 14 optically active α-methylbenzylmercaptoacetic acid leads to the racemic alcohol[12].

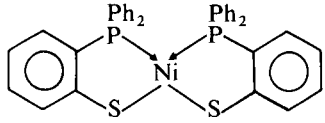
$$2Et_2S + HgCl_2 \longrightarrow (Et_2S)_2HgCl_2 \tag{13}$$

$$PhCH(Me)SCH_2CO_2H + HgCl_2 + H_2O \longrightarrow PhCH(Me)OH + ClHgSCH_2CO_2H + HCl \tag{14}$$

We have seen in Section II how chelated thiols can be alkylated with alkyl halides (reaction 9). The reverse can also occur[13,14] but less readily[15]. Forcing conditions often seem necessary, and also conditions under which it is difficult for the cleaved group to realkylate the S atom (e.g. reaction 15).



$$(ClO_4^-)_2 \xrightarrow[\text{boil}]{\text{EtOH/DMF}} 2MeOEt + 2HClO_4 +$$



(15)

Interesting compounds somewhat analogous to thioethers are the phosphonothiolates. The replacement of EtS^- in diethyl phosphonothiolate by F^- or OH^- in aqueous solution is promoted by silver ions (reactions 16 and 17). In one of the first modern kinetic studies of soft metal ion-promotion Saville[16] showed that the corresponding rate equations are 18 and 19, respectively. Equation 18 suggests the mechanism outlined in reactions 20–23 for the substitution by fluoride. Evidence for two silver ions attached

$$\underset{\text{(2)}}{EtOP(Et)SEt} + F^- + Ag^+ \rightarrow EtOP(Et)F + AgSEt \tag{16}$$

$$\underset{\text{(2)}}{EtOP(Et)SEt} + 2H_2O + Ag^+ \rightarrow EtOP(Et)OH + AgSEt + H_3O^+ \tag{17}$$

$$-d[(2)]/dt = \{k_{16}[Ag^+] + k'_{16}[Ag^+]^2\}[F^-][(2)] \tag{18}$$

$$-d[2]/dt = k_{17}[Ag^+]^2[(2)] \tag{19}$$

$$2 + Ag^+ \rightleftharpoons \underset{\text{(3)}}{EtOP(Et)SEt} \quad \text{fast} \tag{20}$$

$$3 + Ag^+ \rightleftharpoons \underset{\underset{O}{\|}}{EtOP(Et)}\overset{\overset{Ag^+}{\uparrow}}{\underset{\downarrow}{S}}Et \quad \text{fast} \qquad (21)$$

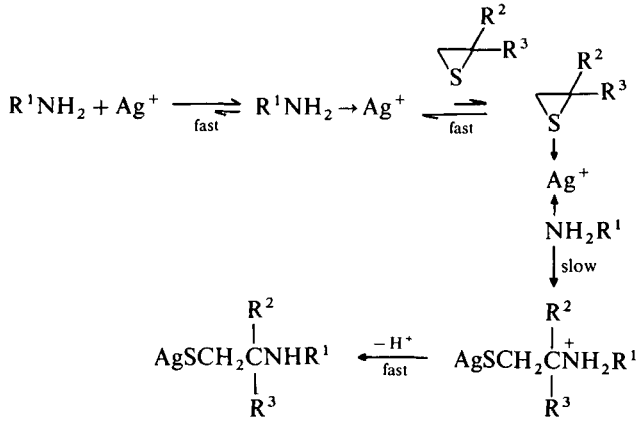
(4)

$$3 + F^- \rightarrow \underset{\underset{O}{\|}}{EtOP(Et)}F + AgSEt \quad \text{slow} \qquad (22)$$

$$4 + F^- \rightarrow \underset{\underset{O}{\|}}{EtOP(Et)}F + [Ag_2SEt]^+ \quad \text{slow} \qquad (23)$$

to sulphur was mentioned in Section I, and kinetic evidence that suggests it has now been found in many other contexts. It seems that attack by neutral water molecules requires powerful promotion of this sort, since no kinetic term first-order in silver is found for reaction 17. The pattern of kinetic behaviour found for these phosphonothiolate reactions has proved to be universal in studies of silver ion promotion with other S-substrates.

Cyclic thioethers have also been cleaved preparatively[17] using Ag^+ ions. An example[18] involving aminolysis is shown in reaction 24. The suggested mechanism is likely to be essentially correct, but kinetic study will probably reveal that $2R^1NH_2$:1 Ag^+ complexes are also involved. More mechanistic work is required on the promoted reactions of thioethers.



(24)

IV. REACTIONS OF DISULPHIDES

The soft metal ion-promoted hydrolysis of disulphides is well known[4], and exploratory kinetic studies were made[19,20] in the 1950s and 1960s. Recently the reaction has been examined in more detail, together with the promoted reaction between disulphides and sulphinate ions which yields thiosulphonate esters[21] (reaction 25). Another similar reaction[22] that still awaits kinetic study is the promoted aminolysis to give sulphenamides

$$RSSR + MeC_6H_4SO_2^- + Ag^+ \longrightarrow RSSO_2C_6H_4Me + RSAg \qquad (25)$$

$$RSSR + ArNH_2 + Ag^+ \xrightarrow{H_2O} RSNHAr + RSAg + H_3O^+ \qquad (26)$$

(reaction 26). Reaction 25 is much faster than the hydrolysis in aqueous solvents, and will be considered first. It has only been studied using promotion by silver ions; it was examined initially[21] for dialkyl disulphides and subsequently[23] for diphenyl disulphide. The mechanism is probably the same for both types of disulphide.

In aqueous ethanol the kinetic form of reaction 25 suggests[23] that Ag^+ ions form complexes both with the disulphide (reactions 27 and 28) and with sulphinate ions (reaction 29). The equilibrium constant for reaction 28 is very small, but those for reactions 27 and 29 can be measured directly for appropriate substrates and compared

$$R_2S_2 + Ag^+ \rightleftharpoons \underset{\textbf{(5)}}{R_2S_2 \rightarrow Ag^+} \qquad \text{fast, } K_{27} \tag{27}$$

$$\mathbf{5} + Ag^+ \rightleftharpoons \underset{\textbf{(6)}}{R_2S_2\begin{matrix}\nearrow Ag^+\\ \searrow Ag^+\end{matrix}} \qquad \text{fast, } K_{28} \tag{28}$$

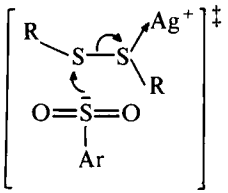
$$\underset{\textbf{(7)}}{MeC_6H_4SO_2^-} + Ag^+ \rightleftharpoons MeC_6H_4\overset{\overset{O^-}{|}}{\underset{\underset{O}{\|}}{S}} \rightarrow Ag^+ \qquad \text{fast, } K_{29} \tag{29}$$

$$\mathbf{5} + \mathbf{7} \longrightarrow RSSO_2C_6H_4Me + RSAg \qquad \text{slow, } k_{30} \tag{30}$$

$$\mathbf{6} + \mathbf{7} \longrightarrow RSSO_2C_6H_4Me + RSAg + Ag^+ \qquad \text{slow, } k_{31} \tag{31}$$

$$-d[R_2S_2]/dt = k_{obs}[R_2S_2] = \{k_{30}[(5)] + k_{31}[\mathbf{6}]\}[\mathbf{7}] \tag{32}$$

with the values deduced from kinetic analysis. Good agreement is found[23]. The overall mechanism is thought to be that given in equations 27–31. It leads to rate equation 32, which, on substitution for species **5**, **6** and **7**, yields an expression containing both first- and second-order terms in $[Ag^+]$ that correctly predicts the observed dependence of k_{obs} on $[Ag^+]$ and provides values of K_{27}, K_{29}, k_{30} and $k_{31}K_{28}$. Most of the reaction is found to take place via step 30 except at the highest silver concentrations. Species **6** is, as expected, more reactive than **5**. At 25 °C for dialkyl disulphides[21], $K_{27} \simeq 50$ $dm^3\,mol^{-1}$ and $k_{30} \simeq 16\,dm^3\,mol^{-1}\,^{-1}$; for diphenyl disulphide[23] $K_{27} \simeq 3\,dm^3\,mol^{-1}$ and $k_{30} \simeq 10^4\,dm^3\,mol^{-1}\,s^{-1}$. These results are in keeping with qualitative expectations about the relative basicities, and the relative reactivities towards nucleophiles, of aliphatic and aromatic disulphides[24]. $K_{29} \simeq 350\,dm^3\,mol^{-1}$ and at high silver ion concentrations the silver sulphinate can be precipitated. The transition state for reaction 30 is probably **8**, in line with other suggestions about the mechanisms of disulphide cleavages[24].



(8)

This reaction of sulphinate ions with disulphides is relevant to the silver ion-promoted hydrolysis of disulphides since the latter reaction is found to proceed via the sulphenic

and sulphinic acids[19,25]. At the high silver ion concentrations required for reasonable rates of hydrolysis, the overall scheme for the hydrolysis of diphenyl disulphide in aqueous dioxane is probably reactions 33–38. This scheme again reflects an observed[25] rate equation containing terms first and second order in $[Ag^+]$. Assuming (reasonably) that $K_{34} \ll 1$, reactions 33–38, lead to equation 39, and the results show that most of the hydrolysis proceeds through **10**, perhaps via transition state **11**, although the species with one silver ion on each S atom could also be involved.

$$Ph_2S_2 + Ag^+ \rightleftharpoons \underset{\textbf{(9)}}{Ph_2S_2 \longrightarrow Ag^+} \qquad \text{fast, } K_{33} \tag{33}$$

$$\textbf{9} + Ag^+ \rightleftharpoons \underset{\textbf{(10)}}{Ph_2S_2\begin{matrix}\nearrow Ag^+\\ \searrow Ag^+\end{matrix}} \qquad \text{fast, } K_{34} \tag{34}$$

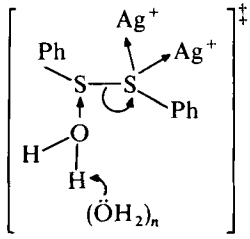
$$\textbf{9} + 2H_2O \longrightarrow PhSAg + PhSOH + H_3O^+ \qquad \text{slow, } k_{35} \tag{35}$$

$$\textbf{10} + 2H_2O \longrightarrow PhSAg + PhSOH + H_3O^+ + Ag^+ \quad \text{slow, } k_{36} \tag{36}$$

$$2PhSOH + H_2O + Ag^+ \longrightarrow PhSAg + PhSO_2H + H_3O^+ \qquad \text{fast} \tag{37}$$

$$Ph_2S_2 + PhSO_2H + H_2O + Ag^+ \longrightarrow PhSAg + PhSSO_2Ph + H_3O^+ \qquad \text{fast} \tag{38}$$

$$k_{obs} = \tfrac{3}{2}(k_{35}K_{33}[Ag^+] + k_{36}K_{34}K_{33}[Ag^+]^2)/(1 + K_{33}[Ag^+]) \tag{39}$$



(11)

The foregoing mechanism applies at pH $\gtrsim 1$. At higher pH a term first order in $[OH^-]$ is found in the rate equation[25]; this represents a route in which an OH^- ion replaces the water molecules in **11**.

The hydrolysis of diphenyl disulphide has also been examined[26] using an aqueous dioxane solvent with promotion by Hg(II) species. The reaction takes a similar course to that found for silver ion promotion except that only a 1:1 complex between the disulphide and Hg(II) species is required to satisfy the kinetic form. With Hg^{2+} the likely mechanism is reactions 40–44. The corresponding rate equation is equation 45 with $K_{40} \simeq 11$ dm^3 mol^{-1} and $k_{41} \simeq 5 \times 10^{-2}$ s^{-1} at 25 °C. With $HgCl^+$ as the promoting ion the corresponding values are 1.8 dm^3 mol^{-1} and 0.2 s^{-1}. This shows that Hg^{2+} is *ca* 6-fold more acidic towards Ph_2S_2 than is $HgCl^+$, but that the complex $Ph_2S_2 \rightarrow HgCl^+$ is attacked by water *ca* 4-fold faster than is **12**. The heats and entropies of formation of such complexes[26] suggest that their stabilities are greatly affected by the extent of desolvation of the metal ion on complex formation, and that freer rotation about the S—S bond is also involved. The overall reactivities of Hg^{2+} and $HgCl^+$ as promoters are similar, but the neutral $HgCl_2$ is *ca* 600-fold less effective. Hg^{2+} is *ca* 5×10^3-fold more reactive than Ag^+. Cd^{2+} and Cu^{2+} ions provide negligible acceleration with diphenyl disulphide at acid pH.

$$Ph_2S_2 + Hg^{2+} \rightleftharpoons Ph_2S_2 \rightarrow Hg^{2+} \quad \text{fast, } K_{40} \tag{40}$$

(12)

$$\mathbf{12} + 2H_2O \longrightarrow PhSHg^+ + PhSOH + H_3O^+ \quad \text{slow, } k_{41} \tag{41}$$

$$2PhSOH + H_2O + Hg^{2+} \longrightarrow PhSHg^+ + PhSO_2H + H_3O^+ \quad \text{fast} \tag{42}$$

$$Ph_2S_2 + PhSO_2H + H_2O + Hg^{2+} \longrightarrow PhSHg^+ + PhSSO_2Ph + H_3O^+ \quad \text{fast} \tag{43}$$

$$2PhSHg^+ \longrightarrow (PhS)_2Hg + Hg^{2+} \quad \text{fast} \tag{44}$$

$$-d[Ph_2S_2]/dt = k_{obs}[Ph_2S_2] = k_{41}K_{40}[Hg^{2+}][Ph_2S_2]/(1 + K_{40}[Hg^{2+}]) \tag{45}$$

V. REACTIONS OF THIOESTERS

Most of the work with thioesters concerns their promoted hydrolysis (reactions 46 and 47) or aminolysis (reaction 48). These reactions have also been known for many years[4]. Early qualitative reports about the relative effectiveness of different soft metal ions are not entirely in agreement, but it was clear that Hg^{2+} and Ag^+ could promote hydrolysis, with Hg^{2+} particularly effective. For aminolysis Schwyzer's preparative experiments[27] suggest the sequence $Pb^{2+} < Cu^{2+} < Hg^{2+} < Ag^+$.

$$R^1COSR^2 + 2H_2O + Hg^{2+} \longrightarrow R^1CO_2H + H_3O^+ + R^2SHg^+ \tag{46}$$

$$R^1CSOR^2 + 3H_2O + 2Ag^+ \longrightarrow R^1CO_2R^2 + 2H_3O^+ + Ag_2S \tag{47}$$

$$R^1COSR^2 + R^3NH_2 + Ag^+ + H_2O \longrightarrow R^1CONHR^3 + H_3O^+ + R^2SAg \tag{48}$$

Subsequent kinetic studies[3,28–33] of the promoted hydrolysis of the ethyl thiolesters p-RC_6H_4COSEt in aqueous solution with a variety of metal perchlorates have revealed a rather coherent pattern of behaviour. With the most powerful metal ions Hg^{2+}, Hg_2^{2+} and Tl^{3+} the rate equation has the simple form of equation 49, and the substituent effects, activation parameters and isotope effects suggest there is a transition from an A1-like mechanism (reaction 50) when R is electron-releasing (e.g. MeO) to an A2-like mechanism (reaction 51) when R is electron-withdrawing (e.g. NO_2). With Ag^+ ions the rate equation 52 again shows evidence for the involvement of two silver ions, and both reaction paths, 53–54 and 55–56, involve an A2-like scheme for all esters.

$$-d[\text{S-ester}]/dt = k[M^{n+}][\text{S-ester}] \tag{49}$$

$$p\text{-}RC_6H_4COSEt + M^{n+} \overset{\text{fast}}{\rightleftharpoons} p\text{-}RC_6H_4COS \begin{matrix} \nearrow M^{n+} \\ \searrow Et \end{matrix} \tag{50}$$

(13)

$$\downarrow \text{slow}$$

$$p\text{-}RC_6H_4CO_2H + EtSM^{(n-1)+} \xleftarrow[2H_2O]{\text{fast}} p\text{-}RC_6H_4\overset{+}{C}O + EtSM^{(n-1)+} + H_3O^+$$

$$\mathbf{13} + H_2O \xrightarrow{\text{slow}} p\text{-}RC_6H_4C\begin{matrix} =O \\ {}^{+}OH_2 \end{matrix} + EtSM^{(n-1)+} \tag{51}$$

$$H_2O \downarrow \text{fast}$$

$$p\text{-}RC_6H_4CO_2H + EtSM^{(n-1)+} + H_3O^+$$

$$-\mathrm{d[S\text{-}ester]}/\mathrm{dt} = \{k_1[Ag^+] + k_2[Ag^+]^2\}[\text{S-ester}] \quad (52)$$

$$p\text{-}RC_6H_4COSEt + Ag^+ \overset{\text{fast}}{\rightleftharpoons} \underset{\textbf{(14)}}{p\text{-}RC_6H_4COS}\begin{matrix}\nearrow Ag^+\\ \searrow Et\end{matrix} \quad (53)$$

$$\textbf{14} + H_2O \xrightarrow{\text{slow}} p\text{-}RC_6H_4CO_2H_2^+ + EtSAg \xrightarrow[H_2O]{\text{fast}} p\text{-}RC_6H_4CO_2H + H_3O^+ + EtSAg \quad (54)$$

$$\textbf{14} + Ag^+ \overset{\text{fast}}{\rightleftharpoons} \underset{\textbf{(15)}}{p\text{-}RC_6H_4COS}\begin{matrix}\nearrow Ag^+\\ \rightarrow Ag^+\\ \searrow Et\end{matrix} \quad (55)$$

$$\textbf{15} + H_2O \xrightarrow{\text{slow}} p\text{-}RC_6H_4CO_2H_2^+ + EtSAg_2^+ \xrightarrow[H_2O]{\text{fast}} p\text{-}RC_6H_4CO_2H + H_3O^+ + EtSAg_2^+ \quad (56)$$

With all the thiolesters and metal ions the pre-equilibria lie well to the left, and the complexes are not spectroscopically detectable under the kinetic conditions. In the A1-like reactions the sequence of metal ion efficiency is $Hg^{2+} > Hg_2^{2+} \simeq Tl^{3+}$; for the A2-like routes the sequence is $Hg^{2+} > Hg_2^{2+} \gg Tl^{3+} \simeq Ag^+$. It has been suggested[29] that the A2-like routes involve intramolecular attack by water coordinated to the metal ion; this may explain the surprisingly low reactivity of Tl^{3+} ions in the A2 mechanism. Hg^{2+} and Ag^+ ions are respectively *ca* 10^6 and 10^3-fold more effective in these hydrolyses than is the H_3O^+ ion. These are fairly typical values throughout the field. Other (borderline) soft metal ions tested (Pb^{2+}, Cu^{2+}, Ni^{2+}, Cd^{2+}) are even less effective (at acid pH) than is H_3O^+.

Almost all metal ion-catalysed and -promoted reactions are believed to occur via pre-equilibria in which the metal becomes rapidly attached to the substrate, some subsequent step being rate-determining, as in the mechanisms outlined so far in this chapter. In Brönsted acid-catalysed reactions rapid pre-equilibrium mechanisms (A1, A2) also greatly predominate, but many examples of slow proton transfer to the substrate (AS_E2) are known too. Slow proton transfer can be regarded as the displacement of H_2O from H_3O^+, or of A^- from HA, by the substrate. One soft metal ion-promoted reaction that probably involves an analogous slow metal ion transfer is the $AuCl_4^-$ ion-promoted hydrolysis of thiolesters[31]. In this case, when interacting with the metal centre the substrate has to displace Cl^- rather than H_2O (reaction 57). Substituent and isotope effects, and activation parameters, are all compatible with the mechanism of reactions 57 and 58, and the absence of a common ion effect at high chloride ion concentrations argues against reaction 57 being a rapid equilibrium. At low ambient Cl^- and H_3O^+ concentrations, $AuCl_4^-$ exists in aqueous solution in equilibrium with $AuCl_3H_2O$ and $AuCl_3OH^-$. These species also promote the thiolester hydrolysis, with $AuCl_3H_2O$ being more effective than either $AuCl_4^-$ or $AuCl_3OH^-$; this may be[31] because H_2O is more easily lost from the gold centre than is Cl^- or OH^-.

$$p\text{-}RC_6H_4COSEt + AuCl_4^- \xrightarrow{\text{slow}} \underset{\textbf{(16)}\quad Et}{p\text{-}RC_6H_4COS} \longrightarrow AuCl_3 + Cl^- \quad (57)$$

$$\textbf{16} + 2H_2O \xrightarrow{\text{fast}} p\text{-}RC_6H_4CO_2H + EtSAuCl_3^- + H_3O^+ \quad (58)$$

The soft metal ion-promoted hydrolysis of a thionester (reaction 47) proceeds much (*ca* 10^6-fold) faster than that of its thiol analogue. This great difference in reactivity was once used to estimate the composition of thion–thiol mixtures[32]. It probably arises because the pre-equilibrium in reaction 59 lies further to the right than does that in reaction 50, and because the positive charge can more easily be delocalized to the carbonyl carbon atom in **17** than in **13**. Preliminary kinetic studies[33] with thionesters show that a similar pattern of soft metal ion reactivity is found to that obtained for thiolesters, but that the mechanism of hydrolysis is A2-like (reactions 59 and 60).

$$p\text{-}RC_6H_4CSOEt + M^{n+} \overset{\text{fast}}{\rightleftharpoons} p\text{-}RC_6H_4C(=S \longrightarrow M^{n+})(OEt) \qquad (59)$$

(17)

$$\mathbf{17} + H_2O \xrightarrow{\text{slow}} p\text{-}RC_6H_4C(SM^{(n-1)+})(OH_2)(OEt) \xrightarrow{2H_2O} p\text{-}RC_6H_4CO_2Et + MS^{(n-2)+} + 2H_3O^+ \qquad (60)$$

Two other classes of thiolester have had their metal ion-promoted hydrolysis studied kinetically: *N*-aryl thiolurethanes and thiol benzimidate esters. Both show interesting features.

For thiolurethanes the following series were studied with Tl^{3+} ions in aqueous acid solution[34]. In the absence of Tl^{3+} ions the reaction is very slow, especially at pH $\gtrsim 2$

$C_6H_5NHC(O)SC_6H_4R\text{-}p$ **(18)** R = MeO, H, Cl

$p\text{-}RC_6H_4NHC(O)SEt$ **(19)** R = MeO, H, Cl

when the elimination–addition mechanism of hydrolysis[35] (reaction 61), which is significant for compounds **18** at higher pH, is suppressed. In the presence of Tl^{3+} ions both **18** and **19** lead to the corresponding aniline (or anilinium ion) and the thalliium salt of the thiol as the only organic products (reactions 62 and 63). The effects of variation in $[Tl^{3+}]$ and $[H_3O^+]$ show that significant amounts of 1:1 Tl^{3+} -S-ester complexes are formed, and that these react preferentially in their deprotonated forms. The observed rate equation for both types of ester takes the form of equation 64, where *a*, *b*, *c* and *d* are constants. The mechanism of reactions 65–69 is compatible with this equation, with the positive $\Delta S^{\ddagger}$ values, and with the small effects produced by substituents R which will exert opposing influences on the different steps[34].

$$ArNHCOSAr + H_2O \rightleftharpoons ArN\overset{\cdots}{C}(SAr)\text{—}O + H_3O^+ \qquad (61)$$

$$ArNH_2 + CO_2 \longleftarrow [ArNHCO_2H] + ArSH \xleftarrow[H_2O]{H_3O^+} ArNCO + ArS^- + H_3O^+$$

$$ArNHCOSEt + H_2O + Tl^{3+} \xrightarrow{H_3O^+} ArNH_3^+ + EtSTl^{2+} + CO_2 \qquad (62)$$

$$ArNHCOSAr + H_2O + Tl^{3+} \xrightarrow{H_3O^+} ArNH_3^+ + ArSTl^{2+} + CO_2 \qquad (63)$$

$$-\mathrm{d[S\text{-}ester]}/\mathrm{d}t = \frac{(a[Tl^{3+}] + b[Tl^{3+}]/[H_3O^+])[\mathrm{S\text{-}ester}]}{(1 + c[Tl^{3+}] + d[Tl^{3+}]/[H_3O^+])} \tag{64}$$

$$\mathbf{18} + Tl^{3+} \overset{\text{fast}}{\rightleftharpoons} \underset{\text{(or 19)}}{\underset{\downarrow}{\underset{\mathbf{(20)}}{\mathrm{PhNHC}(=O)(SC_6H_4R)}}\ Tl^{3+}} \tag{65}$$

$$\mathbf{20} + H_2O \overset{\text{fast}}{\rightleftharpoons} \underset{\mathbf{(21)}}{\underset{\downarrow}{\mathrm{PhN{-}C(=O)(SC_6H_4R)}}\ Tl^{3+}} + H_3O^+ \tag{66}$$

$$\mathbf{20} \xrightarrow[H_2O]{\text{slow}} \mathrm{PhN{=}C{=}O} + H_3O^+ + \mathrm{ArSTl^{2+}} \tag{67}$$

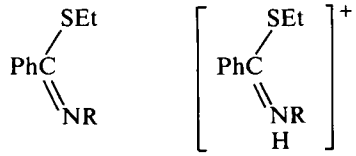
$$\mathbf{21} \xrightarrow{\text{slow}} \mathrm{PhN{=}C{=}O} + \mathrm{ArSTl^{2+}} \tag{68}$$

$$\mathrm{PhNCO} + H_2O \xrightarrow[H_3O^+]{\text{fast}} [\mathrm{PhNHCO_2H}] \xrightarrow[H_3O^+]{H_2O} \mathrm{PhNH_3^+} + CO_2 \tag{69}$$

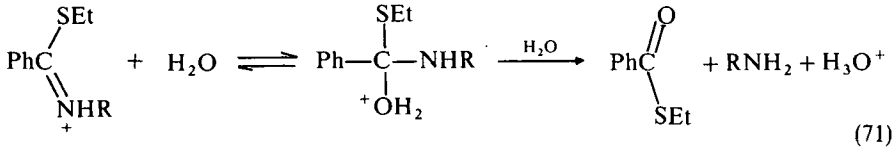
Confirmation that loss of the N-bound proton is essential in the reactions of esters **18** is the negligible reactivity observed for the *N*-methyl derivative $\mathrm{PhN(Me)C(O)SC_6H_4Cl}$. What is evidently happening in this system is that the elimination–addition mechanism of hydrolysis that is important in aqueous solutions at pH 4–5 in the absence of metal ions, is being made available at low pH owing to the formation of a much-improved leaving group containing the metal ion. Routes via steps 67 and 68 correspond to E2 and E1cB eliminations, respectively. It is believed that esters **19** can also employ mechanism 65–69, but an A1-like mechanism (reaction 70) is also available since in this case the *N*-methyl derivative PhN(Me)C(O)SEt is much more reactive than the corresponding N—H compound. This A1 mechanism is analogous to that found[29] in Tl^{3+} ion-promotion of other thiolesters containing electron-releasing substituents (see above). Thiolurethanes are, as a class, much more (*ca* 10^4-fold) reactive than the simpler esters ArCOSEt in Tl^{3+} ion-promotion. The insertion of the NH or NR group is likely to improve both the pre-equilibrium position and the rate of the slow step.

$$\begin{array}{l} \mathrm{PhN(Me)COSEt} + Tl^{3+} \overset{\text{fast}}{\rightleftharpoons} \underset{\downarrow}{\mathrm{PhN(Me)C(=O)(SEt)}}\ Tl^{3+} \xrightarrow{\text{slow}} \mathrm{PhN(Me)\overset{+}{C}O} + \mathrm{EtSTl^{2+}} \\ \qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad \Big\downarrow \text{fast}\ 2H_2O \\ \mathrm{PhN\overset{+}{H}_2Me} + CO_2 + H_2O + \mathrm{EtSTl^{2+}} \xleftarrow{\text{fast}} [\mathrm{PhN(Me)CO_2H}] + H_3O^+ + \mathrm{EtSTl^{2+}} \end{array} \tag{70}$$

Thiol benzimidate esters (e.g. **22**) are relatively basic, and in dilute aqueous solutions of Brönsted acids they exist very largely in their protonated form, **23**. Hydrolysis proceeds slowly under such conditions and leads[36] initially to the thiolester (reaction 71) which undergoes further slow hydrolysis to the acid, $\mathrm{PhCO_2H}$. The rate of hydrolysis of **23**, R = H or R = C_6H_{11}, in dilute acid has been shown[37] to be unaffected by the presence of Ag^+ ions, so that any Ag^+-substrate complexes formed must be rather stable. The presence of silver ions does, however, affect the products that can be isolated because,



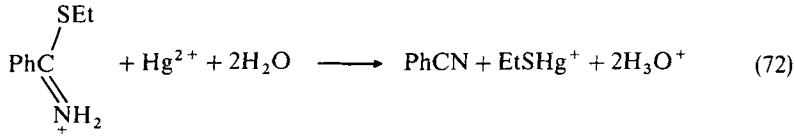
(22) (23)



(71)

under such conditions, the thiolester is relatively rapidly desulphurized (see reactions 53–56).

In the presence of Hg^{2+} ions (or Tl^{3+} or $AuCl_4^-$) a considerable increase in the rate of loss of thiol benzimidate ester occurs[37]. When R = H in **23** the product is benzonitrile (reaction 72) but if $R = C_6H_{11}$ it is the corresponding O-amide (reaction 73). The rate equation for reaction 72 involves both first- and second-order terms in $[Hg^{2+}]$ and in $[H_3O^+]$, and a mechanism including S—N chelates of Hg^{2+}, **24** and **25** has been suggested. For reaction 73, the rate equation 74 is simpler, and the mechanism of reactions 75–78 is likely. The need for an uncharged N atom in reaction 76 and the likelihood that **26** is chelated (cf species **24** and **25**) is shown[37] by the complete unreactivity of compound **27**.



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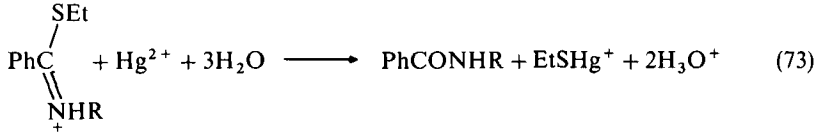
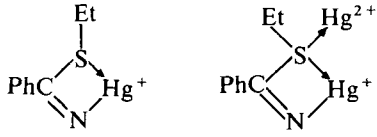


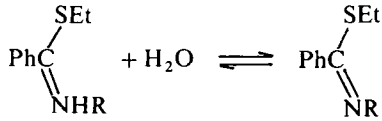
(73)

$$-d[(23)]/dt = k[Hg^{2+}][(23)]/[H_3O^+] \quad (74)$$



(24) (25)

By comparison with hydrolysis, there has been little study of soft metal ion-promoted aminolysis of thiolesters of any type. As noted above, Schwyzer's preparative yields[27]



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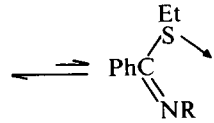

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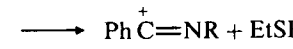

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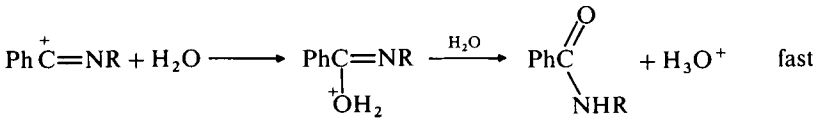

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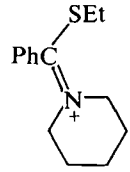
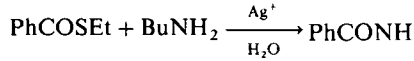


(27)

suggest that $Ag^+ > Hg^{2+} > Cu^{2+} > Pb^{2+}$ is the sequence of effectiveness. So far kinetic work is compatible with this conclusion, although it should be remembered that in preparative work extra (heterogeneous) catalytic effects can be present. The homogeneous *n*-butylaminolysis of ethyl thiolbenzoate (reaction 79) in aqueous solution over a range of pH values in the presence of Ag^+ ions yields[38] a kinetic pattern which shows that the reaction occurs between the known 1:1 and 2:1butylamine–Ag^+ complexes and the thiolester, probably via transition states in which the amine reacts intramolecularly with the ester, **28** and **29**, as first suggested by Schwyzer. A similar mechanism has been proposed[39] for the Ag^+ ion-promoted cyclohexylaminolysis of the ester **30**. In this reaction the SH group acquires two Ag^+ ions to which the ester carbonyl group is believed to coordinate, whilst the Ag^+–hexylamine complexes attack the ester S atom as in **28** and **29**.



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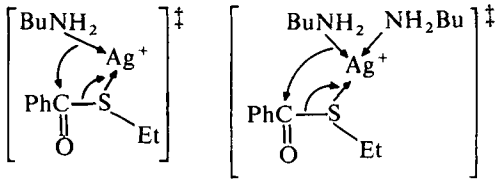
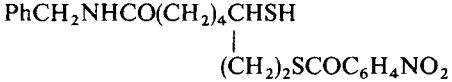


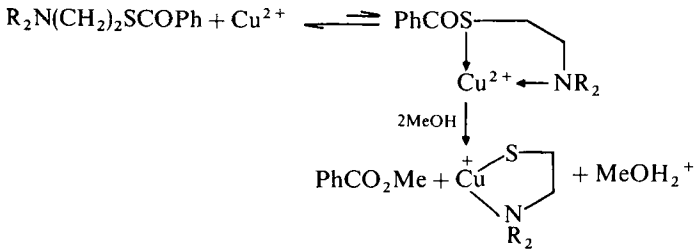
(28) (29)



(30)

No kinetic work involving promotion by Cu^{2+} or Pb^{2+} ions appears to exist, but a recent study[40] using ethyl thiolbenzoate and *n*-butylamine with Hg^{2+} ions indicates that this ion forms complexes with amines that are indeed less effective in bringing about aminolysis than those of Ag^+ (as found by Schwyzer)[27]. This surprising result (Hg^{2+} is normally a much more powerful promoter than Ag^+) possibly arises from a feature of intramolecular reactions between species both coordinated to a metal centre observed in reactions of isocyanates[41]. If an electrophile and a nucleophile that can react intermolecularly are both coordinated to the same (catalytic) metal atom, so that the intermolecular process is converted into an intramolecular reaction, then the overall catalytic efficiency passes through a maximum either as the nucleophilicity of the nucleophile is increased, or as the (Lewis) acidity of the metal centre increases. This effect arises because when the interaction between the nucleophile and the metal is too weak rather little complex is formed, whereas when it is too strong the nucleophilicity of the bound nucleophile is too greatly diminished. In the complexes between Hg^{2+} and butylamine the residual nucleophilicity of the butylamine may be so small that the corresponding Ag^+ complexes are more effecive in transition states like **28** and **29**, even though the activation of the S-ester will be greater in the Hg^{2+} system.

Various pieces of evidence given in this chapter taken together suggest that for soft ions as weak as Cu^{2+} and Pb^{2+} to provide significant promotion with S-substrates, either an anionic or a chelating substrate is required (to give sufficient interaction between metal ion and substrate) and/or a reaction mechanism involving an intramolecular step. The success[27] of preparative aminolyses using Cu^{2+} or Pb^{2+} may depend upon the intramolecular nature of the aminolyses. Another example[42] of the successful use of Cu^{2+} ions with thiolesters, this time involving chelating substrates, is the preparative solvolysis[43] of *β*-amino thiolesters in methanol (reactions 80 and 81). A similar promoted alcoholysis[43] using Ag^+ ions (reaction 82) might also succeed with Cu^{2+} ions.



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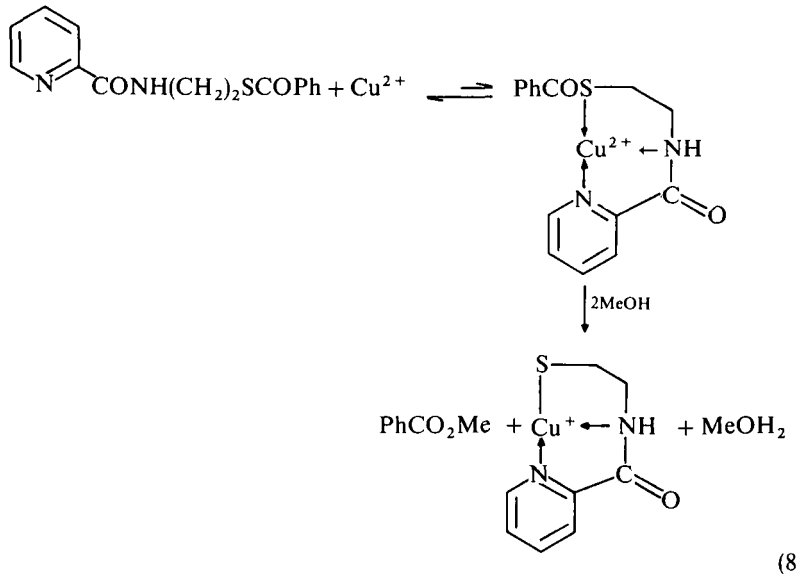

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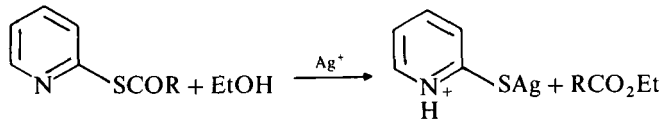
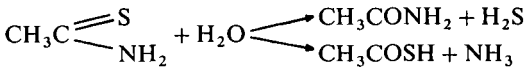


(82)

VI. REACTIONS OF THIOAMIDES

In the 1950s it was found that thioacetamide could be used as an alternative to hydrogen sulphide for precipitating a variety of soft metal ions from aqueous solution as their sulphides[44]. The reactions leading to metal sulphide formation depend upon the pH and upon the metal. Normally[44,45] thioacetamide undergoes fast hydrolysis in solution to hydrogen sulphide and/or thioacetic acid (reaction 83). Both of these compounds can



(83)

then lead rapidly to the metal sulphide (see Section VII for reactions of thioacids). However, under certain conditions a direct reaction between thioacetamide and the metal ion occurs whose rate decreases as the pH falls. The original work[44] on all these reactions involved heterogeneous conditions, and was mainly concerned with rates of precipitation. The organic products were never identified. Subsequently the direct reaction has been studied[46]kinetically with three of the metal ions (Co^{2+}, Cd^{2+} and Pb^{2+}) under homogeneous conditions using acetate buffers (mostly at pH $\approx$ 6). Under the conditions used almost all of the metal ions existed as either $MOAc^+$ or MCl^+. These species were shown to form complexes with thioacetamide via the S atom, and the final organic product was found to be acetonitrile (and not the O-amide, reaction 84). By working at lower pH the free M^{2+} ions were shown to be less effective than the hydrogen ion in hydrolysing (or decomposing) thioacetamide. Although a detailed

mechanism was not suggested for the reaction at higher pH, it was considered[46] probable that the deprotonated complexes **31** were the most reactive species. A cyclic transition state looks possible for the final step of reaction 84, in line with comments made in Section V about the reactivity of borderline soft metal ions.

$$\mathrm{MeC(S)NH_2 + [MOAc]^+ \rightleftharpoons [MeC(NH_2)=S \rightarrow MOAc]^+ \underset{H_3O^+}{\overset{H_2O}{\rightleftharpoons}} MeC(NH)—S—MOAc \; (\mathbf{31}) \longrightarrow AcOH + MeCN + MS} \tag{84}$$

The detailed kinetics of some analogous reactions involving thiobenzamide and N-substituted thiobenzamides have also been investigated[47–51], using homogeneous solutions in dilute aqueous perchloric acid. These amides undergo direct reactions with free Hg^{2+}, Ag^+, Cu^{2+} and Tl^{3+} ions at 25 °C over a range of perchloric acid concentrations in which the hydrogen ion-catalysed hydrolysis is negligible. With thiobenzamide the products were always benzonitrile and the metal sulphide (e.g. reaction 85).

$$\mathrm{PhC(S)NH_2 + Hg^{2+} + 2H_2O \longrightarrow PhCN + HgS + 2H_3O^+} \tag{85}$$

The mercury reaction[48] can serve as an example. Here a 2:1 S-amide:Hg^{2+} complex is formed stoichiometrically and rapidly under all concentration conditions. This complex is stable, but reacts further in the presence of an excess of Hg^{2+} ions. At any fixed value of $[H_3O^+]$ the rate equation is 86 and as $[H_3O^+]$ is raised k_{obs} falls to reach a constant minimum value when $[H_3O^+] \gtrsim 1.0$ mol dm^{-3}. These facts, the detailed dependencies on $[H_3O^+]$ of k_{obs} and of the spectrum of the 2:1 complex, and the behaviour of N-substituted thiobenzamides (see below) all point to the mechanism of reactions 87–95.

$$-\mathrm{d[2{:}1\ complex]}/dt = k_{obs}[Hg^{2+}][\mathrm{2{:}1\ complex}] \tag{86}$$

$$\mathrm{PhC(S)NH_2 + Hg^{2+} \overset{fast}{\rightleftharpoons} PhC(NH_2)=S \rightarrow Hg^{2+}} \quad (\mathbf{32}) \tag{87}$$

$$\mathbf{32} + \mathrm{PhC(S)NH_2} \overset{fast}{\rightleftharpoons} (\mathrm{PhC(NH_2)=S}\rightarrow)_2\mathrm{Hg^{2+}} \quad (\mathbf{33}) \tag{88}$$

$$\mathbf{32} + \mathrm{H_2O} \overset{fast}{\rightleftharpoons} \mathrm{PhC(NH)—S—Hg^+ + H_3O^+} \quad (\mathbf{34}) \tag{89}$$

$$\mathbf{33} + \mathrm{H_2O} \overset{fast}{\rightleftharpoons} \mathrm{PhC(NH_2)=S \rightarrow Hg^+—S—C(NH)—Ph + H_3O^+} \quad (\mathbf{35}) \tag{90}$$

$$\mathbf{35} + \mathrm{H_2O} \overset{fast}{\rightleftharpoons} (\mathrm{PhC(NH)—S}\rightarrow)_2\mathrm{Hg + H_3O^+} \quad (\mathbf{36}) \tag{91}$$

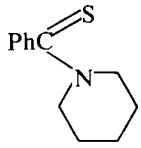
$$\mathbf{33} + Hg^{2+} \xrightarrow{\text{slow}} 2\,\mathbf{32} \tag{92}$$

$$\mathbf{35} + Hg^{2+} \xrightarrow{\text{slow}} \mathbf{32} + \mathbf{34} \tag{93}$$

$$\mathbf{36} + Hg^{2+} \xrightarrow{\text{slow}} 2\,\mathbf{34} \tag{94}$$

$$\mathbf{34} \xrightarrow{\text{fast}} PhC{\equiv}\overset{+}{N}H + HgS \xrightarrow{H_2O} PhCN + HgS + H_3O^+ \tag{95}$$

In this scheme for Hg^{2+} ion-promotion only the deprotonated 1:1 complex **34** leads to the products. The need for N-bound protons is shown by the negligible reaction undergone by **37**. N-monosubstituted thiobenzamides, **38**, display[48] a kinetic form in keeping with reactions 87–95, but modified to include only one N—H ionization, and a product-forming step equation 96; these S-amides can only lead to the corresponding O-derivatives (cf reactions 72 and 73 for the thiobenzimidate ester hydrolysis).



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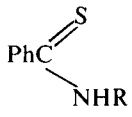

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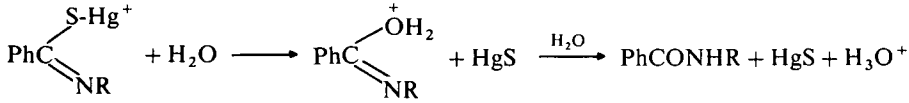


(96)

The reactions of Ag^+ and of Cu^{2+} with thiobenzamides are broadly analogous to those of Hg^{2+}. With Ag^+ only 1:1 complexes **39** (reaction 97) are formed[47]. For thiobenzamide the rapidly and stoichiometrically formed complex undergoes just one N—H ionization to **40** and the slow steps are equations 98 and 99.

$$PhC(S)NH_2 + Ag^+ \rightleftharpoons \underset{\underset{NH_2}{|}}{PhC{=}S}\rightarrow Ag^+ \underset{H_3O^+}{\overset{H_2O}{\rightleftharpoons}} \underset{\underset{NH}{\|}}{PhC\text{-}SAg} \tag{97}$$

(39) (40)

$$\mathbf{40} \longrightarrow PhC{\equiv}\overset{+}{N}H + AgS^- \tag{98}$$

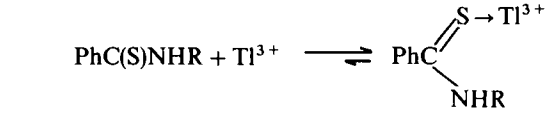
$$\mathbf{39} + H_2O \longrightarrow PhC{\equiv}\overset{+}{N}H + H_3O^+ + AgS^- \tag{99}$$

With Cu^{2+} ions the reaction is similar[49], except that only a low concentration of (possibly N,S-chelated) 1:1 complex is formed. The qualitative sequence of relative reactivities of these metal ions is $Hg^{2+} > Ag^+ \gg Cu^{2+}$. As with thioacetamide (see above), the borderline soft ions Pb^{2+}, Cd^{2+}, Tl^+ and Ni^{2+} have less effect in decomposing thiobenzamides at moderate ambient hydrogen ion concentrations than does H_3O^+ itself[47].

The long-established[52] desulphurization of thioureas [$(R_2N)_2C{=}S$ where R=H or alkyl] by mercury or lead species, under mildly alkaline conditions, shows a qualitative

behaviour pattern reminiscent of the thioamide reactions discussed above. Here again the ability to lose N-bound protons is apparently a crucial feature.

The direct reactions of Tl^{3+} and $AuCl_4^-$ ions with thiobenzamides in dilute aqueous perchloric acid are also of interest[50,51]. These ions have reactivities comparable to that of Hg^{2+}. With an excess of metal ion over thiobenzamide, they both lead to rapid stoichiometric 1:1 complex formation (reactions 100 and 101). For these complexes, in contrast to those of Hg^{2+}, Ag^+ and Cu^{2+}, their subsequent decomposition is not facilitated by the ionization of N-bound protons. This fact permits tertiary amides such as *N*-thiobenzoylpiperidine (**37**) to be desulphurized at rates comparable to those found for thiobenzamide and *N*-cyclohexyl thiobenzamide. For the gold reaction[51] the steps following equation 101 are believed to be given by scheme 102. Changes in the ambient chloride ion concentration show that desulphurization also occurs via **42** at low, and via **43** at high, chloride ion concentrations, these complexes being more reactive than **41**. The gold(III) ions **44**–**47** also promote the hydrolysis of thioamides[53]. With **44**–**46** the mechanism is similar to reactions 101 and 102, but for **47** a slow substitution by the S-amide at gold is believed to control the rate. This is another, as yet rare, slow metal transfer mechanism (cf reaction 57 for S-esters).



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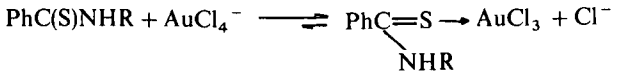
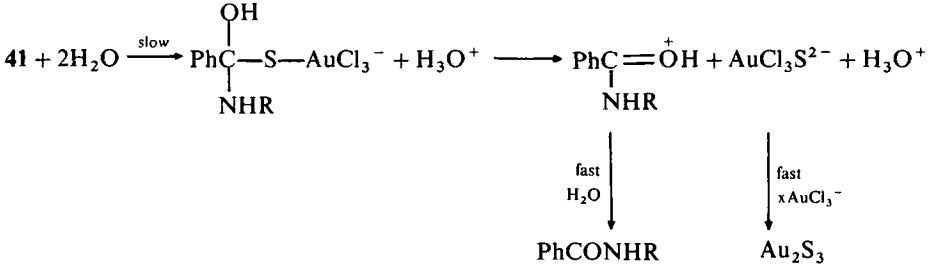


(101)

(41)



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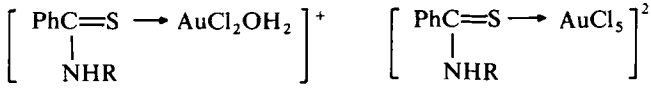


(42) **(43)**

$[Au(dien)Cl]^{2+}$ $[Au(dien\text{-}H)Cl]^+$ $[Au(NH_3)_4]^{3+}$

(44) **(45)** **(46)**

$[Au(phen)Cl_2]^+$ (dien = diethylene triamine; phen = 1,10-phenanthroline)

(47)

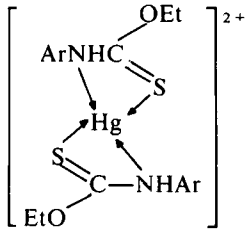
In the thallium ion reaction[50] not only is k_{obs} independent of $[H_3O^+]$, but it is inversely related to the excess thallium ion concentration. This effect suggests that the reactive complex is a 2:1 S-amide: Tl^{3+} species whose low equilibrium concentration falls proportionately as $[Tl^{3+}]$ is increased. Why the 2:1 complex should be the more reactive species in this case is not obvious; the reverse is found with mercury (see reactions 87–95).

Quite recently the kinetics of hydrolysis in dilute aqueous acid of some thionurethanes (**48**) has been studied[54], with promotion by Hg^{2+} ions (reaction 103). Thionurethanes

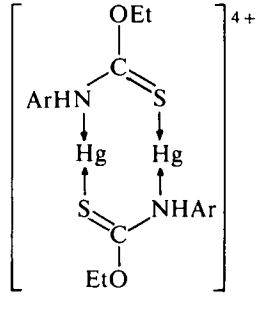
$$p\text{-}RC_6H_4NHC(S)OEt \quad (R = MeO, Me, H, Cl, NO_2)$$

(48)

are both thionesters and thioamides; the results are therefore of particular interest in view of the work described above. Except for the p-NO_2 derivative, it is found that the kinetic behaviour of these thionurethanes is similar, although not identical, to that found for the desulphurization of thiobenzamides (equation 86). A stable 2:1 thionurethane: Hg^{2+} complex (**49**) is again formed rapidly and stoichiometrically, and as for thiobenzamides, if an excess of Hg^{2+} ions is present the 2:1 complex is partially converted into a (reactive) complex of lower stoichiometry. However, with the thionurethanes the rate equation 104 for loss of the 2:1 complex is not simple first order in $[Hg^{2+}]$ as is equation 86, but shows evidence of significant equilibrium complex formation between the 2:1 complex and the excess of Hg^{2+} ions. The new complex formed is believed to be a 2:2 complex (**50**), and the overall mechanism that of reactions 105–108. The cor-



(49)



(50)

$$\mathbf{48} + Hg^{2+} + 2H_2O \longrightarrow p\text{-}RC_6H_4NHCO_2Et + HgS + 2H_3O^+ \qquad (103)$$

$$-\,d[2{:}1\ \text{complex}]/dt = \frac{a[Hg^{2+}]\,[2{:}1\ \text{complex}]}{(1 + b[Hg^{2+}])}$$

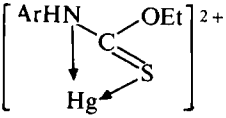
$$= k_{obs}\,[2{:}1\ \text{complex}] \qquad (104)$$

$$2\,\mathbf{48} + Hg^{2+} \rightleftharpoons \mathbf{49} \quad \text{fast} \qquad (105)$$

$$\mathbf{49} + Hg^{2+} \rightleftharpoons \mathbf{50} \quad \text{fast}, K \qquad (106)$$

$$\mathbf{50} + 3H_2O \longrightarrow p\text{-}RC_6H_4NHCO_2Et + HgS + 2H_3O^+$$

$$+ \quad \text{slow}, k \qquad (107)$$



(51)

$$\mathbf{51} + 3H_2O \longrightarrow p\text{-}RC_6H_4NHCO_2Et + HgS + 2H_3O^+ \quad \text{fast} \tag{108}$$

$$k_{obs} = kK[Hg^{2+}]/(1 + K[Hg^{2+}]) \tag{109}$$

responding rate equation is equation 109, in keeping with equation 104. With the p-NO_2 derivative of **48** the 2:2 complex is formed stoichiometrically at low concentrations, and k_{obs} is thereafter independent of the $[Hg^{2+}]$. This result is also in keeping with the mechanism 105–108.

As for the thioacetamide and thiobenzamide systems, the values of k_{obs} for all the thionurethanes rise as $[H_3O^+]$ is lowered; this effect is attributed[54] to ionization of an N-bound proton from **50**, with the deprotonated form being the more reactive. Reactions 105–108 with a small value of K provide an alternative to the mechanism of equations 87–95 originally proposed for thiobenzamides[48].

The (approximate) relative reactivities of the various types of thiol and thionesters, and thioamides studied are:

$$\underset{10^6}{ArC(S)OEt} > \underset{10^4}{ArC(S)NHR} \sim ArNHC(O)SEt > \underset{10^2}{ArNHC(S)OEt} \gg \underset{1}{ArC(O)SEt}$$

By changing the mechanism, the presence of an NH group retards the loss of thion sulphur but accelerates that of thiol sulphur.

VII. REACTIONS OF THIOCARBOXYLIC ACIDS AND THIOANHYDRIDES

There was little to report[4] in this area in 1977, and little or no work has appeared since. One kinetic study[3] has examined the hydrolysis of thiobenzoic acid, PhCOSH, and of thiobenzoic anhydride $(PhCO)_2S$, in aqueous perchloric acid in the presence of Hg^{2+} and other soft ions. As usual for S compounds, the hydrogen ion-catalysed reactions are relatively slow[55]. The presence of Ag^+ or Cu^{2+} ions leads to heavy precipitation of the corresponding salt even in very dilute solutions of thiobenzoic acid; with Ni^{2+}, Cd^{2+} or Pb^{2+} there is little precipitation but no significant increase in the rate of hydrolysis. Once again these borderline ions prove less effective than H_3O^+ at low pH. Only with Hg^{2+} ions is an increase in rate observed and readily studied in homogeneous solution: in this case the precipitation of salt is negligible if $[PhCOSH] \lesssim 10^{-4}$ mol dm^{-3} and $[H_3O^+] \simeq 10^{-3}$ mol dm^{-3}. The hydrolysis (reaction 110) is first order in $[Hg^{2+}]$ and in [PhCOSH], and is independent of the extent of ionization of the thioacid, $[PhCOS^-]/[PhCOSH]$, which can be controlled by changes in $[H_3O^+]$. The entropy of activation $\Delta S^{\ddagger} \simeq 0$. The mechanism is probably reactions 111–114. The involvement of a second metal ion in the reactive complex when this would otherwise carry only a single positive charge, proposed above in species **25**, and in most silver ion-promoted reactions, is again indicated.

$$PhCOSH + Hg^{2+} + 3H_2O \longrightarrow PhCO_2H + HgS + 2H_3O^+ \tag{110}$$

$$PhCOSH + H_2O \rightleftharpoons PhCOS^- + H_3O^+ \quad \text{fast} \tag{111}$$

$$PhCOS^- + Hg^{2+} \rightleftharpoons PhCOSHg^+ \quad \text{fast} \tag{112}$$

$$PhCOSHg^+ + Hg^{2+} \rightleftharpoons PhCOSHg^+ \quad \text{fast} \tag{113}$$

(**52**) Hg^{2+}

$$\mathbf{52} \xrightarrow{\text{slow}} Ph\overset{+}{C}O + HgS + Hg^{2+} \xrightarrow[\text{fast}]{2H_2O} PhCO_2H + H_3O^+ + HgS + Hg^{2+} \tag{114}$$

The hydrolysis of thiobenzoic anhydride occurs in two stages: reactions 115 and 116;

the second stage is much the slower and, as expected, has kinetics identical to those observed for thiobenzoic acid. Reaction 115 is first order in $[Hg^{2+}]$ and in $[(PhCO)_2S]$, and may involve reactions 117 and 118. Under similar conditions the relative reactivities of PhCOSEt, PhCOSH and $(PhCO)_2S$ (first stage) in their Hg^{2+} ion-promoted hydrolysis are $1:2.3 \times 10^2:1.4 \times 10^4$.

$$(PhCO)_2S + Hg^{2+} + 2H_2O \longrightarrow PhCOSHg^+ + PhCO_2H + H_3O^+ \quad (115)$$

$$PhCOSHg^+ + 2H_2O \longrightarrow PhCO_2H + HgS + H_3O^+ \quad (116)$$

$$(PhCO)_2S + Hg^{2+} \rightleftharpoons (PhCO)_2S \longrightarrow Hg^{2+} \quad \text{fast} \quad (117)$$

$$(PhCO)_2S \longrightarrow Hg^{2+} + H_2O \longrightarrow PhCOSHg^+ + PhCO_2H_2^+ \quad \text{slow} \quad (118)$$

VIII. REACTIONS OF ISOTHIOCYANATES

Work on the mechanism of hydrolysis of isothiocyanates using media containing Brönsted acids (reaction 119) has only recently begun to appear[56]. Both alkyl and aryl isothiocyanates are found to be very resistant to catalysis by hydrogen ions in aqueous solution. Their spontaneous hydrolyses are also much slower than those of the corresponding isocyanates. It has been shown, however, that hydrolyses promoted by Hg^{2+}, Tl^{3+} or Ag^+ ions (e.g. reaction 120) is relatively rapid[57,58]. For a series of *o*- and *p*-substituted phenylisothiocyanates the kinetic form for the Hg^{2+} and Tl^{3+} ion-promoted reactions[58] is simple (equation 121). *Para*-substituent effects are small, *ortho*-substituents lead to steric hindrance, $\Delta S^{\ddagger}$ is normally negative, the solvent isotope effect $k_{H_2O}/k_{D2O} > 1$, and there exists no evidence for the formation of a large amount of complex between ArNCS and the metal ion. All these findings are compatible with the mechanism of reactions 122–124 for which the rate equation is equation 125. The behaviour with Ag^+ ions is similar[57], although there is some evidence for a small contribution from a kinetic term in $[Ag^+]^2$. Tl^{3+} ions are surprisingly less effective (*ca* 10^3-fold) than Hg^{2+} ions in this A2-like reaction, and possess a promoting ability similar to that of Ag^+. It has been suggested that Tl^{3+} ions coordinate to isothiocyanates with special difficulty. Although Tl^{3+} ions have usually been found to coordinate less strongly than Hg^{2+} ions to S-substrates (K for the pre-equilibrium smaller) their overall promoting efficiency has almost always been found to be comparable to that of Hg^{2+} ions, since the rate constants, k, for the subsequent slow steps tend to be larger for Tl^{3+}. However, it is not always possible to determine K and k separately (e.g. it is not possible for the present reactions) and the real chemical reason that Tl^{3+} ions are sometimes much less efficient than Hg^{2+} ions is not known. Different abilities to effect intramolecular transfer of hydration water to the substrate in bimolecular slow steps (such as reaction 123, and in the A2-like hydrolysis of thiolesters, Section V) and changes in the usual pattern of relative K values when opportunities for chelation are present, are the features that probably underlie unusual $Hg^{2+}:Tl^{3+}$ reactivity ratios.

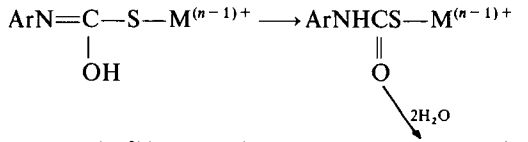
$$RNCS + H_2O \xrightarrow{H_3O^+} [RNHCOSH] \longrightarrow RNH_2 + [COS] \xrightarrow{H_2O} H_2S + CO_2 \quad (119)$$

$$ArNCS + Hg^{2+} + 4H_2O \xrightarrow{H_3O^+} ArNH_2 + HgS + CO_2 + 2H_3O^+ \quad (120)$$

$$-d[ArNCS]/dt = k[M^{n+}][ArNCS] \quad (121)$$

$$ArNCS + M^{n+} \rightleftharpoons ArNCS \longrightarrow M^{n+} \quad K, \text{ fast} \quad (122)$$

$$ArNCS \longrightarrow M^{n+} + 2H_2O \longrightarrow ArN{=}\underset{\displaystyle OH}{\underset{|}{C}}{-}S{-}M^{(n-1)+} + H_3O^+ \quad k, \text{ slow} \quad (123)$$



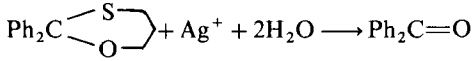
$$ArNH_2 + CO_2 + MS^{(n-2)+} + H_3O^+ \longleftarrow ArNHCO_2H + MS^{(n-2)+} + H_3O^+ \quad (124)$$

$$-d[ArNCS]/dt = kK[M^{n+}][ArNCS] \quad (125)$$

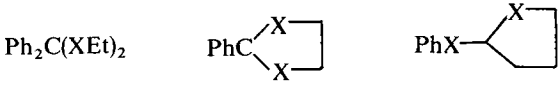
IX. REACTIONS OF THIOACETALS

Kinetic work on promoted reactions of thioacetals is now much more plentiful than[4] in 1977. It is concerned exclusively with solvolysis, mainly hydrolysis (e.g. reactions 126 and 127). Acetals can take three forms[59]: open-chain (e.g. **53**), cyclic (e.g. **54**) and open-chain/cyclic (e.g. **55**). In **53**–**55** X can be O or S. No mechanistic studies of promotion have yet involved bicyclic (spiro) acetals. Acetals are not subject to base catalysis, and for O,S- and S,S-acetals, as usual for S compounds, their susceptibility to Brönsted acid catalysis[59] is much less than that of their O,O-analogues. S,S-acetals are especially resistant to Brönsted acid catalysis but, as expected, can readily be cleaved by suitable soft reagents[60]. As a result they have been much used for the protection of keto and thiol groups during synthesis, and to provide the carbonyl group in the final step of indirect acylation[61]. Reagents used to cleave S,S-acetals in preparative contexts normally involve salts or oxides of soft metals[60], but other types of soft species (e.g. I^+, NO^+, $PhSeO^+$) are also employed[4,62–64]. We shall see that, of soft metal species, Hg^{2+} and Tl^{3+} ions are the most effective kinetically, but in preparative work the speed of the reaction may be less important than the ease of work-up. Soft metal ions do not accelerate the solvolysis of simple non-chelating O,O-acetals[4,65,66]; they are therefore reasonably assumed to interact primarily with the S atoms of O,S-acetals. As for the promotion of reactions of other classes of S substrate dealt with in this chapter, the borderline soft metal ions Cd^{2+}, Ni^{2+} and Cu^{2+} are found to be less effective than the hydrogen ion in bringing about thioacetal hydrolysis[67].

$$PhCH(SEt)_2 + Hg^{2+} + 3H_2O \longrightarrow PhCHO + Hg(SEt)_2 + 2H_3O^+ \quad (126)$$



$$+ Ag^+ + 2H_2O \longrightarrow Ph_2C{=}O + HO(CH_2)_3SAg + H_3O^+ \quad (127)$$



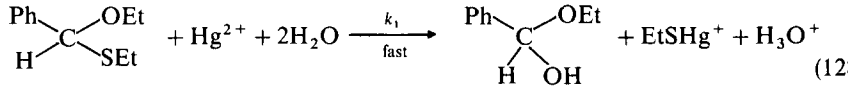
(53) **(54)** **(55)**

A. O,S-acetals

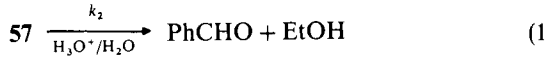
1. Open-chain compounds

Only one open-chain O,S-acetal has been studied kinetically. Compound **56**, however, provided interesting results[68–70] on hydrolysis in aqueous solution. In dilute perchloric acid in the presence of even very low (*ca* 10^{-4} mol dm^{-3}) concentrations of Hg^{2+} or Tl^{3+} ions the rate of hydrolysis is independent of the metal ion concentration, and displays kinetics characteristic of the corresponding O,O-hemiacetal (**57**). The mechanism of reactions 128 and 129 is involved with $k_1 \gg k_2$, so that an effectively quantitative yield

of O,O-hemiacetal is formed (transiently) in solution. This provides a useful route to O,O-hemiacetals from simple O,S-acetals. For **56** probably $k_1 > 10^6\,dm^3\,mol^{-1}\,s^{-1}$ at 25 °C.



(56) (57) (128)

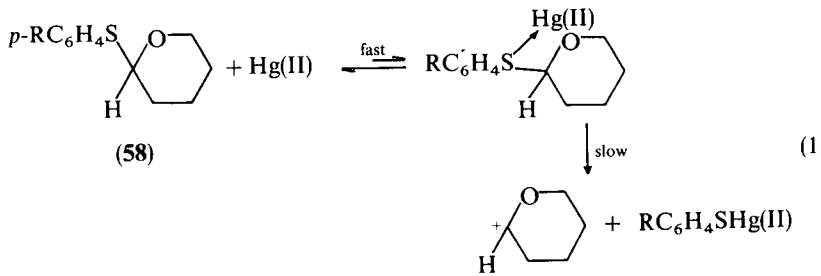


(129)

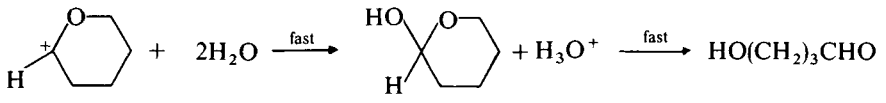
Since in promoted reactions generally Ag^+ ions often lead to rate constants *ca* 10^3-fold smaller than do Hg^{2+} and Tl^{3+} ions, and since[71] for **57** k_{H+} (k_2 in equation 129) $\simeq 10^3\,dm^3\,mol^{-1}\,s^{-1}$ at 25 °C, it would be expected that Ag^+ and H_3O^+ concentration ranges could be chosen in which either reaction 129 or the Ag^+ equivalent of reaction 128, dominates the kinetics of hydrolysis. This proves to be the case[70]. The details of reaction 128 for Hg^{2+} and Tl^{3+} are unknown; for Ag^+ its kinetic form is independent of $[H_3O^+]$ and contains both first- and second-order terms in $[Ag^+]$. The mechanism is similar to that found for disulphides (Section IV) and is given for a cyclic O,S-acetal in Section IX.A.3). In the presence of hydrogen ions only, **56** has $k_{H+} = 1.4\,dm^3\,mol^{-1}\,s^{-1}$ at 25 °C. The hydrogen ion-catalysed hydrolysis is thus very slow compared with both the metal ion-promoted and the hemiacetal hydrolysis; $Hg^{2+}$and Tl^{3+} are at least 10^6-fold more effective than H_3O^+ in cleaving this O,S-acetal. The hydrogen ion route very probably involves initial protonation on oxygen, and slow C—O cleavage[72]. With S,S-acetals, which by comparison will receive protons with difficulty, the relative efficiencies of Hg^{2+} and Tl^{3+} would be expected to be even greater (Section IX.B.2).

2. *Open-chain/cyclic compounds*

As for open-chain O,S-acetals, only one type of open-chain/cyclic compound has been studied. In the original work[73] acetals (**58**, R = NO_2, Cl, H, Me, MeO) were hydrolysed in 40% aqueous dioxane in the presence of a large (*ca.* 2 mol dm^{-3}), fixed concentration of hydrochloric acid and variable concentrations (10^{-4}–10^{-3} mol dm^{-3}) of $HgCl_2$. Under such conditions the Hg(II) species present are largely $HgCl_3^-$ and $HgCl_4^{2-}$ ions. The promoted reaction was found to be first oder in $[Hg(II)_{total}]$ with a Hammett $\rho = +0.9$, and $[\Delta S^{\ddagger} = 190\,J\,K^{-1}\,mol^{-1}$ (for the Me derivative). An Al-like mechanism was suggested (reactions 130 and 131 in line with the A1 scheme proposed for the purely hydrogen ion-catalysed hydrolysis of these acetals[73] (which probably also involves initial C—S cleavage).



(58) (130)



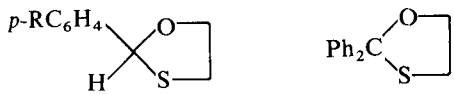
(59) (131)

It was subsequently found[4] that when these hydrolyses are conducted using only mercury(II) perchlorate and perchloric acid, so that the promoting ion is Hg^{2+}, the reaction is much faster. Added Cl^- ions retard the hydrolysis. The relative reactivities of different Hg(II) species were found to be $Hg^{2+} \sim HgCl^+ \lesssim HgCl_2 > HgCl_3^- \gg HgCl_4^{2-}$, with the second-order rate constant for promotion by Hg^{2+}, $k_{Hg} > 10^3\ dm^3\ mol^{-1}\ s^{-1}$, and about 10^6-fold larger than k_{H+} at 25 °C. No accumulation of hemiacetal (**59**) occurs in these systems, even in the absence of added Cl^- ions, at the Hg^{2+} and H_3O^+ concentrations used, but could do so at higher Hg^{2+} and lower H_3O^+ concentrations.

Acetal (**58**, R = H) has also been hydrolysed using a 10% dioxane–water solvent, with Ag^+ as the promoting ion[74]. As for **56** and for other systems, kinetic terms in $[Ag^+]$ and $[Ag^+]^2$ are detected. Ag^+ is *ca* 100-fold less reactive than Hg^{2+}.

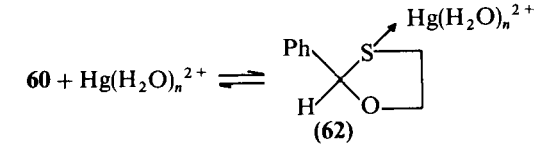
3. Cyclic compounds

Two types of cyclic O,S-acetal have been investigated, **60** and **61**. Initially **60**, R = NO_2, Cl, H, Me, MeO, was studied[75] under conditions similar to those used[73] for **58** when the promoting species would have been mainly $HgCl_3^-$ and $HgCl_4^{2-}$. The hydrolyses were again found to be first order in $[Hg(II)_{total}]$, but for this O,S-acetal electron-release favoured reaction and $\Delta S^{\ddagger} \simeq -30\ J\ K^{-1}\ mol^{-1}$. An A2-like scheme was proposed: a mechanism similar to reactions 130 and 131 but with water in the slow step which leads directly to the hemiacetal.

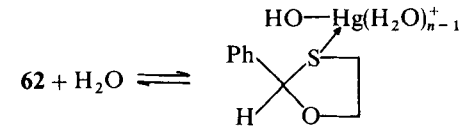


(60) (61)

Further study[76] of **60**, R = H, with mercury(II) perchlorate, using a 1% dioxane–water solvent and various ethanol–water solvents, and a range of added anion and hydrogen ion concentrations, uncovered a complex but interesting mechanism (reactions 132–138). Again the purely hydrogen ion-catalysed path was negligible under the conditions used, and with cyclic acetals, because they tend to hydrolyse more slowly than other types,

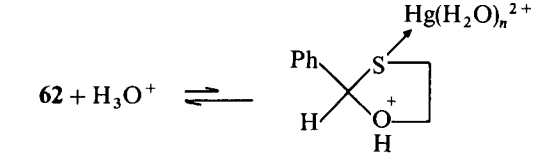


(62) (132)

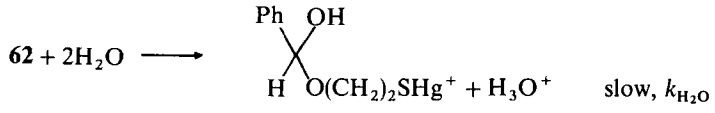


(63) (133)

the intermediate hemiacetals do not normally limit the rate at the metal and hydrogen ion concentrations employed. (See Section IX.A.1 for the behaviour of the open-chain analogue of **60**.)



(64)



(65)

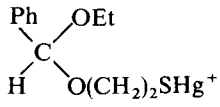
$$\mathbf{63} \longrightarrow \mathbf{65} \quad \text{slow, } k_{OH} \tag{136}$$

$$\mathbf{64} + 3H_2O \longrightarrow \mathbf{65} + 2H_3O^+ \quad \text{slow, } k_H \tag{137}$$

$$\mathbf{65} \xrightarrow{H_2O/H_3O^+} PhCHO + HO(CH_2)_2SHg^+ \quad \text{fast} \tag{138}$$

It is found that at 25 °C, $K \simeq 10^3\,dm^3\,mol^{-1}$, $K_a = 8 \times 10^{-4}\,mol\,dm^{-3}$, $k_{H_2O} = 0.5\,s^{-1}$ (with $\Delta S^{\ddagger} = -45\,J\,K^{-1}\,mol^{-1}$) and $k_{OH^-} = 20\,s^{-1}$ (with $\Delta S^{\ddagger} = -4\,JK^{-1}\,mol^{-1}$). These magnitudes of K and K_a are compatible with independent data. Step 136 is believed to involve the intramolecular transfer of a mercury-bound OH^- ion. This route becomes more prominent in the presence of added anions (which reduce the charge on mercury and facilitate the transfer of OH^- to carbon). The steps 132 and 135 constitute an A2-like mechanism involving Hg^{2+} and alone represent an acceleration of *ca* 10^5-fold over the purely hydrogen ion-catalysed reaction[75,77]. Understandably, the route via **64** is relatively much more important in the presence of added Cl^- ions (which will reduce, or reverse, the charge on the Hg atom).

In ethanol–water mixtures similar behaviour is found[76], except that some of the aldehyde product is formed via **66** produced in the analogue of step 135 with ethanol in place of water. **66** hydrolyses in aqueous acid very slowly compared to **65**; indeed **66** is *ca* 40-fold less reactive than $PhCH(OEt)_2$ towards hydrogen ion catalysis. This is doubtless due to the positive charge on **66**, so that it is again interesting and significant that the effect of added Cl^- ions on this slow hydrogen ion-catalysed reaction of **66** is to accelerate it; its rate eventually reaches a steady value *ca* 4-fold less than that of $PhCH(OEt)_2$ under comparable conditions.

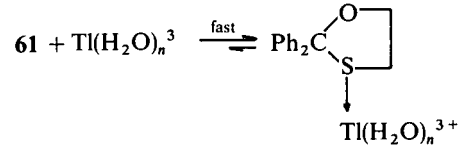


(66)

The Hg^+ ion-promoted hydrolysis of **61** has also been examined[78] in a study similar to that just described. An analogous mechanism is indicated with K and K_H smaller, and k_{H_2O} larger. These changes would be expected to follow from the greater electron

withdrawal provided by the second phenyl group. This group might also be expected to hinder the intramolecular step 136, which is indeed 4-fold smaller for **61** than for **60**.

Acetal (**61**) has also been studied with Tl^{3+} and Ag^+ as the promoting ions[67]. The Tl^{3+}-promoted hydrolysis is especially simple kinetically: the rate is independent of $[Tl^{3+}]$ at least down to $[Tl^{3+}] = 5 \times 10^{-4}$ mol dm^{-3}, and is independent of $[H_3O^+]$ when $[H_3O^+] \gtrsim 0.15$ mol dm^{-3}. A 1:1 complex is formed stoichiometrically (saturation kinetics, reactions 139 and 140). When $[H_3O^+] \gtrsim 0.15$ mol dm^{-3} the rate falls. In this pH region equilibrium 141 begins to move significantly to the right. Probably the Tl^{2+} species are less effective promoters than Tl^{3+}, and it seems that no intramolecular effects are involved with this ion. This result is in agreement with conclusions concerning Tl^{3+} ions reached in Section V. The Tl^{3+} ion is a far more powerful Lewis acid towards **61** than is Hg^{2+}, and **67** may involve chelation with O and S. Surprisingly, Tl^{3+} invariably prefers O,S- to S,S-acetals as substrates.



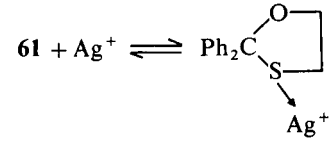
(139)

(67)

$$\mathbf{67} + xH_2O \xrightarrow{\text{slow}} \text{Products} \qquad (140)$$

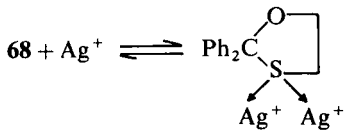
$$Tl(H_2O)_n^{3+} + H_2O \rightleftharpoons Tl(OH)(H_2O)_{n-1}^{2+} + H_3O^+ \qquad (141)$$

The silver ion-promoted hydrolysis of **61** is much slower than the thallium and mercury ion reactions, except at the highest ($\gtrsim 10^{-2}$ mol dm^{-3}) metal ion concentrations. The silver ion rate is able to become comparable to those with Hg^{2+} and Tl^{3+} under these conditions because saturation kinetics do not intervene to limit the rate for silver, and because, as usual, its rate equation contains terms in $[Ag^+]^2$. The Ag^+ reaction is independent of $[H_3O^+]$, and is probably best represented by reactions 142–146. This type of mechanism[67] leads to a rate equation 147 containing four variable parameters, and it can account for a variety of experimental rate equations. It may underlie much Ag^+ ion-promotion.



(142)

(68)



(143)

(69)

$$\mathbf{68} + (2H_2O) \longrightarrow Ph_2C(O(CH_2)_2SAg)(OH)\ (\mathbf{70}) + H_3O^+ \quad \text{slow, } k_1 \qquad (144)$$

$$\mathbf{69} + (2H_2O) \longrightarrow \mathbf{70} + Ag^+ + H_3O^+ \quad \text{slow, } k_2 \qquad (145)$$

$$\mathbf{70} \xrightarrow{H_2O/H_3O^+} Ph_2C{=}O + HO(CH_2)_2SAg \quad \text{fast} \qquad (146)$$

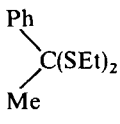
$$k_{obs} = \frac{k_1K_1[Ag^+] + k_2K_1K_2[Ag^+]^2}{(1 + K_1[Ag^+] + K_1K_2[Ag^+]^2)} \qquad (147)$$

B. S,S-Acetals

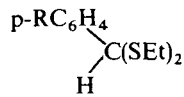
1. *Open-chain compounds*

We deal first with silver ion promotion. Acetals **71**–**73**, R = NO_2, H, Me, MeO were studied[67,79,80] using dioxane–water mixtures (usually 1% dioxane). Their kinetic behaviour is similar to that found for **61**, and the general mechanism 142–146 probably obtains. For all S,S-acetals the (open-chain) O,S-hemiacetal intermediates no doubt also enjoy soft metal ion-promoted hydrolysis. Since open-chain O,S-acetals are much more reactive that S,S-acetals the hemiacetal hydrolysis is unlikely to be rate-limiting during hydrolyses of the latter. The kinetic pattern is simplest for compounds **72** and **73** for which the second-order terms contribute little when $[Ag^+] \lesssim 0.15$ mol dm^{-3}. Under these conditions[79,80] the mechanism reduces to reactions 148–150. The rate equation is equation 151. Values of k_1, and of the corresponding activation parameters for **72** and **73** suggest that, when the substituents in the S-acetal are more electron-releasing than in **73**, R = H, the hydrolysis mechanism is an A1 analogue. With **73**, R = NO_2, however, the reaction is relatively very slow, and the activation parameters have a different pattern with $\Delta S^{\ddagger}$ large and negative. For this compound it is suggested that water is involved in the slow phase of reaction 149, and that the mechanism is thus an A2 analogue. Deuterium isotope effects[81] also indicate a change in mechanism between **73**, R = MeO, and **73**, R = NO_2. Acetal **73**, R = H, may be an intermediate case.

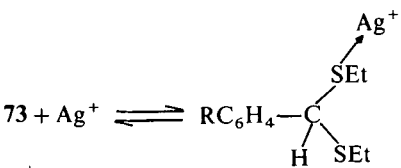
$Ph_2C(SEt)_2$ (**71**)



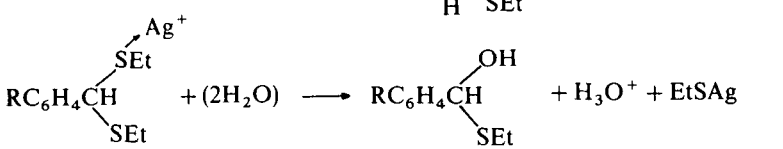
(**72**)



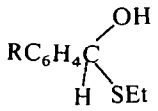
(**73**)



fast, K_1 (148)



(149)



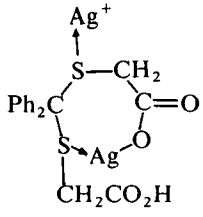
$$\xrightarrow{Ag^+/H_2O} RC_6H_4CHO + EtSAg + H_3O^+ \quad \text{fast} \qquad (150)$$

$$-\text{d[S-acetal]}/dt = \frac{k_1K_1(Ag^+][\text{S-acetal}]}{(1 + K_1[Ag^+])} \qquad (151)$$

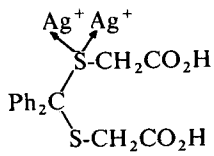
$$\text{or} \quad k_{obs} = \frac{k_1K_1[Ag^+]}{(1 + K_1[Ag^+])} \qquad (152)$$

$Ph_2C(SCH_2CO_2H)_2$ (74) $Ph_2C(SCH_2CH_2OH)_2$ (75)

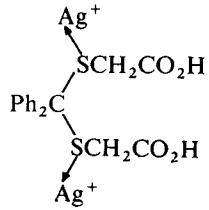
S,S-acetals **74** and **75** display special behaviour arising from their leaving groups[67]. For **74** the hydrolysis is sufficiently slow to allow spectroscopic study of the initial (rapid) Ag^+-S-acetal complex formation: a 2 Ag^+: 1 S-acetal equilibrium is set up, with negligible formation of 1:1 complexes. The kinetics of the subsequent promoted hydrolysis show that the 2:1 complex exists principally in a form with one carboxyl group dissociated, perhaps **76**, but that the hydrolysis occurs only via a fully protonated (doubly charged) complex, probably **77**. **77** will no doubt exist in equilibrium with a greater proportion of **78** but the latter complex seems less attractive as the reactive species. 1:1 Complexes are possibly not observed because they can exist in a neutral form, and therefore easily add another Ag^+ ion to give **76**.



(76)

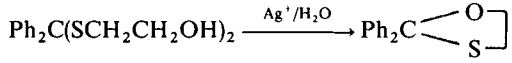


(77)



(78)

S,S-acetal **75** undergoes[4] an initial rapid intramolecular cyclization (reaction 153) to give O,S-acetal **61**. This promoted cyclization is first order in $[Ag^+]$ when $[Ag^+] \gtrsim 0.03\ \text{mol dm}^{-3}$. The subsequent reaction is identical to that observed for **61**.



$$+ HO(CH_2)_2SAg + H_3O^+ \qquad (153)$$

(61)

Turning to promotion by Hg^{2+} and Tl^{3+} ions, we find that the open-chain S,S-acetals **71** and **73**, R = H, react so rapidly with Hg^{2+} that chloride ions, or other anions, must be added to the reaction mixture (to convert the Hg^{2+} ions to species of lower reactivity) to bring the rate into the stopped-flow range[4]. No open-chain S,S-acetal has yet been studied which gives conveniently measurable rates of reaction with Hg^{2+} ions. With Tl^{3+}, acetal **73**, R = H, leads to very rapid reactions, but **71** provides[67] measurable rates and a simple first-order dependence on $[Tl^{3+}]$. It is possible that this corresponds to a slow metal ion transfer mechanism, but more work is required with both Hg^{2+} and Tl^{3+} using less reactive members of this class of thioacetal.

Acetal **74** behaves[67] with Tl^{3+} rather as it does with Ag^+: the 1:1 adduct **79** is formed stoichiometrically, loses a proton to give **80** and can then add a further Tl^{3+} ion, **81**. The overall mechanism (reactions 154–159) is, in principle like that observed for the cyclic O,S-acetals (reactions 139–141). The adducts, especially **80**, are probably chelated. In contrast, acetal **75** does not behave[67] with Tl^{3+} ions as it does with Ag^+: there is no rapid, initial cyclization to the oxathiolan **61**. Instead a direct reaction to give benzophenone is observed (which is faster than the Tl^{3+}-promoted hydrolysis of **61**): it involves reactions corresponding to 155, 156 and 158. Chelation in the complexes **82** and **83** prevents cyclization.

$$Tl(H_2O)_n^{3+} + H_2O \xrightarrow{\text{fast}} Tl(OH)(H_2O)_n^{2+} + H_3O^+ \quad (154)$$

$$Tl(H_2O)_n^{3+} + \text{S,S-acetal} \xrightleftharpoons{\text{fast}} [(H_2O)_{n-1}Tl \leftarrow \text{S,S-acetal}]^{3+} + H_2O \quad (155)$$

(79)

$$\mathbf{79} + H_2O \xrightleftharpoons{\text{fast}} [(H_2O)]_{n-1}Tl \leftarrow \text{S,S-acetal-O}^-]^{2+} + H_3O^+ \quad (156)$$

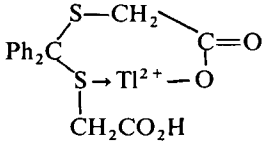
(80)

$$\mathbf{80} + Tl(OH)(H_2O)_{n-1}^{2+} \xrightleftharpoons{\text{fast}} [2Tl\text{:1-S,S-acetal}]^{4+} \quad (157)$$

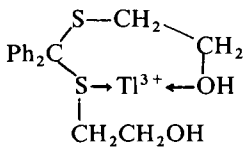
(81)

$$\mathbf{79} \xrightarrow[H_2O]{\text{slow}} \text{Products} \quad (158)$$

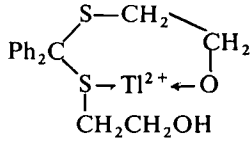
$$\mathbf{81} \xrightarrow[H_2O]{\text{slow}} \text{Products} \quad (159)$$



(80)



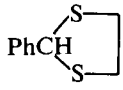
(82)



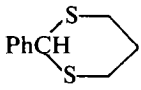
(83)

2. Cyclic compounds

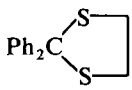
Acetals **84** and **85** hydrolyse inconveniently slowly under the influence of Ag^+ ions, but **86** has been studied kinetically[67]. The reaction, 160, 160 displays the same type of rate equation as found for the corresponding oxathiolan **61**, and for the open-chain analogue, **71**. A mechanism based on steps like 142–146 is probable, with Ag^+ also involved in the rapid hydrolysis of the hemithioacetal in the step corresponding to 146. The overall hydrolysis of **86** is *ca* 10^4-fold slower than that of **71** under the same conditions. Tl^{3+} ion-promotion[67] of the hydrolysis of **86** also has a kinetic form similar to that found for the open-chain compound **71**, but here the difference in reactivity under given conditions appears to be only *ca* 100.



(84)



(85)



(86)

$$Ph_2C\begin{matrix}S\\S\end{matrix}\Big] + 2Ag^+ + 3H_2O \longrightarrow Ph_2C{=}O + AgS(CH_2)_2SAg + 2H_3O^+ \quad (160)$$

With Hg^{2+} ions, in contrast to the situation with the open-chain acetals (Section IX.B.1), conveniently measurable rates of hydrolysis are found for cyclic derivatives, and a detailed comparison with Tl^{3+} ion promotion has been made[78,82] for acetals **84** and **85**. In a 1% dioxane–water solvent, both these acetals give evidence of saturation kinetics arising from simple 1:1 complex formation using either Hg^{2+} or Tl^{3+}. The outline mechanism is probably reactions 161 and 162. Equation 163 gives k_{obs}. Values of K_1, k_1 and of the activation parameters were obtained[82]. The negative $\Delta S^{\ddagger}$ values (which reflect principally k_1) suggest an A2-like mechanism, as shown in equations 161 and 162. Overall, **84** and **85** display similar reactivities with Tl^{3+} and Hg^{2+}: they are both less basic towards Tl^{3+} than towards Hg^{2+}, but both Tl^{3+} complexes react more rapidly than do those of Hg^{2+}. (This seems to be a common feature of Tl^{3+} and Hg^{2+} ion-promotion of reactions of S-substrates unless O,S-chelated complexes are possible, when Tl^{3+} coordination is favoured—see Section IX.A.3.) There are nevertheless interesting differences of detail: **85** is less basic than **84** towards Tl^{3+} but the reverse is true towards Hg^{2+}, and the Tl^{3+} complex of **85** is more reactive with water that is that of **84**, but the opposite is true for the corresponding Hg^{2+} complexes. These subtle differences possibly reflect (unknown) minor differences in the conformations of the complexes.

$$\text{S,S-acetal} + M^{n+} \rightleftharpoons M^{n+} \leftarrow \text{S,S-acetal} \qquad \text{fast, } K_1 \quad (161)$$

$$M^{n+} \leftarrow \text{S,S-acetal} + xH_2O \longrightarrow \text{Products} \qquad \text{slow, } k_1 \quad (162)$$

$$k_{obs} = k_1K_1[M^{n+}]/(1 + K_1[M^{n+}]) \quad (163)$$

X. SUMMARY

The work outlined in this chapter reinforces conclusions drawn earlier[4] concerning soft metal ion-promoted reactions of organo-sulphur compounds: (i) many (possibly all) types of divalent S-compound are susceptible to promotion, (ii) kinetic forms tend to be rather simple, (iii) mechanisms are often analogous to those found for hydrogen ion-catalysed reactions (e.g. Al- or A2-like) but slow metal transfer is rare, and types of mechanisms available only to metals are sometimes observed, (iv) a metal–sulphur derivative is usually formed, (v) in aqueous solutions the fastest reactions have so far been provided by Hg^{2+} and $HgCl^+$ ions, but various Au(III) species, and free Tl^{3+}, Hg_2^{2+} and Ag^+ ions, are also very effective, (vi) borderline soft ions (Cd^{2+}, Cu^{2+}, Pb^{2+} etc.) lead to less rapid reactions of S compounds than does the (hard) H_3O^+ ion unless either the S compound acts as a chelating ligand for the metal ion, or an intramolecular attack by another species within the metal ion–S-substrate complex is involved.

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CHAPTER **13**

Thiol–disulfide interchange

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I. INTRODUCTION

Thiol–disulfide interchange is the reaction of a thiol (RSH) with a disulfide (R'SSR'), with formation of a new disulfide (RSSR') and a thiol (R'SH) derived from the original disulfide (equation 1). The reaction is unique in organic chemistry: although it involves the cleavage and formation of a strong covalent bond (the S—S bond; bond energy *ca* 60 kcal mol^{-1}), it occurs reversibly at room temperature in water at physiological pH (*ca* 7)[1–4]. The reaction is moderately fast: a typical value of the observed rate constant is *ca* 10 M^{-1} min^{-1} at pH 7 and room temperature[5]. The half-life for the reaction is *ca* 2 h for mM concentrations of thiol and disulfide in aqueous solution at pH 7, and for alkanethiols with normal values of pK_a (*ca* 9–10). The yield of the reaction is quantitative if side-reactions—such as air oxidation of thiol to disulfide, and cleavage of disulfide bonds at high pH—are prevented[1].

$$RSH + R'SSR' \rightleftharpoons RSSR' + HSR' \quad (1)$$

Thiol–disulfide interchange is an S_N2 reaction. Thiolate anion (RS^-) is the active nucleophile and the reaction can be stopped if the solution is made acidic[1]. The reaction is overall second-order: first-order each in thiolate and in disulfide (equations 2–4)[6–20]. In this chapter, we will distinguish between *thiol*–disulfide interchange (the overall observed process, equation 1), and *thiolate*–disulfide interchange (the reaction of thiolate anion with disulfide, equation 3). The two processes differ according to the extent to which thiol is dissociated to thiolate anion under the reaction conditions.

$$RSH \rightleftharpoons RS^- + H^+ \quad (pK_a^{RSH}) \quad (2)$$

$$RS^- + R'SSR' \rightleftharpoons RSSR' + {}^-SR' \quad (3)$$

$$H^+ + {}^-SR' \rightleftharpoons HSR' \quad (pK_a^{R'SH}) \quad (4)$$

Thiolate–disulfide interchange is base catalyzed[21–25] and involves the backside nucleophilic attack of thiolate anion along the S—S bond axis of the disulfide[26]. It shows less sensitivity to solvent than most S_N2 reactions involving oxygen and nitrogen nucleophiles[15]. The rates of thiolate–disulfide interchange in polar aprotic solvents (DMSO, DMF) are faster by a factor of approximately 10^3 than rates in polar protic solvents (water, methanol). For comparison, the rate enhancement for oxyanions (which are more highly solvated than thiolates)[15] on moving from protic to polar aprotic solvents is 10^6–10^7.

Biologically important molecules containing the thiol or the disulfide group are widely distributed in nature[1,2], and the unique position of thiols and disulfides in biochemistry has been reviewed in several excellent books and articles[1–3]. The thiol-containing amino acid—cysteine—is present in proteins and peptides; examples include glutathione[27] and trypanothione[28–30]. Several cofactors—coenzyme A, dihydrolipoamide, coenzyme M ($^-O_3SCH_2CH_2SH$)[31]—contain the essential thiol functionality[1,2]. The disulfide bonds

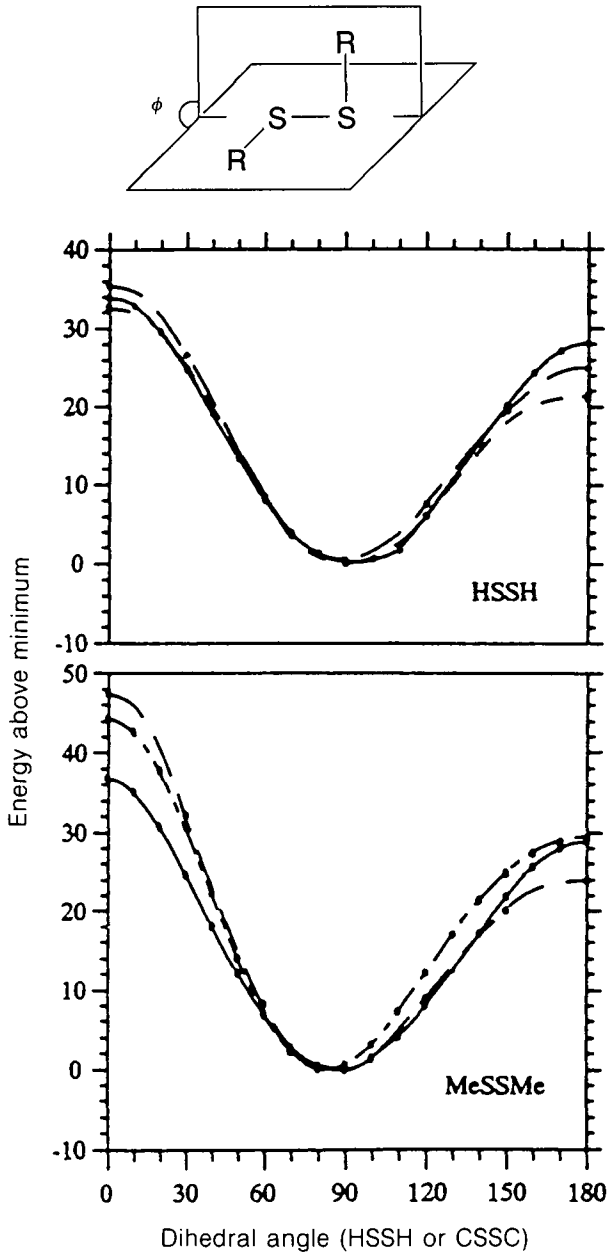


FIGURE 1. Relative energy (kJ mol^{-1}) of HSSH and MeSSMe as a function of the dihedral angle (ϕ, RSSR): (—) MM2 (85); (——) 6-31G* [M. Aida and C. Nagata, *Theor. Chim. Acta*, **70**, 73 (1986)]; (- -) SCF and MP2 [C. J. Marsden and B. J. Smith, *J. Phys. Chem.*, **92**, 347 (1988)]; (— - —) OPLS [W L. Jorgensen, *J. Phys. Chem.*, **90**, 6379 (1986)]. Reprinted with permission from Reference 16. Copyright (1990) American Chemical Society

between cysteine residues are important tertiary and quarternary structural elements in proteins (especially extracellular proteins) such as immunoglobulins, enzymes, hormones, procollagen and albumin[1-3]. The cleavage of the disulfide bond(s) of many proteins (e.g. deoxyribonuclease I) results in loss of activity[32]. Thiol–disulfide interchange may play a role in metabolic regulation of enzymatic activities[3,33,34]. The activities of several chloroplast enzymes such as fructose-1,6-biphosphatase, NADP-malate dehydrogenase, sedoheptulose-1,7-biphosphatase, NADP-glyceraldehyde-3-phosphate dehydrogenase and phosphoribulokinase are enhanced by reduction of their specific disulfide bonds by photogenerated reducing equivalents transferred via ferredoxin and thioredoxin[3,35-37]. The cleavage of disulfide bonds of β-adrenergic and other cell surface receptors by thiols activates the receptor in a manner similar to binding of agonist[38,39].

The thiol functional group is essential for activity of many enzymes[1,2] such as thiol proteases (papain, ficin, bromelain)[40], β-ketoacylthiolase[41-43], enolase[44], creatine kinase, glyceraldehyde-3-phosphate dehydrogenase, phosphofructokinase and adenylate kinase[1-3,11]. These enzymes are inactive in mixed disulfide form, and can be reactivated using strongly reducing thiols (e.g. dithiothreitol, *N,N'*-dimethyl-*N,N'*-bis(mercaptoacetyl)hydrazine)[11,18]. A thiolate anion may be involved in methanogenesis by 2e/1e redox coupling with a Ni cofactor in methyl coenzyme M reductase[31]. The reactive thiol functionality is masked as a trisulfide in the potent DNA-cleavage agents—calichemycin and esperimicin[45-48]. The rate-determining step in the unmasking of these DNA-cleavage agents is the cleavage of the trisulfide by a thiol (e.g. glutathione)[48]. The thiolate anion formed undergoes intramolecular Michael-type attack on an enone system, which in turn facilitates the ring closure of the enediyne moiety to form the reactive aromatic diradical.

Thiolate anion is a strong nucleophile and a good leaving group because of its high polarizability and low degree of solvation. The thiol group is less strongly hydrogen-bonded, and the thiolate anion is less solvated, than the alkoxide anion. The value of pK_a of the SH group of butanethiol in DMSO (*ca* 17) is 7 units higher than in water (*ca* 10); the corresponding pK_a value for the OH group of butanol is 12 units higher in DMSO (*ca* 28) than in water (*ca* 16)[49-51].

The optimum CSSC dihedral angle in the disulfide bond is *ca* 90° (Figure 1). The energy barrier to rotation around CSSC bond is *ca* 7.5 kcal mol^{-1}[52]. Five-membered cyclic disulfides are strained and have a CSSC dihedral angle of *ca* 30°[53]. Sulfur shows concatenation: molecular sulfur S_8 exists as an eight-membered ring; organosulfur compounds containing tri- and polysulfide linkages (RS_nR) are found in nature and have been characterized[54,55].

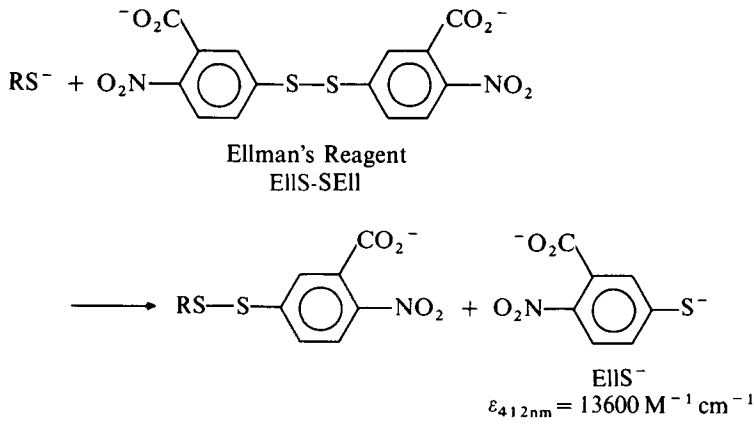
This chapter focuses on the physical-organic aspects of the thiol–disulfide interchange reaction. The biochemical aspects of the reaction are only lightly touched upon here, and we recommend References 1–3 to the reader for a detailed review of the biochemistry.

II. METHODS USED IN FOLLOWING THIOL–DISULFIDE INTERCHANGE

A. Spectroscopic (UV, NMR) Assays

The kinetics of thiol–disulfide interchange reactions involving formation of a chromophoric thiolate are conveniently followed by UV spectroscopy. The reaction of thiolates with excess Ellman's reagent [EllS-SEll, 5,5'-Dithiobis(2-nitrobenzoic acid)] is used for quantitative estimation of thiol by measuring the absorption due to Ellman's thiolate ($EllS^-$) at 412 nm (equation 5)[56-58]. Reactions of thiols with 4,4'-dipyridyl disulfide and 2,2'-dipyridyl disulfide generate chromophoric thiols: 4-thiopyridone ($\varepsilon_{324\,nm}$ = 19600 M^{-1} cm^{-1}) and 2-thiopyridone ($\varepsilon_{343\,nm}$ = 8080 M^{-1} cm^{-1}) respectively[59-62].

The kinetics and equilibria of reactions involving cyclic five- and six-membered disulfides can be followed at 330 nm and 290 (or 310 nm) respectively. Five-membered



(5)

cyclic disulfides absorb in the UV region at 330 nm ($\varepsilon = 147\,M^{-1}\,cm^{-1}$) and six-membered disulfides absorb at 290 nm ($\varepsilon = 290\,M^{-1}\,cm^{-1}$) or 310 nm ($\varepsilon = 110\,M^{-1}\,cm^{-1}$)[5,53,63–65].

^{1}H NMR spectroscopy can be used to determine the position of equilibria in thiol–disulfide interchange reactions[10,13,18], and to follow the kinetics of the reactions (either in the reacting system or after quenching with acid)[18,66–68]. This method is useful where the methylene protons α and β to the sulfur in the reactants and products differ in chemical shift and can be integrated accurately. Dynamic ^{1}H NMR lineshape analysis[15,17] and spin-transfer methods[9,69] have been used to determine the rate constants of degenerate intermolecular thiolate–disulfide interchange reactions: $RS^- + RSSR = RSSR + RS^-$. Analysis of ^{1}H NMR lineshapes, where the resonances are exchange-broadened, is useful for determining the rates of fast degenerate intermolecular interchange reactions between thiolates and disulfides (k_s- *ca* $10–10^7\,M^{-1}\,s^{-1}$)[15,17]. The spin-transfer method between pairs of exchanging protons and carbons (α to sulfur) is applicable for slower rates (k_s- *ca* $2–60\,M^{-1}\,s^{-1}$)[9,69].

B. Enzymatic Assays

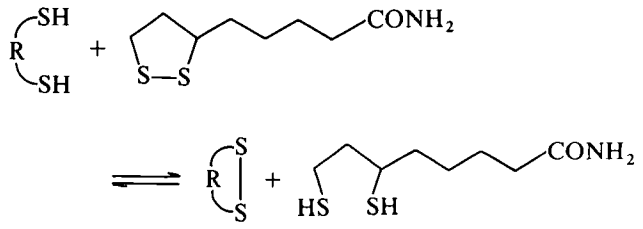
The kinetics of reduction of oxidized glutathione (GSSG) by thiols is conveniently followed[5] using a fast enzymatic reaction involving glyoxalase-I. The glutathione (GSH) that is released is converted to S-lactoyl glutathione by reaction with methylglyoxal in the presence of glyoxalase-I (GX-I), and the appearance of S-lactoyl glutathione is followed spectrophotometrically at 240 nm ($\varepsilon = 3370\,M^{-1}\,cm^{-1}$) (equations 6–8)[5]. The rates of reactions involving aminothiols cannot be determined by this method because they react rapidly with methylglyoxal and form species that absorb strongly at 240 nm and thus interfere with the spectroscopic measurement[5]. This assay is subject to errors due to oxidation of thiol groups if air is not carefully excluded.

$$RS^- + GS{-}SG \rightleftharpoons RS{-}SG + GS^- \quad (6)$$

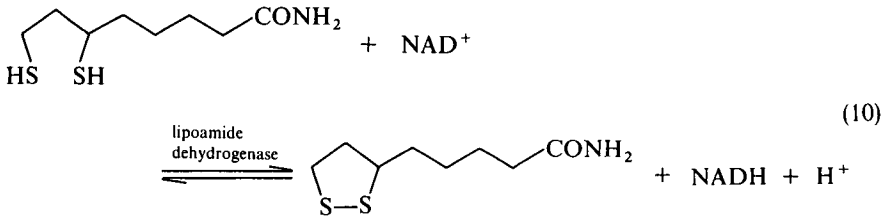
$$GS^- + CH_3COCHO \rightleftharpoons GS{-}CH(OH){-}COCH_3 \quad (7)$$

$$GS{-}CH(OH){-}COCH_3 + GX\text{-}I \rightleftharpoons GS{-}CO{-}CH(OH)CH_3 + GX\text{-}I \quad (8)$$

The equilibria of thiol–disulfide interchange reactions between α,ω-dithiols and lipoamide can be determined conveniently by the addition of lipoamide dehydrogenase and NAD^+. NADH is produced; this compound is coveniently monitored at 340 nm[5,70]



(9)



(10)

(equations 9 and 10). The equilibrium constants for α,ω-dithiol and lipoamide are then calculated from the measured equilibrium constant of the α,ω-dithiol with respect to NAD^+ and from the standard value of the equilibrium constant for lipoamide and NADH.

C. Assays Based on Chromatography

The kinetics and equilibrium constants of thiol–disulfide interchange reactions involving cysteine derivatives or peptides containing cysteine have been determined by HPLC[71] and gel-filtration chromatography[72] on the reaction mixtures after quenching with acid. The equilibrium products of the reaction of glutathione and cystine have been separated by ion-exchange chromatography[73] or by electrophoresis of the ^{35}S-labeled compounds[74]. Gas chromatography of the equilibrium mixture of alkanethiols and disulfides has been used to estimate equilibrium constants[75].

III. MECHANISM

A. Products

Thiol–disulfide interchange of a monothiol (RSH) with a disulfide (R'SSR') involves multiple equilibria (equations 1 and 11): the reaction products include all possible thiols (RSH and R'SH), symmetrical disulfides (RSSR, R'SSR') and mixed or unsymmetrical disulfides (RSSR').

$$RSH + RS—SR' \rightleftharpoons RS—SR + R'SH \tag{11}$$

B. Dependence on Solution pH, and on the pK_a Values of Thiols

Because the thiol–disulfide interchange reaction requires thiolate anion, the observed rate of reaction (and, in systems in which the participating thiols have different values of pK_a, the observed position of equilibrium) depends upon the pH of the solution and

the extent of ionization of the various thiols. For a thiol of pK_a 10, only 0.1% of thiol is present as thiolate at pH 7, and 1% of thiol is in thiolate form at pH 8; the observed rate constant of the thiol–disulfide interchange at pH 8 is therefore 10 times faster than that at pH 7. The thiolate can be generated by addition of base, e.g. potassium *t*-butoxide, in polar aprotic solvents (DMSO, DMF)[15]. Thiol is a much weaker nucleophile than thiolate, and direct reaction between *thiol* and disulfide has not been observed. The reaction of thiolate with disulfide is effectively quenched by addition of acid and conversion of RS^- to RSH.

C. Kinetics

1. Rate law

The thiol–disulfide interchange reaction is overall second-order: first-order in thiolate and in disulfide[6,7]. For a representative reaction of a thiolate (RS^-) with Ellman's disulfide (EllS-SEll, equation 5) the rate laws are given by equations 12 and 13. The rate constant k_{RS^-} derived from equation 12, based on the concentration of the thiolate, is independent of pH; the observed rate constant k_{obsd}, based on total concentration of thiol (equation 13), depends upon pH. The value of the rate constant k_{RS^-} is useful for interpretations of reactivity (such as Brønsted correlations of rates or equilibrium constants with values of pK_a of thiols). The calculation of the observed rate constant k_{obsd} at the pH of reaction is straightforward from equation 13 using the value of the total thiol present in solution, $[RSH]_{total} = [RS^-] + [RSH]$, and is useful for predicting rates at the same pH. The two rate constants k_{obsd} and k_{RS^-} are related to each other by equation 14 and can be interconverted using the values of the pK_a of thiol and the pH of solution[5,6]. Table 1 lists the values of rate constants for representative thiol–disulfide interchange reactions in water.

$$(d[EllS^-]/dt) = k_{RS^-}[RS^-][EllS\text{-}SEll] \tag{12}$$

$$(d[EllS^-]/dt) = k_{obsd}[RSH]_{total}[EllS\text{-}SEll] \tag{13}$$

$$k_{RS^-} = k_{obsd}(1 + 10^{pK_a - pH}) \tag{14}$$

TABLE 1. Representative rate constants of thiol–disulfide interchange reactions in water

Reactants						
Thiol	Disulfide	pK_a (thiol)	k_{RS^-} ($M^{-1}min^{-1}$)	k_{obsd}[a] ($M^{-1}min^{-1}$)	Temp (°C)	Ref.
Mercaptoethanol	Oxidized glutathione	9.6	3.4×10^3	8.7	30	5
3-Mercaptopropanoic acid	Oxidized glutathione	10.6	1.2×10^4	3.2	30	5
Mercaptoethanol	Ellman's disulfide	9.6	1.5×10^7	3.7×10^4	30	6
Propanethiol	Ellman's disulfide	10.5	6.4×10^7	2.0×10^4	25	7
Thiophenol	Ellman's disulfide	6.6	1.3×10^6	9.6×10^5	30	6
Dithiothreitol	Papain-S-SCH_3	9.2	5.3×10^5	3.3×10^3	30	11
Dithiothreitol	Oxidized mercaptoethanol	9.2	3.7×10^2	2.3[b]	25	18

[a]Values of k_{obsd} are at pH 7. [b]The value of the rate constant is corrected statistically for the presence of two thiol groups on dithiothreitol.

2. Brønsted relation

The log of the rate constants (k_{RS^-}) of thiolate–disulfide interchange reactions follows a Brønsted correlation with the values of pK_a of the thiols. The Brønsted plot for the reaction of thiolates with oxidized glutathione[5] has a Brønsted coefficient (slope), β_{nuc}, of 0.5. The Brønsted coefficients are also *ca* 0.4–0.5 for the reaction of thiolates with Ellman's disulfide[6,7]. Alkyl and aryl thiolates show separate correlation lines with Ellman's disulfide[7], but show a similar slope, $\beta_{nuc} = 0.5$. An aromatic thiolate reacts with Ellman's reagent[7] or the mixed disulfide EllS-$SCH_2CH_2CH_2OH$[76] at a rate faster by a factor of 6 than an aliphatic thiolate of the same pK_a. The higher reactivity of aromatic thiolates in comparison to aliphatic thiolates is probably due to greater softness (and weaker solvation) of the former[7,8]. Brønsted correlations have also been reported for the reaction of thiolates with 4,4′-dipyridyl disulfide[59] and 2,2′-dipyridyl disulfide[60].

A Brønsted correlation (equation 15) for thiol–disulfide interchange (equation 16) has been assembled empirically by systematic examination of the influence of pK_a^{RSH} for the nucleophilic (nuc), central (c) and leaving group (lg) thiols on the rate of the reaction. Equations 17 and 18 represent different types of fits to data (k_{RS^-} is in units of $M^{-1}\,min^{-1}$)[5]. Equation 17 represents the best fit to all the available data, although it is suspect because the values of β_{nuc} and β_{lg} are not obviously compatible with a transition state with charge symmetrically distributed between the terminal sulfur atoms. The data included in the correlation are taken from a range of studies and are not necessarily directly comparable. Several different sets of Brønsted coefficients give similar fits to the observed data (equations 17 and 18); this observation suggests that the Brønsted coefficients are not sharply defined. We recommend equation 18 for general use based on the symmetry of the values of β_{nuc} and β_{lg}. The value of β_c for the central thiol has been estimated as *ca* -0.3 to -0.4 from a limited set of data for reactions of RS^- with EllS-SEll, RS-SEll, and $HOCH_2CH_2CH_2S$-SEll[76].

$$\log k_{RS^-} = C + \beta_{nuc} pK_a^{nuc} + \beta_c pK_a^{c} + \beta_{lg} pK_a^{lg} \tag{15}$$

$$R^{nuc}S^- + R^cS{-}SR^{lg} \xrightarrow{k_{RS^-}} R^{nuc}S{-}SR^c + {}^-SR^{lg} \tag{16}$$

$$\log k_{RS^-} = 7.0 + 0.50\,pK_a^{nuc} - 0.27\,pK_a^{c} - 0.73\,pK_a^{lg} \tag{17}$$

$$\log k_{RS^-} = 6.3 + 0.59\,pK_a^{nuc} - 0.40\,pK_a^{c} - 0.59\,pK_a^{lg} \tag{18}$$

The data on which equations 17 and 18 are based cover a range of different (and perhaps not directly comparable) thiol and disulfide structures. A study of the Brønsted coefficients of the nucleophilic, central and leaving group thiols using a carefully limited and consistent set of thiols and disulfides would be useful mechanistically. In the absence of unambiguously interpretable data, these correlations (equations 17 and 18) should be considered as kinetic models for thiolate–disulfide interchange reactions. Although they do not have an unimpeachable mechanistic foundation, they are useful in predicting rate constants (k_{RS^-}) in water. The value of k_{RS^-} can be converted to the observed rate constant (k_{obsd}) at the pH of reaction using equation 14.

The optimum value of pK_a of the nucleophilic thiol for the maximum observed rate (k_{obsd}) of thiol–disulfide interchange at a given pH can be predicted by a Brønsted correlation (equation 19)[5,6]. The optimum value of pK_a of the nucleophilic thiol (based on the assumption of $\beta_{nuc} = 0.50$) is therefore the value of the pH of the reaction mixture; at pH 7 a nucleophilic thiol of $pK_a = 7$ will show the maximum observed rate of thiol–disulfide interchange (Figure 2). This prediction closely matches the observed rates of thiol–disulfide interchange[5,6] and is useful in designing reagents that reduce disulfide bonds rapidly at pH 7[18,20]. For a thiol of $pK_a \gg$ pH, only a small fraction of the total thiol is present as thiolate; for a thiol of $pK_a \ll$ pH, thiol is present as thiolate, but its

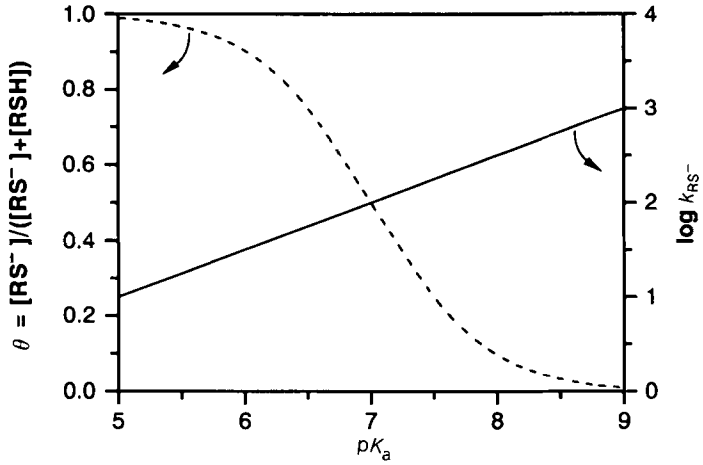


FIGURE 2. Comparison of plots of the log of rate constant of the thiolate–disulfide interchange reaction (log k_{RS^-}, —) vs pK_a of a nucleophilic thiol, and of the degree of dissociation at pH 7 (θ, ----) vs pK_a of thiol. The values of rate constant (k_{RS^-}) are calculated using equation 17, assuming the value of β_{nuc} as 0.5, and the value of pK_a of both the central and leaving group thiols as 8.5. The observed rate constant (k_{obsd}) in terms of the total concentration of thiol and thiolate in solution is given by $k_{obsd} = \theta k_{RS^-}$

nucleophilicity is low. A thiol of pK_a = pH balances the proportion of thiol present as thiolate and adequate nucleophilicity of the thiolate.

$$\text{pH} = \text{p}K_a + \log[(1-\beta)/\beta] \tag{19}$$

3. *Substituent effects*

a. Steric. The steric effect is most pronounced when all three thiols in the transition state are fully substituted at the carbon α to sulfur. It is significantly large even when two of the three adjacent thiols in the transition state are fully substituted at the carbon α to sulfur. The rate constant for reaction of *t*-butyl thiolate with bis(*t*-butyl) disulfide ($k_{s^-} = 10^{-7}\,M^{-1}\,s^{-1}$) in butanol is *ca* 10^6-fold slower than that for 1-butyl thiolate with bis(1-butyl) disulfide ($k_{s^-} = 0.26\,M^{-1}\,s^{-1}$)[24]. The observed rate constant for the reaction of penicillamine ($^-OOC—CH(NH_3^+)—C(CH_3)_2SH$) with the mixed disulfide of penicillamine and glutathione at pH 7.4 ($k_{obsd} = 0.00047\,M^{-1}\,min^{-1}$) is *ca* 10^5-fold slower than that of penicillamine with glutathione disulfide which contains no substitution α to sulfur ($k_{obsd} = 37\,M^{-1}\,min^{-1}$)[66]. The observed rate constant for the reaction of glutathione with penicillamine disulfide ($0.012\,M^{-1}\,min^{-1}$) is also *ca* 2000-fold lower than for glutathione with mixed penicillamine-glutathione disulfide ($27\,M^{-1}\,min^{-1}$)[66]. The equilibrium constant for the formation of bis(*t*-butyl) disulfide is small in the reaction of *t*-butyl thiol with mixed 1-butyl *t*-butyl disulfide, i.e. the formation of bis(*t*-butyl) disulfide is disfavored[75,77].

Steric effects are small for alkyl substitution at carbon β to sulfur: the rate constant for degenerate thiolate–disulfide interchange of neopentyl thiolate with its disulfide is only threefold lower than that of 1-butyl thiolate with its disulfide[15]. The reaction of thiol group of the Bovine serum albumin (BSA) with Ellman's disulfide is anomalously slower, by a factor of 14, than that with cystamine ($^+H_3NCH_2CH_2SSCH_2CH_2NH_3^+$)[78].

The thiol groups in some proteins appear to be relatively inaccessible, possibly due to a combination of steric effect and other factors such as local hydrophobicity or charge–charge repulsion.

b. Acidity. The rate constants of thiolate–disulfide interchange reactions vary significantly with the acidities of the substrate thiols: The reaction of mercaptoethanol with Ellman's disulfide ($k_{RS^-} = 1.5 \times 10^7\ M^{-1}\ min^{-1}$)[6] is significantly faster than that of mercaptoethanol with glutathione disulfide ($k_{RS^-} = 3.4 \times 10^3\ M^{-1}\ min^{-1}$)[5] in water; the relevant values of pK_a are 4.5 for EllSH and 8.7 for GSH. Brønsted correlations (equations 15–18) describe the effect of acidities (pK_a) of the nucleophilic, central and leaving group thiols on the rate constants of thiolate–disulfide interchange reactions. The rate constants for thiolate–disulfide interchange (k_{RS^-}) are larger for increasing values of pK_a for nucleophilic thiols, and for decreasing pK_a values for central and leaving group thiols. The rate constant should be affected more by a change in the pK_a values of the nucleophilic and leaving group thiols than that for the central thiol, because the Brønsted coefficients are larger for the nucleophilic and leaving group thiols than for the central thiol[5].

A mixed disulfide (R'SSR") may have two constituent thiols of different acidities ($pK_a^{R'SH} > pK_a^{R"SH}$). The cleavage of the mixed disulfide R'SSR" by a nucleophilic thiolate RS^- occurs favourably with release of the more acidic thiol (R"SH), and the less acidic R'S group is retained in the new mixed disulfide (RSSR')[76].

c. Charge. The rates of thiol–disulfide interchange reactions in aqueous solutions with charged substituents vary by as much as a factor of 2.5 from the predicted rate constants based on structure–reactivity correlations with uncharged substituents[79]. The deviations from predicted values based on uncharged substituents are the greatest when the charge is on the central group, and the deviations decrease with increasing distance of the charge from the reactive site[79]; e.g., both the rates of reactions of $^-O_2CCH_2CH_2S^-$ with the mixed disulfides $^-O_2CCH_2CH_2SSC_6H_4NO_2$-*p* and $^-O_2CCH_2CH_2CH_2SSC_6H_4$-$NO_2$-*p* are lower than the predicted values based on the Brønsted correlation with uncharged substituents, but the deviation is lower with $^-O_2CCH_2CH_2CH_2SSC_6H_4$-$NO_2$-*p*[79]. A similar effect of the negative charge on R groups is seen in the rate constants for degenerate RS^-/RSSR interchange reactions[9]. Thiolates without charged substituents, such as mercaptoethanol thiolate, react 25 times faster with a positively charged analog of Ellman's disulfide than with the negatively charged Ellman's disulfide; this ratio decreases to *ca* 1 to 3.5 for a thiolate with a positively charged substituent three bonds from sulfur (cysteine ethyl ester), and increases to 120 for a thiolate with a negatively charged substituent ($^-O_2CCH_2S^-$)[80].

The electrostatic influence of the local cysteine environments in peptides has been observed in thiol–disulfide interchange reactions[71,81]. The rate constants in water for the reaction of the negatively charged Ellman's disulfide and a peptide containing cysteine with two positive neighbors, one positive and one neutral neighbor, or two neutral neighbors are 130,000, 3350 and 370 $M^{-1}s^{-1}$ respectively at pH 7 and 20 mM ionic strength[81]. Electrostatic contributions totaling a factor of 2000 ($\Delta G = 4.3$ kcal mol^{-1}) have been estimated for the fastest and the slowest thiol–disulfide interchange reactions of small charged substrates in 50% methanol–water mixture; these contributions to the free energy comprise $+3.0$ kcal mol^{-1} from attraction and -1.3 kcal mol^{-1} from repulsion[71].

d. Hydrogen bonding. The rates of thiolate–disulfide interchange in polar aprotic solvents are not significantly affected by groups capable of intramolecular hydrogen bonding[15]. The rate constant for the degenerate thiolate–disulfide interchange reaction

TABLE 2. Comparison of rate constants for degenerate thiolate–disulfide interchange ($RS^- + RSSR \rightleftharpoons RSSR + {}^-SR$) in polar protic and polar aprotic solvents

RS^-	M^+	Solvent	$10^{-3}\,k^{a,b}$ ($M^{-1}\,s^{-1}$) (297 K)	$\Delta G^{\ddagger}$ (kcal mol^{-1}) (297 K)	$\Delta H^{\ddagger}$ (kcal mol^{-1})	$\Delta S^{\ddagger}$ (cal $K^{-1}\,mol^{-1}$)
$HOCH_2CH_2S^-$	Na^+	D_2O	0.0077	16.2	13	−10
	K^+	D_2O	0.0095	16.1	13	−11
	K^+	CD_3OD	0.0040	16.6	13	−12
	K^+	DMF-d_7	20	11.5	8	−13
	K^+	DMSO-d_6	21	11.5		
$CH_3CH_2CH_2CH_2S^-$	Na^+	DMF-d_7	43	11.1		
	K^+	DMSO-d_6	54	11.0		
$CH_3C(CH_3)_2CH_2S^-$	K^+	DMF-d_7	15	11.7		
	K^+	DMSO-d_6	16	11.7		
$HOC(CH_3)_2CH_2S^-$	K^+	DMSO-d_6	1.1	13.2	10	−10
$HOCH_2C(CH_3)_2CH_2S^-$	K^+	DMSO-d_6	0.67	13.5	9	−16

[a]Uncertainties are: k, ±10%; $\Delta G^{\ddagger}$, ±0.1 kcal mol^{-1}; $\Delta H^{\ddagger}$, ±1 kcal mol^{-1}; $\Delta S^{\ddagger}$, ±2 cal $K^{-1}\,mol^{-1}$.
[b]Rate constants were inferred from visual comparison of the simulated ^1H NMR line shapes with the experimental line shapes. The values for CD_3OD are unpublished observations of R. Singh and G. M. Whitesides; all other values are from reference 15.

of 2-hydroxyethanethiolate is only twofold lower than that of 1-butanethiolate. In sterically hindered thiolates, introduction of a hydroxy group either β or γ to the C—S bond slows the interchange by approximately a factor of 15 in DMSO (Table 2). A *gem*-dimethyl effect and weaker solvation of the hydroxyl group in the sterically hindered substrate may result in greater intramolecular hydrogen bonding than in the sterically unhindered 2-hydroxyethanethiolate[15].

e. Reactions involving cyclic disulfides. The rate constant for degenerate intermolecular thiolate–disulfide interchange involving cyclic five-membered disulfides (1,2-dithiolane) is higher than that involving cyclic six-membered disulfides (1,2-dithiane) by a factor of *ca* 650 ($\Delta\Delta G^{\ddagger}$ *ca* 3.8 kcal mol^{-1})[17]. The rate constants for the cyclic six- and seven-membered disulfides are similar to those for noncyclic disulfides[17]. The ring strain of 1,2-dithiolane (estimated by calorimetry) is higher than that of 1,2-dithiane by 3.7 kcal mol^{-1} [82]. The agreement of the value of $\Delta\Delta G^{\ddagger}$ (3.8 kcal mol^{-1}) from kinetics and the value of ring strain (3.7 kcal mol^{-1}) from calorimetry suggests that the ring strain in the cyclic five-membered disulfide is completely released in the transition state[17]. In the transition state, the S—S bond is expected to be longer than in the ground state of disulfide, and the CSS angle at the central carbon is energetically most favorable at *ca* 90°[83,84]. This geometry expected for the transition state is better matched by the structure of the ground state of the cyclic five-membered disulfide than that of cystine, based on X-ray crystallographic structural parameters[17].

4. Solvent effects

The rates of thiolate–disulfide interchange reactions are larger in polar aprotic solvents (DMSO, DMF) than in polar protic solvents (water, methanol) by a factor of *ca* 10^3 (Table 2)[15]. The nature of the counter ions (Na^+, K^+), or addition of 18-crown-6 to the reaction involving potassium alkanethiolate, has no effect on the rate of thiolate–disulfide interchange in DMSO[15].

The transition state is expected to have a more delocalized negative charge and therefore to be less influenced by solvation than the ground state thiolate. The higher rates of thiolate–disulfide interchange in polar aprotic solvents (DMSO, DMF) than in polar protic solvents (water, methanol) may be explained by a smaller destabilization of the transition state than that of the ground state thiolate, in going from polar protic solvents to polar aprotic solvents (Figure 3)[15]. The log of the rate constant depends linearly on the solvent composition in mixtures of water and DMSO (Figure 4)[15,17].

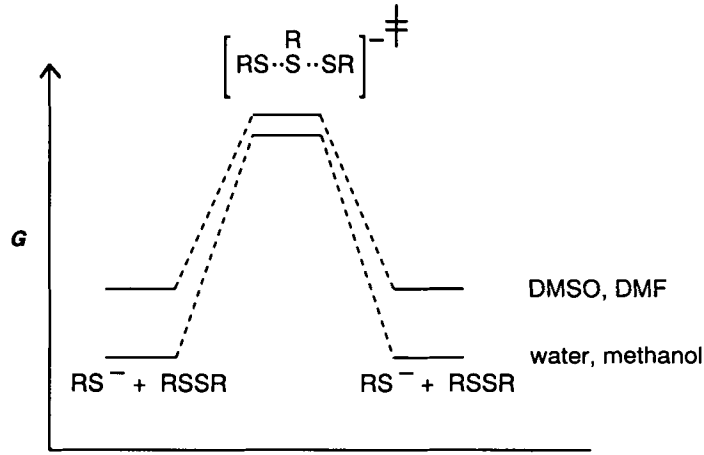


FIGURE 3. Hypothetical plot of free energy vs reaction coordinate for thiolate–disulfide interchange reaction in polar protic solvents (water, methanol) and in polar aprotic solvents (DMSO, DMF)

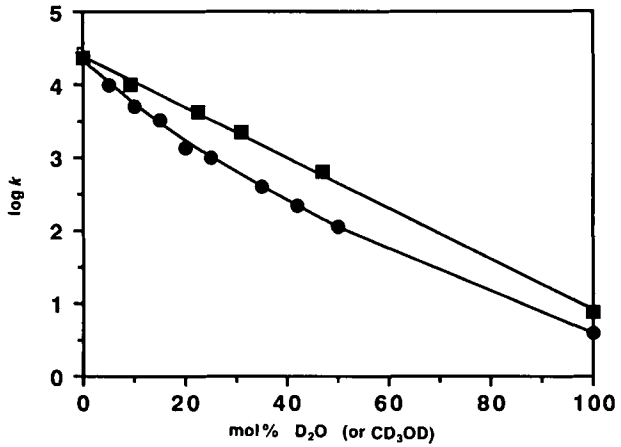


FIGURE 4. Effect of addition of D_2O (■) or CD_3OD (●) on log of rate constants (k) of thiolate–disulfide interchange of potassium 2-hydroxyethanethiolate and bis(2-hydroxyethyl) disulfide in DMSO-d_6. The values of rate constants are for 297 K and are in $M^{-1}s^{-1}$

The corresponding plot for methanol–DMSO mixture, although not linear, also shows a gradual decrease in the log of the rate constant with an increasing mole fraction of methanol (Figure 4)[85]. The absence of a sharp drop in rate on addition of small mole fractions of water or methanol to DMSO suggests the absence of specific solvation of thiolate by polar protic solvents. In going from polar protic to polar aprotic solvents, the increase of approximately 10^3 in rate of reaction involving thiolate anion (RS^-) is less than that (10^6–10^7) involving S_N2 reactions of alkoxide anion (RO^-)[15]. The alkoxide anions are more solvated in water than are thiolate anions[86,87].

The rate of thiolate–disulfide interchange of 1,3-propanedithiolate and 1,2-dithiolane (cyclic five-membered disulfide) is extremely fast in DMSO (k_{RS^-} *ca* $10^8\ M^{-1}\ s^{-1}$) and only *ca* 10^2 slower than the diffusion limit[17] (equation 20). This large rate arises from two factors: (i) the ground state of 1,2-dithiolane is destabilized relative to the transition state because of ring strain, and (ii) the thiolate is relatively more destabilized in DMSO than is the transition state with its more delocalized charge[17].

(20)

A comparison of the strengths of the $RS^-\cdots HOR$ complexes and $RO^-\cdots HOR$ complexes by pulsed high-pressure mass spectrometry shows that complexes incorporating alkoxides are more stable by 2–7 kcal mol^{-1} than those incorporating thiolates[88]. The weak contributions of ionic hydrogen bond to solvation in $RS^-(H_2O)_n$ complexes are effectively dissipated within the first 2–3 solvent molecules ($n = 2$–3)[88].

5. *Gas-phase studies*

The reaction of ethanethiolate ($C_2H_5S^-$) with dimethyl disulfide (CH_3SSCH_3) in the gas phase occurs exclusively with thiolate–disulfide interchange; this reaction yields methanethiolate (CH_3S^-) and mixed ethyl methyl disulfide ($CH_3SSC_2H_5$)[89]. A possible side reaction, the carbon-centered substitution to yield CH_3SS^- and $CH_3SC_2H_5$, is not observed[89]. The value of the rate constant for the reaction of ethanethiolate with dimethyl disulfide in the gas phase is estimated as $3 \times 10^9\ M^{-1}\ s^{-1}$. Comparison of this rate constant with the collisional rate constant suggests that the reaction occurs with a probability of 0.003 per collision[89].

6. *Catalysis*

A number of species—aromatic thiols, nonthiol nucleophiles and cations—have been surveyed as potential catalysts for thiol–disulfide interchange in water[15]; catalysis is observed only with selenols[15,19], and even with these species the magnitudes of the catalysis are not large.

Selenols are only effective as catalysts for thiol–disulfide interchange reactions involving strongly reducing dithiols[19]. The observed rate of reduction of bis(2-hydroxyethyl) disulfide by dithiothreitol in water at pH 7 is enhanced by a factor of 15 in the presence of 5 mol% 2-aminoethaneselenol. This catalytic activity of selenols is probably due to a combination of the low pK_a (*ca* 5.5 to 7) (and hence significantly high concentration of RSe^- at pH 7) for selenols, and weak solvation and high polarizability (and hence high nucleophilicity) of the selenolate anion. The precursors of selenols, diselenides (RSeSeR) and selenocyanates (RSeCN) can also be conveniently used to catalyze the thiol–disulfide interchange reactions involving strongly reducing dithiols[19]. Thiol–disulfide interchange reactions involving monothiols are not catalyzed by selenols, because these disulfides oxidize the selenols to diselenides. Strongly reducing dithiols at

even moderate concentrations can reduce diselenides to selenols, and therefore in the thiol–disulfide interchange reactions involving strongly reducing dithiols, the selenol remains in the reduced (and catalytic) state[19].

7. Comparison with selenolate–diselenide interchange

The observed rate of selenolate–diselenide interchange for selenocysteamine and selenocystamine ($k_{obsd} = 1.65 \times 10^7\ M^{-1}\ s^{-1}$)[69] in water at pH 7 is faster by a factor of 10^7 than the corresponding thiol–disulfide interchange reaction of cysteamine and cystamine ($k_{obsd} = 1.4\ M^{-1}\ s^{-1}$), possibly due to (i) better nucleophilicity and better leaving group ability of selenolate than for thiolate, and (ii) low pK_a of selenols (*ca* 5.5 to 7) and therefore high concentration of the nucleophilic selenolate anion at pH 7[69]. In this system, the absolute rate constant (k_{RSe^-}) for the selenolate–diselenide interchange is higher than that of the structurally analogous thiolate–disulfide interchange (k_{RS^-}) by 2.4×10^5.

D. Transition State Structure

A study of crystal structures of compounds containing divalent sulfur (Y—S—Z; Y,Z ≠ H) shows that nonbonded contacts of nucleophiles are directed along the extension of one of the covalent bonds to sulfur[26]. According to the frontier-orbital model, the HOMO of the nucleophile interacts preferentially with the LUMO (σ^*) orbital of S—Y or S—Z. Attractive nonbonded interactions may represent the incipient stages of chemical reactions[26]. The preferred attack of the thiolate nucleophile on the disulfide (S—S) bond is therefore along the extension of the S—S bond.

In the transition state the negative charge must be delocalized over the three sulfur atoms. The transition state is qualitatively pictured as having greater negative charge at the terminal sulfurs than at the central sulfur, based on the value of the Brønsted coefficients: $\beta_{nuc} = \beta_{lg} \approx 0.5$ (by symmetry); $\beta_c \approx -0.3$ to -0.4[5–8]. The absence of curvature in the Brønsted plots for attack of thiolate anions having a range of pK_a values on a single disulfide suggests that the transition state structure does not change with changes in structure of the thiolate anions or the disulfide groups for these thiol–disulfide interchange reactions[5–7]. Superposition of plots of $\log k_{RS^-}$ (rate constant) vs $\log K_{s^-}$ (equilibrium constant) for a series of thiol–disulfide interchange reactions, varying in equilibrium constant by a factor of approximately 10^{21}, shows gradual curvature of the type expected on the basis of the Hammond postulate[8]. Although these data indicate a change in transition state structure[8], factors other than Hammond postulate behavior, such as solvation, can cause curvature in Brønsted plots. Although thiolate anions are not as strongly solvated as alkoxide anions, interpretations suggesting a change in structure of the transition state from a curved Brønsted plot should be treated with caution[50,90,91].

The value of $\Delta S^{\ddagger}$ for thiol–disulfide interchange in polar protic (water, methanol) and polar aprotic (DMSO, DMF) solvents is *ca* -10 to -16 cal K^{-1} mol^{-1} (Table 2)[15]. This value is less than that expected for complete localization of two particles in the transition state, and suggests that the decrease in entropy in the transition state relative to two particles in the ground state is partially compensated either by release of solvent molecules attached to the thiolate in the ground state[15], or by a relatively loose transition-state structure (with two weak, partial S··S bonds) or both.

E. Theoretical Calculations on Thiol–Disulfide Interchange

An *ab initio* MO study on the thiolate–disulfide interchange reaction indicates that the reaction is a typical S_N2 reaction and proceeds via a single transition state with little

conformational distortion[92]. The charge distribution in the transition state is calculated to be higher on the two terminal sulfurs and lower on the central sulfur, in agreement with the experimental results based on Brønsted coefficients[92]. The geometry of the transition state has been suggested to be a trigonal bipyramidal configuration at the central sulfur with the nucleophilic and leaving sulfurs in apical positions[83]. The participation of d orbitals is not essential in stabilization of the transition state[83].

$$\begin{array}{c} 0.4- \quad 0.2- \quad 0.4- \\ \mathrm{RS\cdots S\cdots SR} \\ \mathrm{R} \end{array}$$

F. Mechanistic Uncertainties

The geometry of the transition state is unclear: the relative dispositions of the alkyl groups on the three sulfur atoms in the transition state are not known. The symmetry of the transition state with respect to the nucleophilic and leaving group thiols is still ambiguous, although microscopic reversibility would indicate a symmetrical structure if there is a single transition state. Unsymmetrical transition states connected by a symmetrical intermediate are possible, but seem unlikely. A more complete characterization of the Brønsted coefficients, and appropriate calculations, will both be useful in understanding this issue. The transition state seems to be less solvated than the ground state thiolate, but the degree of solvation of the transition state is not known. Resolving the question of solvation may be useful in designing strategies for catalysis of thiol–disulfide interchange. Strategies for catalysis based on desolvation and destabilization of the ground state thiolates seem unlikely to produce large effects. A more plausible strategy (although one that represents a difficult problem in molecular design) will be to stabilize the transition state of the catalyzed reaction, perhaps by appropriate charge–charge interactions in the charge-delocalized transition state.

IV. EQUILIBRIUM IN THIOL–DISULFIDE INTERCHANGE REACTIONS

A. Equilibria Involving Monothiols

In the equilibria involving a monothiol (RSH) and a disulfide (R'SSR') (equations 1 and 11), the distribution of species is nearly random or statistical if the pK_a values of the thiols (RSH and R'SH) are similar, i.e.

$$K_1 = \{([\mathrm{RSSR'}][\mathrm{R'SH}])/([\mathrm{RSH}][\mathrm{R'SSR'}])\} \approx 2$$

and

$$K_2 = \{([\mathrm{RSSR}][\mathrm{R'SH}])/([\mathrm{RSH}][\mathrm{RSSR'}])\} \approx 0.5$$

The experimental values of equilibrium constants for the interchange involving glutathione (RSH) and cystine (R'SSR') in water at pH 7 are similar to those expected from random distribution, $K_1 = 3.7$ and $K_2 = 0.79$[23,73,93].

The equilibrium constants for thiol–disulfide interchange reactions for a series of monothiols and disulfides, at values of pH in which the equilibrium concentration of thiolate anion is small, are relatively insensitive to changes in substituents (except for sterically hindered structures with alkyl substituents at carbon α to sulfur)[68]. The formation of bis(*t*-butyl) disulfides is disfavored in equilibria involving *t*-butyl thiol and mixed *t*-butyl 1-butyl disulfide[75,77,94], and the formation of penicillamine disulfide is disfavored in equilibria involving penicillamine and mixed penicillamine cysteine disulfide[68].

The equilibrium constant for the interchange of a monothiol (RSH) with a disulfide

(R'SSR') is pH dependent if the values of pK_a of the thiols (RSH and R'SH) are different. In general, the equilibrium mixture favours the most stable thiolate: the equilibrium is, in effect, driven to one side by the free energy of ionization of the most acidic thiol.

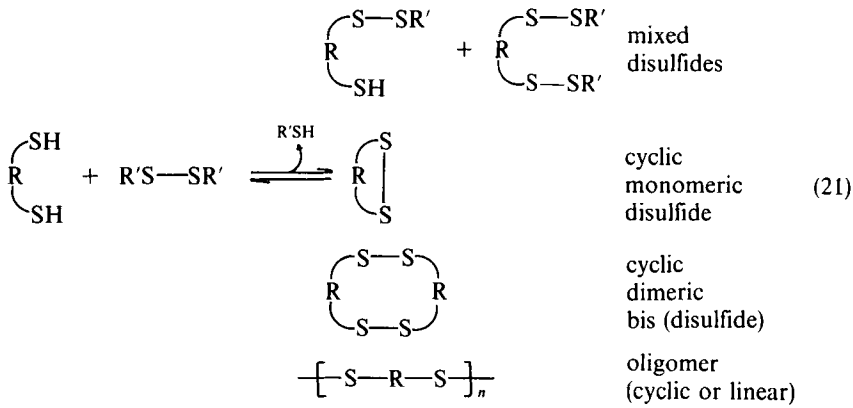
At a value of pH between the values of pK_a of RSH and R'SH, the formation of the thiolate corresponding to the thiol of lower pK_a is preferred[5]. The equilibrium of the thiol–disulfide interchange reaction involving mercaptoethanol ($pK_a = 9.6$) and Ellman's disulfide (pK_a of EllSH *ca* 4.5) in aqueous buffer at pH 7–8 is shifted entirely toward the formation of Ellman's thiolate and the disulfide of mercaptoethanol. The amount of Ellman's thiolate is approximately quantitatively equal to that of initial mercaptoethanol, and hence the utility of Ellman's assay.

The values of the equilibrium constant (K^{obsd}) of thiol–disulfide interchange in aqueous medium can be dissected into K^{SH} (defined for thiols) and K^{S^-} (defined for thiolates)[5]. The equilibrium constant K^{SH} shows no obvious correlation with the values of pK_a, but is influenced by steric effects. The plot of the log of the equilibrium constant K^{S^-} vs $2(pK_a^{RSH} - pK_a^{R'SH})$ is linear (slope *ca* 1.2)[5]. K^{S^-} is therefore strongly influenced by the acidities of the participating thiols[5].

Electrostatic effects on equilibria of thiol–disulfide interchange reactions are small in magnitude, but occur in the expected direction. The formation of mixed disulfide with unlike charges on the two component thiols is favored, and the formation of mixed disulfide with like charges on the two component thiols is disfavored[72]. In the equilibrium involving *N*-acetylcysteine (**A**, bearing one negative charge on the cysteine carboxylate) and the 85–114 peptide fragment of Kunitz soybean trypsin inhibitor (**B**, bearing one positive charge on the *N*-terminal leucine residue next to cysteine), the proportions of disulfides **A**—**B**, **A**—**A** and **B**—**B** in water at pH 7 and low ionic strength (20 mM) are 72%, 10% and 18% respectively, and at high ionic strength (1 M) are 61%, 15% and 24% respectively. The expected statistical distributions are 50%, 25% and 25% respectively. The electrostatic effect at low ionic strength (20 mM) favors the formation of **A**—**B**, and disfavors the formation of **A**—**A** more than that of **B**—**B**, because the two negative charges on **A**—**A** are closer to each other than are the positive charges on **B**—**B**. At high ionic strengths the electrostatic effects are shielded and the observed distribution is similar to that statistically expected[72].

B. Equilibria Involving α,ω-Dithiols

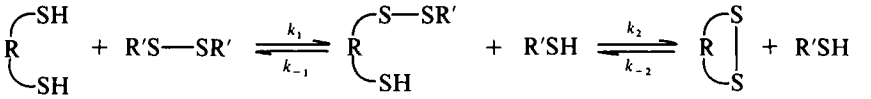
Thiol–disulfide interchange of α,ω-dithiols (HS—R—SH) with a disulfide (R'SSR') can generate a variety of products ranging from cyclic monomeric disulfide, cyclic dimeric



(21)

bis(disulfide) to oligomeric disulfide (equation 21). The product distribution depends on the nature of R, and on the concentrations of the dithiol and the disulfide.

Cyclic monomeric disulfides are the major products for the thiol–disulfide interchange reactions of 1,3-dithiols to 1,6-dithiols in which the two thiol groups are separated by three to six atoms (equations 22 and 23). The formation of the cyclic monomeric disulfide occurs via the intramolecular thiol–disulfide interchange reaction of the intermediate mixed disulfide (k_2, equation 22); this reaction is significantly faster than the corresponding intermolecular reaction. High effective concentration (EC, see below and also Table 3, for footnote *c*) favors the formation of the cyclic monomeric disulfide[17].



(22)

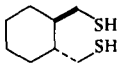
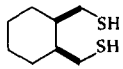
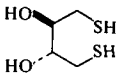
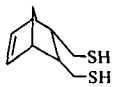
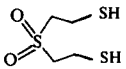
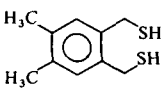
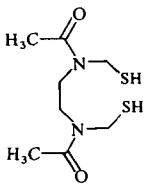
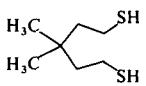
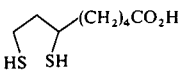
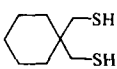
$$K_{eq} = ([\overline{SRS}][R'SH]^2)/([HS—R—SH][R'SSR']) \quad (23)$$

The stability of the cyclic disulfide is an important factor in the overall equilibrium. Cyclic six-membered disulfides have a CSSC dihedral angle of *ca* 60° and are more stable than cyclic five-membered disulfides, which have a CSSC dihedral angle of *ca* 30°[14]. The ring strain in cyclic five-membered disulfides has been estimated as 3.7 kcal mol^{-1} higher than that for the cyclic six-membered disulfides[82]. It has been estimated that the ring cleavage (k_{-2}, equation 22) of cyclic five-membered disulfides is faster by a factor of *ca* 600 than that of cyclic six-membered disulfides[17]. On the other hand, the formation of the cyclic five-membered disulfide (k_2, equation 22) is faster by a factor of *ca* 20 than that of the cyclic six-membered disulfide, based on values of kinetic effective concentrations for analogous reactions[17]. The overall result is that K_{eq} for formation of a six-membered disulfide from the corresponding dithiol is more favorable than that for a five-membered disulfide from its dithiol by a factor of *ca* 30[13,17].

The reducing ability of α,ω-dithiols depends on two factors: (i) the stability of the monomeric cyclic disulfide, and (ii) the kinetic effective concentration for the intramolecular ring-closure step (k_2, equation 22). 1,4-Alkanedithiols that form strain-free cyclic six-membered disulfides are the most reducing (K_{eq} *ca* 10–10^3 M, equation 23); 1,3- and 1,5-alkanedithiols that form five- and seven-membered rings respectively are *ca* 10-fold less reducing (Table 3). Rings smaller than six-membered are less favored primarily for enthalpic reasons (ring strain, including angle strain in the CSSC group). Rings larger than six-membered are less favored because of conformational entropy (low kinetic effective concentration for the intramolecular ring-closure)[13,16]. In 1,8-dithiols, the effective concentration for intramolecular ring-closure is sufficiently low that intermolecular oligomeric disulfide formation becomes competitive with cyclic monomeric disulfide formation[13]. The reduction potentials of dithiols that form oligomeric products are similar to those for monothiols[5,13]. 1,2-Dithiols form cyclic bis(disulfide) dimers in relatively dilute solution (*ca* 1 mM), but polymerize at higher concentrations[13].

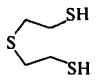
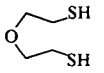
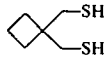
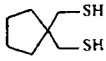
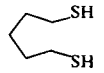
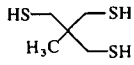
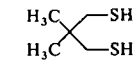
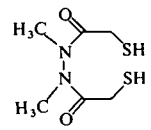
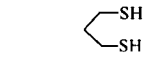
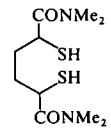
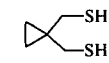
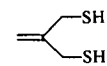
Molecular mechanics calculations of equilibria of thiol–disulfide interchange reactions involving α,ω-dithiols with 1,2-dithiane correlate well with experimental results, but do not give the absolute values of energies[16]. The empirical relationship between calculated differences in strain energy (ΔSE) and the experimental values of ΔG is: ΔG *ca* 0.4ΔSE. Why the molecular mechanics calculations overestimate strain is not known. This correlation may be a useful guide for designing α,ω-dithiols of appropriate reduction potential.

TABLE 3. Equilibrium constants for thiol–disulfide interchange

Structure	$K(ME^{ox})$	$\varepsilon_0(V)^a$	Eq. against[b]	References
Dithiols that form cyclic monomers[c]				
	1500 M	−0.354	DTT	*d,e*
	670 M	−0.344	DTT	*d,e*
	180 M	−0.327	Lip	*d,e*
	77 M	−0.316	DTT	*d,e*
	65 M	−0.314	DTT	*d,e*
	63 M	−0.313	DTT	*f*
	44 M	−0.309	DTT	*d,e*
	19 M	−0.298	DTT	*e,g*
	15 M	−0.295	DTT	*f*
	14 M	−0.294	DTT	*d,e*
	8.6 M	−0.288	ME, DTT	*d,e*
	8.0 M	−0.287	DTT	*d,e*

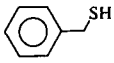
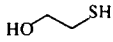
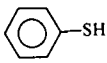
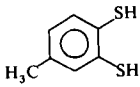
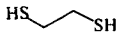
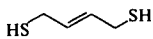
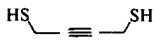
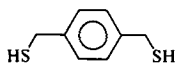
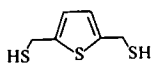
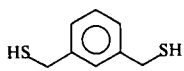
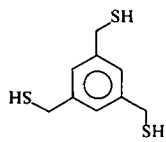
(*continued*)

TABLE 3. (*continued*)

Structure	$K(ME^{ox})$	$\varepsilon_0(V)^a$	Eq. against[b]	References
	6.7 M	−0.285	DTT	*d,e*
	6.1 M	−0.284	DTT	*d,e*
	4.4 M	−0.279	DTT	*d,e*
	3.6 M	−0.277	DTT	*d,e*
	3.6 M	−0.277	DTT	*d,e*
	3.1 M	−0.275	DTT	*d,e*
	2.9 M	−0.274	DTT	*d,e*
	2.5 M	−0.272	DTT	*h*
	2.3 M	−0.271	ME, DTT	*d,e*
	1.8 M	−0.269	DTT	*i*
	1.2 M	−0.263	DTT	*d,e*
	0.67 M	−0.255	DTT	*d,e*
6,6′-sucrose disulfide	0.30 M	−0.245	ME	*j*
$HS(CH_2)_6SH$	0.21 M	−0.240	DTT	*d,e*

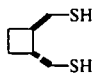
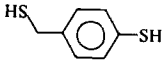
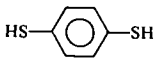
(*continued*)

TABLE 3. (*continued*)

Structure	$K(ME^{ox})$	$\varepsilon_0(V)^a$	Eq. against[b]	References
Monothiols that form dimers				
	2.6	−0.272	ME	*d*
$CH_3(CH_2)_6SH$	1.1	−0.261	ME	*d*
	1.0	−0.260	ME	*d*
	0.31	−0.245	ME	*g*
Dithiols that form cyclic dimers				
	0.40 M	−0.254	ME	*d,e*
	0.38 M	−0.254	ME	*d,e*
	0.32 M	−0.253	ME	*e,g*
	0.035 M	−0.239	ME	*d,e*
Dithiols that form polymers				
	4.8	−0.280	ME	*d*
	4.0	−0.278	ME	*d*
	3.4	−0.276	ME	*g*
	3.1	−0.275	ME	*d*
	3.0	−0.275	ME	*g*
	2.8	−0.274	ME	*k*

(*continued*)

TABLE 3. (*continued*)

Structure	$K(ME^{ox})$	$\varepsilon_0(V)^a$	Eq. against[b]	References
	1.8	−0.268	ME	*d*
$HS(CH_2)_8SH$	1.7	−0.267	ME	*d*
$HS(CH_2)_7SH$	1.4	−0.265	ME	*d*
	1.3	−0.264	ME	*g*
	0.20	−0.240	ME	*g*

[a] $\varepsilon_0(V)$ values vs standard hydrogen electrode at pH 7.0 and 25 °C. All $\varepsilon_0(V)$ values are calculated using the $\varepsilon_0(V)$ values for lipoic acid [−0.288 V, D. R. Sanadi, M. Langley and R. L. Searls, *J. Biol. Chem.*, **234**, 178 (1959) and C. V. Massey, *Biochem. Biophys. Acta*, **37**, 314 (1960)] and the K_{eq} value between lipoic acid and the compound of interest.

[b] Abbreviations: DTT, dithiothreitol; Lip, lipoic acid; ME, 2-mercaptoethand.

[c] The value of $K(ME^{ox})$ for this group of compounds is sometimes called the effective concentration (EC).

[d] Equilibrations were carried out at 25 °C, in a 1/1 mixture of d_4-methanol/phosphate buffer (50 mM, pH 7.0) in D_2O, see Reference 13.

[e] The equilibrium constants (K) in the Houk and Whitesides paper (13) were systematically in correct by a factor of 10^3 (originating in error in manipulation of units during the original calculations) and have been adjusted accordingly. The values of equilibrium constants, which were obtained from equilibrium with DTT, have also been readjusted by a factor of approximately 2 so as to obtain a similar value to that reported in this paper.

[f] Equilibrations were carried out at 25 °C in a 1/1 mixture of d_4-methanol/phosphate buffer (50 mM, pH 7.0) in D_2O, see G. V. Lamoureux and G. M. Whitesides, *J. Org. Chem.*, **58**, 633 (1993).

[g] Equilibrations were carried out in d_4-methanol with 0.02 mM sodium methylate added, see Reference 13.

[h] Equilibrations were carried out in D_2O (pD 7.0, 50 mM phosphate), see Reference 18.

[i] Equilibrations were carried out in D_2O (pD 7.0, 50 mM phosphate), see Reference 20.

[j] Equilibrations were carried out in D_2O (pD 7.0, 50 mM phosphate), see W. J. Less and G. M. Whitesides, *J. Org. Chem.*, **58**, 642 (1993).

[k] Equilibrations were carried out in d_6-benzene with 0.02 mM tetramethylguanidine added, see Reference 13.

The equilibrium constant for the thiol–disulfide interchange of an α,ω-dithiol with a disulfide (equations 22 and 23) has also been termed as the 'effective concentration' (EC)[95,96]. The equilibrium expression for effective concentration is a measure of the propensity of thiols to form the cyclic disulfide[96]. The EC has also been interpreted in terms of the *proximity* of these thiol groups in the ground state (that is, as a kind of local concentration), and thus used to infer information about conformation. Considering that the value of the equilibrium constant is very strongly influenced by strain in the CSSC group and by ring strain (for cyclic disulfides), its interpretation in terms of 'proximity' and 'concentration' must be evaluated with the possibility of contributions from these terms in mind[16]. If the EC is used (and interpreted) just as an equilibrium constant, but as one with an easily remembered reference value (EC *ca* 1–10 M for an α,ω-dithiol forming a strain-free cyclic disulfide) it has the virtue of being easy to remember and to interpret.

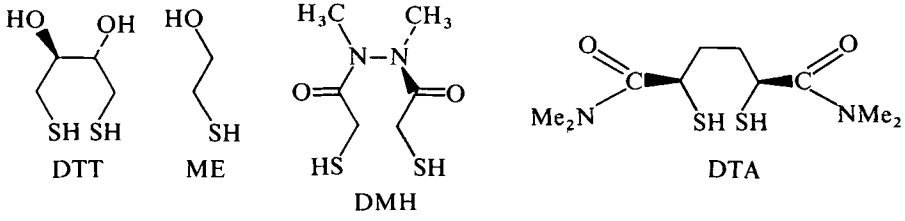
The equilibrium expression for effective concentration ($EC = K_{eq}$, equations 22 and 23) involves a ring-closure step (k_2) in the forward reaction (k_2 is a measure of the kinetic effective concentration), and a ring-cleavage reaction (k_{-2}) in the reverse direction. The ring-cleavage reaction, k_{-2}, is faster for a more strained cyclic disulfide than for an unstrained one, and correspondingly the value of the equilibrium expression for effective concentration ($EC = K_{eq}$) is lower for the more strained cyclic disulfide.

In cases involving cyclic disulfides with ring strain, the trends of the equilibrium expression for effective concentration (equilibrium EC) may be different than the trends of the kinetic values for effective concentration (kinetic EC). In a comparison of the formation of cyclic five-membered disulfide and cyclic six-membered disulfide, the equilibrium EC (related to K_{eq}, equations 22 and 23) is favored for the formation of the six-membered disulfide by a factor of 30 over the five-membered disulfide, whereas the kinetic EC (related to k_2, equation 22) is higher for the ring-closure reaction for formation of the five-membered disulfide than that of the six-membered disulfide by a factor of 20. The value of the equilibrium EC is easier to determine than that of the kinetic EC. As we have indicated, however, the equilibrium EC is a direct measure of proximity only when there is no strain in the disulfides or dithiols, and it is perhaps most useful as a measure of proximity when these other factors (e.g. ring strain reflecting an unfavorable CSSC dihedral angle; terms destabilizing the dithiol relative to disulfide) are absent or can be independently estimated[16].

V. APPLICATIONS OF THIOL–DISULFIDE INTERCHANGE IN BIOCHEMISTRY

The subject of the thiol–disulfide interchange reaction is an important one in biochemistry, and has been discussed extensively elsewhere[1–3]. Here we will only outline some of the issues.

Disulfide-reducing reagents are used in biochemistry for a number of purposes, especially in reduction of cystine groups in proteins and in maintaining essential thiol groups in their reduced state[97]. α,ω-Dithiols, such as dithiothreitol (DTT)[70], *N,N'*-dimethyl-*N,N'*-bis(mercaptoacetyl)hydrazine (DMH)[18] and *meso*-2,5-dimercapto-*N,N,N',N'*-tetramethyladipamide (DTA)[20], have higher reduction potential than cystine groups in proteins, and are useful disulfide-reducing reagents because they react specifically with the cystine disulfide to be reduced without any unwanted side-reaction with the protein. The value of the first pK_a of DTT is 9.2[5], and it is therefore relatively slow as a reducing reagent at pH 7. DMH and DTA (pK_a *ca* 8) reduce small organic disulfides and disulfide bonds in proteins *ca* 7 times faster than does DTT in water at pH 7[18,20]. Mercaptoethanol (ME, pK_a *ca* 9.6) is inexpensive and is used in large amounts (0.1–0.7 M) in biochemical manipulations, for example in conjunction with SDS gel-electrophoresis[97]. Mercaptoethanol is weakly reducing and it often generates complex reaction mixtures containing mixed disulfides[5].



The cyclic five-membered disulfide—lipoamide—is a cofactor of the pyruvate dehydrogenase complex[98,99]. The rate of ring opening of this cyclic five-membered disulfide by thiolate–disulfide interchange is faster by a factor of *ca* 10^3 than that involving cyclic six- or seven-membered disulfides[17]. The evolutionary selection of lipoamide as a cofactor in pyruvate dehydrogenase complex may reflect the fast rate of ring opening of the cyclic five-membered ring by nucleophiles and the resulting ability of the lipoamides to maintain a high flux through the pyruvate dehydrogenase complex[17].

The values of pK_a of thiol groups in proteins have been measured kinetically from the Brønsted correlation of thiol–disulfide interchange reactions[11]. The pK_a of the active-site thiol in papain is estimated as *ca* 4 at pH 6, and *ca* 8.4 at pH 9[11]. At low pH (*ca* 6) the proximate positively charged group increases the acidity of the active-site thiol in papain. The pK_a of the thiol group of reduced lysozyme is *ca* 11. These values of pK_a, although semiquantitative, are useful for comparison with the values of pK_a determined by other methods[11].

The redox equilibria between the cystine-bridged cyclic disulfide structures in proteins and their corresponding reduced open-chain α,ω-dithiol forms have been measured for several proteins[3]. The value of the equilibrium constant (or equilibrium expression for effective concentration, equilibrium EC) for the thiol–disulfide interchange reaction of a protein α,ω-dithiol can be a useful measure of proximity of the two thiol groups in the protein if there is no ring strain associated with the corresponding cyclic disulfide. A high value of the equilibrium EC suggests that the two thiol groups are nearby spatially, are limited in mobility and can form a CSSC group with little or no angle strain[16,95,96].

The disulfide bonds in proteins are formed after translation[100,101]. The pathway of sequential disulfide bond formation has been studied for bovine pancreatic trypsin inhibitor (BPTI)[102,103] and for ribonuclease A[104]. In the case of BPTI, interpretations of different sets of data have led to different conclusions[102,103]. The conclusion of Weissman and Kim—that all well-populated folding intermediates in the oxidative folding of BPTI contain only native disulfide bonds—is still being actively debated[105,106].

The inclusion bodies, obtained from the expression of eukaryotic proteins in genetically engineered *E. coli*, may contain protein with unformed and mismatched disulfide bonds[107,108]. The conversion of the 'wrongly' disulfide-connected protein to the 'correctly' disulfide-connected protein is a major problem in biotechnology. The general approach is to reduce the 'wrongly' disulfide-connected protein completely and to oxidize it gradually with a redox buffer containing a mixture of thiol and disulfide[109]. Protein–disulfide isomerase has been proposed as catalyst for the thiol–disulfide interchange involving proteins[110]. Its low catalytic activity and absence of specificity make its biological role uncertain[111,112]. Thioredoxin has a cysteine of low pK_a and it reacts with disulfides rapidly at pH 7. Thioredoxin is redox-coupled to NADPH via the enzyme thioredoxin reductase, and may be of metabolic significance in thiol–disulfide interchange reactions[113–115].

VI. CONCLUDING REMARKS

Thiol–disulfide interchange is a reversible S_N2 reaction that involves cleavage and formation of a covalent S—S bond. The active nucleophile is the thiolate anion (RS^-); the thiol (RSH) is not active. The rates of reaction of thiolate anions with disulfides show a Brønsted correlation with the values of pK_a of thiols. The value of the Brønsted coefficient for the nucleophilic thiol (*ca* 0.5) is well studied, but a more complete analysis of the Brønsted coefficients for the central and leaving group thiols would be a useful step toward a better understanding of the structure of the transition state.

The rate constant of the thiolate–disulfide interchange reaction (k_{RS^-}, based on the concentration of thiolate anion) is influenced by factors such as pK_a of thiol and CSSC dihedral angle in the disulfide. The rate constant (k_{RS^-}) increases with increasing values of pK_a of the thiols because of the increasing nucleophilicity of the thiolate anions. The observed rate constant of reaction (k_{obsd}), however, is optimum for the value of pK_a of the thiol equal to the pH of the solution. The most stable CSSC dihedral angle in the disulfide is *ca* 90°. Cyclic five-membered disulfides, with CSSC dihedral angle of *ca* 30°, are strained, and are cleaved *ca* 10^3 times faster than the less-strained cyclic six-membered

disulfide. An improved theoretical conformational analysis of the ground state of cyclic disulfides—in terms of the bond angles, bond lengths, and the CSSC and CCSS dihedral angles—would be useful to predict the ring strains and rates of thiol—disulfide interchange reactions involving cyclic disulfides.

Thiolate–disulfide interchange reactions are faster in polar aprotic solvents such as DMSO and DMF than in water. The rate enhancement in going from water to polar aprotic solvents is lower than for reactions of alkoxide anions. The thiolate–disulfide interchange involving strained cyclic five-membered disulfide is extremely fast (k_{RS}-*ca* $10^8\ M^{-1}\ s^{-1}$) in polar aprotic solvents.

Disulfide bonds are present in proteins and are formed from the cysteine thiols after translation. The physical-organic study of several biochemical issues related to the thiol–disulfide interchange—the mode of formation of the 'correct' disulfide bonds, the degree of stability imparted to the protein by the disulfide bond, the strain in the large-ring protein disulfides, the role of thiol–disulfide interchange in regulation of protein activity and the design of reagents that can efficiently reduce disulfide bonds—would be important and useful.

VII. ACKNOWLEDGMENTS

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CHAPTER **14**

Vinyl sulfides

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I. INTRODUCTION

In this chapter the chemistry of vinyl sulfides including theoretical calculations, spectral properties, preparation, synthetic applications, etc., will be reviewed with the aim of giving a comprehensive picture of a variety of special features of these interesting compounds. The term 'vinyl sulfides', however, requires clarification in the present context. On the one hand, ignoring all functional derivatives of vinyl sulfides would in our opinion make the present review scanty. On the other hand, it is unreasonable to completely consider all compounds with the C=C—S— moiety, such as β-alkyl (or aryl)thio-substituted ethylenic carbonyl compounds, nitriles, etc., whose behavior is governed by the nature of the corresponding functional group rather than by the 'vinyl sulfide' moiety. Thiones existing in equilibrium with the corresponding enethiols, C=C—SH, both simple and functionally substituted ones, are also excluded from this chapter except for theoretical calculations and spectral investigations of the simplest representatives, vinyl mercaptan, CH_2=CH—SH and its analogs. The properties of enethiols have been reviewed elsewhere[1]. Therefore, our focus has been mainly upon the alkyl, aryl, heteroaryl, halo and alkoxy vinyl sulfides as well as on bis- and tris-[alkyl(aryl)thio]ethenes.

Vinyl sulfides are commonly considered to be one of the most versatile auxiliaries in organic synthesis and this is supported by a steadily growing number of applications of their synthetic ability[2–5]. They are of value as precursors of aldehydes[6] and ketones[7], including α,β-[2,3,5] and α,β,γ,δ-[8,9] unsaturated carbonyl compounds, cyclopropanes[10] and oxiranes[10] as well as olefins of controlled configuration[11–15]. A series of insect sex pheromones of high stereoisomeric purity were synthesized via bromo-substituted vinyl sulfides[16]. Some vinyl sulfide derivatives were successfully employed in the synthesis of rifamycin[9]. The vinyl sulfide moiety constitutes a part of the ajoene molecule and its homologues, potent antithrombotic agents isolated from garlic (*Alluim sativum*)[17] and the simplest divinyl sulfide was found in onion (*Alluim sativum* L) in the previous century[18].

The vinyl sulfide residue C=C—S is a principal structural unit of tetrathiafulvalenes, first prepared just in 1970[19] and now already grown up to an extension of organo-sulfur compounds, from which the first superconducting 'organic metals' have been discovered[20,21].

Recently, much attention has been paid to divinyl sulfide and its derivatives[22–24] as available monomers, cross-linking agents and building blocks for organic synthesis.

Consequently, the literature on the chemistry of the C=C—S moiety is huge and, of course, cannot be exhaustively covered in a chapter of limited space.

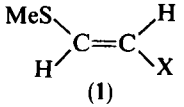
Therefore, in preparing this chapter we tried to concentrate on the basic physico-chemical properties, synthesis and most important reactions of simple vinyl sulfides, emphasizing as far as possible publications of the last two decades.

Since the chemistry of divinyl disulfides has recently been reviewed[25] the chemistry of C=C—S—S systems is not included in this chapter.

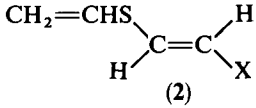
II. STRUCTURE AND CONFORMATIONS

A. Quantum-chemical Calculations

The electronic and spatial structure of vinyl sulfides was the subject of both semi-empirical and *ab initio* calculations as well as of numerous spectral investigations. Many authors paid much attention to the importance of the d-orbitals of sulfur in the interaction of the heteroatom with the double bond. The participation of the excited orbitals of sulfur (3d and 4s-AO) in saturated and unsaturated sulfides was analyzed[26] and it was concluded that their contribution to the ground state is negligible in both cases. The most reasonable valence state of the sulfur atom which makes the largest contribution to the ground state was found to be $2[s^2p^4]$ for saturated and $2[s^2p^4]$ and $3[s^2p^3]^+$ for unsaturated sulfides. Nevertheless the spd-basis set was used in a number of semiempirical and nonempirical calculations. It was found that while neglecting d orbitals at the nonempirical level would not cause any serious drawbacks if extended basis sets are employed, it is impossible to adequately reproduce the acceptor properties of the sulfur atom by applying semiempirical calculations without including its vacant d orbitals. CNDO/2 calculation of the *E*-isomers **1** and **2** in both the spd and sp basis at



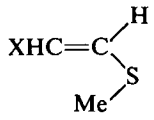
(1)



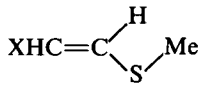
(2)

(X = OMe, Me, H, F, Cl)

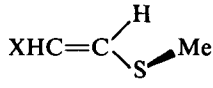
standard fixed geometry was performed[27] with the aim to compare transmission of electronic effects through the oxygen and the sulfur atoms and it was concluded that the higher transmission efficiency of the sulfur atom is due to $p\pi$–$d\pi$–$p\pi$ interaction. The sulfur atom, which in the sp basis acts as a π donor like the oxygen, becomes a π acceptor in the spd basis. The *E* and *Z* isomers of **1** (X = Me, OMe, SMe) were calculated in the sp basis[28] with fixed geometry taken from Reference 29. Using the sp basis has been justified by the fact that the data obtained in the spd basis were in poor agreement with experiment. The relative stabilities of the two planar (*syn* **3** and *anti* **4**) and one



(3)



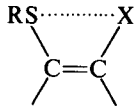
(4)



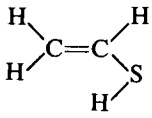
(5)

nonplanar (*gauche* **5**) conformations were estimated for both isomers. Equilibrium measurements[28] showed that the *E* isomer is the more stable one, ΔH values being 1.9, 9.9 and 2.8 kJ mol^{-1} for X = Me, OMe and SMe, respectively. The corresponding calculated values are 2.8, −3.6 and 2.4 kJ mol^{-1}. The discrepancy may be due to the use of the same geometry for both isomers. The *anti* conformation **4** was found to be the most stable one for X = Me, SMe, while the *gauche* form **5** is preferable for X = OMe. An analysis of through-space interactions leading to nonbonded attraction has been performed by Epiotis and coworkers[30] for the *Z* isomers of XCH=CHX molecules using the CNDO/2 method at standard geometry. The *Z* isomer was shown to be more stable than the *E* isomer, the ΔE values being 1.7 kJ mol^{-1} for X = OMe and

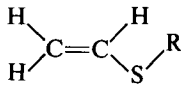
20.4 kJ mol^{-1} for X = SMe. Although only qualitative significance should be given to the latter value, as it is well known that the CNDO method overestimates the contribution of d orbitals, the relative stability is correctly reproduced. The greater stability of the *Z* isomers is due to long-range bonding interactions which may be depicted as follows:



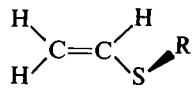
The potential function for internal rotation about the C_{sp^2}—S bond leading to three possible conformations **6–8** has been calculated by an *ab initio* method using different



(6)



(7)



(8)

basis sets[29,31–36] (for experimental evidence see Sections II.B and II.C). The potential curves obtained by fitting four points (for $\phi = 0$, 60, 120 and 180°) into the truncated Fourier expansion

$$V(\phi) = \tfrac{1}{2}[V_1(1 - \cos\phi) + V_2(1 - \cos 2\phi) + V_3(1 - \cos 3\phi)] \quad (1)$$

are depicted in Figures 1 and 2 for R = H and Me, respectively. It is clearly seen that the potential function is strongly dependent on the basis set used. Thus, although the *syn* conformation has been found to be the most stable in all approximations, the second stable form is varied from the *anti* conformation using the STO-3G basis set to the *gauche* conformation with different values of the CCSH torsional angle ϕ using the split basis sets. The preference of the *syn* conformation in spite of its more rigid constraints has for a long time been known experimentally, and recently it has been

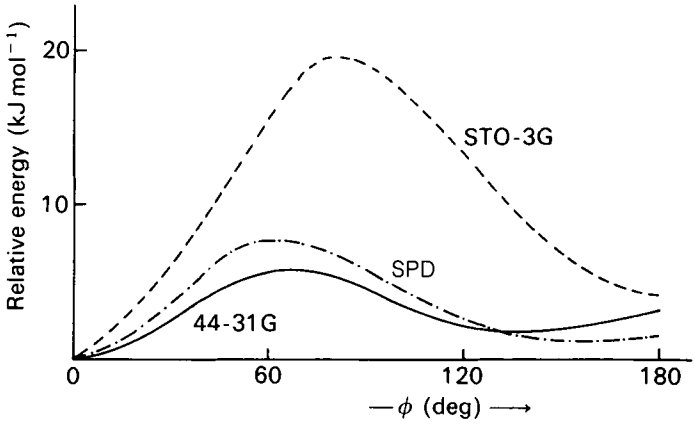


FIGURE 1. Potential functions for internal rotation in $H_2C{=}CH{-}SH$. For abbreviations see footnotes to Table 1. Reprinted with permission from Reference 31. Copyright (1978) American Chemical Society

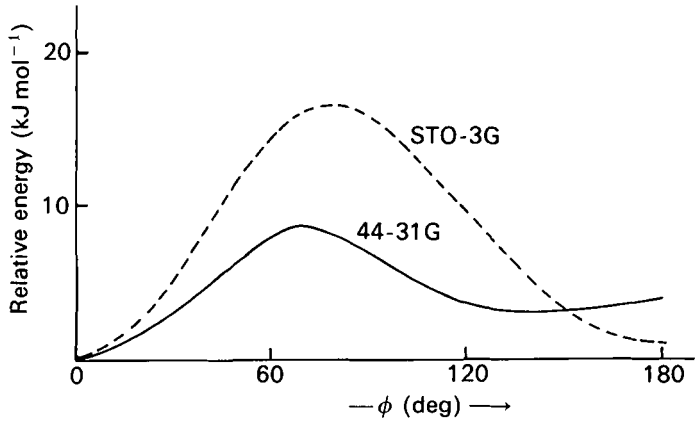
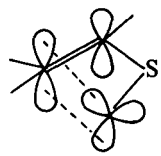


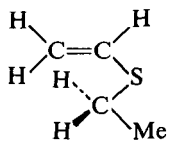
FIGURE 2. Potential functions for internal rotation in $H_2C{=}CH{-}SMe$. For abbreviations see footnotes to Table 1. Reprinted with permission from Reference 31. Copyright (1978) American Chemical Society

suggested that this may be due to an attractive hyperconjugative interaction between the methyl group and the π orbital[37,38] (similar arguments were employed to explain the *syn* preference of vinyl ethers[39]; (cf. Reference 38 and citations therein). Combining the pseudo-π-orbital of the methyl group with the sulfur lone pair and the C=C π bond results in a six-electron pseudoaromatic system which stabilizes the *syn* conformation:

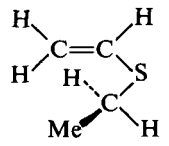


The relative energies of conformers **6**–**8** and the energetic barriers for the *syn* → *gauche* conversion are summarized for R = H, Me and Et in Table 1.

Two staggered conformations of the Et group (referred to as *anti* **9** and *gauche* **10** with respect to the S—C_{sp^3} rather than the C_{sp^2}—S bond[36]) are possible for the *syn*



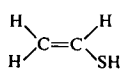
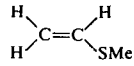
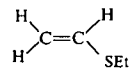
(9)



(10)

conformation of ethyl vinyl sulfide. Conformation **10** was calculated to be 2.1 kJ mol^{-1} less stable[36]. Several conclusions can be drawn by inspecting Table 1 and Figures 1 and 2. First, the energy barriers are overestimated by the STO-3G method which leads to incorrect prediction of the second stable conformation (*anti* instead of *gauche*). High-level 6-31G* computations with complete geometry optimization (MP2/6-31G*//6-31G* basis set) give the value of the barrier taken as the energy difference between the planar *syn*

TABLE 1. Calculated relative energies and barriers for *syn*→*gauche* rotation for simple vinyl sulfides

Compound	Method	Relative energy (kJ mol^{-1})			Barrier (kJ mol^{-1})	Reference
		syn	*gauche*	*anti*	*syn*→*gauche*	
	STO-3G	0	13.4	4.1	19.1[a]	31
	44-31G	0	2.3	3.2	5.6	31
	4-31G	0	1.9	3.3	6.0	32
	4-21G[b]	0	1.4	2.7	7.3	33
	3-21G	0	0	1.4	3.8	34
	SPD[c]	0	1.4	1.4	7.5	29
	MM[d]	0	2.5	3.4	3.8	34
	CNDO/2	0	4.0	3.8	13.0	35
	STO-3G[e]	0	9.5	1.1	16.7[a]	31
	44-31G[e]	0	3.6	3.9	8.3	31
	3-21G	0	0.8	4.6	6.5	34
	MM	0	1.7	4.3	7.1	34
	3-21G*	0	1.7	4.6	—	36

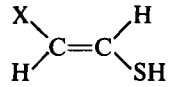
[a] *Syn* to *anti* conversion.
[b] 4-21G for first-row atoms and 33-21G for sulfur.
[c] SPD refers to a [(C/7,3), (H/4), (S/10,6,1)] basis contracted to [[C/4,2], [H/2], [S/6,4,1]].
[d] Molecular mechanics.
[e] The most stable staggered conformation of the Me group is adopted.

and perpendicular form as 8.4 kJ mol^{-1} [40]. Second, all split basis sets give very similar potential functions regardless of whether the polarization functions or d orbitals are included or not, Third, the MM method correctly reproduces the shape of the potential function of the sophisticated *ab initio* computations.

The p–π conjugation energy in vinyl sulfides has also been evaluated from the equilibrium studies of the isomer pairs[41–44], being 7.8 and 5.8 kJ mol^{-1} in methyl and ethyl vinyl sulfides, respectively (cf Table 1).

Of interest also are geometrical variations which accompany the rotation about the C_{sp^2}—S bond. The dominant relaxation was shown to be associated with the CCS valence angle and the C_{sp^2}—S bond length[33]. In going from *syn* **6** to *gauche* **8** and further to *anti* **7** conformation the CCS angle decreases by five degrees, reaching its minimum in the *gauche* form, and then slightly increases in the *anti* conformation. The C—S bond lengthens by 0.02 Å going through its maximum in the *gauche* conformation. The MP2/6-31G*//6-31G* method gives a lengthening of the C—S bond by 0.0195 Å and that of the C=C bond by 0.0008 Å in the perpendicular conformation compared to the *syn*[40]. These results imply that the conjugation between the sulfur lone pair and the π system would be greatest at the planar conformations, being rather larger at the *syn* than at the *anti* conformation.

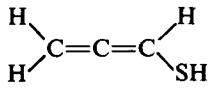
To evaluate the importance of conjugation effects in different conformations a series of related compounds **11** (X = CN, H, Me, F) with both π-acceptor and π-donor substituents has been calculated[33]. Since the substituents are located in the *trans*-β-position to the SH group, it was reasonable to rule out direct steric interactions as the mechanism by which the group X influences the conformation. The variation of the total energy with the torsional angle ϕ is depicted in Figure 3. As can be seen from



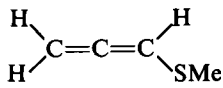
(11)

the figure, the *syn* conformation ($\phi = 0°$) is more stable for X = H and CN (π acceptor), while the *gauche* conformation ($\phi \approx 120°$) is preferable with π-donating substituents (Me and F). The trend observed can be rationalized in terms of the extent to which the sulfur lone pair participates in the π bonding. The cyano group would encourage high conjugation of the C=C bond with the sulfur lone pair thus stabilizing the planar conformations, especially the *syn*. The *gauche* is not a stable conformer in this case (Figure 3). With a π-donor substituent the C_α atom will be π-electron rich, which should prevent conjugation with the sulfur lone pair and hence destabilize the planar conformations, especially the *syn*.

Among other vinylic sulfides calculated one should mention *ab initio* calculations of allenyl thiol **12**[31], methyl allenyl sulfide **13**[31] and divinyl sulfide **14**[34].



(12)



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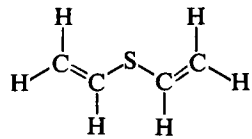


(14)

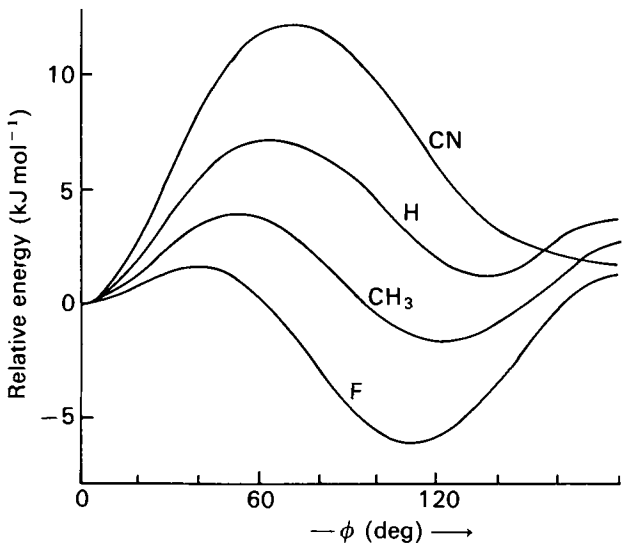
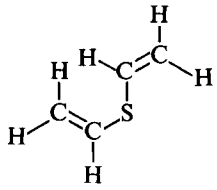


FIGURE 3. Potential functions for internal rotation in vinyl thiols **11** (scaled to the same zero at the *syn* conformation). Reproduced by permission of Elsevier Science Publishers BV from Reference 33

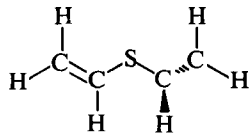
Only two forms, the *syn* and the *anti*, were calculated for allenyl thiol and the results were very similar to that found for vinyl thiol, the energy difference being 4.6 kJ mol^{-1} at the STO-3G level (cf. Table 1).

Methyl allenyl sulfide **13** is apparently less congested than methyl vinyl sulfide due to the absence of a close contact between the methyl group and the vinylic hydrogen. The results for these two molecules are similar in that the STO-3G method predicts the *syn* and the *anti* form to be the stable conformations, while the 44-31G method gives the *gauche* as the second stable conformation in both cases. However, the *syn–anti* energy difference is larger for methyl allenyl sulfide than for methyl vinyl sulfide (4.6 vs 1.1 kJ mol^{-1} at STO-3G and 7.4 vs 3.9 kJ mol^{-1} for 44-31G, respectively). This is probably due to the lower steric hindrance in the *syn* conformation for the former molecule. The *syn*→*gauche* barrier height is 5.0 kJ mol^{-1} which is 3.3 kJ mol^{-1} lower than in methyl vinyl sulfide (at 44-31G), and the *syn*→*anti* barrier height is 12.6 vs 16.7 kJ mol^{-1} (at STO-3G) and this has been ascribed[31] to a weaker π-character of the C—S bond.

Divinyl sulfide has two rotational axes and, hence, a more complicated conformational picture. If one torsional angle is kept fixed at 180° the potential function for internal rotation about the second C—S bond can be calculated; the results are displayed in Figure 4[34]. The major difference from the corresponding curves in Figures 1 and 2 is that the *syn,anti* conformation **15** is a most unstable one and is the result of the steric congestion and of the lower π character of the C—S bond due to the dissipation of n–π conjugation. The *anti,gauche* conformation **16** is a most stable form as can be



(15)



(16)

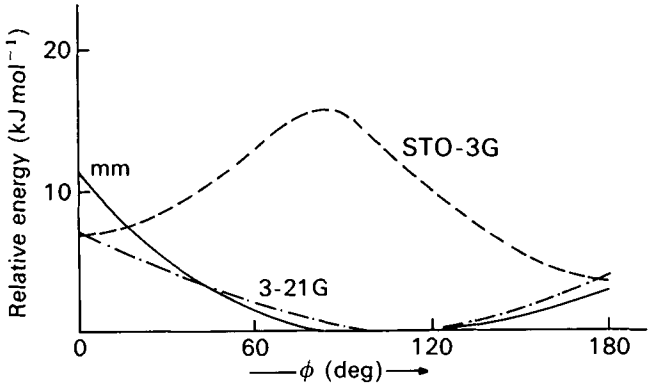
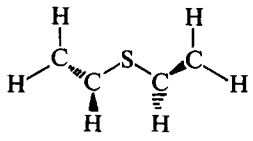
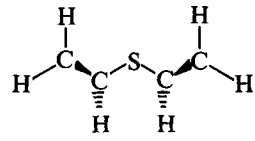


FIGURE 4. Potential functions for internal rotations about the S—C_{sp^2} bond in divinyl sulfide. Reprinted with permission from Reference 34. Copyright (1985) American Chemical Society



(17) C_2



(18) C_S

seen from Figure 4. Note that STO-3G exaggerates the contribution of the conjugative effect and hence the stability of the planar *anti,anti* form). Two *gauche,gauche* conformations **17** and **18** with symmetry C_2 and C_s, respectively, were also found to exist by MM and 3-21G methods, although the two methods do not agree concerning the relative stability of these conformers. The energy of the **17** → **18** transformation is 5 kJ mol^{-1} at 3-21G vs 1.3 kJ mol^{-1} by the MM method. The authors assume that the MM results may be more reliable as the dipole moment of divinyl sulfide calculated by the MM method (1.48 *D*) is in better agreement with the experimental values of 1.07–1.2 *D* (Section II.C) than that obtained from 3-21G (1.91 *D*).

Earlier MM results obtained by Sinegovskaya and coworkers, and referred to in References 23 and 45, are depicted in Figures 5 and 6. Noteworthy is the existence of the two *gauche,gauche* conformations with minimized steric hindrances (i.e. two pairs of minima on the steric hindrance energy surface map, Figure 5). The potential energy surface in Figure 6 is obtained by summing up the energy of steric hindrance and that of conjugation, the latter being determined from equation 2 where the dihedral angle ϕ is the deviation from the C=C plane and the parameters V_1 and V_2 can be estimated by Raman spectroscopy.[23] Even a superficial inspection of Figures 5 and 6 shows that taking into account the conjugation leads to only moderate changes in the potential

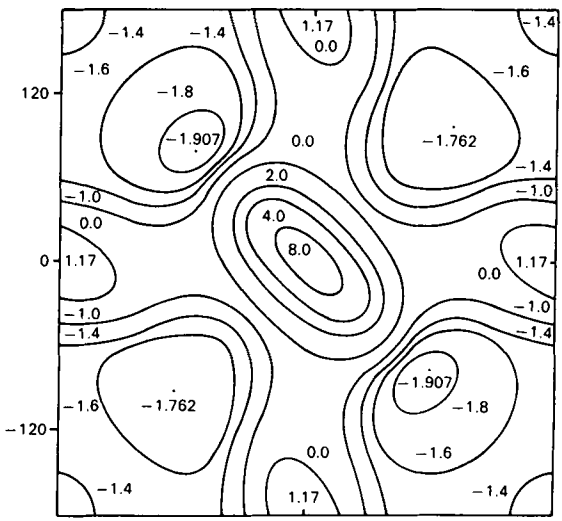


FIGURE 5. Map of the steric hindrance energy surface of divinyl sulfide. Reproduced by permission of Harwood Academic Publisher GmbH from Reference 45

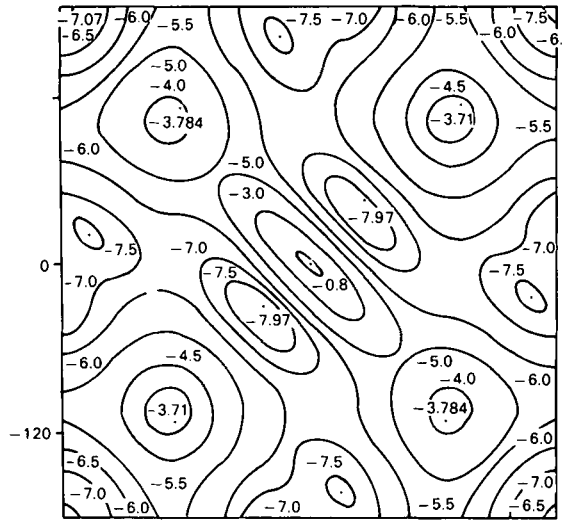


FIGURE 6. Map of the potential energy surface of divinyl sulfide. Reproduced by permission of Harwood Academic Publishers GmbH from Reference 45

energy surface. This is probably the result of a much lower extent of the p,π interaction of the sulfur lone pair with the C=C double bond than that of the oxygen in the corresponding oxygen derivatives, especially in divinyl sulfide where this interaction is dissipated on two C=C bonds.

$$U = (V_1/2)[1 - \cos(\phi - \pi)] + (V_2/2)[1 - \cos 2(\phi - \pi/2)] \quad (2)$$

B. Spectral Properties and Conformational Effects

Different methods were employed to establish the structure and conformations of the simplest vinyl sulfides, vinyl thiol and methyl vinyl sulfide. These include microwave spectroscopy, electron diffraction and photoelectron spectroscopy. Spectral studies of structural parameters are limited to small molecules which, nevertheless, can be regarded as appropriate models for investigating the spatial structure of the larger related species. Much more data concerning the manifestation of conformational effects are available in IR and UV spectra of vinyl sulfides. For related data in NMR spectra see Section III.

The parent member of the series, vinyl thiol, has been extensively studied by two groups[46-51] using MW and IR spectroscopy. The molecule was shown to exist predominantly in the planar *syn* conformation (**6**, R = H)[46,47]. The *syn*[48] and the 'quasi-planar' *anti*[49] conformations together with their different isotopic derivatives were studied by MW spectroscopy. Rotational constants in the ground vibrational state of simple vinyl sulfides are listed in Table 2. The data for vinyl thiol allow an estimate to be made of the C—S bond length and the CCS bond angle[48] and the structure is depicted in Figure 7[51].

The observed variation of the rotational constants with torsional excitation is indicative of extensive relaxation of the CCS angle (decreasing by up to 5°) and the C—S bond (elongation by up to 0.02 Å) during internal rotation in the vinyl thiol. The

TABLE 2. Rotational constants (MHz) and dipole moments (*D*) for vinyl sulfides

Molecule	A	B	C	μ^a	Reference
syn-CH_2=CHSH	49,815.28	5,835.716	5,222.081	0.896	48
syn-CH_2=CHSD	42,210.90	5,797.486	5,096.362		48
anti-CH_2=CHSH	49,422.75	5,897.215	5,279.436	1.117	49
anti-CH_2=CHSD	44,785.79	5,891.532	5,087.542		49
syn-CH_2=CHSMe[b]	10,606.60	4,784.34	3,366.26	1.14[c]	35,52
syn-CH_2=CHSEt (**9**)	8,849.353	2,369.861	1,914.526	4.761[d]	36
syn-CH_2=CHSEt (**10**)	5,409.198	3,201.021	2,257.910	4.890[d]	36

[a]Measured by the Stark effect.
[b]Data from Reference 35; earlier data[52] are very close to these values.
[c]From Reference 52.
[d]Calculated by an *ab initio* method.

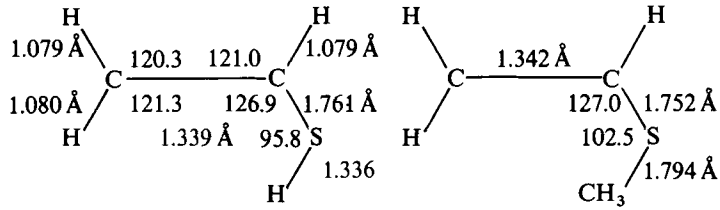


FIGURE 7 Structures of *syn*-vinyl thiol and methyl vinyl sulfide

potential function of Figure 8 confirms that the *anti* conformation is subject to a double minimum potential with a barrier of 0.14 kJ mol^{-1}. As the ground vibrational state of the *anti* form lies above this small barrier, this conformer appears to be essentially planar. Theoretical calculations also shown in Figure 8 are in good agreement with experiment[33]. The *syn* → *anti* barrier is 9.5 kJ mol^{-1}, the former rotamer being more stable by 0.6 kJ mol^{-1}.

Methyl vinyl sulfide has been extensively studied by MW spectroscopy[35,52], electron diffraction[29,35,53,54], IR spectroscopy[55,56], conventional[57] and variable-temperature[58] photoelectron spectroscopy. The reported results were the subject of some controversy. Thus, only the *syn* conformer was reported to exist by MW[52] and PE[57] spectroscopy at room temperature, while the statistical (33%:66%)[53] or nearly so (38%:62%)[29] proportion of the *syn* and *gauche* conformers has been obtained from the electron diffraction studies. Derissen and Bijen, however, have found that only including 11 to 21% of the *gauche* conformer allows one to account for radial distribution curves[54]. Temperature dependence of the IR spectra in the region of ν_{CSC} (in the gas phase)[57] and $\nu_{C=C}$ (in heptane solution)[56] vibrations gave a similar enthalpy difference between the conformers of 5.9–6.1 kJ mol^{-1} in favor of the *syn*-conformation. A somewhat higher value of 9.6 kJ mol^{-1} has been measured by variable-temperature photoelectron spectroscopy[58a]. Different spectral data were analyzed in terms of the two molecular models, that of a large (dynamic model) or a small (static model) amplitude motion, and the discrepancies noted above were explained[35] by the fact that the static model should not be used at high temperatures or when the barrier between the conformations is high, which is the case for methyl vinyl sulfide.

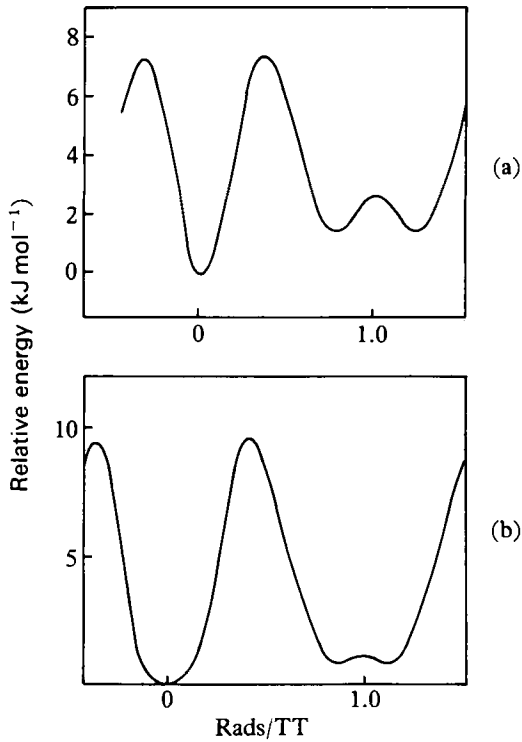


FIGURE 8. Calculated (a) and experimental (b) potential functions for internal rotation about the S—C bond in vinyl thiol. Reproduced by permission of Elsevier Science Publishers BV from Reference 33

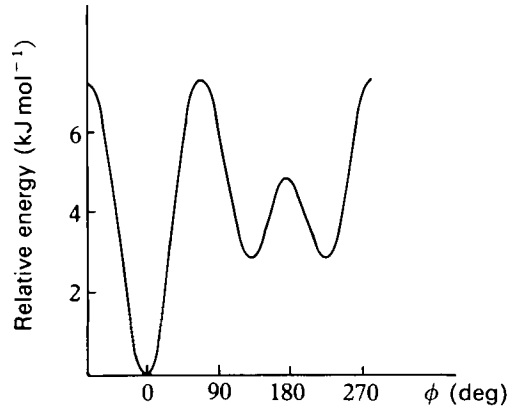


FIGURE 9. Experimental potential function for internal rotation in methyl vinyl sulfide[56]

Analysis of the PE spectra of methyl vinyl sulfide, (methylthio)ketene $CH_3SCH{=}C{=}O$ and other similar species led to the conclusion that the first band is associated with the ejection of an electron from the $(n_s + \pi)$ orbital, and the second one with that from the $(n_s - \pi)$ orbital[58b]. The conclusion is supported by the approximately similar (2.60 eV) $(n_s - \pi)/(n_s + \pi)$ orbital splitting for the species studied.

The potential function for the internal rotation in methyl vinyl sulfide[56] depicted in Figure 9 is qualitatively similar to that in vinyl thiol (Figure 8). The *syn* → *gauche* barriers are practically equal, but the barrier separating the two *gauche* conformers is substantially higher for methyl vinyl sulfide (2.9 kJ mol^{-1} vs 0.14 kJ mol^{-1}) and therefore the potential well for the *gauche* conformer may contain 2 or 3 vibrational levels.

It is of interest to compare some geometrical parameters for vinyl thiol and methyl vinyl sulfide[54] (Figure 7). The observed shortening of the C—S bond and the slight elongation of the C=C bond are probably the result of stronger n–π conjugation due to the donating nature of the Me group, while the substantial increase in the CSC angle is caused by the more strained structure of methyl vinyl sulfide.

Some characteristic bands in the IR spectra can be used for establishing the conformation of vinyl sulfides[59]. The assignment of the fundamental frequencies (Table 3) is according to Reference 55. The only discrepancy between this assignment and that in an earlier work[60] is concerned with the interpretation of the band at 1430 cm^{-1}. Popov and Kagan have assigned this band to the deformational vibrations of the vinyl group ($\delta_{=CH_2}$) and recommended it as characteristic for identification of β-substituted and nonsubstituted vinyl sulfides[60]. Fabian and coworkers[55] assigned it to the vibrations of the methyl group (δ_{Me}) in the nonplanar form while the deformational vibrations of the vinyl group were represented by a band at 1360–1390 cm^{-1}. The results of the later measurements on deuteriated species[61] are in better agreement with the assignment given in Reference 55.

The $\nu_{C=C}$ band is represented by a doublet in the region 1575–1585 cm^{-1} with the exception of vinyl sulfides containing bulky substituents (entries 6–9, 11). The low-frequency component of the doublet has been assigned to a more stable *syn* conformer, the high-frequency component to a nonplanar *gauche* conformer. With increasing alkyl group branching the intensity of the low-frequency component drops and that of the high-frequency component rises. Wagging vibrations (ω_{CH_2}) seem to be most suitable for identifying the rotamers of vinyl sulfides. It was suggested[55] that the low-frequency band at 860 cm^{-1} should be assigned to a planar *syn* conformer and the high-frequency band at 880 cm^{-1} to a *gauche* conformer. It has been noted[59] that the band at 678 cm^{-1} (ν_{CSC}) dominating in the spectrum of methyl vinyl sulfide noticeably losses its intensity in the spectra of *n*-alkyl vinyl sulfides and disappears in the spectra of *s*- and *t*-alkyl vinyl sulfides (Table 3). The latter show in this region only one band at 728–729 cm^{-1} assigned to the *gauche* rotamer[59]. Comparing the relative intensities of bands in the regions 650–750 cm^{-1} and 890–900 cm^{-1} one can see that on increasing the alkyl branching, the population of the planar *syn* rotamer rapidly diminishes and *t*-alkyl vinyl sulfides exist at ambient temperature mainly in the *gauche* conformation.

Near-ultraviolet spectra of vinyl sulfides show two typical bands with the position only slightly dependent on the solvent or on the substituent within each type of compound (Table 4).

The nature of the corresponding transitions is, however, still questionable. Thus, the high-frequency band with partly resolved vibrational structure at 225 nm has been assigned to the π–π^* transition, and the less intensive low-frequency band at 242 nm to the π–4s transition[66]. Based on comparison of the UV spectra of vinyl ethyl and diethyl sulfides, Frolov and coworkers assigned the low-frequency band to the π–π^* transition while that at 225 nm can, in their opinion, be attributed to the σ–σ^* transition[68]. The possibility for conformational effects to affect the UV spectra of vinyl sulfides[55] has been

TABLE 3. Fundamental frequencies of the vinyl thio group of vinyl sulfides (cm^{-1})

No.	Compound	$\nu_{=CH_2}$	$\nu_{C=C}$	$\delta_{=CH_2}$	$\delta_{=CH}$	ρ_{CH_2}	τ_{CH_2}	ω_{CH_2}	ν_{CSC}	$\omega_{(CH)_2}$
1	$MeSCH{=}CH_2$	3105 w 3033 w sh 3010 w	1584 s 1574 s sh	1388 m	1276 w	1036 s	960 s	885 s sh 860 s	742 m 735 m 699 w 678 s	596 m
2	$EtSCH{=}CH_2$	3092 w 3033 w sh 3010 w	1582 s 1574 s sh	1376 m	1260 m	1012 w	958 s	880 s sh 860 s	718 m 674 w 647 w	590 m
3	n-$PrSCH{=}CH_2$	3094 w 3020 w sh 3000 w	1584 s 1576 m sh	1376 m	1290 m 1275 m	1020 m	958 s	880 s sh 857 s	715 m 655 m	590 m
4	i-$PrSCH{=}CH_2$	3088 w 3020 w sh 3000 w	1584 s 1576 m sh	1366 m	1276 w	1022 m	958 s	880 s 860 s sh	726 m 707 m 648 w	592 s
5	n-$BuSCH{=}CH_2$	3105 w 3030 w sh 3000 w	1586 w 1574 m sh	1385 m	1275 m	1056 w 1024 s	964 s	880 s sh 860 s	744 m 716 m 696 w	595 s
6	s-$BuSCH{=}CH_2$	3097 w 3020 w sh 3002 w	1585 s	1388 m	1282 w	1061 w 1020 m	953 s	880 s sh 862 s	745 s 725 m 705 m 688 m	595 s
7	t-$BuSCH{=}CH_2$	3092 w 3028 w sh 3000 w	1587 s	1360 s	1270 w	1036 w 1017 w	959 s	890 s	728 s	590 m
8	t-$PenSCH{=}CH_2$	3088 w 3023 w	1585 s	1358 s 1368 s	1278 m	1056 m 1025 m	958 s	884 s	729 s	598 m 577 m
9	c-$HexSCH{=}CH_2$	3105 w 3030 w sh 3003 w	1585 s	1382 m	1270 m	1025 m	963 s	888 s 865 s sh	742 m 722 m 694 m	594 m
10	$S(CH{=}CH_2)_2$	3092 w 3025 w 3008 w	1592 s 1580 s 1560 m sh	1388 m 1380 s	1276 m 1260 s	1038 m 1014 m	965 m sh 954 s	903 m sh 880 s	735 s 728 s 684 m	612 m 590 m 574 w
11	$PhSCH{=}CH_2$	3078 m 3063 m 3027 w 3008 w	1585 s	1382 m	1275 m	1069 m 1024 s	962 m	900 m 882 m	746 s 720 w 695 s 620 w	596 s

TABLE 4. UV data for vinyl sulfides

No.	Compound	Solvent	λ_{max}(nm)	ε	λ_{max}(nm)	ε	Reference
1	MeSCH=CH_2[a]	hexane	227.1	11,300	240.8 sh	4,700	62
		ethanol	225.4	9,900	239 sh	5,700	62
2	EtSCH=CH_2[b]	hexane	229.1	7,500	253.5 sh	2,700	62
		ethanol	227.5	6,500	240.6 sh	3,500	62
3	*n*-PrSCH=CH_2	hexane	228.5	6,400	250 sh	3,500	62
		ethanol	227.7	6,000	250 sh	3,400	62
4	*n*-BuSCH=CH_2	hexane	229.6	6,400	250 sh	3,300	62
		ethanol	228.3	5,900	250 sh	3,500	62
5	*t*-BuSCH=CH_2[c]	hexane	235	6,100	251.3	6,100	62
		ethanol	235.2	4,200	249.5	4,500	62
6	CH_2=CHSCH=CH_2[d]	hexane	242	8,400	259.3	7,400	62
		ethanol	239.9	7,900	257.5	6,900	62
7	PhSCH=CH_2	hexane	245	9,000	266.5	8,600	62
		ethanol	247	8,700	264.6	8,200	62
8	*E*-EtSCH=CHPh	hexane	224	10,700	289.4	19,200	62
		ethanol	223.8	13,000	290	25,000	62
9	*Z*-EtSCH=CHPh	hexane	223.6	9,600	287	16,900	62
		ethanol	223.8	9,300	288.7	17,800	62
10	PhCH=CHSCH=CHPh	hexane	233.2	23,000	272	34,800	62
		ethanol	232.6	20,500	314.9	27,700	62
11	*E*-MeSCH=CHBu-*t*	decane	229.4	8,390	256.4	3,590	63
12	*E*-EtSCH=CHBu-*t*	decane	231.5	6,420	253.2	4,550	63
13	*E*-*i*-PrSCH=CHBu-*t*	decane	232.6	5,460	252.8	4,640	63
14	*E*-*t*-BuSCH=CHBu-*t*	decane	232.8	4,340	256.1	4,240	63
15	*Z*-MeSCH=CHCl	cyclohexane	236	8,560	246	5,770	64
		methanol	233	8,280	246	5,680	64
16	*E*-EtSCH=CHCl	cyclohexane	237	4,880	256	5,860	64
		methanol	236	4,830	254	5,650	64
17	*Z*-EtSCH=CHCl	cyclohexane	235	8,360	246	5,750	64
		methanol	233	7,500	245	5,110	64
18	*E*-*i*-PrSCH=CHCl	cyclohexane	239	3,330	258	5,750	64
		methanol	239	3,900	256	5,970	64

(*continued*)

TABLE 4. (*continued*)

No.	Compound	Solvent	λ_{max}(nm)	ε	λ_{max}(nm)	ε	Reference
19	*Z*-*i*-PrSCH=CHCl	cyclohexane	235	8,360	246	5,290	64
		methanol	233	7,750	245	5,040	64
20	*E*-*t*-BuSCH=CHCl	cyclohexane			260	5,380	64
		methanol			258	5,280	64
21	*Z*-*t*-BuSCH=CHCl	cyclohexane	233	7,840	245	5,530	64
		methanol	231	8,000	246	5,680	64
22	$EtSCH{=}CCl_2$	cyclohexane	247.3	7,600	257.1 sh	7,000	65
23	*n*-$PrSCH{=}CCl_2$	cyclohexane	247.7	7,500	255.8 sh	7,200	65
24	*t*-$PrSCH{=}CCl_2$	cyclohexane	247.4	6,800	256.7 sh		65
25	*n*-$BuSCH{=}CCl_2$	cyclohexane	247.5	7,700	256.1	7,300	65
26	*t*-$BuSCH{=}CCl_2$	cyclohexane	246.8	7,100	256 sh	6,200	65
27	*E*-MeSCH=CHOEt	cyclohexane			252	5,480	64
		methanol			250	5,270	64
28	*Z*-MeSCH=CHOEt	cyclohexane	228	6,430	256 sh	3,340	64
		methanol	225	6,550	251 sh	3,310	64
29	*E*-ELSCH=CHOEt	cyclohexane			251	3,250	64
		methanol			249	2,950	64
30	*Z*-ELSCH=CHOEt	cyclohexane	224	6,440	252 sh	3,820	64
		methanol	224	6,300	249 sh	3,420	64
31	*E*-*i*-PrSCH=CHOEt	cyclohexane			250	3,380	64
		methanol			246	3,770	64
32	*Z*-*i*-PrSCH=CHOEt	cyclohexane	224	9,200	252 sh	4,950	64
		methanol	223	9,440	249 sh	4,720	64
33	*E*-*t*-BuSCH=CHOEt	cyclohexane			252	4,360	64
		methanol			248	4,520	64
34	*Z*-*t*-BuSCH=CHOEt	cyclohexane	205	9,630	252 sh	3,960	64
		methanol	205	9,370	248 sh	4,130	64

[a] In the gas phase λ_{max} = 225.2 and 242 nm[66].
[b] λ_{max}(hexane) = 234.2 and 250 nm[67].
[c] λ_{max}(hexane) = 229.4 and 250 nm[67].
[d] λ_{max}(hexane) = 241.6 and 259.1 nm[67].

TABLE 5. Ionization potentials (IP) of vinyl sulfides

No.	Compound	IP(eV)	Reference	No.	Compound	IP(eV)	Reference
1	MeSCH=CH_2	8.45 v	57	8	PhSCH=CH_2	7.96 a	70
2	EtSCH=CH_2	8.21 a	70	9	*i*-PrSCH=CCl_2	8.14 a	64
3	*n*-PrSCH=CH_2	8.16 a	70	10	*E*-MeSCH=CHSMe	7.85 v	57
4	*i*-PrSCH=CH_2	8.15 a	70	11	*Z*-MeSCH=CHSMe	7.80 v	57
5	*n*-BuSCH=CH_2	8.15 a	70	12	$(MeS)_2C=CH_2$	8.20 v	57
6	*t*-BuSCH=CH_2	8.07 a	70	13	$(MeS)_2C=C(SMe)_2$	7.75 v	57
7	$S(CH=CH_2)_2$	8.25 a 8.45 v	70 71	14		8.06 v	66

discussed by Ratovskii, Panov and coworkers[63,65]. The high-frequency band has been assigned to the π–π^* transition in the planar *syn* conformer while the low-frequency band belongs to the *gauche* conformation and is of the *l*–a_π type where *l* is the molecular orbital centered mainly on the lone pair of the sulfur atom and partly including the π orbital, while a_π is a combination of the π^* orbital and lowest vacant orbitals of the sulfur atom. Temperature dependence of the molar extinction coefficients and the effect of the alkyl substituent are in line with this assignment. With increasing bulkiness of the alkyl group the ratio of the oscillator strengths changes in favor of the low-frequency band owing to the increasing percent of the *gauche* conformer (entries 1–5 and 11–14 in Table 4). The significant drop in the intensity of the high-frequency band with temperature, together with that of the low-frequency band being insensitive or slightly increasing in intensity, results in the same changes of the ratio of the oscillator strengths[63].

This analysis has, however, been criticized[23] as it suggests a significant difference in the electronic structure of the conformers. A detailed recent analysis of UV and PE spectra of vinyl sulfides[69] has led the authors to the conclusion that the low-frequency band is of the π–σ^* type rather than of the π–π^* type[68] or Rydberg transition[66]. The conclusion is based on the isotope effects: the ratio of the intensities of the low- and high-frequency bands is 0.225 for both $CH_3SCH=CH_2$ and $CH_3SCD=CD_2$ and increases to 1.35 for $CD_3SCH=CH_2$[69]. The high-frequency band has been assigned to the π–π^* transition[69].

Valuable information on the energy and composition of molecular orbitals is provided by photoelectron spectroscopy. First ionization potentials obtained from PES or by direct photoionization are shown in Table 5.

Only approximate correlation of the IP of alkyl vinyl sulfides with inductive substituent constants has been obtained[70] ($r = 0.93$). Nevertheless, estimation of the energy of conjugation of the double bond with the cation-radical center on the sulfur atom can be made from the deviations of the corresponding points for vinyl sulfides from the correlation of the IP of thiols and dialkyl sulfides with $\Sigma\sigma^*$[70]. The value was found to be *ca* 96–125 kJ mol^{-1}.

C. Dipole Moments

Measurements of the dipole moments of vinyl sulfides can provide additional information on their spatial structure and the effects of conjugation. The dipole moments of the related species, alkyl vinyl ethers, were shown to be very sensitive to the branching of the alkyl radical[72,73] and one might expect the same behavior for vinyl sulfides. Experimental values of the dipole moments of vinyl sulfides obtained mainly by the group of one of us are shown in Table 6.

TABLE 6. Dipole moments of vinyl sulfides

Compound	Solvent	μ, D	Reference
$MeSCH{=}CH_2$	benzene	1.35	74
$EtSCH{=}CH_2$	benzene	1.47 (1.38)	74 (75)
n-$PrSCH{=}CH_2$	benzene	1.44	74
i-$PrSCH{=}CH_2$	benzene	1.58	74
n-$BuSCH{=}CH_2$	benzene	1.41 (1.40)	74 (75)
i-$BuSCH{=}CH_2$	benzene	1.60	74
s-$BuSCH{=}CH_2$	benzene	1.59	74
t-$BuSCH{=}CH_2$	benzene	1.69	74
t-$PenSCH{=}CH_2$	benzene	1.70	74
c-$HexSCH{=}CH_2$	benzene	1.60	74
$S(CH{=}CH_2)_2$	benzene	1.07 (1.20)	59 (76)
$PhSCH{=}CH_2$		1.27	75
p-$TolSCH{=}CH_2$		1.73	77
(*Z*)-*p*-TolSCH=CHSTol-*p*		2.61	77
(*E*)-*p*-TolSCH=CHSTol-*p*		2.37	77
$(p\text{-TolS})_2C{=}CH_2$		2.46	77
$(p\text{-TolS})_2C{=}CHSTol\text{-}p$		2.38	77
(*Z*)-*p*-TolSC(Cl)=C(Cl)STol-*p*		2.39	77
(*E*)-*p*-TolSC(Cl)=C(Cl)STol-*p*		2.60	77
(*E*)-PhSCH=CHCl		1.56	78
(*E*)-PhSC(Pr)=C(Pr)Cl		1.29	78
(*E*)-PhSC(Bu)=CHCl		1.56	78
(*E*)-*p*-TolSCH=CHCl		2.13	77
(*E*)-*p*-TolSC(Cl)=CHCl		1.87	77
$Me_3SiSCH{=}CH_2$	octane	2.00	79
$Me_3GeSCH{=}CH_2$	octane	2.10	79
$Me_3SnSCH{=}CH_2$	octane	2.61	79
$Ph_3SnSCH{=}CH_2$	octane	2.50	79

The data for alkyl vinyl sulfides in Table 6 conform to this expectation, although the dipole moments vary in more narrow limits (0.35 *D*) than those in vinyl ethers[73] (0.84 *D*) on going from Me to *t*-Pen. Increasing dipole moment with branching of the alkyl group is indicative of the change of conformation from *syn* for R = Me to *gauche* for *t*-alkyl groups. A vector scheme gives the addition of the σ and π-moments (Figure 10) in the *gauche* conformer, while in the *syn* conformer they are subtracted. When the *syn* conformation is unfavorable (with *t*-alkyl radicals) and all molecules exist in the *gauche* form, the dependence of μ on R should be weakened which, indeed, has been shown experimentally[79] (Figure 11).

The possibility of the π-induced moment, caused by polarization of the $\pi_{C=C}$ bond due to electronegativity of the sulfur atom, to act as an additional effect has also been discussed. This effect, although small, could explain the slight exhaltation of the dipole moment of *t*-alkyl vinyl sulfides over alkyl ethyl sulfides (1.60 *D*)[74].

The best correlation of the dipole moments of alkyl vinyl sulfides with the structural parameters of R is that with the hyperconjugative constant $\Delta n = n_{C-H} + 0.4\, n_{C-C}$ where n_{C-H} and n_{C-C} are the numbers of C—H and C—C bonds, respectively, in the α position:

$$\mu = 1.95 - 0.21\Delta n, \quad r = 0.98, \quad s_0 = 0.027 \tag{3}$$

FIGURE 10. Addition (in the *gauche*) and subtraction (in the *syn*) π moments in vinyl sulfides

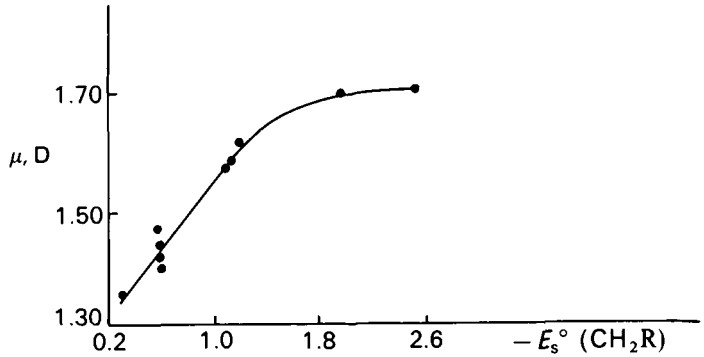


FIGURE 11. Dependence of the dipole moments on the steric parameter E_s^0 of the alkyl group of alkyl vinyl sulfides[79]

Correlation of nearly the same reliability is fulfilled with the steric constants $E_s^\circ(CH_2R)$:

$$\mu = 1.32 - 0.2\ E_s^\circ(CH_2R), \quad r = 0.97, \quad s_0 = 0.031 \tag{4}$$

Similar correlation with Δn for alkyl vinyl ethers has a slope of 0.47[73]. If we accept that correlation with Δn has a steric nature[74] and it reflects steric hindrance to resonance, one can conclude that the efficiency of transmittance of the electronic effects of R in vinyl sulfides is more than a factor of 2 lower than in vinyl ethers (see Section III for more details).

The temperature dependence of the dipole moment of vinyl sulfides has also been studied[79]. As the calculated moments of the *syn* (1.40 *D*) and *gauche* (1.90 *D*) conformers are different, the direct dependence which has been observed for R = Me and Et should be indicative of the predominance of the *syn* conformer at lower temperatures. On the other hand, the reciprocal dependence for R = *i*-Pr and *t*-Bu is due to the growing population of higher vibrational levels in the *gauche* form of these species at higher temperature, thus approaching the *anti* conformation rather than increasing the contribution of the *syn* conformation[79].

Calculated moments for elementorganic vinyl sulfides (last four entries) are very close for all three conformations (*syn*, *gauche* and *anti*). The absence of a temperature dependence is consonant with these calculations[79].

D. Basicity of Vinyl Sulfides

In order to evaluate the various effects operating in α,β-unsaturated sulfides, the measurement of the relative basicity of different sulfides including vinyl, allyl, aromatic

TABLE 7. Phenol OH stretching vibration shifts ($\Delta\nu$) on hydrogen bonding with sulfides in CCl_4[83]

Sulfide	$\Delta\nu$ (cm^{-1})	Sulfide	$\Delta\nu$ (cm^{-1})
Me_2S	227	EtSPh	180
$MeSCH{=}CH_2$	164	*n*-Bu_2S	248
MeSEt	237	$PhSCH_2CH{=}CH_2$	176
$S(CH{=}CH_2)_2$	123	$EtSCH{=}CHPh$	175[a]
$EtSCH{=}CH_2$	175	Ph_2S	122
Et_2S	242	$(PhCH_2)_2S$	179
n-$PrSCH{=}CH_2$	173	$EtSCH{=}CHCl$	130[b]
i-$PrSCH{=}CH_2$	189	*n*-$PrSCH{=}CHCl$	136[b]
$EtSCH_2CH{=}CH_2$	227	*i*-$PrSCH{=}CHCl$	131[b]
i-PrSEt	254	*n*-$BuSCH{=}CHCl$	129[b]
$S(CH_2CH{=}CH_2)_2$	216	*i*-$PrSCH{=}CCl_2$	132
i-$BuSC{\equiv}CH$	76	$Me_3SiCH_2SCH{=}CH_2$	182
n-$BuSCH{=}CH_2$	172	$Me_3SiSCH{=}CH_2$	171[c]
t-$BuSCH{=}CH_2$	202	$Me_3GeSCH{=}CH_2$	205[c]
n-Pr_2S	245	$Me_3SnSCH{=}CH_2$	218[c]
EtSBu-*i*	254	$Et_3SnSCH{=}CH_2$	211[c]
i-Pr_2S	256	*E*-$Et_3SiSCH{=}CHBu$-*t*	193[c]
MeSPh	172	*E*-$Et_3GeSCH{=}CHBu$-*t*	223[c]
n-$BuSC{\equiv}CMe$	107	*E*-$Et_3SnSCH{=}CHBu$-*t*	234[c]
$PhSCH{=}CH_2$	140		

[a]80% of the *E* isomer in mixtures; for mixtures with 70% and 30% of *E* isomer $\Delta\nu$ = 174 and 176 cm^{-1}, respectively.
[b]No assignment of configuration.
[c]Reference 84.

and acetylenic sulfides together with the saturated species has been performed[80–84]. The shift of the phenol OH stretching frequency upon hydrogen bonding to relevant sulfide has been used as a probe of electron density on the center of basicity, the sulfur atom. Correlation of relative basicities ($\Delta\nu$) shown in Table 7 with the sum of polar ($\Sigma\sigma^*$), hyperconjugative ($\Sigma\Delta n$) and steric (ΣE_s°) constants revealed that the only statistically significant dependence is that on the polar effect (points for elementorganic sulfides, the last seven entries, have not been included) (equation 5).

$$\Delta\nu = 227 - 90\Sigma\sigma^*, \quad r = 0.98 \tag{5}$$

Noteworthy is the higher basicity (by *ca* 30 cm^{-1}) of vinyl sulfides relative to the corresponding vinyl ethers while an opposite relation is observed for the saturated species[81]. Electron density on the oxygen atom in simple ethers is higher than on the sulfur atom in dialkyl sulfides and thus the former are stronger bases, as one could expect. In vinyl ethers strong $p{-}\pi$ conjugation reduces sharply their basicity (by *ca* 120 cm^{-1}) while the same decrease in vinyl sulfides is much less pronounced (by *ca* 65 cm^{-1}) and, according to equation 5, is caused mainly by the inductive effect of the vinyl group.

After applying usual statistical criteria, all deviations from the straight line of equation 5 are found to be random. Points for elementorganic vinyl sulfides (the last seven entries) are substantially shifted towards lower basicities, probably due to $p_\pi{-}d_\pi$ interaction of the lone pair of the sulfur atom and vacant d orbitals of the metal.

The sulfur atom was assumed to be the preferred site of protonation, which is certainly the case for long-range interactions like hydrogen-bond formation. On the other hand, complete protonation of vinyl sulfides as well as of vinyl ethers and selenides takes place on the C_β atom leading to the corresponding carbocations[79]. It is because of the drastic structural changes in the ionic species compared to their neutral precursors that the electrostatic potential contour maps are not appropriate for predicting the site of protonation. Thus, the energy difference between the C_β- and S-protonated species is 174.5 kJ mol^{-1} for methyl vinyl sulfide (3–21G*)[85]. Measuring gas-phase basicities of vinyl ethers and sulfides[85] showed that the stabilization of the adjacent positive charge is nearly the same by the oxygen and the sulfur atom, in contrast with what has been found in solution.

III. NUCLEAR MAGNETIC RESONANCE

It may seem discriminatory to devote a separate section to NMR while other spectral methods are discussed in one section. However, this can be justified by the large amount of information on the NMR spectra of vinyl sulfides and the special attention paid by many chemists to this field. Although nuclear magnetic resonance is one of the most powerful methods for investigating conformations, or the degree of conjugation in unsaturated species, etc., only in the last two decades have researchers begun to extensively investigate the NMR spectroscopy of vinyl sulfides. Since then a wealth of information has been accumulated and is partly represented in Tables 8 and 9. The main questions here are how the sulfur atom itself and the substituent acting through it affect the spectral parameters, and how the electronic and spatial structure of vinyl sulfides can be rationalized from the analysis of their ^{1}H (Table 8) and ^{13}C (Table 9) spectra.

A. ^{1}H NMR

The α-olefinic proton signal in both alkyl[86] and aryl[88] vinyl sulfides was found at 0.9 to 1.3 ppm lower field than in ethylene, due to deshielding by the electronegative sulfur atom. The upfield shift of the olefinic *β-cis* and *β-trans* protons has been attributed to the conjugation of the lone pair of the sulfur atom with the double bond. The downfield shifts of the β-protons of vinyl sulfides relative to the vinyl ethers has been interpreted in a similar manner[88]. With increasing branching of the alkyl group the degree of conjugation diminishes due to loss of planarity and the signals of the β-protons are shifted downfield (first eight entries, Table 8). A similar effect is caused by electron-withdrawing substituents in aryl vinyl sulfides. Fueno and coworkers[88] addressed the issue quantitatively, in correlating olefinic proton shifts in vinyl sulfides and ethers with the Hammett substituent constant for the X substituent (entries 10–16 in Table 8). The following values were obtained: $\rho_{cis} = -0.54$, $\rho_{trans} = -0.45$ for aryl vinyl sulfides and $\rho_{cis} = -0.32$, $\rho_{trans} = -0.38$ for aryl vinyl ethers. From these values it follows that (i) the chemical shifts of the *β-cis* protons are more sensitive than those of the *β-trans* protons to the substituent effects in vinyl sulfides, while the opposite is true for the vinyl ethers; and (ii) the efficiency of transmission of substituent effects through the sulfur atom is higher than through the oxygen. While there is no good explanation for the first fact, the efficiency of the sulfur atom in transmitting the electronic effects has been discussed thoroughly (see also next section). In addition to conventional electron-donating conjugation that the sulfur atom can show, p_π–d_π conjugation of acceptor type and also 'through-conjugative' contribution of the p_π–d_π–p_π type when it is placed between two π systems[88] were ascribed to the higher transmission efficiency of the sulfur atom.

TABLE 8. ^{1}H NMR data (δ values in ppm and coupling constants in Hz) for vinyl sulfides[a]

Compound	Solvent	H_{gem}	H_{cis}	H_{trans}	J_{gem}	J_{cis}	J_{trans}	Reference
$MeSCH{=}CH_2$	neat	6.35	4.84	5.08	−0.3	10.3	16.4	86
$EtSCH{=}CH_2$	neat	6.25	4.97	5.11		10.0	16.4	86
n-$PrSCH{=}CH_2$	$CDCl_3$	6.35	5.09	5.16				87
s-$BuSCH{=}CH_2$	neat	6.32	5.12	5.13	0.3	10.0	16.8	86
t-$BuSCH{=}CH_2$	neat	6.46	5.28	5.21	1.1	9.6	16.5	86
$EtCH(Me)(CH_2)_2SCH{=}CH_2$	neat	6.28	5.00	5.07	0.2	10.2	16.6	86
$Et(Me)CHCH_2SCH{=}CH_2$	neat	6.28	5.00	5.06	0.2	9.8	17.0	86
c-$HexSCH{=}CH_2$	$CDCl_3$	6.35	5.07	5.15				87
$PhCH(Me)SCH{=}CH_2$	neat	6.14	5.11	4.98	0.2	10.0	16.8	86
$XC_6H_4SCH{=}CH_2$								
X=H	CCl_4	6.44	5.23	5.25		9.4	16.4	88
X=*p*-OMe	CCl_4	6.37	4.98	5.13				88
X=*p*-Me	CCl_4	6.40	5.12	5.18				88
X=*m*-Me	CCl_4	6.45	5.23	5.26				88
X=*p*-Cl	CCl_4	6.42	5.27	5.32				88
X=*m*-Cl	CCl_4	6.46	5.38	5.39				88
X=*p*-NO_2	CCl_4	6.54	5.62	5.63				88
$CH_2{=}CHSCH{=}CH_2$	$CDCl_3$	6.39	5.26	5.26		9.6	16.8	89
$ClCH_2CH(Cl)SCH{=}CH_2$	$CDCl_3$	6.46	5.52	5.52				90
(*E*)-$MeSCH{=}CHMe$	CCl_4	5.97	5.49	—			15.0	91
(*Z*)-$MeSCH{=}CHMe$	CCl_4	5.89	—	5.59		9.5		91
(*E*)-$EtSCH{=}CHMe$	CCl_4	5.93	5.65	—			14.9	91
	CD_3OD	5.83	5.43	—			14.5	92
(*E*)-$Na^+\bar{S}CH{=}CHMe$	CD_3OD	6.70	5.68	—			15.0	92
(*Z*)-$EtSCH{=}CHMe$	CCl_4	5.92	—	5.62		9.1		91
	CD_3OD	5.80	—	5.48		9.5		92
(*Z*)-$Na^+\bar{S}CH{=}CHMe$	CD_3OD	6.72	—	5.60		10.0		92
(*E*)-*i*-$PrSCH{=}CHMe$	CCl_4	5.99	5.75	—			14.6	91
(*Z*)-*i*-$PrSCH{=}CHMe$	CCl_4	6.00	—	5.64		9.4		91
(*E*)-*t*-$BuSCH{=}CHMe$	CCl_4	6.09	5.90	—			14.6	91
(*Z*)-*t*-$BuSCH{=}CHMe$	CCl_4	6.11	—	5.74		9.2		91
(*E*)-$PhSCH{=}CHMe$	CCl_4	6.05	5.88	—			14.8	91

(Z)-PhSCH=CHMe	CCl_4	6.15	—	5.78	9.3			91
$PhSCMe=CH_2$	CCl_4	—	5.05	4.83				93
(E,E)-$S(CH=CHMe)_2$	CCl_4	5.90	5.62	—			14.7	91
(Z,Z)-$S(CH=CHMe)_2$	CCl_4	5.89	—	5.72		9.4		91
(E,Z)-$S(CH=CHMe)_2$	CCl_4							91
(E)-fragment		5.92	5.61	—			14.7	
(Z)-fragment		5.93	—	5.61		9.2		
(Z)-$ClCH=CHSCH=CH_2$	$CDCl_3$							90
$ClCH=CH$-fragment		6.46	—	6.18		7.5		
$CH=CH_2$-fragment		6.44	5.35	5.35		11	18	
$MeSCH=CMe_2$	CCl_4	5.46	—	—				91
(E)-MeSCH=CHEt	CCl_4	5.1	—	6.0				91
(Z)-MeSCH=CHEt	CCl_4	5.1	—	5.8				91
(E)-MeSCH=CHPr-*i*	CCl_4	5.84	5.30	—			14.9	91
(Z)-MeSCH=CHPr-*t*	CCl_4	5.65	—	5.27		9.0		91
(E)-MeSCH=CHPh	CCl_4	6.58	6.11	—			16	94
	neat	6.68	6.20	—			16	94
(E)-MeSCH=CDPh	neat	6.68	—	—				94
(Z)-MeSCH=CHPh	CCl_4	5.93	—	6.23		11		94
	neat	5.98	—	6.34		11		94
(Z)-MeSCH=CDPh	neat	5.98	—	—				94
(E)-$MeSCH=CHC_6H_4OMe$-*p*	CCl_4	6.47	6.20	—			16	94
(Z)-$MeSCH=CHC_6H_4OMe$-*p*	CCl_4	5.90	—	6.23		11		94
(E)-$MeSCH=CHC_6H_4NO_2$-*p*	CCl_4	7.03	6.25	—			16	94
(Z)-$MeSCH=CHC_6H_4NO_2$-*p*	CCl_4	6.4	—	6.4				94
$EtSCMe=CH_2$	CCl_4	—	4.58	4.88				91
$EtSCH=CMe_2$	CCl_4	5.50	—	—				91
(E)-EtSCH=CHEt	CCl_4	5.87	5.57	—			15.1	91
(Z)-EtSCH=CHEt	CCl_4	5.85	—	5.49		9.4		91
(E)-EtSCH=CHPr-*i*	CCl_4	5.81	5.51	—			15.7	91
(Z)-EtSCH=CHPr-*i*	CCl_4	5.71	—	5.33		9.6		91
(Z)-*n*-BuSCH=CHBu-*n*	$CDCl_3$	5.89	—	5.54		9.2		95
(Z)-*n*-BuSCH=CHBu-*t*	$CDCl_3$	5.74	5.44	—		11.2		95
(Z)-*n*-BuSCH=CHPh	$CDCl_3$	6.24	—	6.42		11.2		95
(Z)-*c*-HexSCH=CHBu-*n*	$CDCl_3$	5.97	—	5.55		9.7		95

(*continued*)

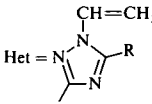
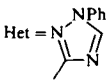
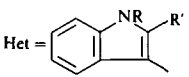
TABLE 8. (*continued*)

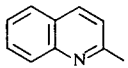
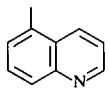
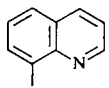
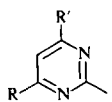
Compound	Solvent	H_{gem}	H_{cis}	H_{trans}	J_{gem}	J_{cis}	J_{trans}	Reference
(*Z*)-PhSCH=CHBu-*n*	$CDCl_3$	6.18	—	5.82		9.2		95
	CCl_4	6.14	—	5.70		9.5		96
(*Z*)-*p*-TolSCH=CHBu-*n*	$CDCl_3$	6.14	—	5.75		9.2		95
(*E*)-PhSCH=CHBu-*s*	CCl_4	6.05	5.75	—		9.0		97
(*Z*)-PhSCH=CHBu-*s*	CCl_4	6.08	—	5.50			15.0	97
(*E*)-PhSCH=CHPen-*n*	CCl_4	6.08	5.86	—			14.8	98
(*Z*)-PhSCH=CHPen-*n*	CCl_4	6.08	—	5.68		9.0		98
(*E*)-PhSCH=CHPh	CCl_4	6.60	6.92	—			16	96
(*Z*)-PhSCH=CHPh	CCl_4	6.46	—	6.66		10.5		96
(*Z*)-EtSCH=CHPh	$CDCl_3$	6.18	—	6.45		10.6		96
(*E*)-EtSCMe=CHMe	CCl_4	—	5.37	—				91
(*Z*)-EtSCMe=CHMe	CCl_4	—		5.55				91
(*E*)-EtSCEt=CHMe	CCl_4	—	5.27	—				91
(*Z*)-EtSCEt=CHMe	CCl_4	—		5.60				91
(*E*)-*n*-BuSCPr=CHMe	$CDCl_3$	—	5.46	—				99
(*Z*)-*n*-BuSCPr=CHMe	$CDCl_3$	—	—	5.53				99
$EtSCH=CEt_2$	CCl_4	5.47	—	—				91
(*E*)-PhSCH=CHF	$CDCl_3$	6.11	6.92	—	82.5[b]	11.1[b]	13.0	100
(*Z*)-PhSCH=CHF	$CDCl_3$	5.58	—	6.74	81.0[b]	4.2	37.7[b]	100
(*E*)-MeSCH=CHCl	$CDCl_3$	6.30	5.95	—			13.0	101
(*Z*)-MeSCH=CDCl	$CDCl_3$	6.20	—	6.00		6.5		101
(*E*)-EtSCH=CHCl	$CDCl_3$	6.34	5.95	—				101
(*Z*)-EtSCH=CHCl	$CDCl_3$	6.27	—	6.01				101
(*E*)-*n*-BuSCH=CHCl	*c*	6.38	5.97	—			13.0	102
(*Z*)-*n*-BuSCH=CHCl	*c*	6.27	—	6.01		6.5		103
(*Z*)-*i*-PrSCH=CHCl	$CDCl_3$	6.33	—	6.01		6.5		101
(*Z*)-*t*-BuSCH=CHCl	$CDCl_3$	6.40	—	6.03		6.5		101
(*E*)-EtSCH=CHBr	$CDCl_3$	6.75	6.10	—				101
(*Z*)-EtSCH=CHBr	$CDCl_3$	6.74	—	6.15				101
(*E*)-*i*-PrSCH=CHBr	$CDCl_3$	6.78	6.10	—			13.0	101
(*Z*)-*i*-PrSCH=CHBr	$CDCl_3$	6.76	—	6.14		6.5		101
(*E*)-*t*-BuSCH=CHBr	$CDCl_3$	6.88	6.08	—			13.0	101

(Z)-*t*-BuSCH=CHBr	$CDCl_3$	6.84	—	6.15		6.5		101
(*E*)-PhSCH=CHCl	*c*	6.47	6.20	—				102
(*Z*)-PhSCH=CHCl	*c*	6.58	—	6.18				102
(*E*)-PhSCH=CHBr	CCl_4	6.76	6.24	—				104
(*Z*)-PhSCH=CHBr	CCl_4	6.91	—	6.23				104
$PhSCF{=}CH_2$	$CDCl_3$	—	4.93	5.08		9.8[b]	43.9[b]	105
$PhSCCl{=}CH_2$	$CDCl_3$	—	5.48	5.52	1.9			106
(*E*)-PhSCCl=CHCl	*c*	—	—	—	6.50			102
$MeSCH{=}CCl_2$	$CDCl_3$	6.52	—	—				101
$EtSCH{=}CCl_2$	$CDCl_3$	6.57	—	—	—			101
i-$PrSCH{=}CCl_3$	$CDCl_2$	6.65	—	—				107
n-$BuSCH{=}CCl_2$	CCl_4	6.11	—					101
(*E*)-PhSCF=CHBr	$CDCl_3$	—	6.13	—			22.0[b]	109
(*Z*)-PhSCF=CHBr	$CDCl_3$		—	—	6.35	8.3[b]		109
$PhSCH{=}CCl_2$	CCl_4	6.45	—	—				108
p-$XC_6H_4SCH{=}CBr_2$								
X = H	$CDCl_3$	7.05	—	—				110
X = OMe	$CDCl_3$	6.94	—	—				110
X = Me	$CDCl_3$	7.10	—	—				110
X = Cl	$CDCl_3$	7.04	—	—				110
(*E*)-MeSCH=CHOEt	$CDCl_3$	5.13	6.58	—			12.0	101
(*Z*)-MeSCH=CHOEt	$CDCl_3$	4.70	—	6.10		5.5		101
(*E*)-EtSCH=CHOEt	CCl_4	5.20	6.65	—			12.0	91
(*Z*)-EtSCH=CHOEt	CCl_4	4.73	—	6.16		6.0		91
(*E*)-*i*-PrSCH=CHOEt	$CDCl_3$	5.33	6.68	—			12.2	101
(*Z*)-*i*-PrSCH=CHOEt	$CDCl_3$	4.93		6.27		5.5	5.5	101
(*E*)-*t*-BuSCH=CHOEt	$CDCl_3$	5.36	6.68	—			12.1	101
(*Z*)-*t*-BuSCH=CHOEt	$CDCl_3$	5.00	—	6.23		5.6		101
(*E*)-EtSCH=C(Me)OEt	CCl_4	4.79	—	—				42
(*Z*)-EtSCH=C(Me)OEt	CCl_4	4.73	—	—				42
(*E*)-EtSCH=CHSEt	CCl_4		6.06					91
(*E*)-EtSCH=CHSEt	CCl_4			6.02				91
(*E*)-EtSCH=C(Me)SEt	CCl_4	5.79	—	—				42
(*Z*)-EtSCH=C(Me)SEt	CCl_4	5.66	—	—				42
(*Z*)-*n*-BuSCH=CHSBu-*n*	*c*			6.13				102
(*Z*)-PhSCH=CHSPh	*c*			6.50				102

(continued)

TABLE 8. *(continued)*

Compound	Solvent	H_{gem}	H_{cis}	H_{trans}	J_{gem}	J_{cis}	J_{trans}	Reference
(*Z*)-PhSCCl=CHSPh	*c*		6.91					102
$(PhS)_2C$=CHPh	CCl_4		7.05					96
$CH_2(SCH{=}CH_2)_2$	$CDCl_3$	6.39	5.23	5.29				87
(*E*)-EtSCH=C(Cl)SePh	$CDCl_3$	6.77	—	—				111
(*Z*)-EtSCH=C(Cl)SePh	$CDCl_3$	6.90	—	—				111
(*E*)-*i*-PrSCH=C(Cl)SePh	$CDCl_3$	6.82	—	—				111
(*Z*)-*i*-PrSCH=C(Cl)SePh	$CDCl_3$	6.95	—	—				111
(*E*)-*n*-BuSCH=C(Cl)SePh	$CDCl_3$	6.76	—	—				111
(*Z*)-*n*-BuSCH=C(Cl)SePh	$CDCl_3$	6.87	—	—				111
(*E*)-EtSCH=C(Cl)SeBu-*n*	$CDCl_3$	6.63	—	—				111
(*Z*)-EtSCH=C(Cl)SeBu-*n*	$CDCl_3$	6.70	—	—				111
Het—SCH=CH_2								
								
R = H	$CDCl_3$	6.88	5.48	5.41		9.8	17.2	112
R = Me	$CDCl_3$	6.88	5.45	5.38		9.9	17.0	112
R = Ph	$CDCl_3$	7.00	5.51	5.40		9.6	17.2	112
R = 2-furyl	$CDCl_3$	7.00	5.57	5.48		9.9	17.2	112
	$CDCl_3$	6.94	5.52	5.43		9.7	16.9	112
								
R = R′ = H	$CDCl_3$	6.34	4.83	5.04		9.7	16.5	112
R = H; R′ = Me	$CDCl_3$	6.24	4.68	4.98		9.6	16.3	112
R = Et; R′ = H	$CDCl_3$	6.33	4.82	5.02		9.6	16.5	112
R = CH=CH_2; R′ = H	$CDCl_3$	6.33	4.90	5.07		9.7	16.5	112
R = CH=CH_2; R′ = Me	$CDCl_3$	6.23	4.73	4.99		9.5	16.4	112

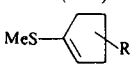
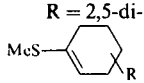
Het = 	$CDCl_3$	7.43	5.51	5.45	10.1	17.4	112
Het = 	$CDCl_3$	6.41	5.02	5.24	9.6	16.5	112
Het = 	$CDCl_3$	6.68	5.65	5.54	9.3	16.6	112
							
R = R′ = H	$CDCl_3$	7.24	5.54	5.48	9.9	17.3	112
R = Me; R′ = OCH=CH_2	$CDCl_3$	7.23	5.48	5.41	10.2	17.6	112

[a] *Gem*, *cis* and *trans* are in relation to the sulfur atom.
[b] ^1H–^{19}F coupling.
[c] Solvent not given.

TABLE 9. ^{13}C NMR chemical shifts (δ in ppm) for C_α and C_β of vinyl sulfides

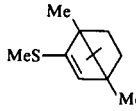
Compound	C_α	C_β	Solvent	Reference
MeSCH=CH_2	133.35	107.71	neat	114
EtSCH=CH_2	132.68	109.74	neat	115
n-PrSCH=CH_2	132.98	109.63	neat	114
i-PrSCH=CH_2	131.98	112.00	neat	115
n-BuSCH=CH_2	132.97	109.45	neat	115
i-BuSCH=CH_2	133.32	109.38	neat	115
s-BuSCH=CH_2	132.02	111.80	neat	114
t-BuSCH=CH_2	130.19	115.69	neat	115
c-HexSCH=CH_2	131.90	111.50	neat	114
$XC_6H_4SCH=CH_2$				
X = H	132.18	114.58	CCl_4	116
X = *p*-NH_2	134.70	110.63	CCl_4	116
X = *p*-OMe	133.93	111.71	CCl_4	116
X = *p*-Me	133.00	113.27	CCl_4	116
X = *m*-Me	132.3	114.9	neat	117
X = *p*-F	132.59	113.87	CCl_4	116
X = *p*-Cl	131.66	115.47	CCl_4	116
X = *p*-Br	131.29	115.73	CCl_4	116
X = *m*-Cl	130.6	117.5	neat	117
X = *p*-CF_3	129.73	118.48	CCl_4	116
X = *p*-NO_2	128.23	120.88	CCl_4	116
CH_2=CHSCH=CH_2	129.88	114.34	neat	114
$ClCH_2CH(Cl)SCH=CH_2$	126.73	119.32	$CDCl_3$	90
(*E*)-MeSCH=CHMe	124.67	122.39	$CDCl_3$	91
(*Z*)-MeSCH=CHMe	127.75	123.04	$CDCl_3$	91
(*E*)-EtSCH=CHMe	123.45	125.72	$CDCl_3$	91
	124.52	123.74	CD_3OD	92
(*E*)-$Na^+\bar{S}CH$=CHMe	139.92	114.65	CD_3OD	92
(*Z*)-EtSCH=CHMe	125.64	123.78	$CDCl_3$	91
	125.82	122.96	CD_3OD	92
(*Z*)-$Na^+\bar{S}CH$=CHMe	141.3	113.5	CD_3OD	92
(*E*)-*i*-PrSCH=CHMe	122.64	128.73	$CDCl_3$	91
(*Z*)-*i*-PrSCH=CHMe	124.26	124.26	$CDCl_3$	91
(*E*)-*t*-BuSCH=CHMe	120.93	132.46	$CDCl_3$	91
(*Z*)-*t*-BuSCH=CHMe	122.07	125.80	$CDCl_3$	91
(*E*,*E*)-$S(CH=CHMe)_2$	127.75	122.23	$CDCl_3$	91
(*Z*,*Z*)-$S(CH=CHMe)_2$	124.67	123.94	$CDCl_3$	91
	(or *vice versa*)			
(*E*,*Z*)-$S(CH=CHMe)_2$			$CDCl_3$	91
(*E*)-fragment	126.61	122.64		
(*Z*)-fragment	124.05	125.15		
	(or *vice versa*)			
MeSCH=CMe_2	120.21	133.02	$CDCl_3$	91
(*E*)-MeSCH=CHEt	123.00	129.21	$CDCl_3$	91
(*Z*)-MeSCH=CHEt	126.18	130.53	$CDCl_3$	91
(*E*)-MeSCH=CHPr-*i*	121.68	134.25	$CDCl_3$	91
(*Z*)-MeSCH=CHPr-*i*	124.61	136.26	$CDCl_3$	91
MeSCMe=CH_2	142.3	104.7	$CDCl_3$	118
MeSC(Pr-*n*)=CH_2	147.3	103.7	$CDCl_3$	118
MeSC(Bu-*t*)=CH_2	157.9	101.0	$CDCl_3$	118
EtSCMe=CH_2	140.91	106.31	$CDCl_3$	91

TABLE 9. (*continued*)

Compound	C_α	C_β	Solvent	Reference
EtSCH=CMe_2	118.01	134.09	$CDCl_3$	91
(*E*)-EtSCH=CHEt	121.65	132.57	$CDCl_3$	91
(*Z*)-EtSCH=CHEt	124.00	131.37	$CDCl_3$	91
(*E*)-EtSCH=CHPr-*i*	120.04	137.66	$CDCl_3$	91
(*Z*)-EtSCH=CHPr-*i*	122.07	136.76	$CDCl_3$	91
(*E*)-MeSCH=CHBu-*t*	120.19	136.86	neat	107
(*Z*)-*n*-BuSCH=CHBu-*n*	124.95	129.53	$CDCl_3$	95
(*E*)-*n*-BuSCH=CHBu-*t*	119.40	139.77	neat	107
	123.25	137.75	$CDCl_3$	95
(*E*)-*i*-PrSCH=CHBu-*t*	117.87	143.04	neat	107
(*E*)-*t*-BuSCH=CHBu-*t*	115.85	147.67	neat	107
(*Z*)-*n*-BuSCH=CHPh	125.20	127.70	$CDCl_3$	95
(*Z*)-*c*-HexSCH=CHBu-*n*	123.03	129.89	$CDCl_3$	95
(*Z*)-PhSCH=CHBu-*n*	122.50	133.68	$CDCl_3$	95
(*E*)-MeSCMe=CHEt	130.6	124.2	$CDCl_3$	118
(*Z*)-MeSCMe=CHEt	130.0	130.4	$CDCl_3$	118
(*E*)-EtSCMe=CHMe	129.54	121.42	$CDCl_3$	91
(*Z*)-EtSCMe=CHMe	130.11	125.48	$CDCl_3$	91
(*E*)-MeSCEt=CHMe	138.5	115.7	$CDCl_3$	118
(*Z*)-MeSCEt=CHMe	138.2	123.2	$CDCl_3$	118
(*E*)-EtSCEt=CHMe	136.45	120.28	$CDCl_3$	91
(*Z*)-EtSCEt=CHMe	136.52	125.56	$CDCl_3$	91
(*E*)-MeSC(Pr-*n*)=CHEt	135.9	124.0	$CDCl_3$	118
(*Z*)-MeSC(Pr-*n*)=CHEt	134.8	132.1	$CDCl_3$	118
(*Z*)-MeSC(Bu-*t*)=CHMe	148.2	127.1	$CDCl_3$	118
(*E*)-*n*-BuSC(Pr-*n*)=CHMe	128.99	126.77	$CDCl_3$	99
(*Z*)-*n*-BuSC(Pr-*n*)=CHMe	129.18	131.21	$CDCl_3$	99
(*E*)-*n*-BuSC(Pr-*n*)=CHPn-*n*	134.17	127.82	$CDCl_3$	99
(*Z*)-*n*-BuSC(Pr-*n*)=CHPr-*n*	133.93	132.41	$CDCl_3$	99
(*E*)-MeSC(Bu-*i*)=CHPr-*i*	133.1	131.0	$CDCl_3$	118
(*Z*)-MeSC(Bu-*i*)=CHPr-*i*	132.1	139.1	$CDCl_3$	118
(*E*)-*n*-BuSCBu=CHEt	134.36	126.61	$CDCl_3$	99
(*Z*)-*n*-BuSCBu=CHEt	133.50	133.93	$CDCl_3$	99
EtSCH=CEt_2	116.63	144.68	$CDCl_3$	91
MeSCMe=CMe_2	123.2	131.7	$CDCl_3$	118
EtSCMe=CMe_2	121.25	134.33	$CDCl_3$	91
MeSC(Pr-*i*)=CMe_2	136.8	137.1	$CDCl_3$	118
				
R = H	138.7	120.4	$CDCl_3$	118
R = 3-Me	138.4	126.3	$CDCl_3$	118
R = 4-Me	137.8	119.2	$CDCl_3$	118
R = 2,5-di-Me	134.2	139.3	$CDCl_3$	118
				
R = H	134.0	118.6	$CDCl_3$	118
R = 2-Me	125.6	133.5	$CDCl_3$	118
R = 3-Me	133.6	124.8	$CDCl_3$	118
R = 4-Me	133.4	118.4	$CDCl_3$	118
R = 5-Me	133.4	118.3	$CDCl_3$	118

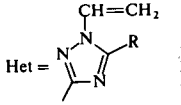
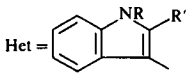
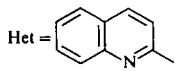
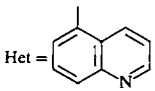
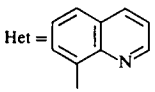
(*continued*)

TABLE 9. (*continued*)

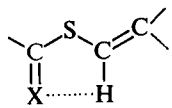
Compound	C_α	C_β	Solvent	Reference
R = 6-Me	139.7	118.5	$CDCl_3$	118
R = 2-Et	125.0	139.7	$CDCl_3$	118
R = 6-Et	139.0	119.4	$CDCl_3$	118
R = 2,6-di-Me	136.3	131.8	$CDCl_3$	118
R = 4-*t*-Bu	133.4	119.1	$CDCl_3$	118
R = 3,3,5-tri-Me	131.7	128.6	$CDCl_3$	118
R = 3,5,5-tri-Me	132.5	123.4	$CDCl_3$	118
R = 3,3,5,5-tetra-Me	130.2	127.1	$CDCl_3$	118
R = 2-*i*-Pr-5-Me	123.9	142.2	$CDCl_3$	118
	146.8	122.0	$CDCl_3$	118
$EtSCH{=}CCl_2$	126.11	113.16	neat	115
i-$PrSCH{=}CCl_2$	124.86	113.38	neat	115
n-$BuSCH{=}CCl_2$	126.47	113.06	neat	115
i-$BuSCH{=}CCl_2$	126.91	112.91	neat	115
t-$BuSCH{=}CCl_2$	122.86	114.38	neat	115
p-$XC_6H_4SCH{=}CCl_2$				
X = H	125.33	116.15	$CHCl_3$	119
X = OMe	127.44	113.92	$CHCl_3$	119
X = Me	126.28	115.03	$CHCl_3$	119
X = Cl	124.45	117.19	$CHCl_3$	119
(*E*)-EtSCH=CHOEt	94.87	154.07	$CDCl_3$	91
(*Z*)-EtSCH=CHOEt	98.68	145.62	$CDCl_3$	91
(*E*)-EtSCH=C(Me)OEt	89.10	160.81	$CDCl_3$	42
(*E*)-EtSCMe=C(Me)OEt	109.07	153.99	$CDCl_3$	42
(*Z*)-EtSCMe=C(Me)OEt	104.00	163.00	$CDCl_3$	42
(*E*)-EtSCH=CHSEt	122.96	122.96	$CDCl_3$	91
(*Z*)-EtSCH=CHSEt	123.20	123.20	$CDCl_3$	91
(*E*)-EtSCH=C(Me)SEt	121.34	129.46	$CDCl_3$	42
(*Z*)-EtSCH=C(Me)SEt	124.10	128.56	$CDCl_3$	42
(*Z*)-EtSCMe=C(Me)SEt	129.30	129.30	$CDCl_3$	42
$CH_2(SCH{=}CH_2)_2$	130.69	113.52	$CDCl_3$	87
(*E*)-$MeSCH{=}CHSiMe_3$	139.70	121.27	neat	107
(*E*)-*n*-$BuSCH{=}CHSiMe_3$	139.57	122.70	neat	107
(*E*)-*i*-$PrSCH{=}CHSiMe_3$	139.47	125.33	neat	107
(*E*)-*t*-$BuSCH{=}CHSiMe_3$	137.10	128.50	neat	107
(*E*)-$MeSCH{=}CHSiEt_3$	140.86	117.60	neat	107
(*E*)-*n*-$BuSCH{=}CHSiEt_3$	140.75	119.15	neat	107
(*E*)-*i*-$PrSCH{=}CHSiEt_3$	140.04	121.27	neat	107
(*E*)-*t*-$BuSCH{=}CHSiEt_3$	138.47	125.10	neat	107
(*E*)-$MeSCH{=}CHSiMe_2OMe$	142.45	119.09	neat	107
(*E*)-*n*-$BuSCH{=}CHSiMe_2OMe$	142.31	120.35	neat	107
(*E*)-*i*-$PrSCH{=}CHSiMe_2OMe$	142.07	122.50	neat	107
(*E*)-*t*-$BuSCH{=}CHSiMe_2OMe$	139.84	125.25	neat	107
(*E*)-$MeSCH{=}CHSiMe(OMe)_2$	144.97	115.13	neat	107
(*E*)-*t*-$BuSCH{=}CHSiMe(OMe)_2$	142.46	120.74	neat	107
(*E*)-MeSCH=CHCOMe	146.26	123.08	neat	107
(*E*)-*n*-BuSCH=CHCOMe	145.76	123.41	neat	107
(*E*)-*i*-PrSCH=CHCOMe	143.03	124.21	neat	107

(*continued*)

TABLE 9. (*continued*)

Compound	C_α	C_β	Solvent	Reference
(*E*)-*t*-BuSCH=CHCOMe	143.28	124.93	neat	107
Het—SCH=CH_2				
Het =  R = H	127.55	116.79	$CDCl_3$	112
R = Me	127.25	116.26	$CDCl_3$	112
Het = 				
R = R′ = H	133.14	110.68	$CDCl_3$	112
R = H; R′ = Me	132.90	109.92	$CDCl_3$	112
R = CH=CH_2; R′ = H	132.81	111.21	$CDCl_3$	112
R = CH=CH_2; R′ = Me	132.60	110.12	$CDCl_3$	112
Het = 	127.84	115.98	$CDCl_3$	112
Het = 	130.21	115.03	$CDCl_3$	112
Het = 	129.32	120.12	$CDCl_3$	112

In a series of papers[87,112,113] Afonin and coworkers proposed the formation of an intramolecular hydrogen bond in vinyl sulfides of the type shown below in heteroaryl vinyl sulfides and *S*-vinyl dithiocarbamates. This is reflected in the downfield shift of the H_α signal from conventional values of 6.3–6.4 ppm to 7.1–7.4 ppm.



B. ^{13}C NMR

The ^{13}C chemical shifts allow one to estimate electronic effects, such as the degree of conjugation and charge distribution, more directly than by the corresponding measurements of ^1H chemical shifts because the latter are more affected by the diamagnetic and paramagnetic effects and by the solvent. The first measurements of the ^{13}C chemical shifts for alkyl and aryl vinyl sulfides revealed that the C_α atom is deshielded by 7–10 ppm relative to ethylene by the sulfur atom while the C_β atom is shielded by 8–16 ppm in alkyl[114] and by 5–10 ppm in aryl[117] sulfides. These values, although attenuated in comparison with those in the corresponding vinyl ethers[89,114], are clearly indicative of the p–π conjugation. With increasing branching of the alkyl groups in RSCH=CH_2 the C_β signal is shifted downfield, and hence the electron density on it decreases. This is contrary to what one might expect from the donating power of R,

which increases with branching and must therefore cause the upfield shift of the C_β atom. The correlation of the C_α and C_β chemical shifts with polar (σ^*), hyperconjugative (Δn) and steric (E_s°) parameters of R in $RSCH{=}CH_2$ showed[120] that the best correlation is that with the $E_s^\circ(CH_2R)$ constants. This implies the predominance of the steric effect which has been interpreted as steric hindrance to conjugation[114].

Measurements of the ^{13}C chemical shifts confirmed that the transmission of electronic effects is more efficient in vinyl sulfides than in vinyl ethers. Thus, correlation of the C_β chemical shifts with Hammett σ values in $ArYCH{=}CH_2$ gave the ρ values of 4.84 and 6.94 for Y = O and S, respectively[116]. Correlation of the C_β shifts with σ_I and σ_R by a dual-parameter equation gave ρ_I 4.32 and 6.56, and ρ_R 5.73 and 8.97 for Y = O and S, respectively[119]. The same correlation with $E_s^\circ(CH_2R)$ in alkyl vinyl sulfides and ethers also showed the slope for the sulfides (−4.54) to be higher than that for the ethers (−3.43)[120]. Besides the concept of p_π–d_π–p_π through-conjugative polarization[88] (see Section II.A) the possibility that steric effects are responsible for the enhanced transmittance of the sulfur has been discussed[114]. The higher selectivity in the correlation with E_s° for vinyl sulfides is ascribed to the less rigid conformation because of the weaker p–π conjugation[114].

However, Reynolds and McClelland[116] assumed that the ratio of C_β to C_1 chemical shifts in aryl vinyl sulfides, rather than the slope itself, should be used as a measure of the ability of the linking group to transmit electronic effects. With this approach, they obtained a different order of transmission ability, i.e. O > S. Correlation of the chemical shifts by a dual-parameter equation with σ_I and σ_R substituent constants showed that the same order (O > S) is predicted for both conjugative and π-inductive effects.

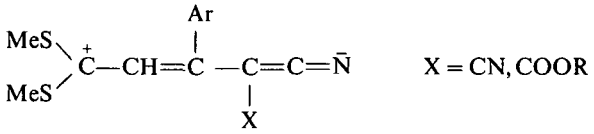
Returning to the original question, of whether the sulfur atom possesses higher transmittance than the oxygen atom, one should distinguish between the sensitivity (the slope of the corresponding correlation) and the actual ability to transmit electronic changes[115]. It is generally accepted that the efficiency of transmission is measured as a slope of the correlation with substituent constants and, on this basis, this efficiency is *ca* 1.5 times greater for the sulfur atom.

Explanation for the C_β downfield shift with increasing bulkiness of R in $RSCH{=}CH_2$ by out-of-plane twisting and reduced conjugation is based on the assumption that the ^{13}C shift can be used as a measure of the π-electron density on the corresponding atom. Virtanen[91] proposed another reasoning based on the ^{13}C NMR measurements of β-substituted vinyl sulfides. Thus, the C_α signal in *Z*-RSCH=CHMe is shifted substantially upfield on going from R = Me to R = *t*-Bu, whereas the C_β downfield shift points to only a slight decrease in the p–π conjugation. In the *E* isomers, on the contrary, the C_β signal is strongly affected by R. The trends observed have been rationalized in terms of the 'through-space shielding' effect which depends on the distance between the group R and the corresponding nucleus. It is more pronounced in the *E* isomers which can adopt the *syn* conformation for the small alkyl groups. For branched R the *gauche* conformer becomes energetically preferable, the $R\cdots C_\beta$ distance increases, resulting in the deshielding of the C_β atom. For the *Z* isomers even with small alkyl groups the *syn* conformation is unfavorable and they exist in the *anti* form with rather long $R\cdots C_\beta$ distance. Therefore it is reasonable to assume that the through-space shielding effect of R is small enough, and varying the size of R has no practical effect on the chemical shift of the C_β atom[91]. Apparently, both effects, i.e. steric hindrance to conjugation[114] and through-space shielding[91], are operative and should be taken into account.

The importance of spatial interaction of R with the substituent at the C_β atom has also been shown for β,β-dichlorovinyl sulfides and ethers. Chemical shifts of the C_β atom in both series were shown to only slightly vary with the branching of R. Unfortunately, no ^{13}C NMR data are available for β-chlorovinyl sulfides, but for β-chlorovinyl ethers it was shown that on going from R = Me to *t*-Bu the C_β signal is shifted > 4 ppm downfield in the *E* isomers while no effect was found for the *Z* isomers[115].

Dependence of the steric inhibition of the resonance effect on the nature of R′ in *E*-RSCH=CHR′ has been demonstrated for R′ = *t*-Bu, H, $SiEt_3$, $SiMe_3$, $SiMe_2OMe$, $Si(OMe)_2Me$ and COMe[107]. The slope of the correlation of the C_β chemical shifts with the steric parameters E_s° decreases in this series from −6.3 to −1.1, which has been attributed to increasing p–π resonance[107]. Electron-withdrawing substituents R′ stabilize the *syn* conformation due to increase of the donating power of the sulfur atom, so that variations of the shielding effect of the alkyl group R become less pronounced.

With increase in the electron-acceptor character of the substituent in the β-position, the extreme polar structure $RS—\overset{+}{C}=CH—\bar{C}HR'$ can be stabilized to such an extent that the C=C double bond acquires a single bond character, as in push–pull butadienes[121].



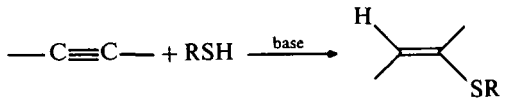
Extremely high polarization due to direct polar resonance in this system is manifested in the ^1H and ^{13}C NMR spectra, were coalescence of the SMe signals has been observed at 420–450 K, depending on R and X.

IV. SYNTHESIS

A. Addition of Thiols to Acetylenes

1. Nucleophilic addition

Nucleophilic addition of thiols to the carbon–carbon triple bond (equation 6) constitutes a classic, general and widespread method for the synthesis of vinyl sulfides.

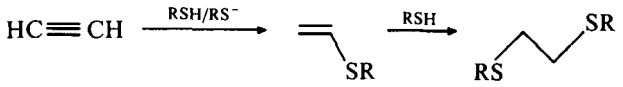


(6)

(19)

The literature on the nucleophilic vinylation of thiols is vast but, fortunately, well documented in reviews and monographs[22–24,80,122–134], which allows consideration of only the main regularities of the reaction, using representative examples.

a. Conditions. The reaction conditions depend strongly on the nature of the substituents at the triple bond (see Section IV.A.1.b) and to a lesser extent on that of the thiol (see Section IV.A.1.c). In the case of acetylene, the reaction in its classical version[123,124,126,131] was carried out under pressure (of up to *ca* 35 atm) at 100–160 °C with acetylene being diluted by nitrogen (up to *ca* 1:2 ratio) using basic catalysts such as alkali metal hydroxides, alkoxides, thiolates etc. The yield of alkyl vinyl sulfides (**19**, R = alkyl) was moderate rather than good, because with small amounts of the catalysts the reaction tends to proceed by reaction with an additional molecule of thiol to form the saturated 1,2-bis adduct **20** (equation 7)[123,124,126,135–137].



(7)

(20)

This side reaction becomes the major one, when zinc or cadmium salts of carboxylic acids are used as catalysts.

Aryl vinyl sulfides (**19**, R = aryl) are formed in better yields: e.g. benzenethiol is vinylated in the presence of KOH/BuOH, under 15 atm of acetylene at 160 °C to afford phenyl vinyl sulfide in > 90% yield. The vinylation of arenethiols with Zn and Cd carboxylates is also possible although 1,2-bis(arylthio)ethanes (**20**) are also formed.

Yields of alkyl vinyl sulfides exceeding 60% were obtained using dioxane as a solvent and KOH catalyst at 70–90 °C and 30 atm, whereas in aqueous solution the yields dropped to 30% and in EtOH, benzene or toluene the reaction did not take place[137]. The vinylation of thiols in water also proceeds in the presence of alkali metal carbonates, amines or ion exchange resins at 140 °C and 30 atm[138].

The thiols released upon the *in situ* hydrolysis of alkyl isothiuronium salts (**21**) with excess alkali are vinylated in aqueous or aqueous alcohol solution with high efficiency at 95–100 °C and 30 atm with yields at the 90% level[139,140]. This allowed a one-pot synthesis of alkyl vinyl sulfides directly from alkyl halides (equation 8).

$$RX \xrightarrow[H_2O \text{ or } EtOH]{(H_2N)_2CS} \underset{\textbf{(21)}}{RSC(NH)NH_2 \cdot HX} \xrightarrow{NaOH} RSH \xrightarrow{C_2H_2} \underset{}{\overset{}{\diagdown\!\!=\!\!\diagup}SR} \qquad (8)$$

This method was successfully employed for the preparation of optically active alkyl vinyl sulfides (**23**) starting from the corresponding alkyl bromides (**22**) (equation 9)[141,142].

$$\underset{\textbf{(22)}}{Et\overset{*}{C}H(Me)(CH_2)_nBr} \xrightarrow[2.\ NaOH/C_2H_2]{1.\ (H_2N)_2CS} \underset{\textbf{(23)}}{\overset{}{\diagdown\!\!=\!\!\diagup}S(CH_2)_n\overset{*}{C}H(Me)Et} \qquad (9)$$

$n = 0, 2, 3$

The reaction was carried out in water at 90–100 °C with 10–15 atm of acetylene using a molar ratio of NaOH:isothiuronium salt of 2. The yield of **23** was 50–80% and the optical purity was as high as 99%. Under similar conditions (H_2O, 90 °C, KOH:thiol ratio = *ca* 1), optically active 1-phenylethyl vinyl sulfide (**25**) was synthesized in 78% chemical and 100% optical yields by vinylation of 1-phenylethanethiol (**24**)[143] (equation 10).

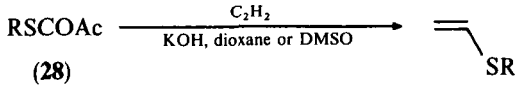
$$\underset{\textbf{(24)}}{Ph\overset{*}{C}H(Me)SH} \xrightarrow[KOH/H_2O,\ 90\,^\circ C]{C_2H_2,\ 10\text{–}15\ atm} \underset{\textbf{(25)}}{\overset{}{\diagdown\!\!=\!\!\diagup}S\overset{*}{C}H(Me)Ph} \qquad (10)$$

Hydrolysis–vinylation of aqueous ω-aminoalkyl isothiuronium halides (**26**) at 120–132 °C and 33 atm with 3-fold excess NaOH leads to ω-aminoalkyl vinyl sulfides (**27**) in 14–78% yields (equation 11). Higher yields (39–78%) were obtained using the ω-dialkylamino derivatives[144].

$$\underset{\textbf{(26)}}{R_2N(CH_2)_nSC(NH)NH_2 \cdot 2HX} \xrightarrow[NaOH/H_2O]{C_2H_2} \underset{\textbf{(27)}}{\overset{}{\diagdown\!\!=\!\!\diagup}S(CH_2)_nNR_2} \qquad (11)$$

R = H, Me, Et; $n = 2, 3$

Alkyl thioacetates (**28**) react readily with acetylene under pressure in the presence of excess alkali in dioxane[145] or in dimethyl sulfoxide (DMSO)[146] to form vinyl sulfides in 56–63% yields (equation 12).

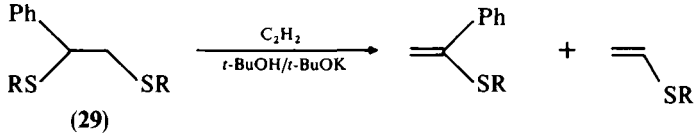


(12)

(**28**)

R = Bu-*n*, *c*-C_6H_{11}

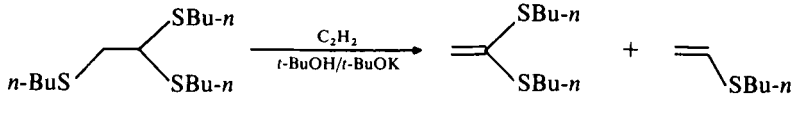
Generally, many other compounds capable of eliminating thiols under base catalysis can be transformed into vinyl sulfides under the combined action of a strong base and acetylene, the latter often facilitating the elimination process. Among such compounds are 1-phenyl-1,2-di(alkylthio)- (**29**)[147] and 1,1,2-tris(alkylthio)ethanes (**30**)[148], which form vinyl sulfides in 32–96% yields upon treatment with acetylene at 90–120 °C and 15–35 atm in *t*-BuOH/*t*-BuOK medium (equations 13 and 14).



(13)

(**29**)

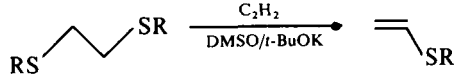
R = Me, Et, $(CH_2)_2OH$



(14)

(**30**) 92% 96%

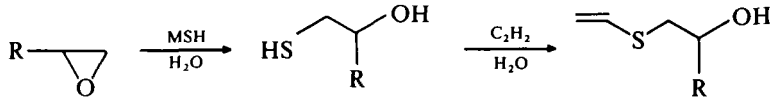
With a stronger base, such as a *t*-BuOK in DMSO, even 1,2-di(alkylthio)ethanes (**31**) undergo the elimination–vinylation reaction (equation 15) at 145–165 °C and 15–32 atm to give alkyl vinyl sulfides[149,150].



(15)

(**31**)

Thiols (**32**) formed from oxiranes and MSH (M = Na, K) in water or alcohols can be intercepted by acetylene in a simultaneous one-pot process to furnish 2-hydroxyalkyl vinyl sulfides (**33**)[151] (equation 16).

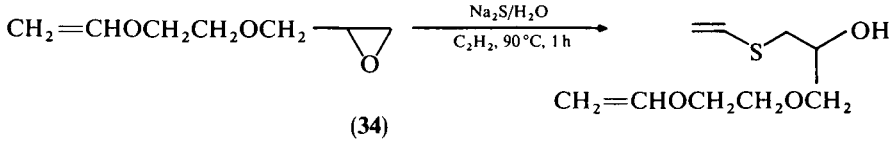


M = Na, K
R = H,Me

(**32**) (**33**)

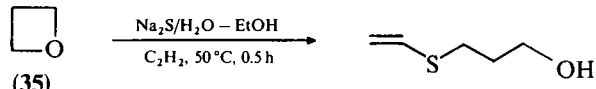
(16)

Similar reactions occur when oxiranes (**34**), oxetanes (**35**) or 1-chloro-2-hydroxyalkanes (**36**) are allowed to react simultaneously with Na_2S and acetylene at 50–90 °C and 15–20 atm in water or in a water–ethanol mixture (equations 17–19)[80,152].



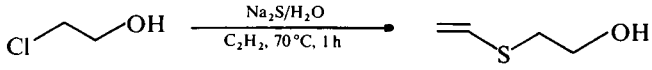
(34)

30% (17)



(35)

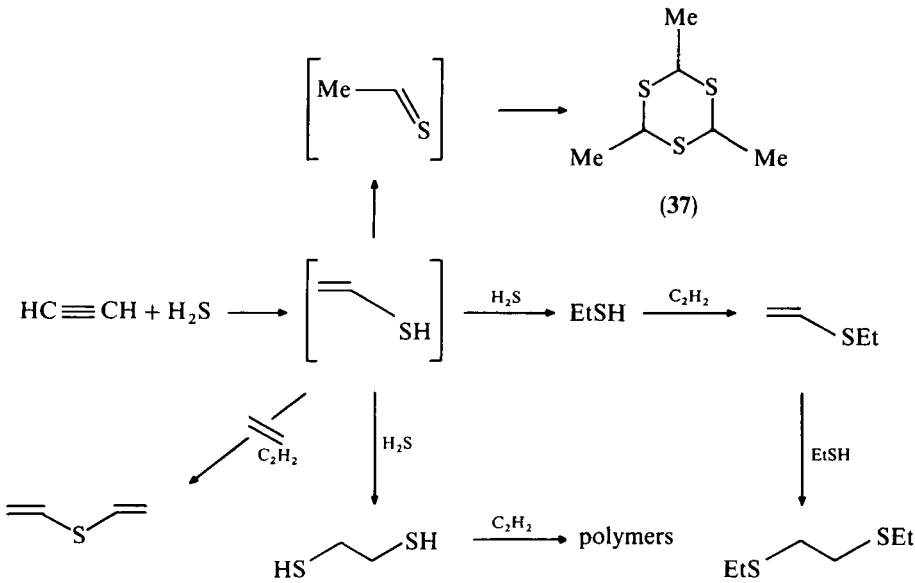
40% (18)



(36)

30% (19)

However, all Reppe's and others' attempts[123,124,126,153,154] to add hydrogen sulfide to acetylene in the presence of an alkali and alkaline earth metal as well as ammonia or ammonium, Cu, Fe or Ni hydrosulphides, sulfides or polysulfides in water or in

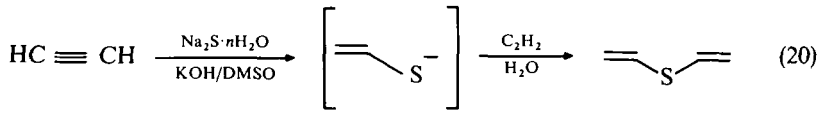


SCHEME 1

polyethylene glycol (100 °C, 10–20 atm) resulted in a complicated mixture containing trimeric thioacetaldehyde (**37**), ethanethiol, ethyl vinyl sulfide, 1,2-di(ethylthio)ethane, 1,2-ethanedithiol and 'thiokol'-like resins. In none of the cases was the expected divinyl sulfide (**39**) found even in traces (Scheme 1).

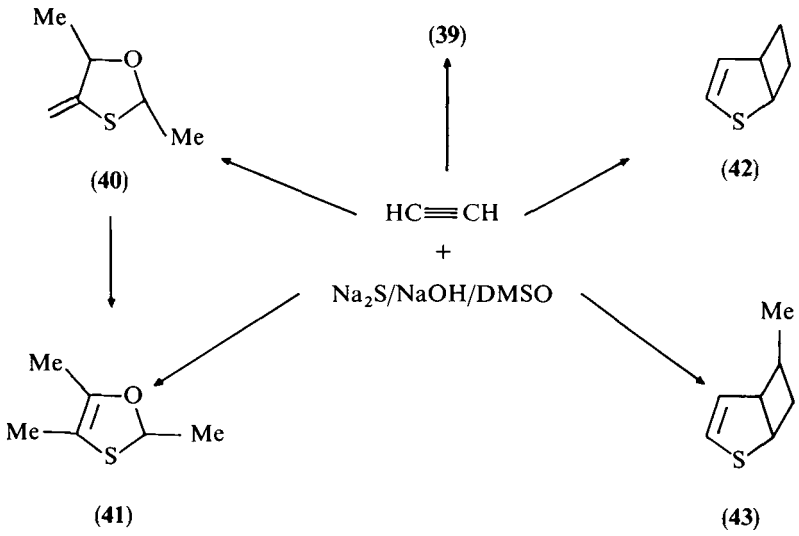
The first reaction of acetylene with sulfide ions to give divinyl sulfide (**39**) in 60–82% yields was carried out in DMSO at 100–110 °C under pressure[22–24,80,155,156]. An almost quantitative yield (98%) was achieved when a 4-fold molar excess of KOH relative to $Na_2S \cdot 4H_2O$ was used[22–24,80].

The use of excess MOH (Na, K) in a two-phase reaction mixture (since metal alkoxides are poorly soluble in DMSO) is the most essential feature of the synthesis (equation 20). A superbasic system capable of highly activating both the sulfide anions and the acetylene is formed[22–24,80,157–159]. The intermediate vinyl thiol is retained as its anion (**38**) thus preventing its participation in other transformations, except for its nucleophilic addition to acetylene which is accelerated by many powers of ten due to the superbasicity of the reaction mixture[22–24,80,157–160].



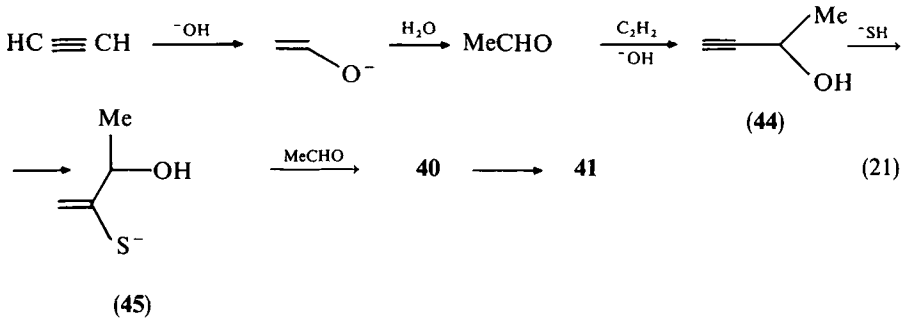
(38) (39) (20)

Under certain conditions, the addition of sulfide ions to acetylene is accompanied by peculiar cyclooligomerization reactions. Thus, in the system Na_2S/NaOH/DMSO, cyclic vinyl sulfides **40** and **41** are formed in a total yield of *ca* 15% in addition to the major product **39** (Scheme 2). In addition, three bridged cyclic vinyl sulfides: **42** and its *exo* and *endo* 6-methylated derivatives **43**, are commonly present in the reaction mixture in *ca* 3% yield[22–24,80,157–161].



SCHEME 2

Compounds **40** and **41** appear to be formed in the reaction sequence shown in equation 21[160]: acetylene is first converted to vinyl alcohol, which then tautomerizes to acetaldehyde, which in turn is ethynylated to 3-methyl-1-butyn-3-ol (**44**), which then adds the hydrosulfide ion to give **45** and one additional molecule of acetaldehyde (equation 21). The intermediate **44** and *Z*-vinylthio-1-buten-3-ol (a further vinylation product of **45**) have been trapped in a similar process[162,163]. Regardless of the low yield of the cyclic vinyl sulfides **40** and **41**, their one-pot formation from very cheap raw materials makes them rather accessible for synthetic applications.



The solvent (DMSO) is of primary importance in the reaction[22-24]. If hexamethylphosphortriamide (HMPA) or sulfolane are used instead under analogous conditions, the yield of **39** becomes much lower (43 and 18%, respectively), and a partial decomposition of the solvent takes place. In water, dimethylformamide (DMF), dioxane and tetrahydrofuran (THF), **39** is formed under the same conditions in yields as low as 1–5%.

A synthesis of perdeuterated **39** and **40** based on the same reaction (equation 22) has been developed[164]. The deuterated acetylene was obtained from reaction of CaC_2 with D_2O. The reaction of CaC_2 and Na_2S in the presence of D_2O in HMPA afforded **39**-d_6 and **40**-d_{10} in 34 and 9% yield, respectively.

$$Na_2S + CaC_2 \xrightarrow[80\,^\circ C]{D_2O/HMPA} (CD_2{=}CD)_2S + \textbf{40}\text{-}d_{10} \qquad (22)$$

39-d_6

A similar impressive enhancement in the rate of the alkanethiolate addition to acetylene has been found[165] when a dipolar aprotic solvent such as HMPA or DMSO was employed. Under atmospheric pressure (10% of sodium thiolate, NaOH or KOH, 10–20 °C), the yields of *n*-alkyl vinyl sulfides spanned 68–90%.

Thus, a rapid development of the acetylene-based chemistry of vinyl sulfides in the last decade has been a result of systematic applications of superbasic catalytic systems (such as alkali/DMSO or alkali/HMPA) for acceleration of the addition of sulfur nucleophiles across the triple bond[20-24,80,157-160]. Due to a combination of a high extent of dissociation of the alkali metal thiolates in these media[166] and the weak solvation of the formed anions[167] ('naked anions') the nucleophilic attack on acetylene (which is also assisted by its higher solubility in these media and its activation under these conditions[168-173]) by the thiolate anion resulting in vinyl sulfides is strongly assisted. In particular, this gives rise to a new one-pot synthesis of alkyl vinyl sulfides directly from sodium sulfide, alkyl halides and acetylene as exemplified by the preparation

$$Na_2S + CD_3I + HC{\equiv}CH \xrightarrow{KOH/DMSO} \underset{SCD_3}{\overset{}{\diagdown\!\!=}} \quad (23)$$

(46)

of methyl-d_3 vinyl sulfide (**46**) in 95% yield at ambient temperature and atmospheric pressure (equation 23)[174].

In the system M_2S (M = alkali or alkaline earth metal)–alkylating agent–H_2O, acetylene was shown to behave as a good trap for the intermediate alkylthio anions, forming alkyl vinyl sulfides in satisfactory yields[80,152]. Consequently, in this case the nucleophilic addition to the triple bond is as fast as the concurrent nucleophilic substitution of the alkylating agent by alkynyl anion. In order to avoid the latter as much as possible it is necessary to use NaSH instead of Na_2S. A highly reactive NaSH can be prepared[175] by using the ability of DMSO to extract NaSH from hydrated Na_2S (equation 24).

$$Na_2S{\cdot}n(H_2O) \xrightarrow[90\text{–}100\,^\circ C]{DMSO} \underset{\text{liquid phase}}{NaSH{\cdot}l(DMSO){\cdot}m(H_2O)} + \underset{\text{solid phase}}{NaOH{\cdot}k(H_2O)} \quad (24)$$

With $Na_2S{\cdot}4H_2O$, up to 90% of the maximum quantity of NaSH is transferred to the DMSO. The solutions obtained are stable enough and do not undergo hydrolysis, as is the case for aqueous and alcoholic NaSH solutions. Since the acidity of H_2S in DMSO is comparable to that of strong acids[166], all the NaSH is dissociated in this medium[176]. These solutions, obtained by filtering off the solid phase (mainly NaOH), can be successfully used in the synthesis of both vinyl sulfides[174] and thiols[177].

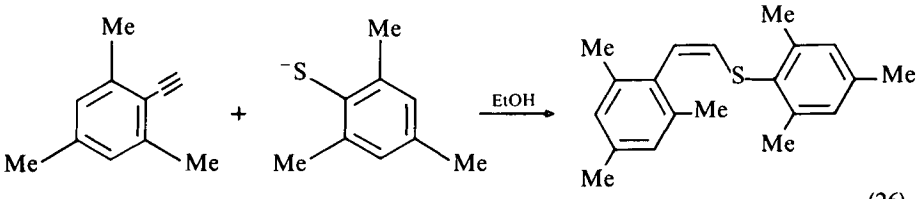
Hence, the classic reaction of vinylation of thiols by acetylene has progressed a long way from the high-temperature, nonselective procedure under pressure up to the modern high-yield synthesis, operating at ambient or moderate temperatures and atmospheric pressure, starting from free thiols or (in equal or higher efficiency) from alkyl halides and other electrophiles.

b. The effect of the structure of the acetylene. As expected, the electron-withdrawing substituents at the triple bond facilitate the reaction. Especially facile are the base-catalyzed additions of thiols to 'activated acetylenes' bearing one or two strongly electronegative functions such as ROC(O)—, RC(O)—, $R_2NC(O)$—, NC—, RS(O)—, $RS(O)_2$— and the like. Normally, the synthesis of vinyl sulfides from activated acetylenes is carried out at room or at a lower temperature and gives an almost quantitative yield of the adducts. Mono-α-substituted activated acetylenes are universally attacked by thiolate anions at the β-position.

As a rule, in the presence of a proton-transfer agent (AH), the reactions follow a concerted *anti* addition mechanism (equation 25) to give *Z* adducts, a stereochemical course that is common for most nucleophilic additions to acetylenes[133,134].

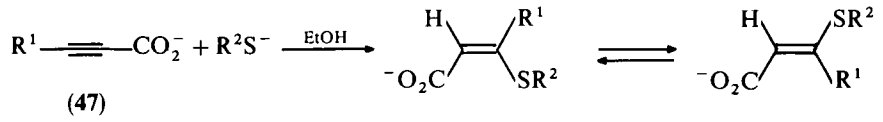
(25)

The steric factor appears to play a negligible role in this route as demonstrated by the example shown in equation 26[178].



(26)

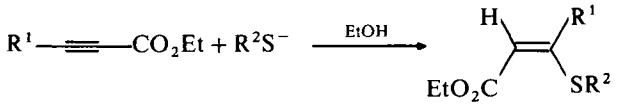
Although some exceptions were apparently found in the additions to propiolate anions (**47**)[179–182], it was later shown that *anti* addition did indeed initially occur[183,184] but an $E \leftrightarrows Z$ postisomerization of the adducts confused the picture (equation 27).



(**47**)

$R^1 = H, Ph; R^2 = 4\text{-}MeC_6H_4$ (27)

For a similar reaction of ethyl propiolates the following kinetic parameters have been determined (equation 28)[185]. The data show a remarkable sensitivity of the reaction rate to a relatively small change in the nature of the triple bond substituent.



(28)

R^1	R^2	$10^2k(M^{-1}s^{-1})$ at 0 °C	$\Delta E^{\ddagger}$(kJ mol^{-1})	$\Delta S^{\ddagger}$(J mol^{-1} K^{-1})
Ph	Ph	2.18	52.3	−50.2
4-$MeOC_6H_4$	4-MeC_6H_4	0.72	60.7	−58.6

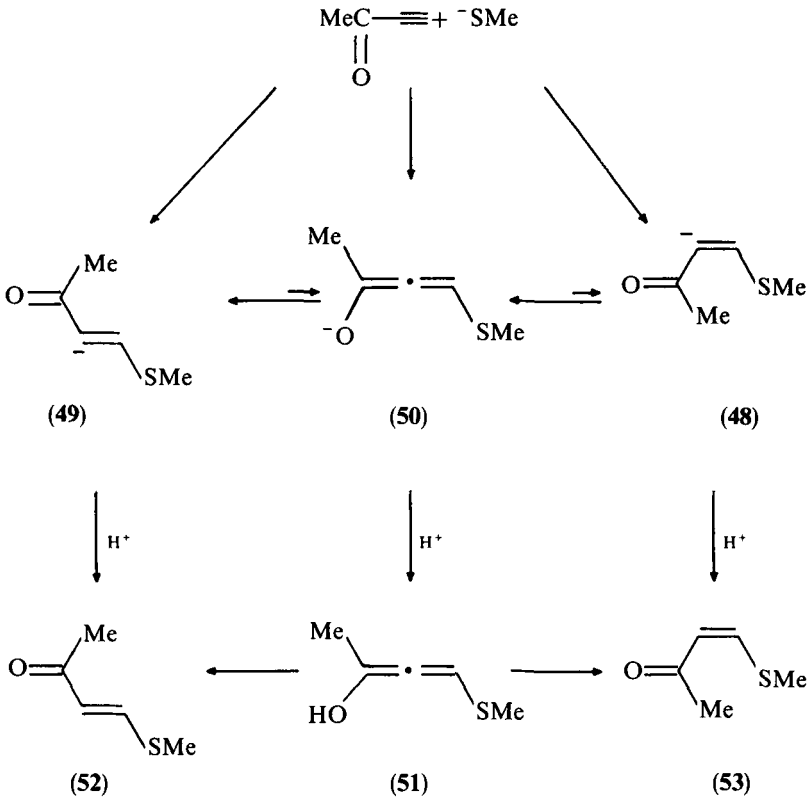
A numerous, although not an exhaustive, list of examples of the high *anti* selectivity of the addition (equation 25) of a great variety of thiols are given in References 186–195.

In the addition of methylthiolate ion to alkynyl methyl ketone the formation of the allenic intermediate **51**[196], which may result not only from the anions **48** and **49** but also from the directly formed anion **50**, explains the formation of both the *E* and *Z* adducts (**52**, **53**) without the requirement of a postisomerization process (Scheme 3)[134].

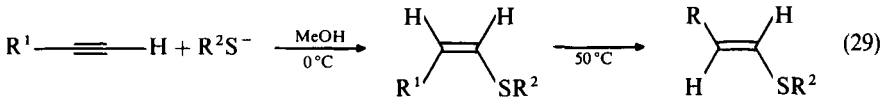
Kinetic and thermodynamic control of the stereoselectivity in the addition reaction 29[197] are functions of the temperature and delocalization of the negative charge by the substituent, as illustrated in Table 10.

In reactions of acylethynes with thiols, similar to those shown in Scheme 3, the appearance of a small proportion of the *E* adducts at low temperature and the stereoconvergence at higher temperature may be associated with the formation of intermediates of types **50** or **51**[196,198,199].

For terminal alkynes (**54**) the regiospecificity of the thiolate addition (equation 30) mostly obeys the Markovnikov rule giving **55**[129,130,186]. The formation of a minor

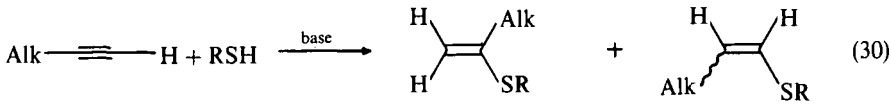


SCHEME 3



Z, 82–100% E, 22–100% (29)

R^1 (Table 10); $R^2 = 4\text{-}MeC_6H_4$



(54) (55) major (56) minor (30)

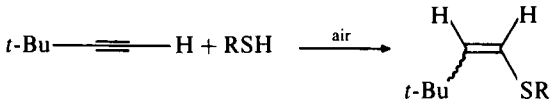
R = Alkyl, Aryl

TABLE 10. Kinetic and thermodynamic control of the stereoselectivity of the nucleophilic addition of 4-$MeC_6H_4S^-$ in equation 29[197]

R^1	% Conversion	% Z isomer	
		under kinetic control, 0 °C	at equilibrium, 50 °C
CN	100	100	33
4-$MeC_6H_4SO_2$	65	100	0
4-$O_2NC_6H_4$	98	100	0
$MeCO_2$	95	92	22
H_2NCO	97	87	23
MeCO	93	82	22

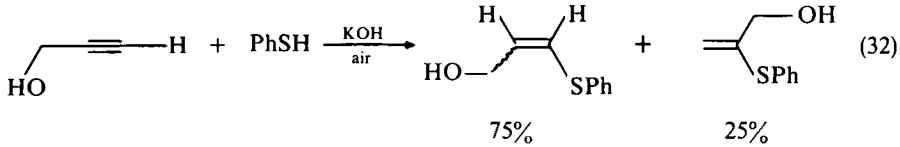
anti-Markovnikov adduct (**56**) which is sometimes detected in the reactions is commonly ascribed to a concurrent radical addition[133].

However, the addition of thiols to *t*-butylacetylene in the presence of KOH (equation 31) gives the anti-Markovnikov product[129,130]. It was suggested that the reaction proceeds via free radicals, since oxygen was not excluded in the procedure[133].

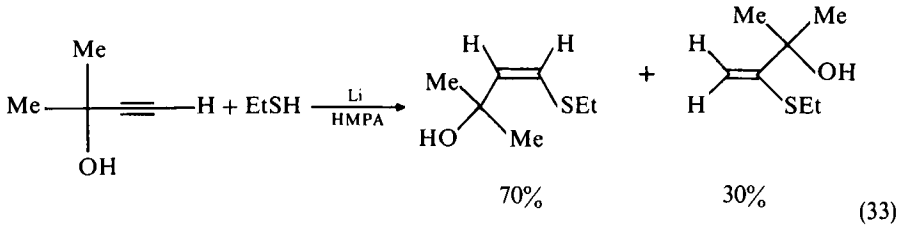


(31)

The anti-Markovnikov adducts that predominate in the addition of thiols to terminal alkynes[200,201] or alkynols (equations 32 and 33) in the presence of oxygen[202] or lithium[203] may also result from the incursion of radical or radical–ion mechanisms. In fact, thiolates usually produce a higher percent of the anti-Markovnikov product than alkoxides of comparable size, a difference which is consistent with their greater proclivity to form radicals[134].

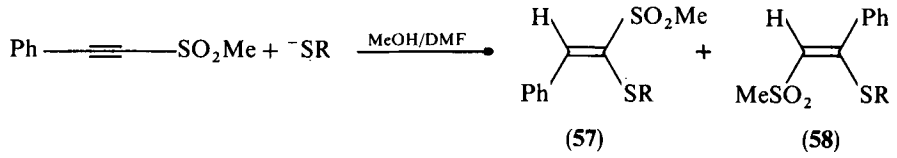


(32)



(33)

Disubstituted acetylenes with substituents of regioselective activation of the same type often display a puzzling regioselectivity of thiolate addition. For instance, in reaction 34 the thiolate attack might be expected to occur predominantly β to the sulfonyl group[204]. Instead, an equimolar mixture of both possible adducts **57** and **58** was formed.

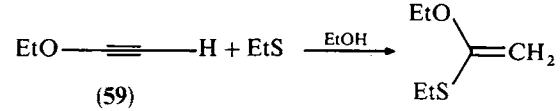


(57) (58)

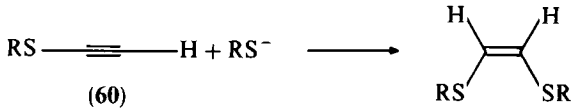
(34)

The ability of the phenyl group to stabilize negative charge may account for this unexpected result. Indeed, with 4-$MeSO_2C_6H_4$, or 4-$O_2NC_6H_4$ instead of Ph, the addition, when R = *n*-Bu, gives exclusively adducts of structure **57**.

α,β-Acetylenic ethers (**59**) and sulfides (**60**) add thiolates with opposite regioselectivities[128,132,205–212] as exemplified by equations 35 and 36. A rationalization of this is the opposite polarization of the triple bond by the adjacent oxygen and sulfur atoms as demonstrated in **61** and **62**[128,132,207].



(59) (35)



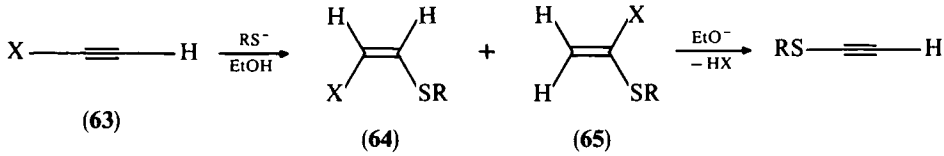
(60) (36)

R = 4-MeC_6H_4

Whether d-orbital participation of the sulfur atom in **62** or some alternative rationalization[213] is valid, the fact is that the elements of the second and higher rows promote the formation of anions at the α position to the element by attack of the thiolate anion on C_β[134]. On the other hand, CNDO/2 estimations[214–217] of the directive power of oxygen towards the two carbons of the triple bond are in accord with reaction expected by structure **61**.

(61) (62)

Nucleophilic substitution on the haloalkynes **63** may proceed by addition–elimination (equation 37), as well as by halophilic attack. The initial adducts, i.e. the corresponding vinyl sulfides **64** and **65**, can be often isolated[218–224]. Thiolates attack almost exclusively on bromine of 1-bromoalkynes[225,226], whereas 1-bromo-3,3,3-trifluoropropyne undergoes addition.[227].



(63) (64) (65)

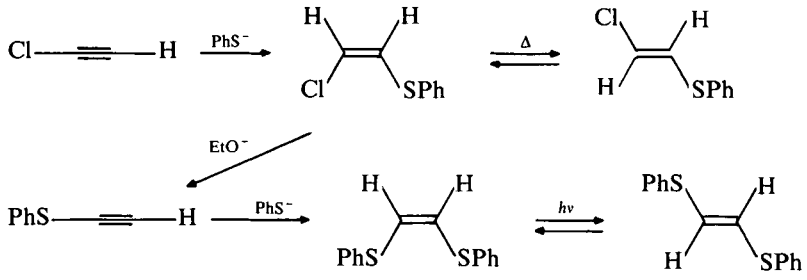
X = F, Cl (37)

TABLE 11. Vinyl sulfides via addition of R^1S^- anions to 1-halo-1-alkynes, $R^2—\equiv—X$

R^2	X	R^1	Vinyl sulfide, %	Reference
H	F	4-MeC_6H_4	CH_2=$CFSC_6H_4$Me-4, 59	221
H	Cl	*t*-Bu	ClCH=CHSBu-*t*	134
Me	Cl	Ar	ClCH=C(Me)SAr	222
F	Cl	Ph	ClCH=C(F)SPh, 70	223
t-Bu	Cl	Ph	ClCH=C(Bu-*t*)SPh, 76	224

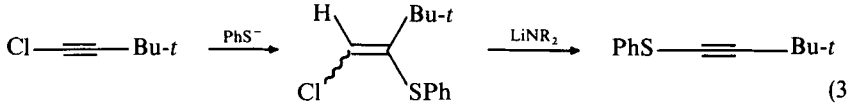
Some representative examples of the regioselectivity in the addition of thiolates to 1-halo-1-alkynes to afford vinyl sulfides are given in Table 11.

It should be noted that the 'true' isomer ratio obtained by a kinetic stereoselectivity in the synthesis may be sometimes obscured by isomerization processes which lead to thermodynamic control. Either heat, light or the presence of basic, acidic or radical species can initiate isomerizations. The interconversions shown in Scheme 4 are representative examples among many which are now available[133,205,206].



SCHEME 4

An alternative mechanism to the nucleophilic substitution at the sp-carbon involves the Fritsch–Buttenberg–Wiechell rearrangement (equation 38)[228]. Depending on the conditions, the intermediate vinyl sulfide (**66**) may be sometimes isolable.



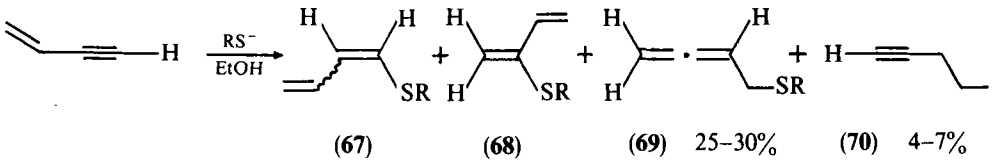
(38)

(**66**)

Vinylacetylene adds thiolates in ethanol to give the alkyl 1,3-dienyl thioethers (**67**) as the major adducts (equation 39) together with the three minor adducts (**68**, **69** and **70**) and the ratio of the products depends on the structure of the thiol[191,229]. The allene (**69**) becomes the exclusive product in aprotic solvents such as dioxane or THF[229].

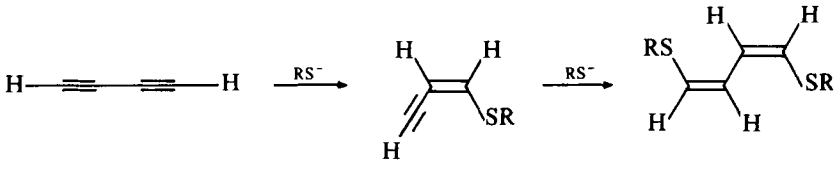
In additions to diacetylene, both monoadducts (**71**) and diadducts (**72**) are formed (equation 40)[130,189,190].

In the case of substituted diacetylenes, alkanethiolates attack preferentially the less hindered sites (equation 41)[134,230]. With symmetrically disubstituted diacetylenes, both *Z*-1,3-enynic and *Z,Z*-1,3-dienic sulfides are formed (equation 42)[231–233].

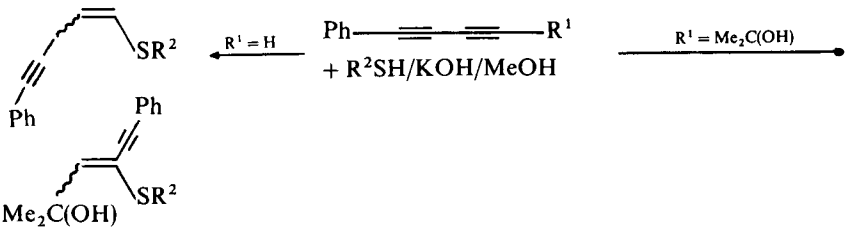


(67) (68) (69) 25–30% (70) 4–7%

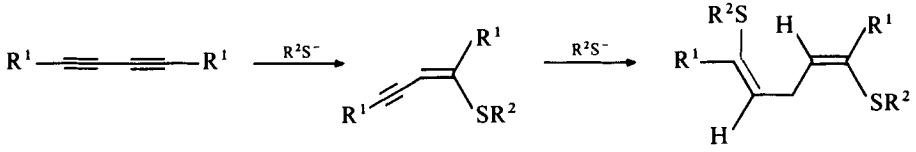
R = Me, Et, *n*-Pr, *n*-Bu, *t*-Bu (39)



(71) (72) (40)

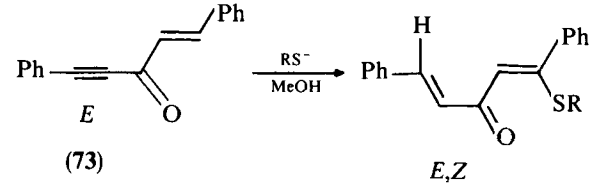


(41)



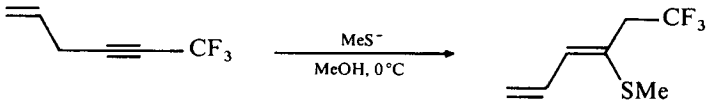
R^1 = H, Alk, Ar; R^2 = $PhCH_2$ (42)

In attack on the enynic ketone **73**, the reaction takes place preferentially on the triple bond in its competition with the double bond for the thiolate (equation 43)[234,235].



(73) *E,Z* (43)

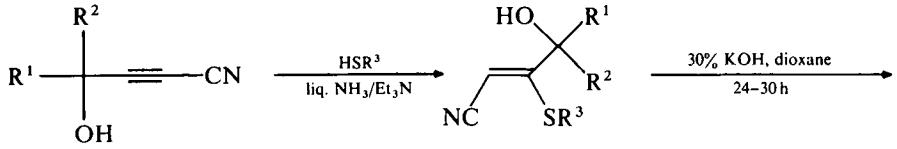
R = 4-MeC_6H_4



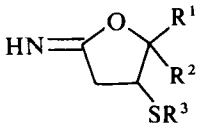
(74) (75) (44)

The addition of methanethiolate to the unconjugated enyne (**74**) is accompanied by a complete shift of the triple bond to form the conjugated dienic sulfide (**75**) (equation 44)[236].

Hydroxyalkyl acetylenic nitriles (**76**) add thiols in liquid ammonia [237] or in ethanol or dioxane in the presence of Et_3N at ambient temperature[238] to afford the corresponding functionally substituted vinyl sulfides (**77**), preferentially of the *Z* configuration, in 91–96% yields. These can be cyclized with 30% KOH at ambient temperature in 86–94% yields the iminodihydrofurans (**78**), which retain the vinyl sulfide moiety (equation 45). Obviously a $Z \rightarrow E$ isomerization precedes the cyclization.



(**76**) (**77**)

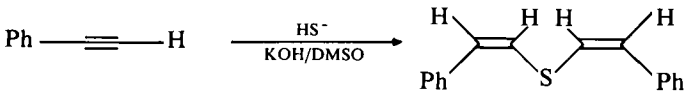


(**78**) (45)

R^1 = Me; R^2 = Me, Et; R^3 = Et, *i*-Pr, *n*-Bu, *neo*-Pen, $C_{12}H_{25}$, CH_2Ph, Ph

c. Effects of the thiol structure. As shown in Section IV.A.1.b, in the addition to acetylene the reaction conditions are most strongly affected when hydrogen sulfide, the simplest thiol, is used instead of aliphatic or aromatic thiols. The same is true for some other substituted acetylenes, though with conjugated or activated acetylenes the SH^- and S^{2-} ions react almost as readily as alkanethiolate or arenethiolate ions.

The hydrosulfide ion generated from hydrated sodium sulfide and activated by the KOH/DMSO system adds smoothly to phenylacetylene to afford the bis-vinyl sulfide **79** in a yield of up to 91% (equation 46)[24,157].

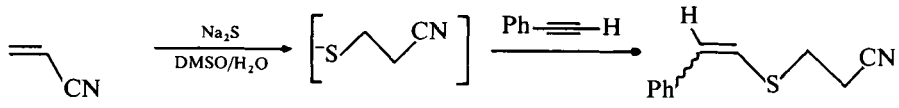


(**79**) (46)

This synthesis was also successful, giving 90% yield, in a KOH–triethylphosphine oxide (TEPO) superbasic system[239] and, to a lesser degree, under two-phase conditions with tetraalkylammonium salts or dibenzo-18-crown-6 as catalysts[240]. Kinetic studies of the hydrosulfide ion addition to phenylacetylene (equation 46)[241] indicate that the reaction rate decreases in the following order of solvents: HMPA > DMSO > TEPO.

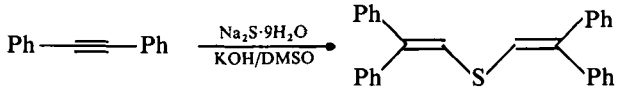
Acrylonitrile reacts with a mixture of phenylacetylene and sodium sulfide in aqueous DMSO at 30–35 °C to form vinyl sulfide (**80**) in 30% yield (equation 47)[242].

Sulfide ions generated in the system $Na_2S \cdot 9H_2O$/KOH/DMSO add to diphenylacetylene to afford an anomalous diadduct (**81**), in 20% yield (equation 48)[243].



(80)

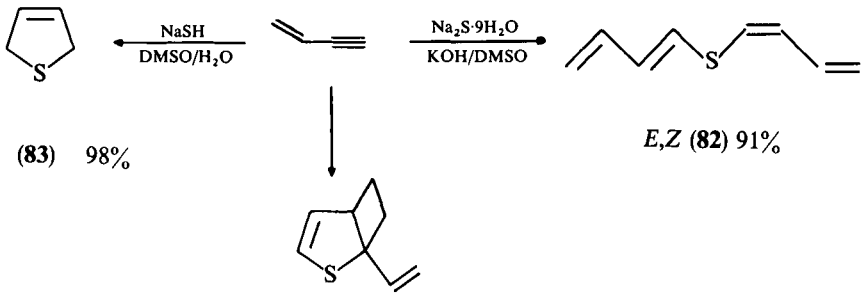
(47)



(81)

(48)

Vinylacetylene interacting at 70–110 °C with the activated sulfide ions in the system $Na_2S \cdot 9H_2O$/KOH/DMSO gives the bis-dienic sulfide (**82**) in a yield exceeding 90%[244]. Under other conditions, the heterocyclization gives either dihydrothiophene (**83**)[245,246] or the bicyclic vinyl sulfide (**84**)[247–252] (Scheme 5)[23–25,160].



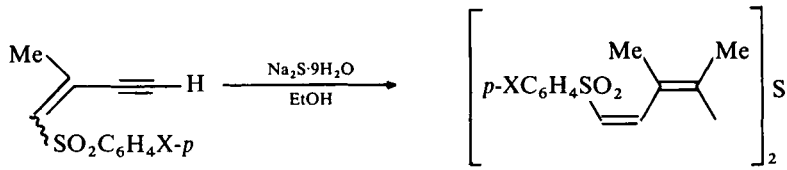
(**83**) 98%

E,Z (**82**) 91%

(**84**) 26%

SCHEME 5

The reaction of sulfide ions with the vinylacetylenic sulfones (**85**) proceeds with isomerization and results in the dienic sulfides (**86**) (equation 49)[253].

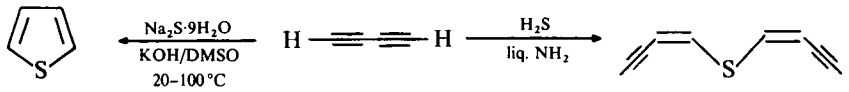


(**85**) (**86**)

(49)

X = H, Me, Cl, Br, NO_2

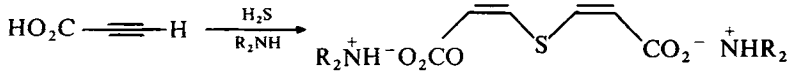
Diacetylene reacts with sulfide ions to give thiophene (**88**) in essentially quantitative yield[254,255]. With H_2S in liquid ammonia it gives the vinyl sulfide (**87**) in 90% yield (equation 50)[256].



(50)

(**88**) (**87**)

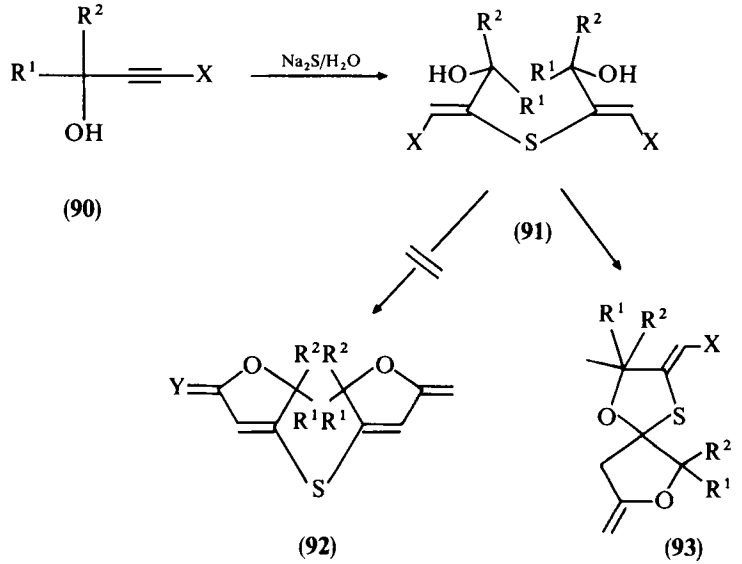
A simple stereospecific synthesis of diammonium salts (**89**) in 81–90% yield from propiolic acid and hydrogen sulfide in liquid ammonia or diethylamine has been developed (equation 51)[257].



(51)

(**89**)

Acetylenic esters and nitriles (**90**) readily react with alkali metal sulfides in water to yield spiroheterocycles (**93**) containing the vinyl sulfide moiety, instead of the divinyl sulfides **91** and **92** (Scheme 6)[258–260].

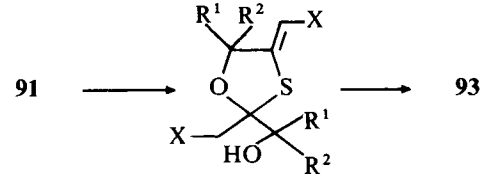


R^1, R^2 = Alkyl, or $(CH_2)_4$

X = CO_2Me, CN; Y = O, NH

SCHEME 6

Apparently, in the intermediate divinyl sulfide (**91**) one of the two hydroxyl groups adds in a crossover mode to the double bond of the other acrylic moiety to form the 1,3-oxathiolane ring of **94**, whereas the remaining hydroxyl group reacts with the ester or the nitrile function to produce the 2-oxo- or the 2-imino-tetrahydrofuran moiety of **92** (equation 52)[260].



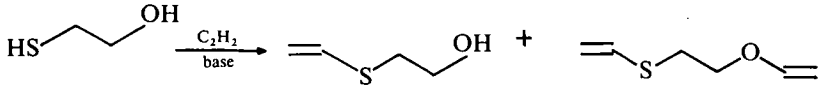
(52)

(**94**)

In concluding the discussion on the nucleophilic addition of hydrogen sulfide to acetylenes, it is noteworthy that satisfactory preparative results are attainable only with sulfide or hydrosulfide ions, i.e. with at least a stoichiometric amount of a base.

As far as alkanethiolate or arenethiols are concerned, they behave normally in the sense that the higher their nucleophilicity, the more active they are in the nucleophilic addition. Steric requirements seem of little importance[129,130,133,134].

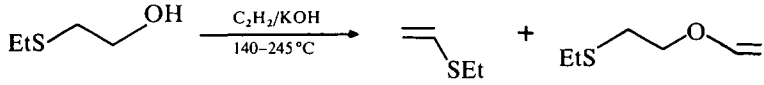
The vinyl sulfides **96** and **97** were prepared by vinylation of 2-mercaptoethanol (**95**) under pressure (equation 53)[80,261–263].



(53)

(**95**) (**96**) 30–70% (**97**) 21%

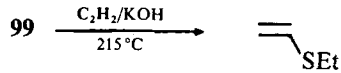
Vinylation of 2-(ethylthio)ethanol (**98**) gave, besides the expected vinyl ether (**99**), ethyl vinyl sulfide in a yield up to 36% (equation 54). This elimination reaction proceeds more easily starting from 2-(ethylthio)propan-1-ol[80].



(54)

(**98**) (**99**)

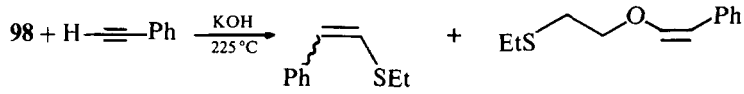
2-Vinyloxyethyl ethyl sulfide (**99**) underwent similar cleavage to 15% of ethyl vinyl sulfide when treated with acetylene and 5% KOH at 215 °C under pressure (equation 55)[80].



(55)

In the reaction of **98** with phenylacetylene the cleavage of the C—S bond which leads to vinyl sulfide (**100**) becomes the major reaction (equation 56)[264].

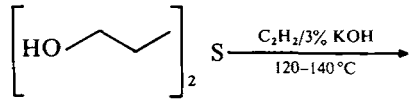
Likewise, upon vinylation of di(2-hydroxyethyl) sulfide (**101**) with acetylene it undergoes up to 50% cleavage to the vinyl sulfides **96** and **97** which are formed along with the expected vinyl ethers (equation 57)[80,261,262].



(56)

(100) 11%

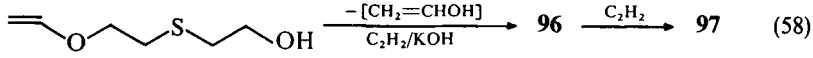
57% $E:Z = 7:3$



(57)

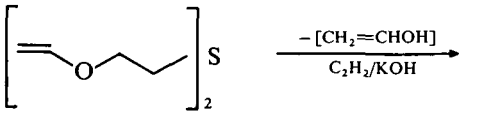
(101)

Experiments in the absence of acetylene did not confirm the probable dehydration step, and participation of the acetylene in the cleavage of the C—S bond during the vinylation has been postulated[262]. However, in the light of new data on the facile base-catalyzed elimination of vinyl alcohol from vinyl ethers of 1,2-diols[265], the vinyl sulfides **96** and **97** as well as the ethyl vinyl sulfide (equation 55) could be formed from the vinyl ethers **102** and **103** (equations 58 and 59).



(58)

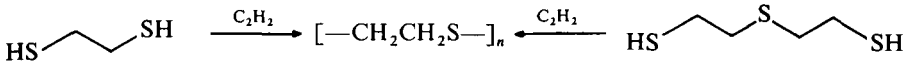
(102)



(59)

(103)

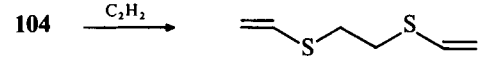
1,2-Di(mercapto)ethane (**104**) and di(2-mercaptoethyl) sulfide (**105**) absorb acetylene vigorously upon vinylation at 80–100 °C to form almost quantitatively polyethylene sulfide (**106**) (equation 60)[80,261,266].



(60)

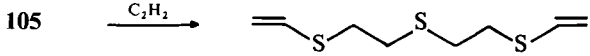
(104) (106) (105)

1,2-Di(vinylthio)ethane (**107**) and di(2-vinylthioethyl) sulfide (**108**) were prepared in 36 and 69% yields, respectively, under special conditions inhibiting the competitive thiylation of the vinylthio group (equations 61 and 62)[80,261]; these include a 2-fold or larger excess of acetylene under 10–15 atm, solvent *t*-BuOH or dioxane, a temperature of 80–100 °C, 1.5–7% of alkali metal hydroxides or alkoxides and 0.3–1% of pyrogallol or hydroquinone as inhibitors of the free radical thiylation.



(61)

(107)

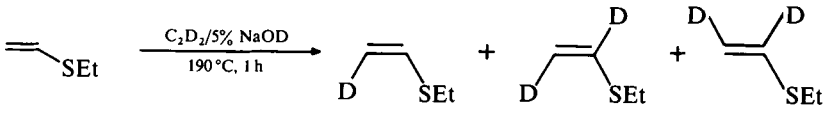


(62)

(108)

The trisulphide (**108**) is also formed during vinylation of **104** in a *ca* 30% yield[261]. On the other hand, from the vinylation products of **104** at 80 °C, **107** was isolated in 10% yield[80,261]. These results indicate the occurrence of side condensation and elimination processes, respectively.

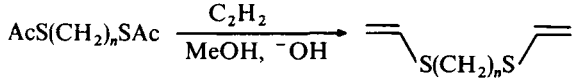
Ethyl vinyl sulfide exchanges its vinylic hydrogens for deuterium under the vinylation conditions with C_2D_2; the major amount of deuterium appears in the *Z* forms (equation 63)[80]. This serves as evidence for a reversible vinylation.



(63)

6% 2% 2%

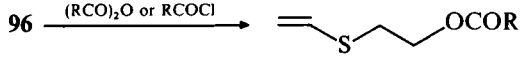
An efficient preparation of ω,ω-di(vinylthio)alkanes (**110**) is based on solvolytic vinylation (equation 64) of α,β-di(acetylthio)alkanes (**109**)[147,267]. In HMPA or DMSO the synthesis is carried out at a temperature as low as 10–15 °C and the yield of **110** spans 60–76%[47]. The precursor di(acetylthio)alkanes can be prepared from dihaloalkanes and sodium thioacetate or by addition of thioacetic acid to dienes.



(64)

(**109**) (**110**)

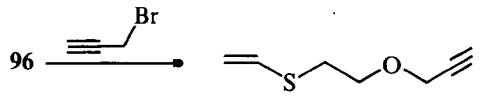
A number of functional vinyl sulfides with base-sensitive functionalities have been synthesized starting from **96** (equations 65–69)[268–271].



(References 80, 272, 273) (65)

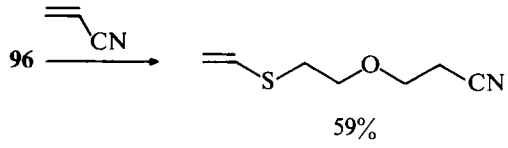
70–73%

R = Me, Et, Ph

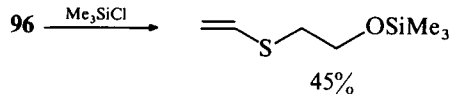


(References 80, 272) (66)

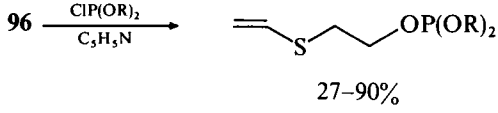
22%



(References 80, 272) (67)



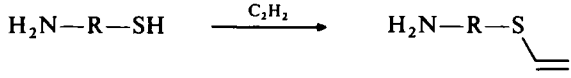
(References 80, 272) (68)



(References 80, 272) (69)

R = Et, *n*-Pr; R—R = $(CH_2)_2$, $CH_2CH(Me)$, $CH(Me)CH(Me)$

Aminoalkyl vinyl sulfides (**112**) are readily prepared by reaction of the corresponding thiols (**111**) with acetylene in the presence of a basic catalyst, such as alkali metal hydroxides or carbonates in benzene, toluene or high boiling ether at 120–180 °C under a pressure of 14–35 atm (equation 70)[272].

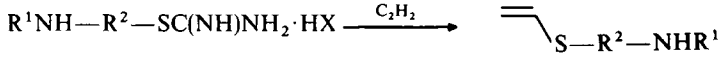


(70)

(**111**) (**112**)

R = $(CH_2)_2$, $(CH_2)_3$, $CH(Me)CH_2$, $CH_2CH(Me)$

Other aminoalkyl vinyl sulfides (**114**) are best made by vinylation of the corresponding isothiuronium salts (**113**) under essentially the same conditions (equation 71)[272].

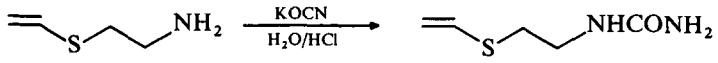


(71)

(**113**) (**114**)

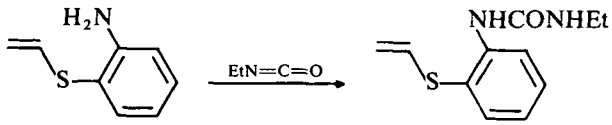
R^1 = H, Me, *n*-Bu; R^2 = $(CH_2)_2$, $CH_2C(Me)_2$

Ureido-substituted vinyl sulfides of types **115–118** which could not survive direct vinylation were prepared by reactions of aminoalkyl or aminoaryl vinyl sulfides with potassium cyanate, alkyl isocyanates, *N*,*N*-dialkylcarbamoyl chlorides, urea or thiourea. Typical examples are given in equations 72–75[272].



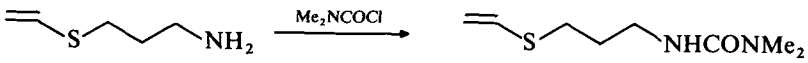
(72)

(115)



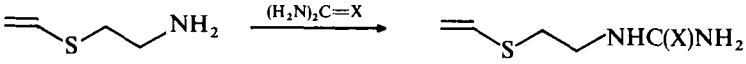
(73)

(116)



(74)

(117)

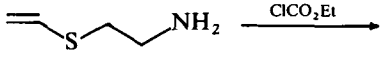


(75)

X = O, S

(118)

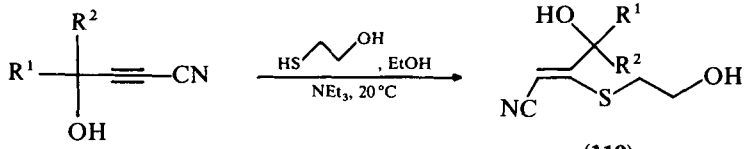
Vinyl sulfides with a carbamate function were prepared[273] according to equations 76 and 77.



(76)

(77)

2-Hydroxyethanethiol adds to hydroxyalkyl acetylenic nitriles in ethanol or dioxane at 20 °C to form the corresponding functional vinyl sulfides (**119**) in yields up to 93% (equation 78)[274].

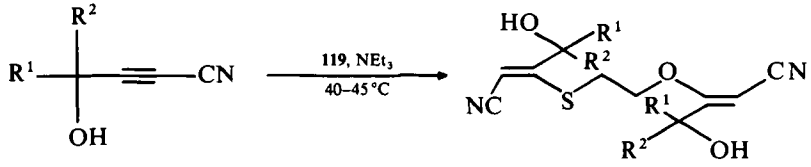


(78)

(119)

R^1 = Me; R^2 = Et; R^1–R^2 = $(CH_2)_5$

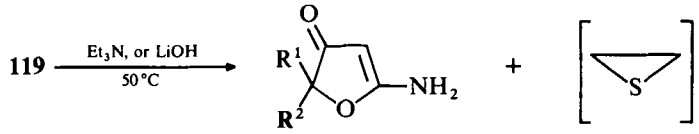
At a higher temperature (40–45 °C) the vinyl sulfides (**119**) are capable of adding via their primary hydroxyl group to a second molecule of acetylenic nitrile to afford the diadduct **120** (equation 79)[274].



(79)

Z,Z (**120**)

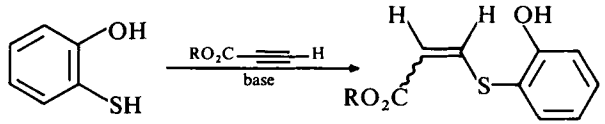
In contrast to the related vinyl sulfides (**77**) obtained from alkanethiols (equation 45), **119** do not cyclize into iminodihydrofurans similar to **78**, but are transformed into 2-amino-5,5-dialkyl-4,5-dihydro-4-furanones (**121**), apparently with elimination of thiiran (equation 80)[274].



(80)

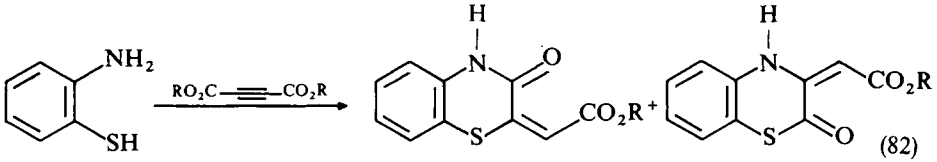
(**121**)

Thus, generally, when a thiolate anion competes with RO^- or RNH_2 sites within the molecule for the acetylenic carbon, the former usually wins. Three additional representative examples of this rule are given in equations 81[133,134,275], 82[133,134,276] and 83[133,134,195].



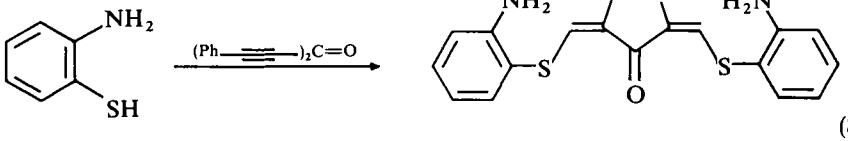
(81)

E,Z



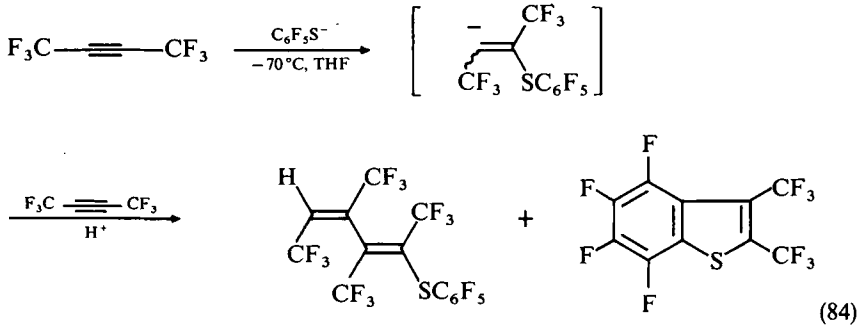
(82)

major minor



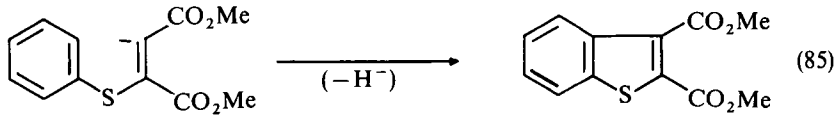
(83)

In some cases further transformations of the intermediate carbanions occur to give derivatives (**122**) resulting from two acetylene molecules or/and cyclic products (**123**) (equation 84)[277].



(84)

(**122**) (**123**)

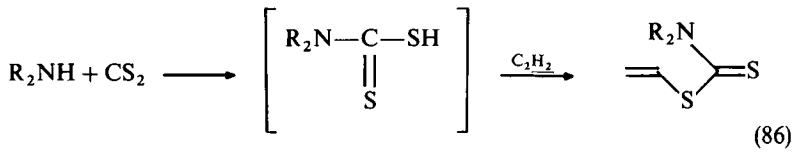


(85)

(**124**)

Equation 85 is an example of the oxidative cyclization of the anion (**124**) derived from the addition of benzenethiols to dimethyl acetylenedicarboxylate[278].

Dithiocarbamic acids (**125**), formed *in situ* from carbon disulfide and a dialkylamine, add to acetylene at 100–140 °C under a pressure of 7–21 atm in THF or DMF to produce *S*-vinyl *N*,*N*-dialkyldithiocarbamates (**126**) in 50–60% yields (equation 86)[279,280].



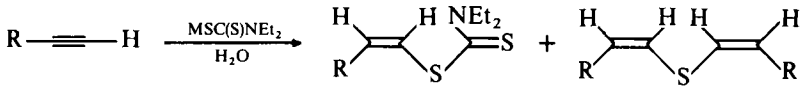
(86)

(**125**) (**126**)

R = Et, *n*-Pr, *n*-Bu; R-R = $(CH_2)_5$, $(CH_2)_2O(CH_2)_2$

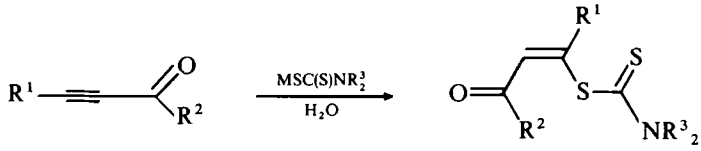
When the reaction is carried out with sodium or potassium *N*,*N*-dialkyldithiocarbamates in DMSO, HMPA, THF or dioxane containing 1–6% water, both adducts (**127**) and divinyl sulfides (**128**) are formed (equation 87)[281–283].

The same reaction, using substituted acetylenic ketones in a two-phase water–Et_2O system at ambient temperature, gives the corresponding *S*-vinyl *N*,*N*-dialkyldithiocarbamates in quantitative yield (equation 88)[284].



(127) (128) (87)

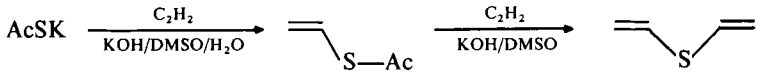
R = H, Ph; M = Na, K



(88)

R^1 = H, Ph; R^2 = Me, Ph; R^3 = Me, Et; M = Na, K

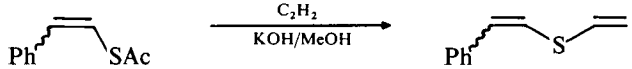
Potassium thioacetate (**129**) and acetylene under pressure in the systems KOH/DMSO and KOH/HMPA containing small amounts of water at 130–140 °C give divinyl sulfide (**39**) in 60% yield (equation 89)[285].



(**129**) (**130**) (**39**) (89)

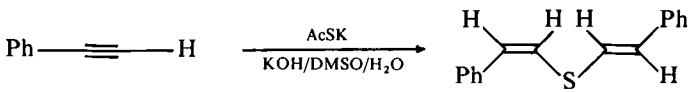
It is not clear whether **39** is formed via the sulfide ions resulting from hydrolysis of **129** or via the hydrolytic vinylation of the intermediate vinyl thioacetate (**130**) or via both routes, although **130** affords **39** readily under similar conditions[80].

Vinyl (2-phenylvinyl) sulfide (**132**) was obtained in 50% yield from 2-phenylvinyl thioacetate (**131**) and acetylene (equation 90)[80].



(**131**) (**132**) (90)

Phenylacetylene reacts with **129** and a suspension of KOH in DMSO at 120–130 °C to form *E,Z*-di(2-phenylvinyl) sulfide (**133**) in 57% yield (equation 91)[80].

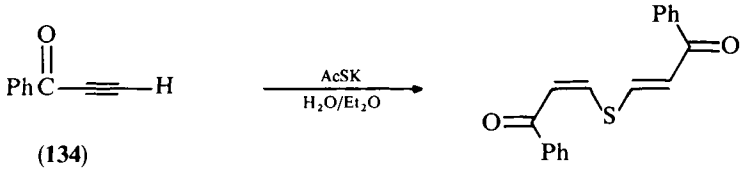


(**133**) (91)

Interestingly, the same reaction in a suspension of KOH in TEPO gives the isomeric *Z,Z*-**133** in 90% yield[239]. In the presence of phase-transfer catalysts (dibenzo-18-crown-6

or TEBA) in an aqueous–organic medium at 70–80 °C the yields of **133**, which is formed in a 1:1 *Z,Z* to *E,E* ratio, were 72 and 37%, respectively. A noncatalytic reaction under comparable conditions gave 20–22% yield of **133**[80].

3-Phenyl-1-propyn-3-one (**134**) reacts with potassium thioacetate in a two-phase H_2O–Et_2O system at room temperature to afford *E,Z*-di-(2-benzoylvinyl) sulfide (**135**) in 90% yield (equation 92)[80].



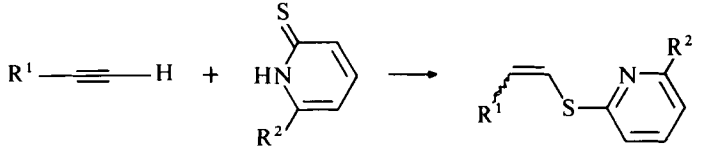
(92)

(**134**) (**135**)

The products of the reaction of vinylacetylene with potassium thioacetate and KOH suspension in DMSO containing *ca* 3% of H_2O at 90 °C are di(buta-1,3-dienyl-1) sulfide (**82**), 1-vinyl-2-thiobicyclo[3.2.0]hept-3-ene (**84**) and 2,5-dihydrothiophene (**83**)[80], i.e. the same products formed with sulfide ions. Analogously, diphenylacetylene with AcSK in KOH/DMSO/H_2O at 140–150 °C gives after 15 h bis(2,2-diphenylvinyl) sulfide (**81**) in 57% yield[80].

d. Additions of thiono compounds. Diverse thiono compounds such as thioketones, thioamides, thioureas and similar compounds add in their thiol tautomeric form to activated acetylenes to produce products containing a vinyl sulfide structural unit. These reactions were thoroughly considered in reviews[78–80,286]. Some representative examples are given below.

Kinetic data for the addition of a thioamide to monosubstituted acetylenes (equation 93)[287] in $CDCl_3$ at 0 °C show that the rate constants decrease in the following order for R^1: COMe > $CO_2Et \gg$ CONHEt and for the R^2 (when R^1 = CONHMe) in the order H > *n*-Pr ≫ Me.

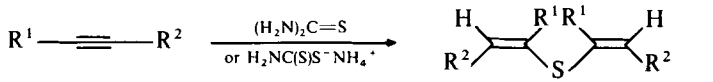


(93)

E, Z

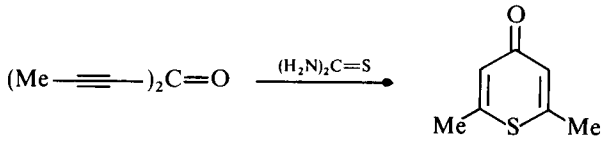
Ammonium dithiocarbamates, thiourea and its derivatives could be often regarded as merely a concealed version of H_2S in such reactions (equations 94 and 95)[80,257,288–291].

Isothiuronium salt (**136**), which contains a vinyl sulfide moiety, is the initial adduct of thiourea to acetylenic mono- or dicarboxylic acids and their esters in an aqueous



(94)

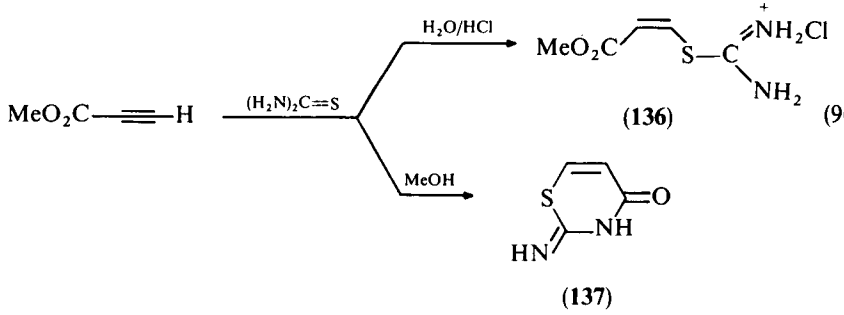
R^1 = H, Me, Ph; R^2 = CN, CO_2H



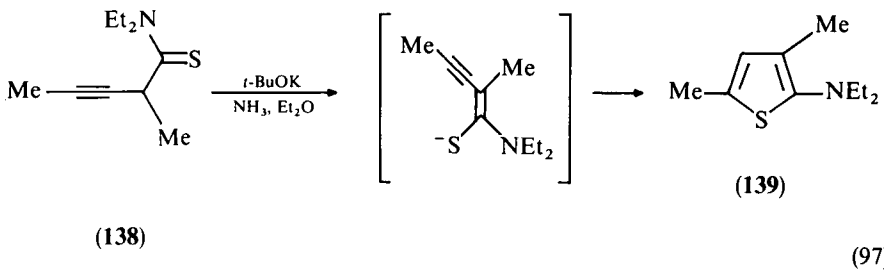
(95)

HCl while in MeOH the thiazine (**137**), which is a cyclic vinyl sulfide, was isolated (equation 96)[288,292].

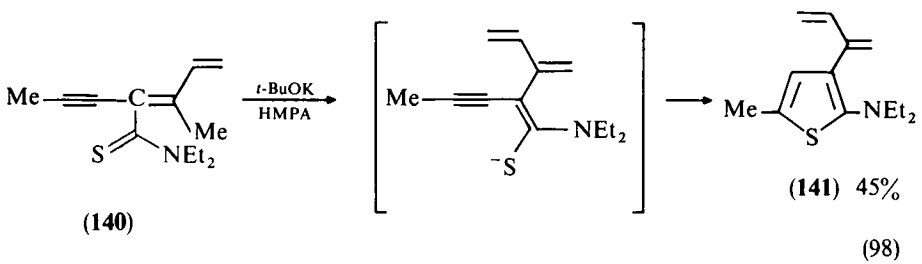
The acetylenic thioamides **138** and **140** cyclize to the thiophenes **139** and **141** in a process initiated by prototropic isomerization under superbasic conditions (equations 97 and 98)[293–296].



(96)



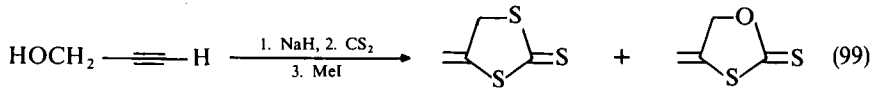
(97)

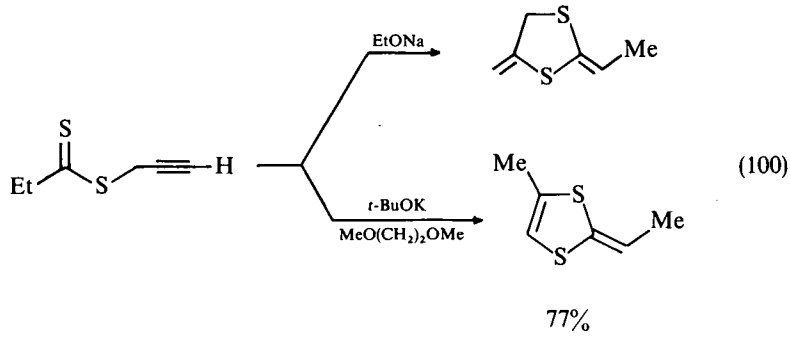


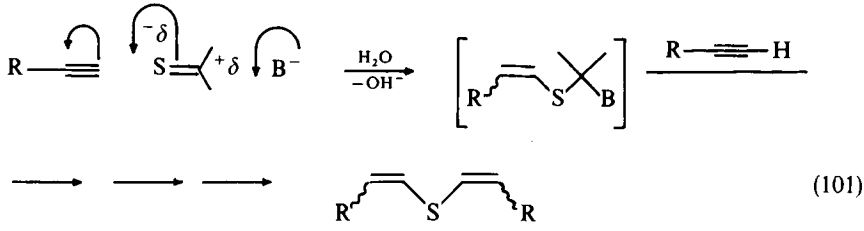
(98)

Dithiocarboxylic acids and related compounds give with acetylenes mostly cyclic adducts containing vinyl sulfide moieties (equations 99 and 100)[295,296].

In superbasic suspensions of MOH in DMSO (M = Na, K) various thione derivatives react with acetylenes to furnish easily divinyl sulfides in high yields. It was suggested[80]



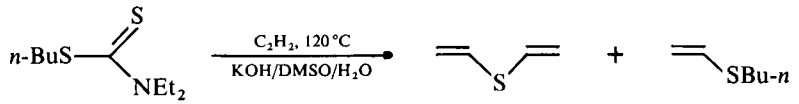




B = MOH/DMSO (HMPA); M = Na, K

that the thione moieties can behave as uncharged, highly polarizable nucleophiles in the presence of a strong base (equation 101).

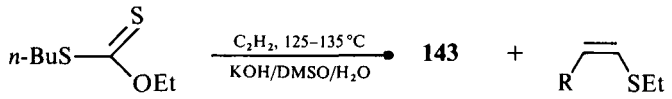
Thione compounds employed in the preparation of vinyl sulfides as generalized by equation 101 include carbon disulfide[80], thiourea[80,297,298], esters of dithiocarbonic[80,281,299], trithiocarbonic[80,300] and some thiophosphoric[80,301] acids and sodium thiosulfate[302]. For example, *N,N*-diethyl-*S*-*n*-butyl dithiocarbamate (**142**) affords with acetylene divinyl sulfide (**39**) and *n*-butyl vinyl sulfide (**143**) in 68 and 93% yields, respectively (equation 102)[80,191,281,300].



(142) **(39)** **(143)**

(102)

In the reaction of *O*-ethyl *S*-*n*-butyl dithiocarbonate (**144**) with acetylenes (equation 103)[80,299] apart from **143**, ethyl vinyl sulfides (**145**) are formed. The formation of **145** indicates a migration of the ethyl group from oxygen to sulfur.

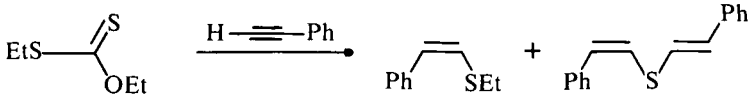


(103)

(144) up to 76% (145)

R = H, Ph

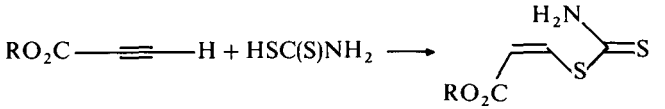
The reaction of *O,S*-diethyl dithiocarbonate with phenylacetylene under similar conditions gives ethyl *Z*-(2-phenylvinyl) sulfide (**145**, R = Ph) in a yield exceeding the stoichiometric amount (128%) based on the *O,S*-diethyl dithiocarbonate. This serves as evidence for a transfer of the ethyl group from EtO to the thione sulfur (equation 104)[80,299].



(104)

(145) 128% 22%

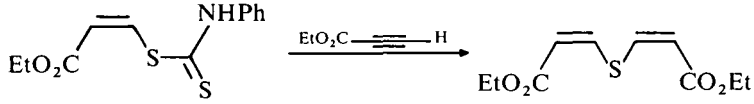
For the preparation of *S*-(2-carboxyvinyl)dithiocarbamates (**146**) the free dithiocarbamic acid is liberated from its amine salt *in situ* at low temperature, and its addition to propiolic acid or ester is effected under mildly acidic conditions (equation 105)[303]. This gives better yields than those earlier reported[304].



(105)

R = H, Et (146)

The reaction between the ammonium salt of *N*-phenyldithiocarbamic acid and ethyl propiolate produced an essentially quantitative yield of the divinyl sulfide (**148**) via the intermediate (**147**) (equation 106)[305]. Basic hydrolysis of **148** gave the corresponding diacid, which with diazomethane gave the dimethyl ester[305].

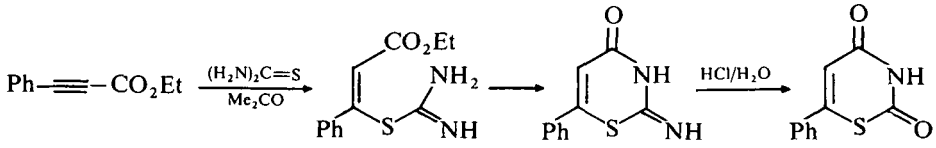


(106)

(147) *Z,Z* (**148**)

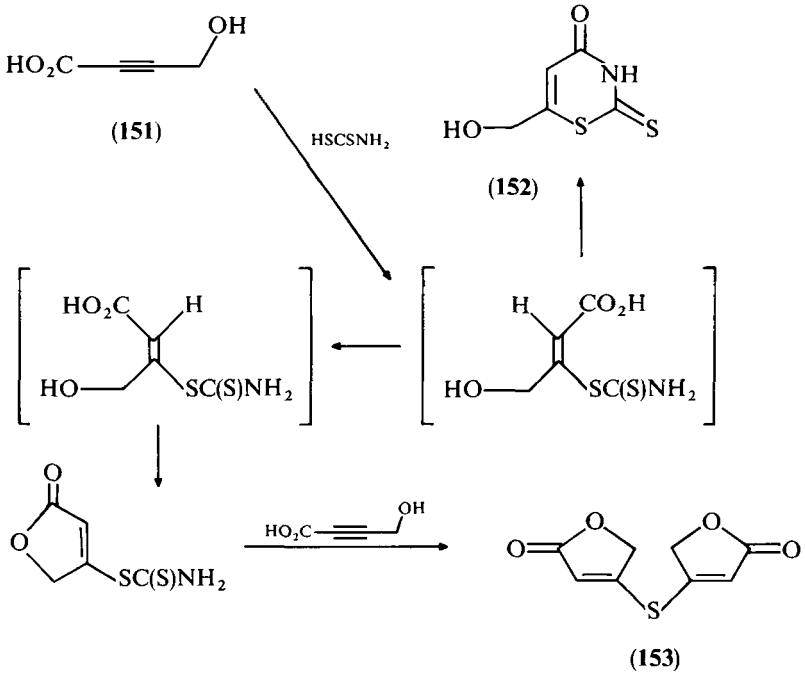
In contrast, the reaction of thioamides with methyl propiolate gives *Z,Z* and *E,Z* isomers of the corresponding divinyl sulfide[306], similar to that observed in the reaction with N-substituted thioureas in refluxing methanol. However, ethyl phenylpropiolate (**149**) and thiourea in refluxing acetone afford 6-phenyl-2,4-dioxo-1,3-thiazine (**150**) (equation 107)[307].

γ-Hydroxytetrolic acid (**151**) gave no acyclic adduct with dithiocarbamic acid (Scheme 7).



(149) (150)

(107)



SCHEME 7

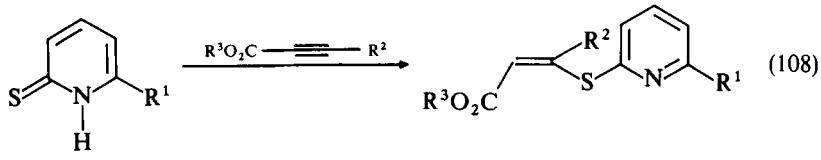
Although a small yield of the desired 1,3-thiazine (**152**) was obtained, the major product was the divinyl sulfide (**153**)[308].

A similar reaction with ethyl γ-hydroxytetrolate or with ethyl tetrolate gives an excellent yield of **152** and its methyl homolog[221].

Pyridine-2(1*H*)-thiones (**154**) afford with propiolic acids or their esters vinyl sulfides (**155**) (equation 108)[309,310].

Monoalkyl thioureas react with dimethyl acetylenedicarboxylate (DMAD) to give good yields of the isomeric dihydrothiazinones **156** and **157** having a vinyl sulfide moiety (equation 109)[311–314].

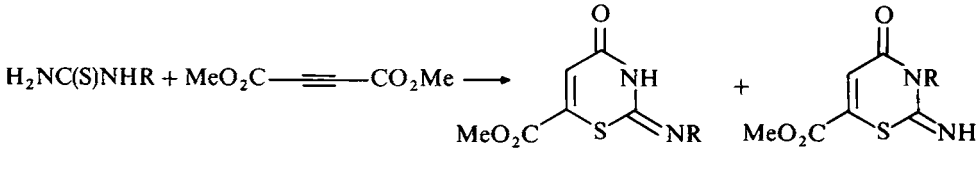
Benzimidazole-2-thione (**158**) and DMAD react in an aqueous MeCN solvent to give the vinyl sulfide (**159**), which could be cyclized into fused thiazolidones (**160**) in dry MeCN or into fused thiazinones (**161**) in dry MeOH (Scheme 8)[315].



(108)

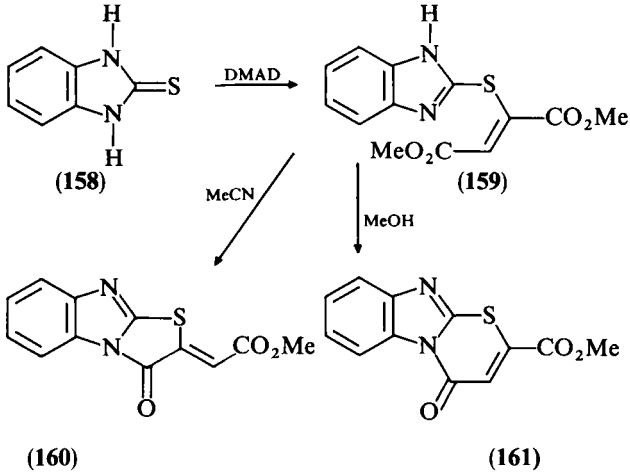
(154) (155)

R^1 = H, Me; R^2 = H, Ph; R^3 = H, Me



(109)

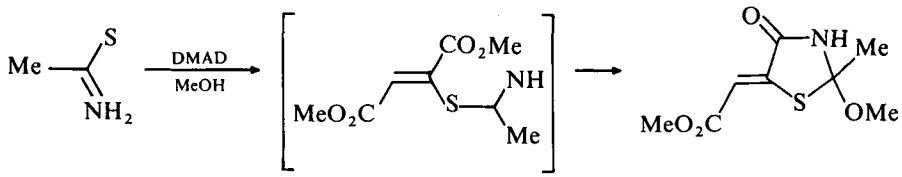
(156) (157)



(158) (159) (160) (161)

SCHEME 8

Ethanethioamide was reported to give the vinyl sulfide (**162**) with DMAD in MeOH[306], but according to its ^{13}C NMR spectrum[315] the structure of the product is that of **163** (equation 110).

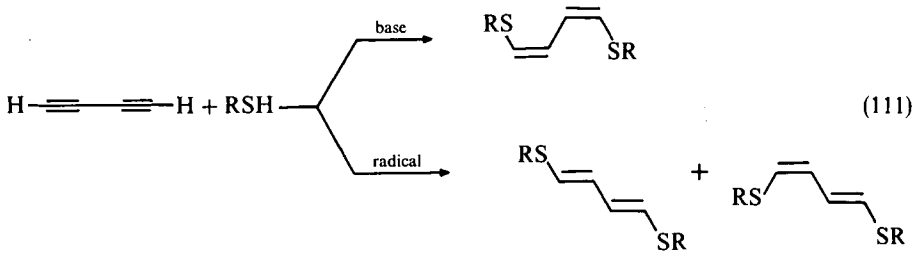


(162) (163) (110)

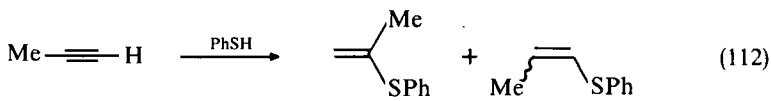
Similar reactions of DMAD with trisubstituted thioureas, 2-oxo-2-phenylethanethioamide, indoline-2-thione, pyridine-2(1*H*)-thione and pyrimidine-2(1*H*)-thione were also described[315].

2. Free-radical addition

Thiols also add to acetylenes in the absence of base and the problem of competing nucleophilic and free radical attacks has long been recognized[123]. Radical processes are normally associated with low stereoselectivity and anti-Markovnikov regioselectivity[128,130,186]. A representative example of the products obtained by the two routes is given in equation 111[130].



(111)



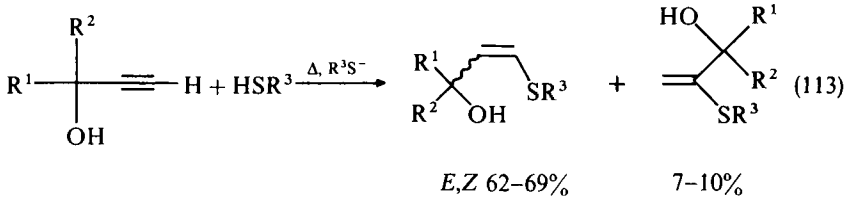
(112)

Other radical or combined radical and nucleophilic additions of thiols to acetylenes have been published (e.g. equation 112)[316,317].

Photochemical addition of *n*-butanethiol to propyn-3-ol afforded 1-hydroxy-2,3-di(*n*-butylthio)propane admixed with a small amount of the expected vinyl sulfide[318]. In the presence of an alkali, thiols add to acetylenic alcohols by both radical and nucleophilic mechanisms giving both the Markovnikov and the anti-Markovnikov products (equation 113)[319,320].

The Markovnikov adducts of arenethiols to propyn-3-ol (**164**) rearrange into 2-(arylthio)-propanals (**165**) upon distillation (equation 114)[321].

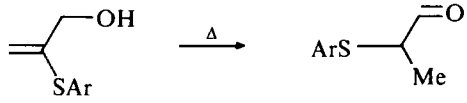
Normally, free-radical addition of thiols to alkoxyalkynes is faster than the nucleophilic addition and produce much of the *Z* and a little of the *E* adducts (equation 115)[127,128,321], whereas the nucleophilic addition of thiolate ions yields 1-alkoxy-1-(alkylthio)ethenes.



(113)

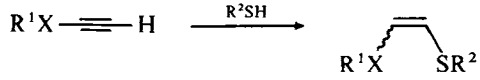
E,Z 62–69% 7–10%

R^1 = H, Me, Et, *n*-Pr; R^2 = H, Me; R^3 = Ph, 4-MeC_6H_4



(114)

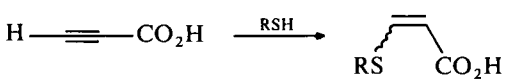
(164) (165)



(115)

X = O, S

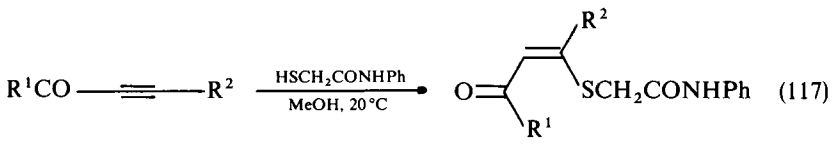
There is a number of papers on the free-radical synthesis of vinyl sulfides from thiols and arylacetylenes[322,323], and the substituent effects on the reaction of arylthiyl radicals with arylacetylenes have recently been studied[324]. The corresponding vinyl sulfides have been prepared by the free-radical addition of thiols to (alkylthio)vinylacetylenes and their analogs[325]. The noncatalytic addition of thiols to propiolic acid leads to the expected vinyl sulfides in almost quantitative yields (equation 116)[326,327].



(116)

E, Z

R = Et, *n*-Pr, *n*-Bu, *n*-C_6H_{13}, *n*-C_8H_{17}, *n*-$C_{12}H_{25}$



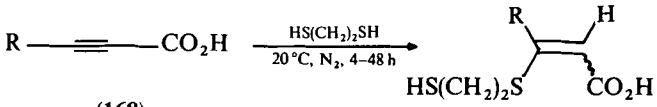
(117)

(166) mainly *Z* (167)

R^1 = Ph, 2-thienyl, MeO; R^2 = H, Ph

A facile catalyst-free synthesis of functional vinyl sulfides (**167**) from mercaptoacetanilide and activated acetylenes (**166**) has been described (equation 117)[328].

The noncatalytic reaction of polyfluoroalk-2-ynoic acids (**168**) with 1,2-dimercaptoethane gives vinyl sulfides (**169**) (equation 118)[329].



(118)

(**168**)

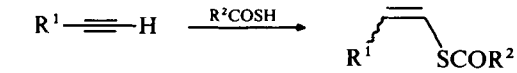
$R = CHF_2$, $CH(CF_3)_2$

E,Z (**169**)

Thiols RSH ($R = CH_2CO_2H$, CH_2CO_2Me) and phenylacetylene freshly distilled under nitrogen in the dark react to give the corresponding vinyl sulfides only in light or in the presence of ascaridole, indicating the radical character of the addition[330]. Light-induced addition of *E*-4-mercapto-2-butenoates to alkynes furnishes 2,3-dihydrothiophenes[331]. UV photolysis of acetylenic thiols $HC{\equiv}C(CH_2)_nSH$ ($n = 2$–7) gives cyclic vinyl sulfides having an endocyclic and an exocyclic double bond in 9–50% yields and oligomers, depending on the structure, temperature and concentrations[332]. Triethylboron proved to be an efficient initiator of the radical addition of thiols to various acetylenes, acetylenic alcohols and trimethylethynyl silane[333].

Diverse versions of radical thiylations of acetylenic derivatives of silicon[334–338], germanium[335,339] and tin[335,339] were also reported. Polymers containing a vinyl sulfide structural unit are obtained by radical polyaddition of 1,4-benzenedithiol to 1,4-diethynylbenzene[340,341] and by similar reactions[342].

Thiocarboxylic acids react readily with various acetylenes[343,344] under UV irradiation or in the presence of peroxides or, more often, noncatalytically to yield anti-Markovnikov adducts (equation 119).

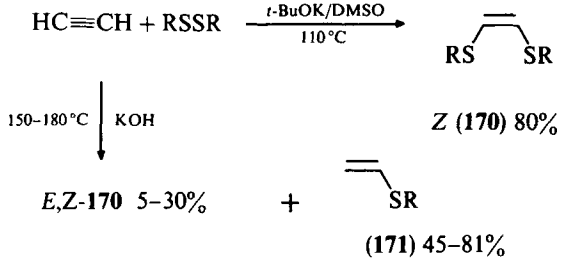


(119)

$R^1 = n$-Bu, t-Bu, c-C_6H_{11}, Ph, $R^3R^4C(OH)$; R^2 = Me, Et

B. Other Additions of Sulfur Compounds to Acetylenes

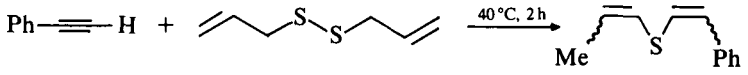
The base-catalyzed addition of organic disulfides to acetylene affords two types of vinyl sulfides: 1,2-di(alkylthio)ethenes (**170**) and/or alkyl or aryl thioethenes (**171**) in satisfactory to good yields (Scheme 9)[80,345–356].



SCHEME 9

With the catalytic superbase system *t*-BuOK/DMSO the reaction proceeds smoothly at a temperature of 110 °C to give selectively and stereospecifically *Z*-**170** in a yield up to 80%[355], whereas in the presence of KOH the process is neither chemo- nor stereospecific and normally requires a higher temperature to give lower yields of both **170** and **171**[80,346]. The stereochemistry of this synthesis and the formation of side products such as 1,2,3-tris(alkylthio)ethenes and poly(alkylthio)acetylenes are in keeping with an anionic chain substitution–addition[353,356]. The reaction of dialkyl (or diphenyl) disulfides with acetylene in 20% aqueous KOH at initial pressure of 14–15 atm C_2H_2 at 160–180 °C for 3 h gives only **171** in 45–81% yields[355].

1-Propenyl 2-styryl sulfide (**172**) was prepared in a 43% yield by the reaction of diallyl disulfide with phenylacetylene in a KOH/DMSO suspension (equation 120)[357]. The same reaction with acetylene is complicated by a number of side reactions and has no preparative value[358].

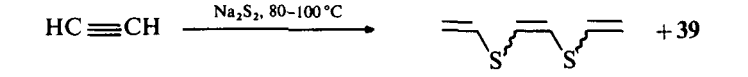


(120)

(**172**)

Z,Z:*E,Z* = 2:1

1,2-Di(ethenylthio)ethene (**173**) along with divinyl sulfide (**39**) have been isolated from the reaction of acetylene with sodium disulfide (equation 121)[359,360].

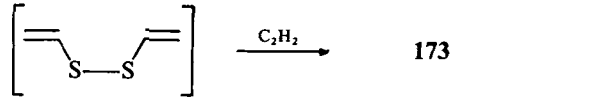


(121)

(**173**) 10%

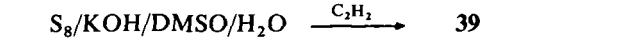
E:*Z* = 2:3

The vinyl sulfide (**173**) appears to be formed by addition of the intermediate divinyl disulfide to acetylene (equation 122) according to Scheme 9.



(122)

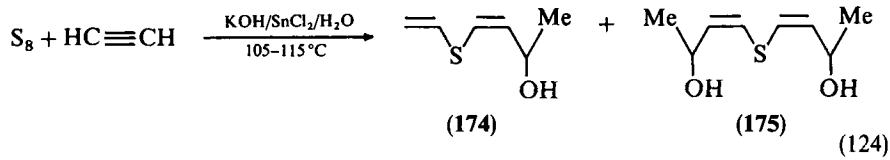
In the superbasic suspensions KOH/DMSO or KOH/HMPA, cyclooctasulfur is readily cleaved at 80–120 °C to form with acetylenes (12 atm) the same products as in the case of sodium sulfide (see Section IV.A.1.a). For example, with acetylene the main product is divinyl sulfide (**39**), which can be prepared by this reaction in a yield of up to 80% (equation 123)[361–364].



(123)

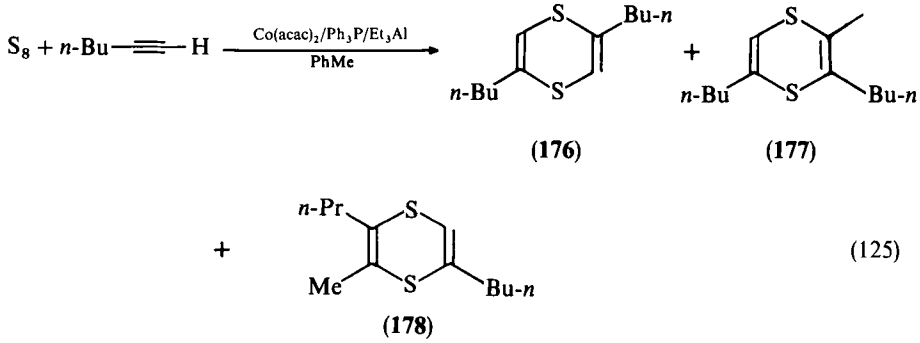
The same reaction in water with $SnCl_2$ as a reducing agent leads to the functionalized divinyl sulfides **174** and **175** in low yields (equation 124)[365].

1-Hexyne reacts with sulfur in toluene in the presence of $Co(acac)_2/Ph_3P/Et_3Al$ to form a mixture of the disubstituted 1,4-dithiines **176** and **177** in 98% yield, whereas when



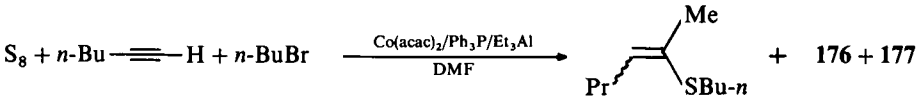
(174) (175) (124)

Et_2NH, Et_3N or Bu_3P are added the trialkyl substituted 1,4-dithiines of type **178** are also formed (equation 125)[366–369]. A similar reaction takes place with 1-pentyne and 1-heptyne.



(176) (177) (178) (125)

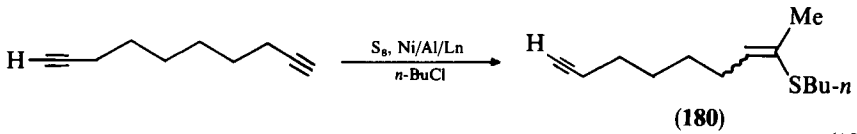
The vinyl sulfide (**179**) together with **176** and **177** has been obtained in 64% total yield from sulfur, 1-hexyne and *n*-BuBr in the presence of $Co(acac)_2/Ph_3P/Et_3Al$ in DMF (equation 126)[366–369].



E,Z (**179**) (126)

Complexes of Ni, Pd or Fe allow the preparation of only the vinyl sulfide **179** in 76–98% yields. The selectivity and the yields fall in the order: *n*-BuCl > *n*-BuBr > *n*-BuI. The system $Ni(acac)_2/Ph_3P/Et_3Al$ proved to be the most efficient. With internal alkynes, the reaction is less selective[366–369].

Under similar conditions vinyl sulfide (**180**) has been obtained in 18% yield from sulfur, 1,9-decadiyne and *n*-BuCl (equation 127)[367].

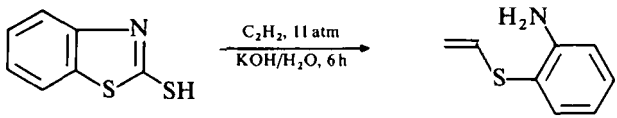


(180) (127)

In the same superbase multiphase system, alkali metal polysulfides behave with acetylene like sulfide ions to afford divinyl sulfide (**39**) in 70–90% yields[22–24].

DMSO itself reacts with acetylene in the presence of alkali and water to give a mixture of products, among which methyl vinyl sulfide and divinyl sulfide are the major ones[370]. By the reaction of the suspension $Na_2S{\cdot}4H_2O$/NaOH/DMSO with acetylene (0.8–1.0 atm at 120 °C) methyl vinyl sulfide of high purity has been prepared in 60% yield in a pilot (400 l) reactor[371,372].

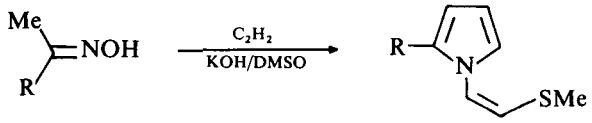
2-Mercaptobenzothiazole (**181**) reacts with acetylene to quantitatively produce 2-aminophenyl vinyl sulfide (**182**) (equation 128)[373].



(128)

(**181**) (**182**)

Methyl *Z*-2-(1-pyrrolyl)vinyl sulfides (**183**) have been isolated in low yield[374] from the Trofimov reaction (pyrrole synthesis from ketoximes and acetylene in a KOH/DMSO system) together with the major products, pyrroles (equation 129).

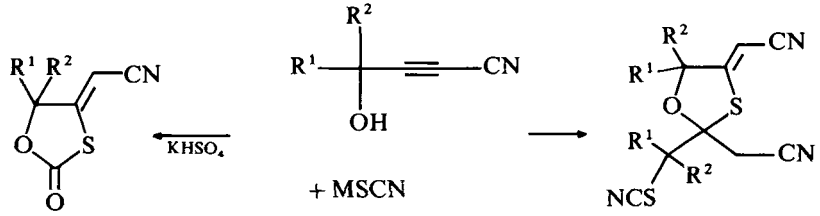


(129)

(**183**)

R = Me, 4-ClC_6H_4, 4-HOC_6H_4, 4-$CH_2{=}CHOC_6H_4$

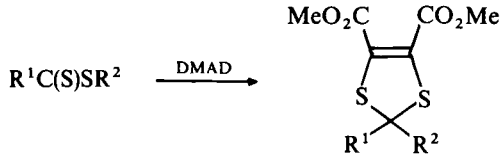
γ-Hydroxy-α,β-acetylenic nitriles react with the system MSCN/$KHSO_4$ (M = NH_4, Na, K) in water at *ca* 20 °C to give 76–88% of 4-(cyanomethylene)-1,3-oxathiolan-2-ones (**184**) containing a vinyl sulfide moiety. The same reaction without $KHSO_4$ affords more heavily functionalized cyclic vinyl sulfides (**185**) in 90–93% yields (equation 130)[375].



(**184**) (**185**)

R^1 = Me; R^2 = Me, Et; R^1–R^2 = $(CH_2)_5$ (130)

Dithiocarboxylic acids and related compounds yield with acetylenes not only acyclic vinyl sulfide derivatives[286] but often cyclic adducts from 1,3-dithioles to tetrathiafulvalenes, which are also vinyl sulfides, at least formally. These reactions have recently been reviewed[286]. In a typical example, allyl, benzyl and propargyl dithiocarboxylates cyclize



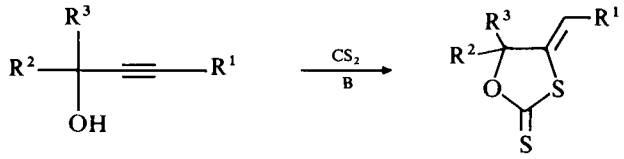
(131)

(186)

R^1 = Me, Ph; R^2 = $CH_2CH{=}CH_2$, $CH_2C(Me){=}CH_2$, $CH_2CH{=}CHPh$-*E*, CH_2Ph, $CH_2C_6H_4OMe$-4, $CH_2C_6H_4NO_2$-4, $CH_2C{\equiv}CH$, $CH_2CH{=}CMe_2$, $CH{=}C{=}CH_2$, $C(Me)_2CH{=}CH_2$, $CH(Ph)CH{=}CH_2$

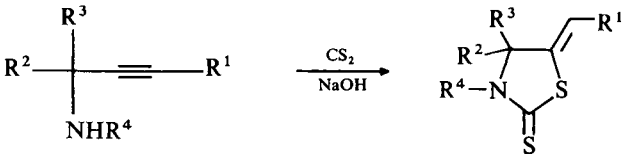
with dimethyl acetylenedicarboxylate with simultaneous [2,3]- or [1,2]-sigmatropic shifts to form substituted 1,3-dithioles (**186**) in 41–98% yields (equation 131)[376,377].

Cyclizations of acetylenic alcohols (equation 132)[378–380] and acetylenic amines (equation 133)[381,382] with CS_2 are also known. The cyclizations of activated acetylenes with diverse carbon disulfide derivatives[383–385] including 1,1-ethylenedithiolates are also under current study.



(132)

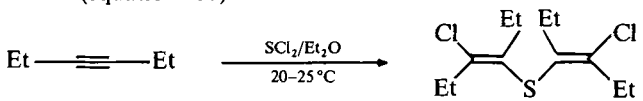
R^1 = H, Me, Ph; R^2, R^3 = H, Me, Et, *n*-Pr;
$R^2 - R^3 = (CH_2)_5$; B = NaOH, KOH



(133)

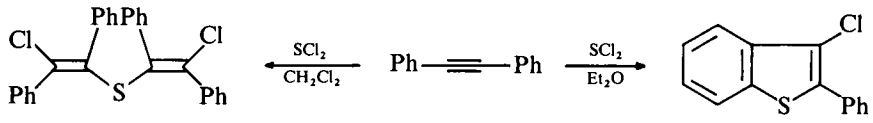
R^1, R^2, R^3, R^4 = H, Me, *i*-Pr

Electrophilic additions of sulfur halides to acetylenes represent a special group of easy syntheses of 2-halovinyl sulfides. Thus, internal alkynes form divinyl sulfides (**187**) with SCl_2 in quantitative yield (equation 134), while diphenylacetylene provides either the divinyl sulfide (**188**) or 3-chloro-2-phenylbenzo[*b*]thiophene (**189**), depending upon the reaction conditions (equation 135)[386].



(134)

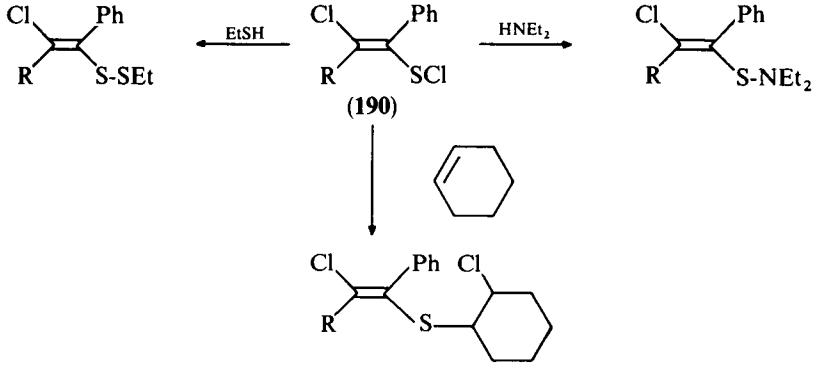
(187)



(188) (189)

(135)

In certain cases it is possible to isolate in good yield the intermediate vinylsulfenyl chloride (**190**). It can be utilized in numerous syntheses of the corresponding 2-chlorovinyl sulfides (Scheme 10)[386].



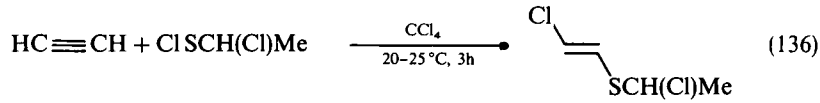
R = H, Me, Ph

SCHEME 10

The stereochemistry of the additions in equations 134 and 135 is *trans* and the orientation in case of unsymmetrical acetylenes is largely anti-Markovnikov. The thiochlorination of acetylenic fatty esters with SCl_2 in Et_2O at 0 °C follows the same regularities and produces substituted vinyl sulfides of types **187**–**189**[387].

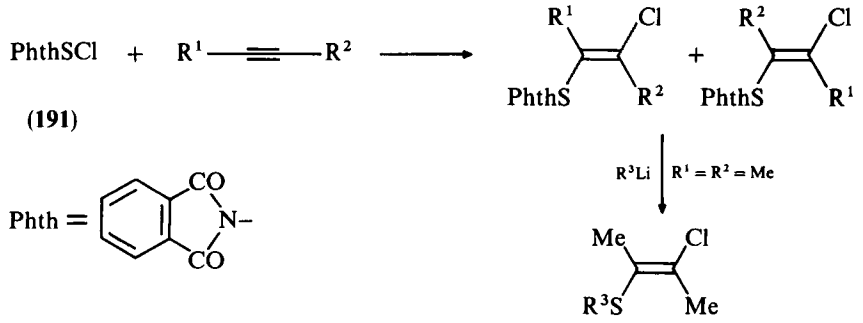
Dichlorodisulfane, S_2Cl_2, adds to diphenylacetylene in DMF to provide 50% yield of **188**, instead of the expected disulfide[388].

The addition of alkyl sulfenyl halides to acetylenes (e.g. equation 136)[389] also proceeds very smoothly to afford the corresponding 2-halovinyl sulfides, almost exclusively of *E* configuration[390–392].



(136)

Syntheses of the type represented by equation 136 received wide coverage[128,393–404]. Phtalimidosulfenyl chloride (**191**) was used to furnish not-easily-accessible vinyl sulfides such as vinyl ethynyl sulfide (R^3 = *t*-BuC≡C) which represents an almost unknown class of unsaturated sulfides (Scheme 11)[405]. The reaction proceeds by an electrophilic addition of **191** to the corresponding acetylene followed by the replacement of the phthalimidoyl moiety at the sulfur by Me, Ph, *t*-Bu or *t*-BuC≡C derived from the corresponding lithium derivatives. In some cases, e.g. with 2,4-$(O_2N)_2C_6H_3SCl$, the

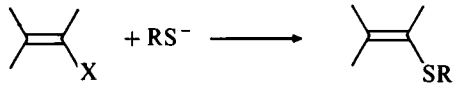


SCHEME 11

reaction is catalyzed by $AlCl_3$[403]. The kinetics and the substituent effects on the addition of arylsulfenyl chlorides to arylacetylenes have been studied[406].

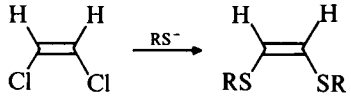
C. Vinylic Substitution by Sulfur Anions

Vinyl sulfides had been prepared via nucleophilic substitution of alkenyl halides by thiolates (equation 137)[407–411], even before their direct synthesis from acetylenes.



(137)

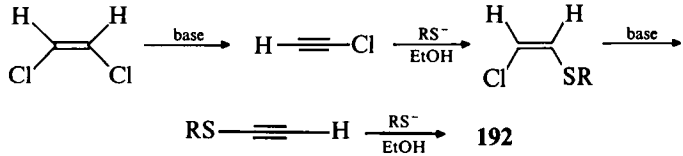
Since alkenyl halides are easily available and the simplest of them (e.g. vinyl chloride, di-, tri- and tetrachloroethenes) are cheap and large-scale commercial products, this method is steadily developing.[411–424]. For example, 1,2-di(alkyl- or arylthio)ethenes (**192**) were prepared by refluxing *Z*-1,2-dichloroethene with a thiol and excess alkali in alcohol[407–421] or in liquid ammonia[424] (equation 138). The yields are high, particularly with arenethiols[409].



(138)

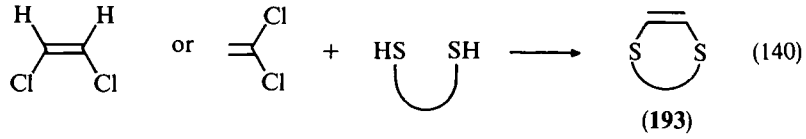
(**192**)

Only *Z*-1,2-dichloroethene reacts under these conditions and the mechanism consists of elimination–addition, and the final products (**192**) retain the *Z* configuration (equation 139)[126]. However, a recent modification allows one to achieve 80% yields of *Z*-bis(methylthio) and *Z*-bis(ethylthio)ethenes from either *Z*- or *E*-1,2-dichloroethene and a mixture of sodamide and the corresponding sodium alkanethiolate in a one-pot synthesis[425].



(139)

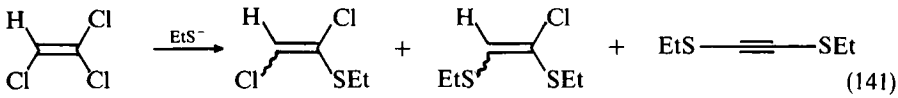
Both isomers of 1,2-dichloroethene eliminate HCl under the action of sodium amide to give sodium chloroethynide, which with a thiol affords **192**[419]. *Z*-1,2-Di(*p*-tolylthio)ethene and 1,2-di(benzylthio)ethene were obtained from 1,1-dichloroethene and *p*-thiocresol or benzyl mercaptan[426,427], and the lack of dependence on the configuration of the precursor confirms the elimination–addition sequence. Both *Z*-1,2- and 1,1-dichloroethenes were employed for cyclovinylation (equation 140) of α,ω-dithiols[428]. Cyclic vinyl sulfides like **193** were also obtained from either $Cl_2CHCHCl_2$, $Br_2CHCHBr_2$, or from $PhCH(Cl)CHCl_2$ via the preceding elimination[428].



(193) (140)

The effect of the solvent (DMF, HMPA, DMSO, EtOH) and the substituents in RSNa (R = *i*-Pr, *n*-Bu, *t*-Bu, CH_2Ph, Ph, 4-MeC_6H_4) on the mono-substitution of *E*- and *Z*-ClCH=CHCl affording *E*- and *Z*-RSCH=CHCl and the disubstitution affording *E*- and *Z*-RSCH=CHSR under mild reaction conditions (20 °C, N_2, 30 min) has been examined by GLC[429].

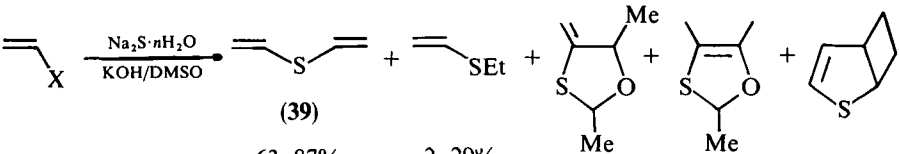
A mixture of vinyl sulfides **194**, **195** and di(ethylthio)ethyne (**196**) was obtained from trichloroethene and ethanethiolate (equation 141)[430].



(194) (195) (196) (141)

Under phase-transfer conditions (NaOH, organic solvent and dibenzo-18-crown-6) or in the system NaOH/DMSO, the polychloroethenes ClCH=CHCl, Cl_2C=CHCl, and Cl_2C=CCl_2 react with RSH (R = *n*-Pr, *i*-Bu, Ph) to give RSCH=CHCl, RSCH=CHSR, RSCCl=CHCl and RSCCl=CCl_2, respectively, the yields being in a range of 25–76% depending on the structure of the reactants and the reaction conditions[431].

In KOH/DMSO and KOH/HMPA suspensions the thiylation of vinyl halides with sodium sulfide affords mainly divinyl sulfide (**39**) in 63–87% yields. Ethyl vinyl sulfide and the cyclic vinyl sulfides **40–42** are formed as side products (Scheme 12)[160,432–434]. The yields of these heterocycles, especially of **42**, are much higher than in the reactions



(39) 63–87% 2–20%

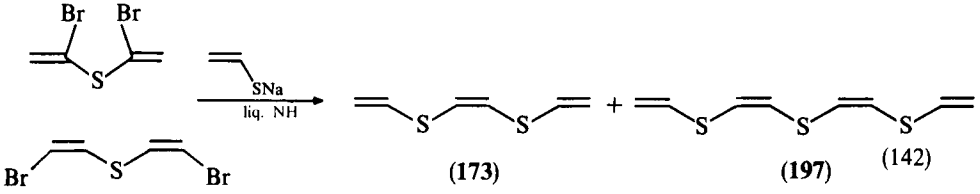
(40) 9% (41) 28% (42) 21%

X = Cl, Br

SCHEME 12

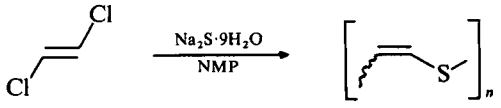
using acetylene as precursor (Section IV.A.1.c). In HMPA, the yield of **39** decreases and that of ethyl vinyl sulfide increases, indicating a larger contribution of electron-transfer processes[160,433,434]. Typical inhibitors of radical processes such as hydroquinone, *N,N*-di-β-naphthyl-*p*-phenylenediamine or phenyl-β-naphthylamine decrease the rate of the reaction[433,434]. Acetylene is usually evolved in the reaction course showing the expected elimination. Consequently, the results imply at least two concurrent pathways leading to **39**, i.e. nucleophilic vinylic substitution (apparently, as a single-electron transfer process) and elimination–addition[433]. Divinyl sulfide (**39**) is also formed in *ca* 35% yield from dihaloethenes and $Na_2S{\cdot}nH_2O$ ($n = 4$–9) in a KOH/DMSO system via a sequence of elimination, substitution and addition processes[435].

Di(1-bromovinyl) and *Z*-di(2-bromovinyl) sulfides react with sodium ethenethiolate in liquid ammonia to give *Z*-1,2-di(ethenylthio)ethene (**173**)[436,437] and *Z,Z*-di[2-ethenylthio)ethenyl]sulfide (**197**)[346] in yields of up to 65 and 90%, respectively (equation 142). The same products were obtained in a total yield of 50% from di-1,2-dibromoethyl sulfide under similar conditions[437]. Likewise, sulfide (**197**) is formed in 30–40% yields from 1,2-dibromoethyl and di-(1-bromovinyl) sulfides[437].



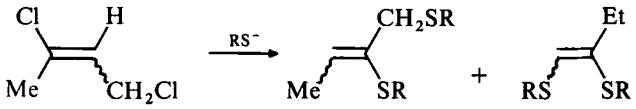
(142)

Poly(vinylene sulfide) of unspecified configuration has been prepared by the reaction of *E*-1,2-dichloroethene with $Na_2S{\cdot}9H_2O$ in *N*-methyl-2-pyrrolidone (NMP) (equation 143)[438].



(143)

1,3-Dichlorobut-2-ene (**198**) reacts with alkanethiols in the presence of excess alkali in ethyl cellosolve at 130–140 °C to produce di(alkylthio)butenes **199** and **200** (equation 144)[439].



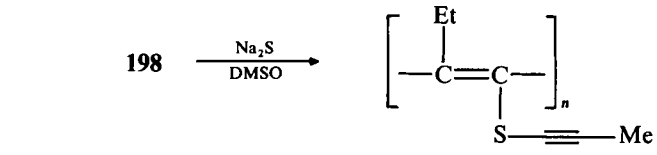
(144)

(**198**) (**199**) (**200**)

In DMSO, a mixture of **198** and sodium sulfide at 110–140 °C undergoes a series of eliminations, substitutions and polymerization to furnish a soluble semiconducting polymer (**201**) having a vinyl sulfide moiety together with other structural units (equation 145)[440].

A number of substituted vinyl sulfides were obtained from thiolates and $CCl_2{=}CHCCl_2CHCl_2$ in ethanol or in DMSO[441,442]. The reaction of $ArCOCH{=}CCl_2$ with thiols in MeCN (Et_3N, −40 °C) leads to the corresponding monosubstituted vinyl sulfides[443].

Apart from the examples above, there are additional data on the vinylic substitution by thiolates, e.g. of vinyl halides[444–450], 1,1-dihaloalkenes[444,451], 1,2-dihaloalkenes[451–453],

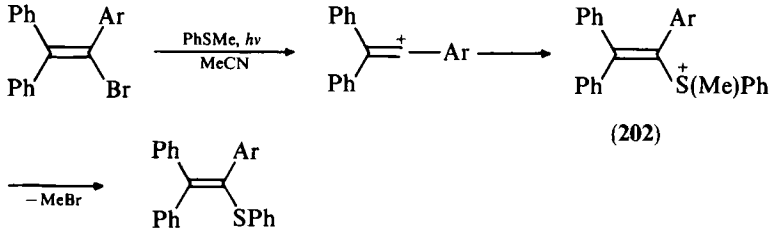


(145)

(201)

tri- and tetrachloroethenes[451,454–456]. The substitution of the halogen in a vinyl halide by thiolate ion to furnish the vinyl sulfide can be catalyzed by transition metals[457–459], and especially good results (63–89%) were recently obtained[459] by using bis(dipyridine)-nickel(II) bromide in dimethoxyethane at 120 °C.

Phenyl triarylvinyl sulfides are formed by UV irradiation of triarylvinyl bromides and PhSMe. The suggested mechanism involves formation of an intermediate triarylvinyl cation, which is captured by the sulfide to form the sulfonium ion (**202**). Attack of Br^- on the methyl group of the latter gives the vinyl sulfide (**203**) and MeBr (equation 146)[460].



(146)

(202)

(203)

D. Free-radical Substitution by Thiols and Disulfides

Free-radical thiylation of haloethenes has been known for a long time to lead to saturated sulfides by the addition of thiols to the double bond (see Reference 461 and references cited therein). However, in 1966 Cristol and Jarvis found that β,β-dichlorovinyl phenyl sulfide can be obtained in an excellent yield by reaction of thiophenol with trichloroethylene in the presence of benzoyl peroxide (Bz_2O_2)[462]. Further investigations showed that the UV- or peroxide-initiated reaction of alkyl and aryl thiols with trichloro-[461–464], tribromo-[104] and fluorobromoethylenes[109] is a convenient route to the β,β-dihalovinyl sulfides (**204**) (equation 147). To reduce the amount of the disulfide RSSR byproduct, a 5–10-fold excess of $CHX{=}CX_2$ is used, and with trichloroethylene the yields reach 90%. With tribromoethylene the yield is somewhat lower (up to 82%) due to the formation of 15–20% of β-bromovinyl phenyl sulfides, *E*,*Z*-$PhSCH{=}CHBr$[104].

In principle, diaryl disulfides which are more convenient to handle than the corresponding thiols can also be used as a source of thiyl radicals. It has been shown, however, that the absence of the $H^\bullet$ radical in the reaction mixture substantially reduces the selectivity of the reaction and addition and substitution products **204–208** were formed (equation 148)[465,466].

$$RSH + CHX{=}CX_2 \xrightarrow[-HX]{Bz_2O_2 \text{ or } h\nu} RSCH{=}CX_2 + RSSR \qquad (147)$$

(204)

R = Alk, Ar; X = Cl, Br

$$ArSSAr + ClCH{=}CCl_2 \xrightarrow{Bz_2O_2 \text{ or } h\nu} \underset{(204)}{ArSCH{=}CCl_2} + \underset{(205)}{ClCH{=}C(Cl)SAr} +$$

$$\underset{(206)}{ArSC(Cl){=}CCl_2} + \underset{(207)}{ArSCHClCCl_3} + \underset{(208)}{CCl_2{=}CHCCl_2CHCl_2} \quad (148)$$

Free-radical substitution of *E*-CHCl=CHCl with thiols also gives the vinyl sulfides (**209**) along with the disubstituted ethenes (**210**) and the adduct (**211**) (equation 149)[103,461]. The rearranged structure of the adduct results from an α,β-chlorotropic rearrangement in the intermediate radical RSCHCl—ĊHCl[461].

$$RSH + E\text{-}CHCl{=}CHCl \xrightarrow{h\nu} \underset{(209)}{E,Z\text{-}RSCH{=}CHCl} + \underset{(210)}{E,Z\text{-}RSCH{=}CHSR} +$$

$$\underset{(211)}{RSCH_2CHCl_2} + RSSR \quad (149)$$

When exposed to UV irradiation, BuSH and 1,1-dichloroethylene afforded the adduct (**212**), which underwent dehydrochlorination to the rearranged substitution product under reflux (equation 150).

$$BuSH + CH_2{=}CCl_2 \xrightarrow{h\nu} \underset{(212)}{BuSCH_2CHCl_2} \xrightarrow[-HCl]{\Delta} E,Z\text{-}BuSCH{=}CHCl \quad (150)$$

The reaction of thiols with tetrachloroethylene, which leads to several products including **204** and **213–216** (equation 151), is very complicated and, thus, has no preparative value[467].

$$RSH + Cl_2C{=}CCl_2 \xrightarrow{h\nu} \underset{(204)}{RSCH{=}CCl_2} + \underset{(213)}{RSC(Cl){=}CCl_2} + RSC(Cl){=}CHCl +$$

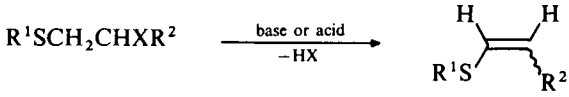
$$\underset{(214)}{RSCCl_2CHCl_2} + \underset{(215)}{RSCH(Cl)CCl_3} + \underset{(216)}{RSCCl{=}CClSR} + (RS)_2C{=}CCl_2 + RSSR \quad (151)$$

Contrary to the reactions of trichloroethylene (equations 147 and 148), that of tetrachloroethylene with diaryl disulfides is more selective than with thiols[466]. In this case, the aryl trichlorovinyl sulfides (**206**) and hexachloro-1,3-butadiene are the reaction products (equation 152).

$$ArSSAr + Cl_2C{=}CCl_2 \xrightarrow{h\nu} \underset{(206)}{ArSC(Cl){=}CCl_2} + Cl_2C{=}C(Cl)\text{-}C(Cl){=}CCl_2 \quad (152)$$

E. Elimination Reactions

The elimination reactions of α- or β-heterosubstituted alkyl sulfides constitute one of the classical syntheses of vinyl sulfides (equation 153). It is documented in a review[127]. Representative illustrations and some recent examples are given below.

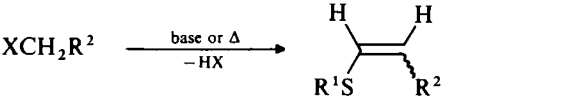


(153)

$X = Cl, Br, I, OR^3, SR^3, \overset{+}{S}R^3_2, \overset{+}{N}R^3_3$, etc.

1. Elimination with bases

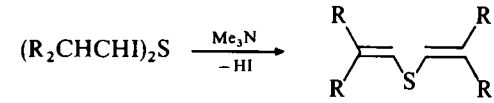
Normally, elimination of hydrogen halides from α-halosulfides occurs under the action of tertiary or secondary amines at a temperature up to 150 °C or, sometimes, just upon heating (equation 154)[321,394,468–475].



(154)

$R^1 = alkyl, Ar, CH{=}CH_2, CH{=}CHMe, CH{=}CHEt, C{\equiv}CH$, etc.
$R^2 = H, alkyl, Ar, Br$, etc.;
base = $PhNEt_2$; $i\text{-}Pr_2NEt$, etc;
X = Cl, Br

Various vinyl sulfides[476,477] including symmetric and unsymmetric divinyl sulfides (**218**) have been prepared almost quantitatively by a Me_3N promoted elimination of HI at 0–20 °C from the di-α-iodo-substituted sulfides (**217**) (equation 155). The latter were obtained *in situ* from α,α-bis(trimethylsiloxy)sulfides and iodotrimethylsilane under mild conditions. (The mono-α-iodosulfides are prepared from the corresponding aldehydes and thiols)[476].



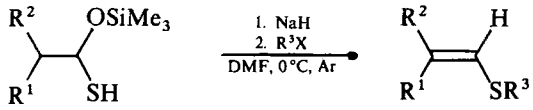
(155)

(**217**) (**218**)

R = Me, Et; R—R = $(CH_2)_5$

An interesting α-elimination occurs when thiols (**219**), prepared from aldehydes, H_2S and chlorotrimethylsilane, are allowed to react with NaH in DMF at 0 °C, and then with alkyl halides. The vinyl sulfides (**220**) are formed in 68–91% yields (equation 156)[478].

α-Chlorosulfides, obtained from the sulfides $R(CH_2)_2SPh$ (R = *n*-Pr, *i*-Pr, *n*-C_5H_{11}, *n*-Hex, Ph), *i*-BuSPh, *c*-HexSPh and $PhCH_2CH(Me)SPh$ by chlorination with SO_2Cl_2, form the corresponding vinyl sulfides RCH=CHSPh, upon boiling with pyridine[479].



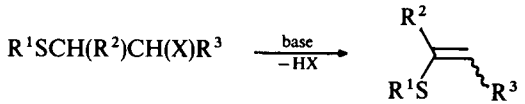
(156)

(219) (220)

$R^1 = H, Me; R^2 = H, Me, Et; R^1\text{–}R^2 = (CH_2)_5;$
$R^3 = n\text{-Pr}, sec\text{-Bu}, c\text{-Hex}, CH_2Ph, (CH_2)_2Ph$

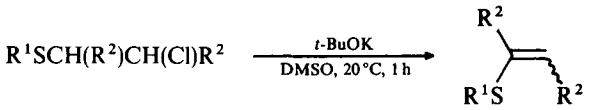
Likewise, α-chlorosulfides obtained from the reaction of thioacetals with PhSCl at −78 °C in CH_2Cl_2 react with $i\text{-Pr}_2NEt$, to furnish vinyl sulfides in good to high yields[480].

The early procedures of β-elimination were mostly developed by using di(2-chloro- or 2-bromoethyl)sulfides to prepare divinyl sulfide[474–479]. However, many other β-haloalkyl sulfides were involved later in the synthesis of diverse vinyl sulfides (**221**) (equation 157)[394,487–499].



(157)

(221)



(158)

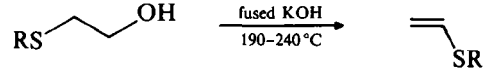
(222) (223)

R^1	Configuration	Yield of **223** (%)	*Z*:*E*
Me	*R*,*R*	80	95:5
	S,*R*	84	2:98
Ph	*R*,*R*	60	80:20
	S,*R*	76	5:95

$R^2 = n\text{-}C_8H_{17}$

Dehydrochlorination of the optically pure β-chlorosulfides (**222**) to the vinyl sulfides (**223**) with *t*-BuOK/DMSO follows the anti-elimination mechanism (equation 158)[500].

Dehydration of the β-hydroxyalkyl sulfides (**224**) under the action of fused KOH gives the vinyl sulfides (**225**) (equation 159)[321,501–506].

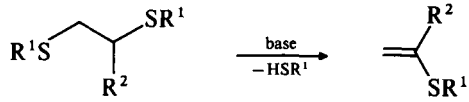


(159)

(224) (225) 36–66%

$R = (CH_2)_2OH$[516,517], CH_2OR^1 (R^1 = Me, n-C_8H_{17})

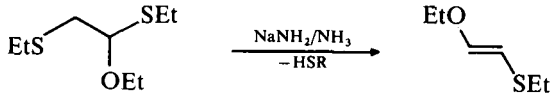
A method for the preparation of α-(alkylthio)styrenes involves the base-catalyzed elimination of thiol from 1-phenyl-1,2-di(alkylthio)ethanes in the presence of acetylene[147]. Similarly 1,1-di(alkylthio)ethenes have been prepared[147,507] from 1,1,2-tri(alkylthio)ethanes (equation 160, R^2 = SAlk) (Section IV.A.1).



(160)

R^1 = alkyl; R^2 = Ph[147], SAlk[148,522];
base = KOH/ROH/C_2H_2[147,148], t-BuOK[522]

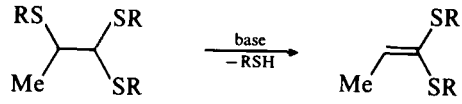
The reaction of 1-ethoxy-1,2-di(ethylthio)ethane with sodium amide in liquid ammonia leads to the vinyl sulfide (**226**), predominantly the E isomer (equation 161)[127].



(161)

(226) 63%

1,1-Di(alkylthio)prop-1-enes (**228**) were obtained by elimination of thiols from 1,1,2-tri(alkylthio)propanes (**227**) with t-BuOK or KOH (equation 162)[508].



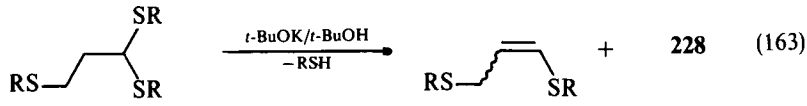
(162)

(227) (228) 33–38%

R = n-Pr, i-Pr, n-Bu, i-Bu

Elimination of thiols from 1,1,3-tri(alkylthio)propanes (**229**) by t-BuOK/t-BuOH proceeds with partial rearrangement to give **228** along with the expected 1,3-di(alkylthio)-prop-1-enes (**230**) in a 1:3 to 1:5 E:Z ratio (equation 163)[509,510].

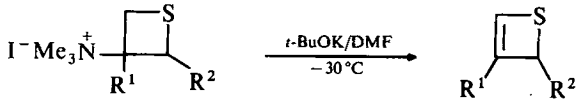
The base-catalyzed elimination of $Me_3NH^+I^-$ from the quaternary ammonium thietanes (**231**) results in the thietes (**232**), a highly interesting group of cyclic vinyl sulfides (equation 164)[511–518].



(229) (230) $E{:}Z = 1{:}3–1{:}5$

60–70%

R = *n*-Bu, *i*-Bu

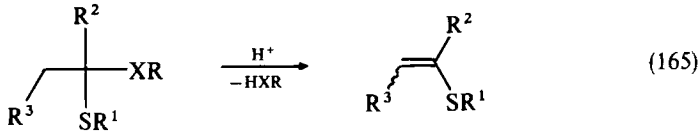


(231) (232)

R^1 = H, Et, *n*-Pr, Ph, β-$C_{10}H_7$, 2-C_4H_3S;
R^2 = H, Me, Et; R^1–R^2 = $(CH_2)_n$ (n = 4, 5, 10)

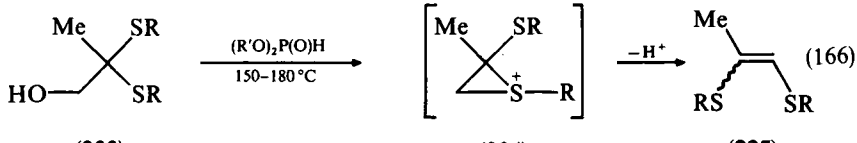
2. Acid-catalyzed and other eliminations

Orthothioesters or thioacetals undergo elimination in the presence of a Brönsted or Lewis acid to form the C=C—S moiety (equation 165)[127,128,471,489,519,520].



R^1 = alkyl, aryl; R^2 = H, alkyl, aryl or SR^1;
R^3 = H, alkyl, SR^1; R^2–R^3 = $(CH_2)_n$; X = O, S

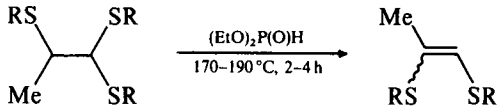
The dithioacetals (**233**), upon dehydration with dialkylphosphite, afford 1,2-di(alkylthio)prop-1-enes (**235**) in 53–73% yields. The migration of the alkylthio group apparently results from ring opening of the intermediate cation (**234**) (equation 166)[521].



(233) (234) (235)

R = *n*-Pr, *n*-Bu, *i*-Bu

An efficient procedure for elimination of thiols from dithioacetals of 2-alkylthiopropanals (**227**) employs diethyl phosphite as a catalyst. The yields of the 1,2-di(alkylthio)prop-1-enes (**235**) range from 70 to 99% (equation 167)[522].



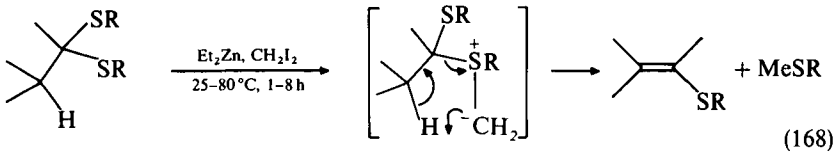
(167)

(**227**) (**235**)

R = *n*-Pr, *i*-Pr, *n*-Bu, *i*-Bu

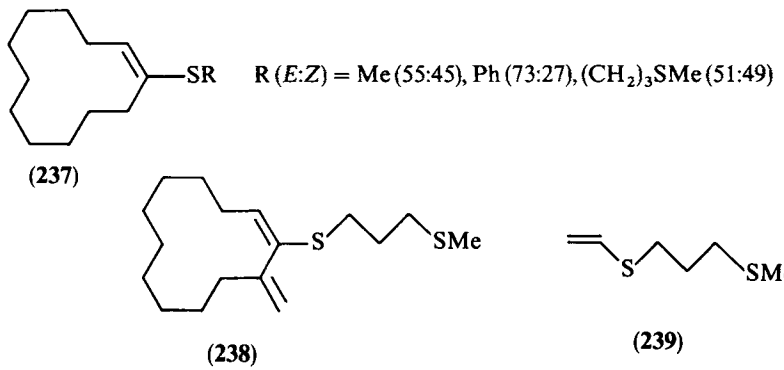
Generally, dithioacetals of ketones are appealing starting materials for the preparation of vinyl sulfides because they are readily available from ketones or by alkylation of dithioacetals of aldehydes[523]. Consequently, direct elimination of thiols from dithioacetals is actively investigated, particularly by using reagents such as copper(I) triflate[524], mercuric triflate/Li_2CO_3[525] or Cu(II) salts in the presence of tertiary amines[526].

A fairly general one-step procedure[527] that converts dithioacetals to vinyl sulfides is their treatment with diethylzinc and methylene iodide. Fast capture of the intermediate carbene by a sulfur is assumed to produce an intermediate sulfonium ylide (**236**) which undergoes a *syn* α,β-elimination (equation 168)[527]. Vinyl sulfides **237**, **238** and **239** have been synthesized by this method[527].



(168)

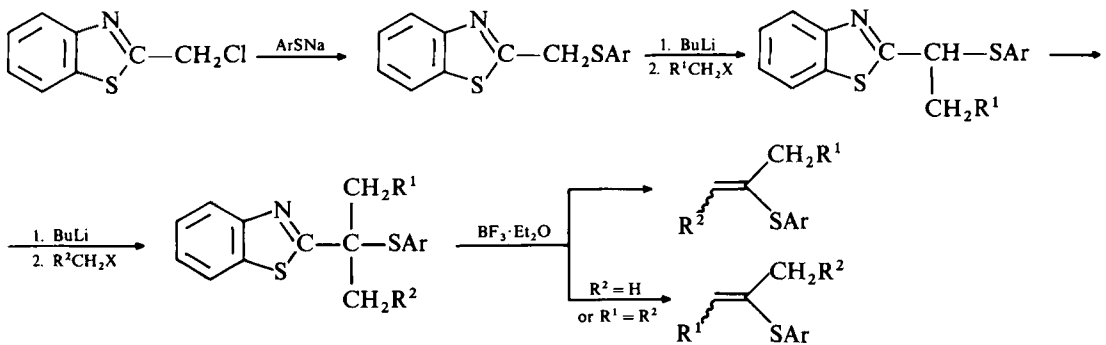
(**236**) 67–92%



(**237**)

(**238**) (**239**)

In another approach, diphenyl dithioacetals have been oxidized to monosulfoxides and then thermolyzed to produce vinyl phenyl sulfides[523,528,529].

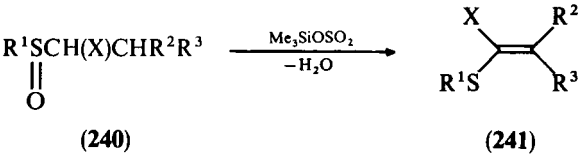


SCHEME 13

A recently developed convenient synthesis of vinyl sulfides in up to 92% yield is based on a sequence of reactions including nucleophilic substitution at the side chain of 2-chloromethylbenzothiazole, consecutive alkylation at the carbon α to the sulfur and, finally, elimination of the heterocyclic residue (Scheme 13)[530].

Vinyl sulfides can be obtained by pyrolytic elimination[531], e.g. from monothioacetals[532], dithioacetals[533] and ethyl 2-(alkylthio)acetates[534], as well as from dithioacetals in the presence of peroxides[535–538].

The eliminative deoxygenation of α-halosulfoxides (**240**) with trimethylsilyl triflate leads to vinyl sulfides (**241**) in 72–92% yields (equation 169)[539].

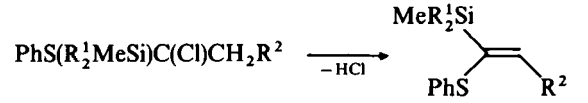


(169)

(**240**) (**241**)

R^1 = *t*-Bu, Ph; R^2 = H, Me, Et, Ph, CH_2 = CH;
R^2 = Me, Ph; X = Cl, Br

Dehydrochlorination of the α-silyl substituted α-chlorosulfides (**242**) proceeds smoothly without base at ambient temperature to give exclusively *Z*-vinyl sulfides (**243**) in 65–94% yield (equation 170)[540].



(170)

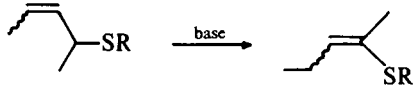
(**242**) (**243**)

R^1 = Me, Ph; R^2 = H, Me, Ph, CH=CH_2, CH=CHPh

F. Miscellaneous

1. Prototropic rearrangement of allyl sulfides

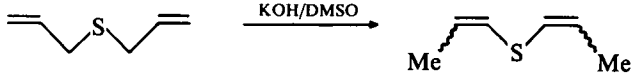
A prototropic shift of the double bond of an allyl sulfide to the sulfur is known to be a versatile route to vinyl sulfides, for instance[489,541–543] (equation 171).



(171)

Base = EtONa/EtOH[556], *t*-BuOH/DMSO (40–50 °C, 10–30 min)[504], KNH_2/liq. NH_3[504]

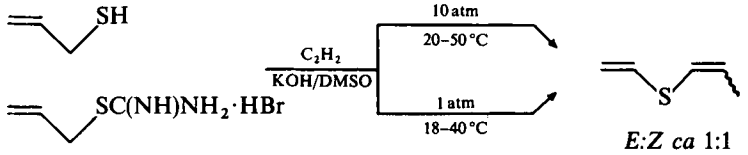
Thus, di(prop-1-enyl) sulfide (**245**) has been obtained in 91% yield by isomerization of di(allyl) sulfide (**244**) with a KOH/DMSO suspension (equation 172)[543].



(172)

(244) (245)

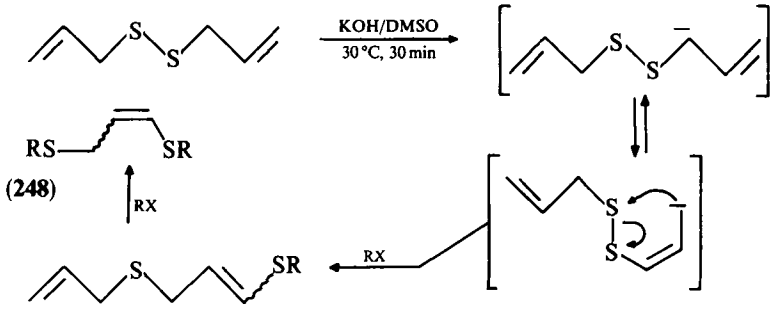
The vinylation of allyl mercaptan[544] or of allylisothiuronium bromide[545] under basic conditions results in quantitative isomerization of the allylic moiety, affording vinyl prop-1-enyl sulfide in quantitative yield (equation 173).



(173)

E:Z ca 1:1

Alkylation of the anion (**246**) generated from diallyl disulfide in a KOH/DMSO suspension leads to 1-alkylthio-3-prop-2-enylthioprop-1-enes (**247**) in 30–40% yields[546,547], 1,3-Di(alkylthio)propenes (**248**)[547] result from decomposition of the sulfonium salts of **247** (Scheme 14).

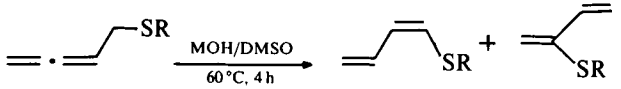


R = Me, Et, *n*-Pr, *i*-Pr; X = Br, I

SCHEME 14

It was assumed that a rearrangement leading to **247** which involves an intramolecular nucleophilic S—S bond cleavage in the prototropically isomerized anion **246** to the anion of **247** takes place. The latter is consequently alkylated. Under similar conditions, the reaction of $(MeCH{=}CHCH_2S)_2$ with *n*-PrI follows the same scheme[548].

1-Alkylthiobuta-2,3-dienes (**249**) isomerize under basic conditions to 1-alkylthiobuta-1,3-dienes (**250**) at 125–135 °C. The reaction does not occur at a lower temperature (60–70 °C)[191,549,550]. In superbase media MOH/DMSO (M = Li, Na, K) **249** are readily converted into both 2-alkylthiobuta-1,3-dienes (**251**) and *Z*-**250** (equation 174)[551,552].



(174)

(249) (250) (251)

R = Me, Et, *i*-Pr

TABLE 12. The effect of the structure of the alkyl group on the **250:251** ratio in the KOH/DMSO-induced isomerization (equation 174)[552]

R	**250**	**251**
Me	10	90
Et	45	55
i-Pr	91	9

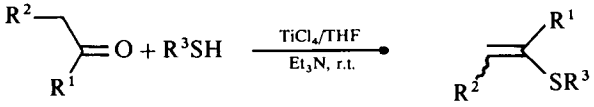
TABLE 13. The effect of the metal cation (M) on the **250:251** ratio in the MOH/DMSO-induced isomerization of **249** (when R = Et)[552]

M	**250**	**251**
Li	None	None
Na	50	50
K	45	55

The **250:251** ratio depends on the structure of R (Table 12) and on the nature of the alkali metal cation (Table 13). The results are in accordance with an elimination–addition scheme[552].

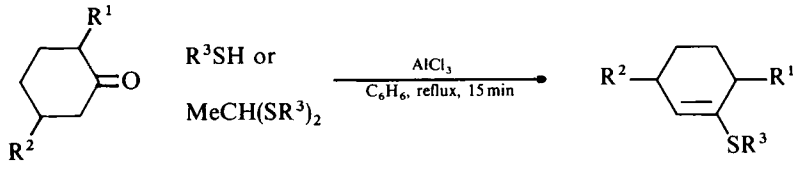
2. From carbonyl compounds and thiols

A convenient method for preparation of vinyl sulfides is based on the reaction of carbonyl compounds with thiols in the presence of titanium tetrachloride and triethylamine (equation 175)[553,554].



(175)

Substituted 1-cyclohexenyl alkyl sulfides (**252**) are synthesized from cyclohexanones and thiols or thioacetals in the presence of $AlCl_3$ (equation 176)[555,556].



(176)

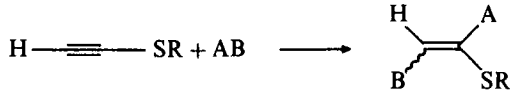
(**252**) 29–64%

R^1 = Me, *i*-Pr; R^2 = H, Me; R^3 = Et, *n*-Pr

Likewise, 1-cycloalkenyl ethyl sulfides were obtained in good yields by 1 h reflux of cyclohexa-, -hepta- and -octanones and thiols with P_2O_5 as a catalyst[556]. Other examples of this synthesis are also known[557].

3. *From α,β-acetylenic sulfides*

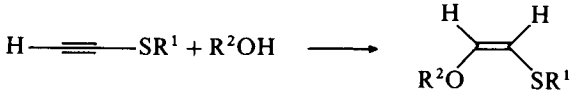
Substituted vinyl sulfides are readily prepared by diverse additions to α,β-acetylenic sulfides (**253**) (equation 177).



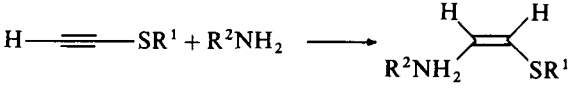
(177)

(253)

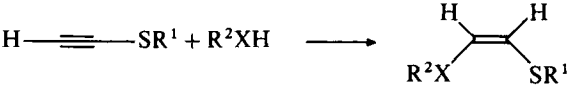
Alcohols and phenols (AB = ROH, ArOH) add to **253** in the presence of a strong base (equation 178)[127,128,205,393,394,471,558,559]. Amines add noncatalytically, and in the case of primary amines the adducts have an enamine structure (equation 179)[128,411,471]. Thiols and selenols also afford the corresponding vinyl sulfides with **253** (equation 180)[128,321,471,558,560].



(178)



(179)

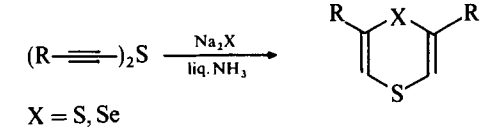


(180)

X = S, Se

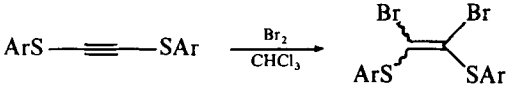
Di(2-alkynyl)sulfides react smoothly with Na_2S or Na_2Se to yield 1,4-dithiins and thiaselenins (equation 181)[561,562].

Di(arylthio)ethynes react with bromine to form dibromides (equation 182)[128].



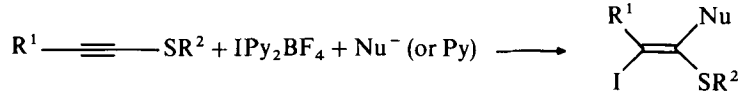
(181)

X = S, Se

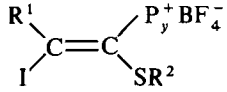


(182)

Conjugate addition of an iodine atom and a nucleophile moiety to α,β-acetylenic sulfides leads to a variety of functionalized vinyl sulfides (equation 183)[563].



(183)

or 

R^1 = Ph, Bu; R^2 = Me, Ph
Nu = HCO_2, CH_3CO_2, NCS, Cl, Br, I

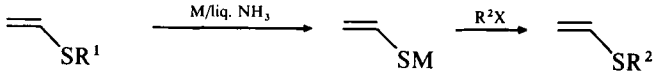
Bis(methylthio)- and bis(ethylthio)acetylenes are easily formed by reaction of acetylene with alkyl thiocyanates or dialkyl disulfides in liquid ammonia in the presence of sodium metal. The bis(alkylthio)acetylenes formed can further react with thiolate anions formed under the reaction conditions from the dialkyl disulfides, giving tris(alkylthio)ethenes[564].

A stereospecific synthesis of *E*- and *Z*-1-alkenyl sulfides from 1-alkynyl sulfides and Grignard reagents in the presence of copper(I) salts[565] or a complex of lithium tetrahydroaluminate or copper hydride complexes[566] has been developed. A number of other additions to α,β-acetylenic sulfides to yield vinyl sulfides, including that of diethylamine to di(alkylthio)acetylenes[567] as well as electrophilic reactions with carboxylic acids[568], hydrogen halides[569,570], *O,O*-diethyl-*N,N*-dimethylamidophosphite[571], phosgene[572], phosphorus tribromide[573] and phosphorus pentachloride[574] were reported.

4. *From enethiolates*

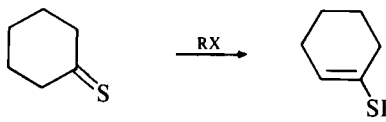
Enethiolate anions prepared readily by cleavage of vinyl sulfides with alkali metals in liquid ammonia can be alkylated to form the same or different vinyl sulfides (equation 184)[575].

Thioketones are also alkylated in their enethiol form. An example is given in equation 185[575].



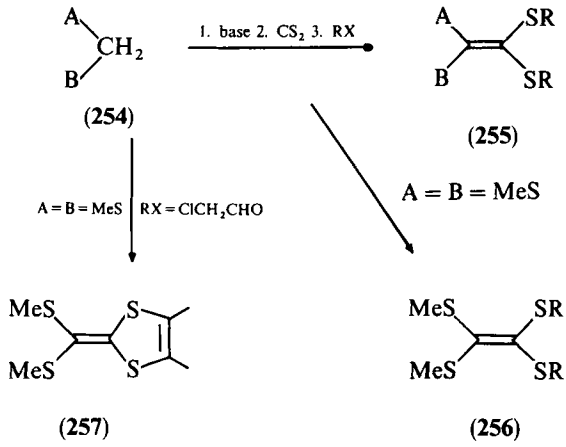
(184)

M = Li, Na



(185)

Various ketene mercaptals (e.g. **255**)[576,577], tetrakis(alkylthio)ethenes (**256**)[578] and 1,3-dithiole derivatives (**257**)[579] which are essentially substituted vinyl sulfides, are produced via the condensation of diverse activated methylene compounds (**254**) with carbon disulfide in the presence of base, followed by alkylation (Scheme 15). A review on this extremely wide and rapidly developing area has recently been published[580].

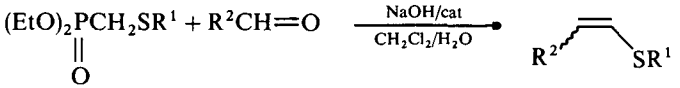


A, B = Ph, PhCO, CN, MeS, RSO, etc.

SCHEME 15

5. Other syntheses

a. Wittig and Wittig–Horner reactions. Vinyl sulfides can be obtained by Wittig[581,582] or Wittig–Horner[583–585] reactions. The latter reaction, applying α-phosphorylalkyl sulfides (**258**), can advantageously be performed in a two-phase catalytic system to afford 40–80% yields of vinyl sulfides (equation 186)[584].



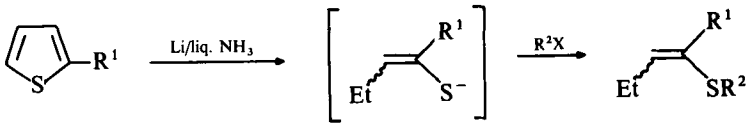
(186)

(**258**) *E*:*Z* 6:1–4:5

R^1 = Me, Ph; R^2 = Ph, 4-$Me_2NC_6H_4$

The reaction is specific to aromatic aldehydes. Ketones and aldehydes capable of enolization are unreactive. The *E*:*Z* ratio of the vinyl sulfides obtained depends on the structure of phase-transfer catalyst. The preference for the *E*-isomers increases with Br^- and I^- anions and in the presence of crown ethers.

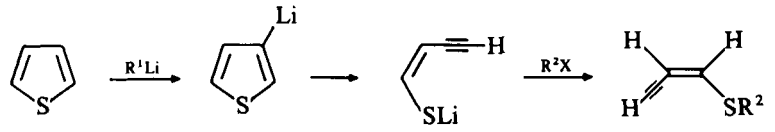
b. From thiophene derivatives. The reductive cleavage of thiophenes with alkali metals in liquid ammonia, followed by alkylation, is a convenient route to vinyl sulfides (equation 187)[586–588].



(187)

R^1, R^2 = Alkyl

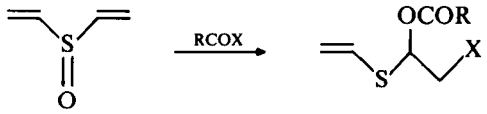
The ring-opening reaction of 3-thienyllithium derivatives constitutes a regio- and stereospecific synthesis of alkyl ene–ynyl sulfides (equation 188)[589]. This reaction has recently been used for the total synthesis of natural products occurring in the plant *genus Anthemis*[590]. The scope and limitations of this and similar reactions have been reviewed[591–596].



(188)

R^1, R^2 = alkyl

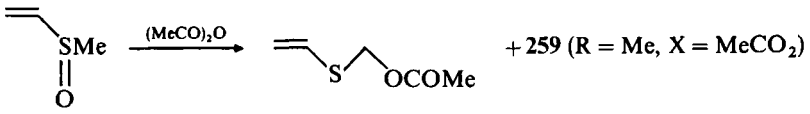
c. Pummerer rearrangement of vinyl sulfoxides. When vinyl sulfoxides react with carboxylic acid anhydrides or acyl halides, they undergo a Pummerer rearrangement to produce the corresponding acyloxy-substituted vinyl sulfides **259** and **260**. The yields are from satisfactory to good (equations 189 and 190)[597–600]. With divinyl sulfoxide and trifluoroacetyl chloride or trifluoroacetic anhydride the yields are 77–90%[599,600].



(189)

(259)

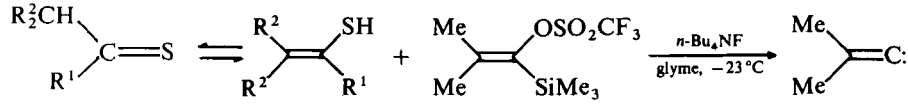
R = Me, Et, *n*-Bu, CF_3; X = RCO_2, Cl



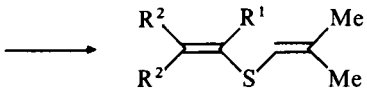
(260)

(190)

d. Carbene synthesis. Isopropylidenecarbene inserts into the enethiol form of thiones (**261**) to give divinyl sulfides (**263**) in 25–40% yields (equation 191)[601]. As the thiones react with strong bases, the carbene was generated from the silyl vinyl triflate (**262**). Since the enethiol content of **261** is in the 20–40% range[602] and the thione–enethiol tautomerism is very slow[602], the conversion of **261** to **263** may be quantitative[601].



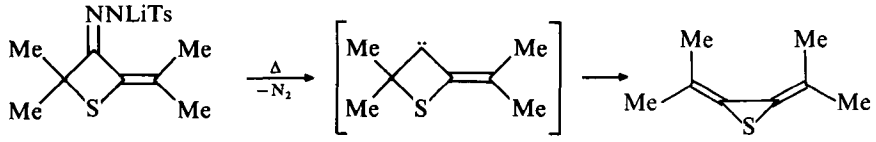
(261) **(262)**



(191)

(263) 25–40%

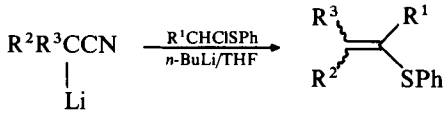
2,3-Diisopropylidenethiirane (**265**), a particular divinyl sulfide, was prepared in 60–70% yield by pyrolysis of the lithium salt of tosylhydrazone (**264**) via rearrangement of the intermediate carbene (equation 192)[603].



(**264**) (**265**)

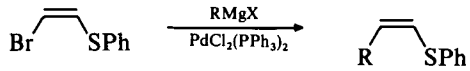
(192)

Reactions of the α-anions of the nitriles (**266**) with (phenylthio)carbenes generated from 1-chloroalkyl phenyl sulfides lead to the vinyl sulfides (**267**) (equation 193)[604].

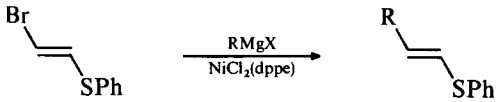


(**266**) (**267**) (193)

e. Cross-coupling reactions of 2-halovinyl sulfides. *Z*- and *E*-1-bromo-2-(phenylthio)-ethenes **268** and **270** are cross-coupled stereospecifically with alkyl Grignard reagents in the presence of Pd(II), Ni(II) or Fe(III) catalysts to yield the vinyl sulfides **269** and **271**, respectively (equations 194 and 195)[97,605].



(**268**) (**269**) (194)

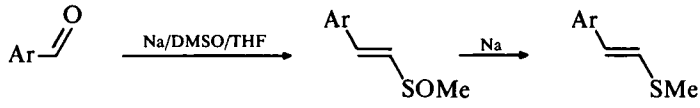


(**270**) (**271**) (195)

dppe = 1,2-bis(diphenylphosphino)ethane

f. Miscellaneous reactions. A facile method for the preparation of *E*-vinyl sulfides (**273**) is the reaction of aryl aldehydes with DMSO in the presence of sodium metal (equation 196)[606]. The reaction proceeds through the selective reduction of the intermediate vinyl sulfoxides (**272**).

The reaction of benzoyl peroxide with 1,1-di(alkylthio)methanes leads to tetrakis-(alkylthio)ethenes. With 1,1-di(*n*-propylthio)ethane the major product is 1,1-di(propylthio)-ethene (equation 197)[607,608].

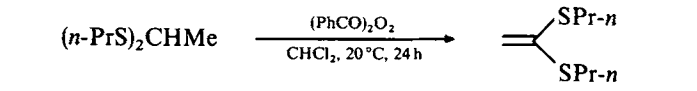


(196)

(272) (273)

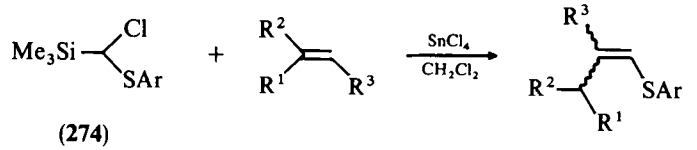
64–84%

Ar = Ph, 4-MeC_6H_4, 2-MeC_6H_4, 4-$MeOC_6H_4$, 2-furyl, 1-naphthyl



(197)

80%



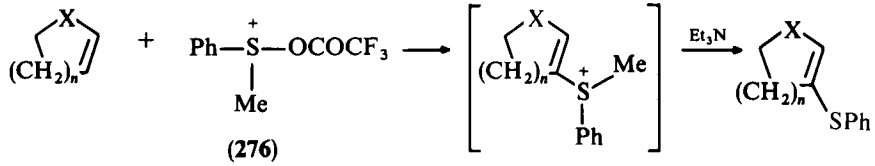
(198)

(274) (275)

Ar = 4-ClC_6H_4, 3,4-$Cl_2C_6H_3$;
$R^1 = R^2 = Me$; $R^3 = Et$; $R^1 - R^3 = (CH_2)_3$, $(CH_2)_4$; $R^1 - R^2 = (CH_2)_5$

A synthesis of vinyl sulfides (**275**) by Lewis acid promoted reaction of [chloro(arylthio)-methyl]trimethylsilanes] (**274**) with trisubstituted alkenes has been described (equation 198)[609].

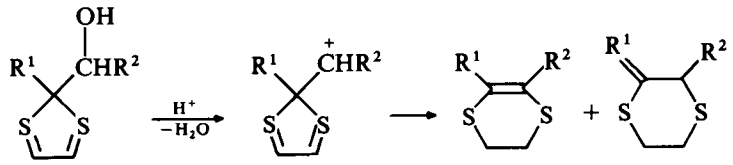
Vinyl sulfides have been obtained via electrophilic substitution at the electron-rich C=C double bond by the trifluoroacetoxysulfonium salt (**276**)[610]. The reaction proceeds with formation of the intermediate sulfonium salt (**277**) which undergoes *in situ* dealkylation with triethylamine (equation 199).



X = O, NH; $n = 1, 2$ (**277**)

(199)

Acid-catalyzed ring expansion in 2-(1-hydroxyalkyl)-1,3-dithiolanes by 1,2-sulfur migration in the intermediate carbocation leads to both exo- and endocyclic vinyl sulfides (equation 200)[611]. The former products are formed under kinetic control whereas their isomers with the endocyclic C=C double bond are the thermodynamic controlled products.



(200)

$R^3 = (R^1 - CH_2)$

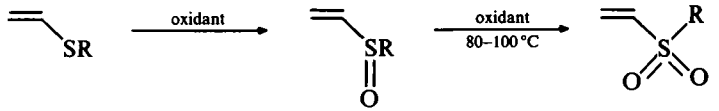
Syntheses of vinyl sulfides via quaternary phosphonium salts are known[612]; an efficient reduction of alkenyl sulfoxides to the corresponding alkenyl sulfides has been reported[193]. Divinyl mercury vinylates thiols to vinyl sulfides[613]. Other reactions affording the vinyl sulfide moiety which have a limited scope are left out of this chapter due to lack of space.

V. REACTIVITY

Vinyl sulfides exhibit typical properties of both sulfides and electron-rich olefins. They are capable of being oxidized to the corresponding sulfoxides and sulfones, as well as adding diverse reagents, particularly electrophiles, across the double bond. They are less reactive than vinyl ethers towards electron-deficient reagents and more reactive than these towards free radicals due to a weaker p–π conjugation (Section II). Nucleophilic addition is not typical of vinyl sulfides, except for those having strong electron-withdrawing substituents on the double bond.

A. Oxidation

Vinyl sulfides are oxidized with retention of the double bond to vinyl sulfoxides, or to vinyl sulfones with excess oxidant under harsher conditions. The traditional oxidants are sodium hypochlorite or hydrogen peroxide which transform vinyl sulfides at ambient temperature to the corresponding sulfoxides. Heating with excess hydrogen peroxide leads to the corresponding sulfones (equation 201)[22–24,123,124,126–131].

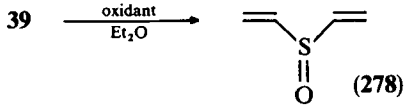


(201)

Oxidant = $NaClO, H_2O_2, MeCO_3H, PhCO_3H, SeO_2$, etc.

The preparation of vinyl sulfoxides is treated in a number of publications, such as References 614–620. A recent review[621] dealt with the synthesis, reactions, structure, physicochemical properties and applications of divinyl sulfoxide, which is a promising monomer and synthon derived from divinyl sulfide.

Divinyl sulfoxide (**278**) was prepared by oxidation of divinyl sulfide (**39**) with perbenzoic acid[622] or with acetyl peroxide in ether[623,624] (equation 202). The sulfoxide (**278**) was reported[621] not to be formed by oxidation of **39** with 30% H_2O_2 in acetone or in acetic acid. In contrast, other vinyl sulfides are known[618,619] to be readily oxidized with 30–90%

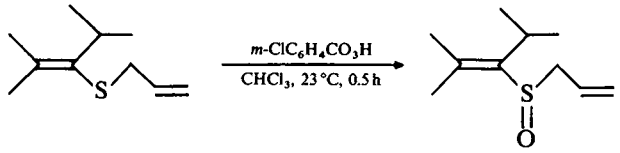


(202)

(**278**)

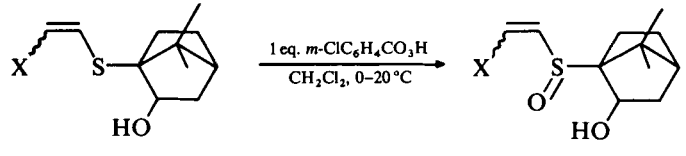
H_2O_2 in acetone, acetic acid or acetic anhydride. For example, oxidation of di(2-phenylvinyl)sulfide (**79**) with H_2O_2 affords di(2-phenylvinyl)sulfone[625].

Comprehensive studies on the oxidation of divinyl sulfide with diverse oxidants have been recently undertaken[621,626,627]. They result in finding conditions which allow an effective application of dilute aqueous hydrogen peroxide for this oxidation. The reaction proceeds at 50–70 °C in the presence of emulsifiers (salts of higher carboxylic acids, alkyl cellosolves, higher alkyl sulfates and sulfonates, polyacetals of various structure) and a borax buffer (pH 8–9) with *ca* stoichiometric amounts of the reactants to give **278** in a yield up to 90%[621,627]. Under these conditions the divinyl sulfone contamination in the crude product is *ca* 0.5%[621]. The availability of the starting materials (acetylene, H_2S, H_2O_2) and a safe and facile technology for handling them make divinyl sulfoxide a potential industrial product. Its chemistry is now rapidly developing[22–24,80,597–600,621,628–638].



(203)

Another oxidant of vinyl sulfides to the corresponding sulfoxides is *m*-chloroperbenzoic acid (such as in equation 203)[639]. One equivalent of this oxidant gave the best results compared with other peroxides in the self-induced diastereoselective oxidation of vinyl sulfides bearing a chiral hydroxy group (**279**) to optically active vinyl sulfoxides (**280**) with $1S,2S,R_s$:$1S,2S,S_s$ diastereoisomeric ratio of *ca* 8–9:1 (equation 204)[640].



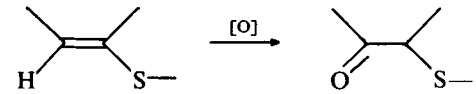
(204)

(**279**) 1*S*;2*S* (**280**)

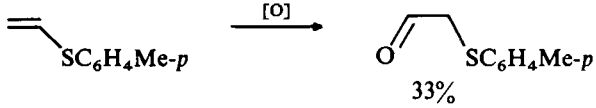
X = CO_2Me, $PhSO_2$, 4-$ClC_6H_4SO_2$

When 2 equivalents of *m*-$ClC_6H_4CO_3H$ were used, the oxidation of **279** gave the corresponding sulfones[640].

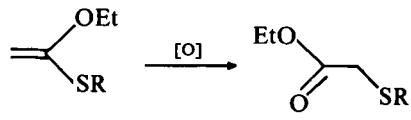
The general oxidative rearrangement of vinyl sulfides depicted by equation 205 is exemplified by equations 206 and 207[641].



(205)



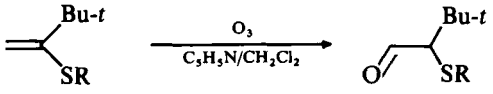
(206)



(207)

R = Bu-*t*, Ph > 50%

A similar oxidative rearrangement occurs upon ozonation of the vinyl sulfides (**281**) to give the aldehydes (**282**) in *ca* 55% yield (equation 208)[642].

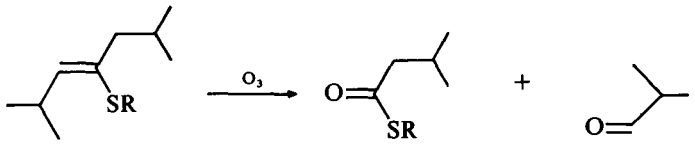


(208)

(**281**) (**282**)

R = Me, Et

In contrast, ozonation of the vinyl sulfides (**283**) under the same conditions led to the classical double-bond cleavage to afford the thioesters (**284**) together with isobutyric aldehyde (equation 209)[642].

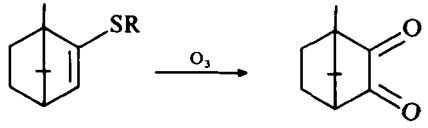


(209)

(**283**) (**284**) 70–80%

R = Me, Et

The third type of reaction occurring with ozone is shown by the vinyl sulfides (**285**) derived from thiocamphor, which gave camphorquinone (**286**) in *ca* 65% yield (equation 210)[642].

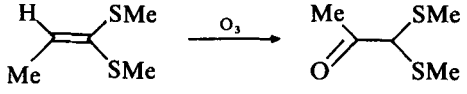


(210)

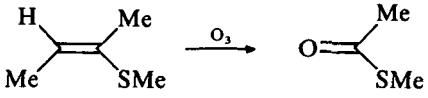
(**285**) (**286**)

R = Me, Et

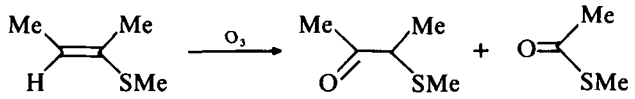
From these results it appears that the presence of a hydrogen atom *cis* to the alkylthio group is necessary for the 'abnormal ozonation' which retains an unmodified carbon chain. The double-bond cleavage always takes place when this structural feature is lacking. Equations 211–213 are consistent with this generalization[642].



(211)



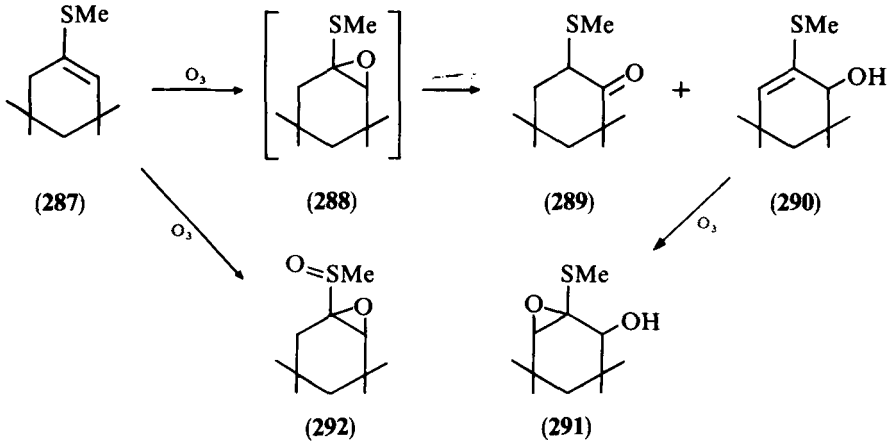
(212)



(213)

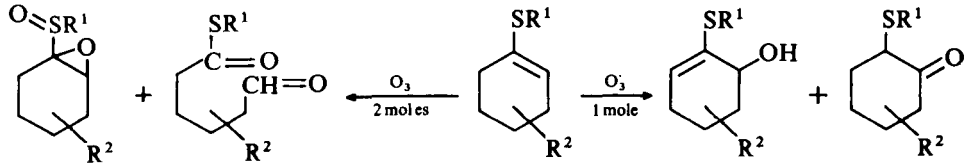
30%

When 1-methylthio-3,3,5,5-tetramethylcyclohexene (**287**) is treated with 1 mole of O_3 in CH_2Cl_2 in the presence of pyridine at $-70\,^{\circ}C$ the ketone (**289**) and the alcohol (**290**), together with the epoxide (**291**), a further ozonation product of the latter, are obtained. Upon ozonation of **287** with 2 moles of O_3, two isomers (1:1) of the epoxide (**292**) have been obtained. It was suggested that epoxide (**288**) is the intermediate of the ozonation reaction which gives **289–291** (Scheme 16)[643].



SCHEME 16

The stereochemistry and mechanism of the ozonation of the vinyl sulfides (**293**) which resemble **287** have been investigated by IR, ^1H and ^{13}C NMR and mass spectroscopy, and the products **294–297** have been identified (Scheme 17)[644].



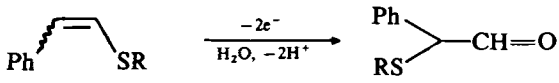
$R_s + S_s$ | *E* or *Z* or *E* + *Z* | *E*:*Z* = 4:1–9:1

R^1 = Me, Et, Ph; R^2 = 4*t*-Bu; 3,5,5-Me_3; 3,3,5,5-Me_4

SCHEME 17

Other reactions of vinyl sulfides with oxygen are also known[645–647]. These include the metal-catalyzed photooxidation in the presence of iron(III) chloride (high-pressure Hg lamp, O_2, pyridine, 30–60 min) to give regioselectively α-chloroketones[648].

Microbial asymmetric oxidation of 2-alkoxyethyl sulfides was reported to be a facile method for synthesis of chiral vinyl sulfoxides[649]. Anodic oxidation of vinyl sulfides in aqueous MeCN gives α-thiolated aldehydes in 50–93% yields (equation 214)[650].



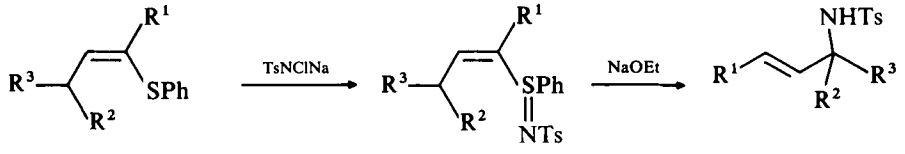
(214)

R = *n*-Bu, Ph, 4-MeC_6H_4, 4-*t*-BuC_6H_4, 4-ClC_6H_4

Various types of oxidation of vinyl sulfides are now widely employed in organic synthesis. Some representative examples of this are given below. Thus, vinyl sulfides (**298**) react with chloramine-T to give sulfimines (**299**), which, in the presence of a base, give allylamides (**300**) via a [2,3]-sigmatropic rearrangement (equation 215)[5,651].

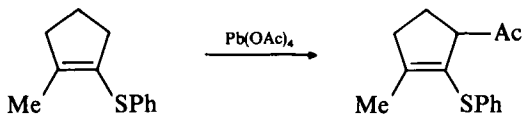
Vinyl sulfides, such as **301**, are capable of allylic acetylation by $Pb(OAc)_4$ without oxidation of the sulfur, as in equation 216[5,651].

The selective oxidation of the vinyl sulfides (**302**) by $NaIO_4$ is a key step[652] in the preparation of synthetically important[5,651] 2-(phenylthio)enones (**303**) (equation 217).



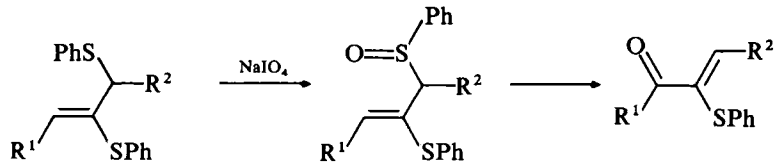
(**298**) (**299**) (**300**)

(215)



(**301**) 56%

(216)



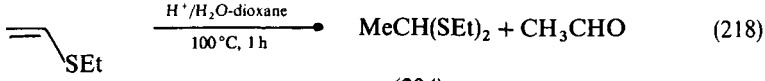
(**302**) 89% (**303**)

(217)

B. Reactions with Electrophiles

1. *Electrophilic additions*

a. Acid-catalyzed hydrolysis. Ethyl vinyl sulfide with 5% HCl in aqueous dioxan gave thioacetal (**304**) and acetaldehyde (equation 218)[131,653]. On prolonging the reaction

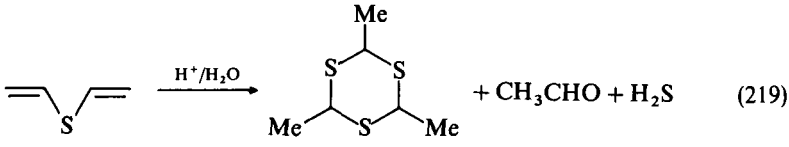


(218)

(304)

time the thioacetal (**304**) is further hydrolyzed slowly and incompletely to acetaldehyde and ethylmercaptan[131,653].

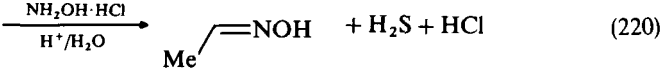
The hydrolysis of divinyl sulfide (**39**) with HCl in H_2O/dioxan leads to H_2S, acetaldehyde, 2,4,6-trimethyl-1,3,5-trithiane and a small amount of thioacetaldehyde oligomers (equation 219)[24,654].



(219)

(**39**)

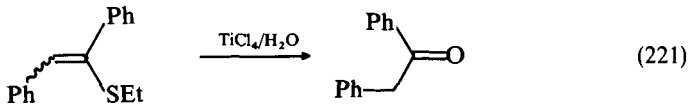
The same products are initially formed when **39** is hydrolyzed in an acidic solution of hydroxylamine hydrochloride. However, the acetaldehyde released is converted to the oxime (equation 220)[24,654]. The extent of hydrolysis as determined by the amount of HCl and H_2S released is 62–68% in the reaction with HCl and 80–85% in the case of $NH_2OH \cdot HCl$[24,654].



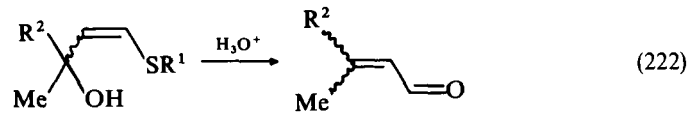
(220)

A convenient method for the hydrolysis of vinyl sulfides to ketones is based on the use of $TiCl_4$ (equation 221)[655].

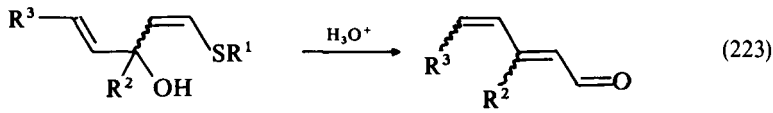
Some examples of the hydrolysis of vinyl sulfides are also reported in References 141–143 and 656. The hydrolysis is the last step in the preparation of α,β- and α,β,γ,δ-unsaturated aldehydes (e.g. equations 222 and 223)[5,8].



(221)



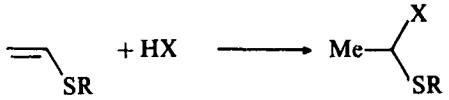
(222)



(223)

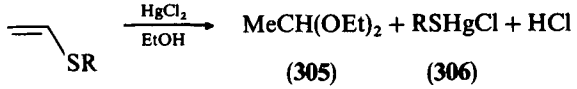
The acid catalyzed hydrolysis of vinyl sulfides proceeds via a mechanism analogous to that of the hydrolysis of vinyl ethers. It involves a slow proton transfer to the double bond to produce a sulfur-stabilized carbenium ion[657] and therefore the reaction represents the simplest case of electrophilic addition.

b. Addition of other electrophilic reagents. The addition of diverse acidic compounds to vinyl sulfides was known for a long time[482,483,658–660]. Hydrogen halides add to the vinylthio group in a Markovnikov manner (equation 224)[482,483,653,658].



(224)

X = Cl, Br



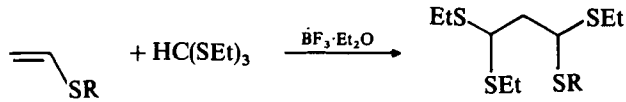
(225)

(305) (306)

In ethanolic $HgCl_2$, vinyl sulfides form acetal (**305**), HCl and the mercury salt **306** (equation 225)[137,654,661]. The HCl liberation is quantitative and can be used analytically. In water the reaction gives acetaldehyde, and in ether a precipitate of $3RSCH{=}CH_2 \cdot 4HgCl_2$, treatment of which with alcohol or water affords acetaldehyde.

In the presence of SO_2, ethyl vinyl sulfide reacts with ethanol to give $MeCH(SEt)_2$ and $MeCH(OEt)_2$; if HCl is also present, then ethanethiol and a small amount of the mixed acetal MeCH(OEt)(SEt) are also formed[653]. In the presence of SO_2 ethyl vinyl sulfide also adds ethanethiol to afford both the Markovnikov and anti-Markovnikov adducts, indicating a competition between electrophilic and free-radical addition, the latter being almost completely suppressed in the presence of 5% hydroquinone[662]. In the presence of $BF_3 \cdot Et_2O$ the trithioorthoformate (**307**) reacts with vinyl sulfides to form bis(dithioacetals) (**308**) in 82% yield (equation 226)[663].

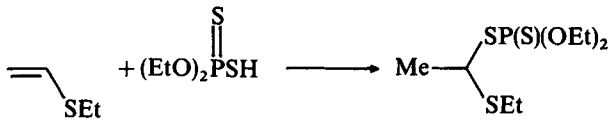
Dialkyl dithiophosphoric acids add to vinyl sulfides according to equation 227[664,665].



(226)

(307) (308)

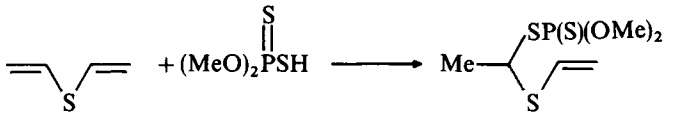
R = Et, Ph



(227)

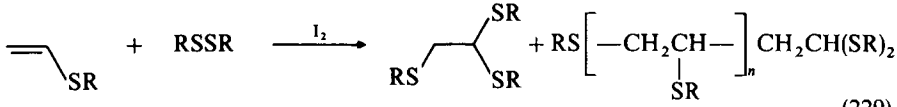
The adduct of dimethyl dithiophosphoric acid (**309**) to divinyl sulfide (**39**) has been shown, contrary to a patent[659], to possess the Markovnikov structure **310** (equation 228)[666].

In the presence of catalytic amounts of iodine, disulfides react with vinyl sulfides to



(39) (309) (310) (228)

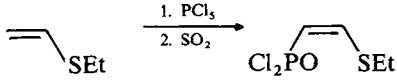
give alkylthioacetaldehyde dialkyl mercaptals together with telomeric products involving the reaction of two or more moles of vinyl sulfide (equation 229)[148].



(229)

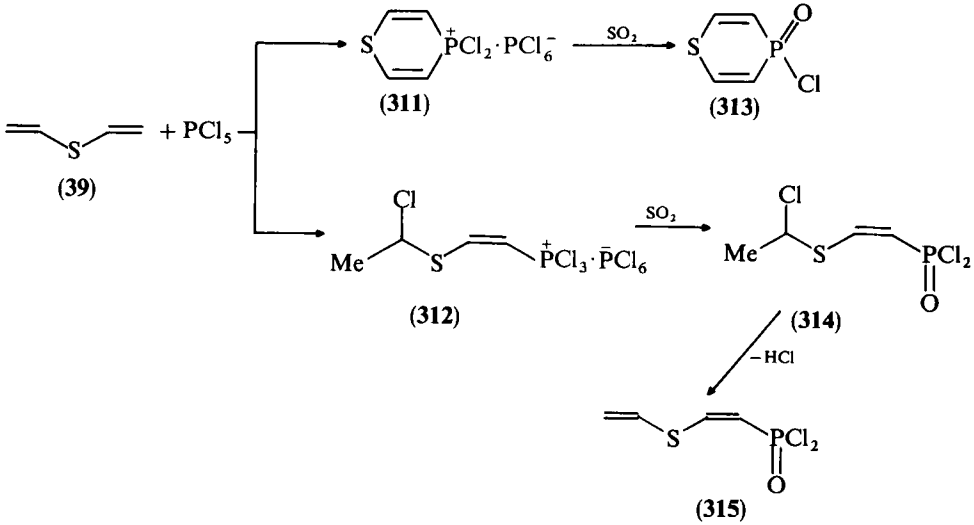
2. *Electrophilic substitutions*

Alkyl vinyl sulfides react with PCl_5 and SO_2 to form 2-alkylthiovinylphosphonic acid dichloride (equation 230)[664,665].



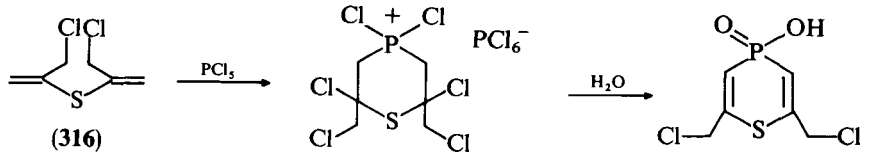
(230)

A similar reaction with divinyl sulfide (**39**) affords two different complexes **311** and **312** which, when decomposed with SO_2, give 4-chloro-4*H*-1,4-thiaphosphorin 4-oxide (**313**) and the dichlorophosphonyl derivatives **314** and **315** (Scheme 18)[667].



SCHEME 18

A similar reaction of di[1-chloromethyl(ethenyl)] sulfide (**316**) with PCl_5 has been reported earlier (equation 231)[668].



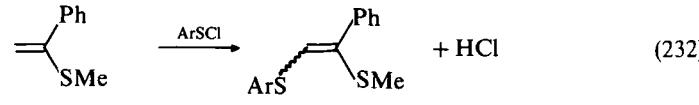
(316) (231)

Arenesulfenyl chlorides react with the vinyl sulfide (**317**) by an electrophilic substitution of the vinylic hydrogen giving preferentially *Z*-**318**, which is the geometrically more stable isomer (when Ar = Ph, $\Delta H = -9.2 \pm 3$ kJ mol^{-1}, $\Delta S = -21 \pm 8$ J mol^{-1} K^{-1} for the $E \rightleftarrows Z$ equilibrium) (equation 232)[669].

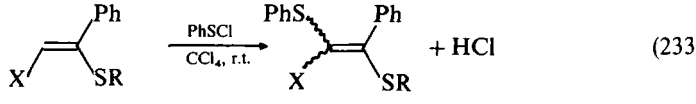
Likewise, the reaction of vinyl sulfides (**319**) with one equivalent of benzenesulfenyl chloride affords the substitution products (**320**) (equation 233)[670].

2,5-Diphenyl-1,4-dithiin (**321**) gives the corresponding disubstitution product (**322**) with benzenesulfenyl chloride (equation 234)[670].

The vinyl sulfides (**323**) form with ArSCl the chlorination product **324** (equation 235)[670].

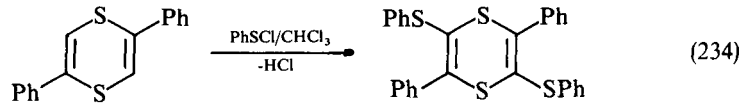


(317) (318) *E*:*Z* *ca* 1:3 (232)

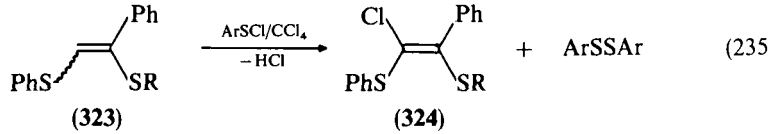


(319) (320) (233)

R = Me, Ph; X = H, Cl

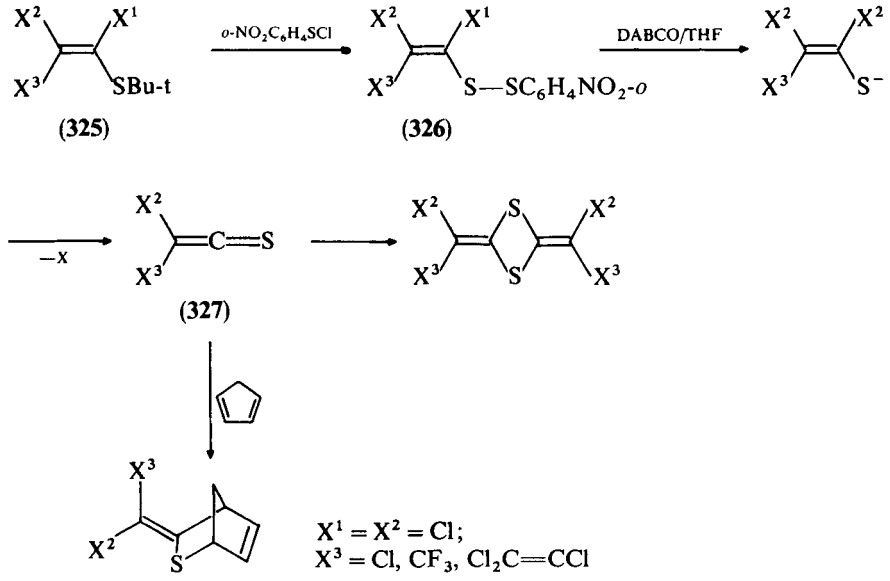


(321) (322) 54% (234)



(323) (324) (235)

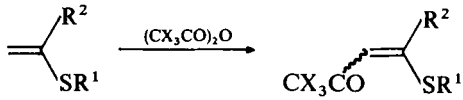
Besides the substitution at the β-position, vinyl sulfides can react by substitution at the sulfur atom. Thus, the α-haloalkenyl sulfides (**325**) react with 2-nitrobenzenesulfenyl chloride to afford alkenyl 2-nitrophenyl disulfides (**326**) in good yields [671]. The S—S bond in the latter compounds can be cleaved with DABCO. The generated thiolates then expel the chloride anion from the α-position, giving thioketenes (**327**). The latter can either dimerize or be trapped by cyclopentadiene (Scheme 19)[671].



SCHEME 19

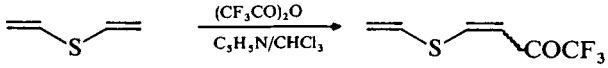
The electrophilic substitution of the β-hydrogen in vinyl sulfides by trihaloacetyl cations derived from trihaloacetic anhydride proceeds smoothly (equation 236)[672,673].

With divinyl sulfide (**39**), only one vinyl group undergoes trifluoroacetylation (equation 237)[674].



(236)

R^1 = Alk, Ar; R^2 = H, Alk, RS; X = F, Cl



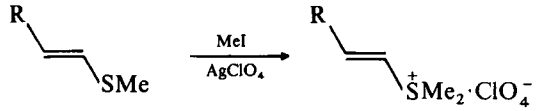
(237)

(**39**) *E*:*Z* *ca* 2:1

Recently, the rates of trifluoroacetylation of $ArSCH{=}CH_2$, $ArSCH{=}CD_2$, and *E*- and *Z*-ArSCH=CHD have been determined and the results indicated that the reaction proceeds by a single-step mechanism[675]. This reaction finds wide application in organic synthesis (see, e.g., References 676–681 and references cited therein).

3. *Alkylation*

Like saturated sulfides, vinyl sulfides can be alkylated on the sulfur atom by activated alkyl halides or by other alkylating reagents[10,682–688]. For example, vinyl sulfonium



(238)

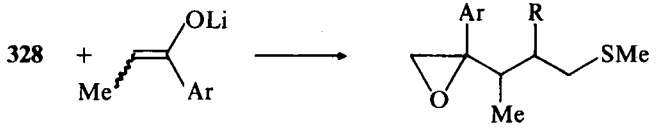
R = *i*-Pr, Ph (**328**)

perchlorates (**328**) are prepared by reacting vinyl sulfides with methyl iodide in the presence of silver perchlorate (equation 238)[10].

Vinyl sulfonium salts are versatile reagents, particularly in the synthesis of cyclopropanes[689-692] and oxiranes[10]. An example is the reaction of the salts **328** with the lithium enolates (**329**) to form the aroylcyclopropanes (**330**) in 42–80% yields (equation 239)[10].

(239)

(**329**) (**330**)

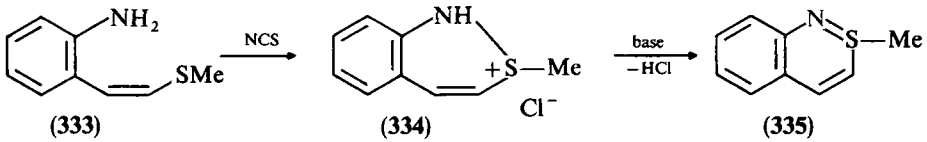


(240)

(**331**) (**332**)

In the case of the enolates **331**, the same reaction leads to the oxiranes **332** (equation 240)[10].

Under the action of *N*-chlorosuccinimide (NCS) the vinyl sulfide (**333**) forms the aminosulfonium salt (**334**) which is converted in the presence of base to the cyclic sulfimide (**335**) (equation 241)[693,694].



(**333**) (**334**) (**335**)

(241)

C. Free-radical Additions

Vinyl sulfides add thiols and H_2S noncatalytically and readily to form anti-Markovnikov adducts, indicating a free-radical addition (equation 242)[123,124,126,131,137,661,695,696].

(242)

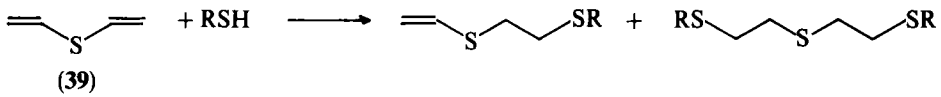
R^1 = Alk, Ar; R^2 = H, Alk, Ar

Although Reppe[126] believed that this addition is catalyzed by alkali, no evidence

for this was found in further studies. On the contrary, diverse vinyl sulfides react exothermally with excess alkane or arenethiols in air to form the corresponding 1,2-di(organylthio)alkanes[661,695,696]. This is consistent with the known tendency of vinyl sulfides to undergo homolytic processes due to the stability of the intermediate radical adjacent to sulfur[614]. Normally, the free-radical thiol addition to vinyl sulfides competes with the electrophilic addition and, when the former is inhibited, e.g. by hydroquinone, the Markovnikov adducts (mercaptals) are mostly formed. In the presence of SO_2 at liquid nitrogen temperature both adducts are detected, with the mercaptal formed in a larger amount[131,661].

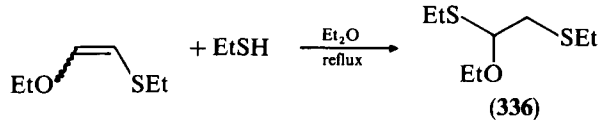
The addition of thiols to divinyl sulfide (**39**) is initiated by AIBN, UV irradiation or by heating alone to 35–75 °C[666,697], whereas thioacetic acid reacts exothermally with **39**[666] to form mono- and/or diadducts (equation 243).

The addition of ethanethiol to 1-ethoxy-2-(ethylthio)ethene (equation 244)[127,128] affords the adduct **336**, thus confirming the higher stability of the intermediate radical adjacent to sulfur as compared with that stabilized by oxygen.



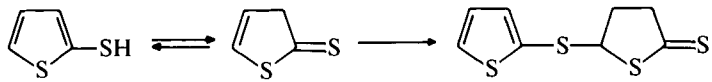
(**39**)

R = Et, *n*-Pr, *n*-Bu, *i*-Bu, *t*-Bu, Ph, Ac, $(MeO)_3Si(CH_2)_n$ (243)



(**336**) (244)

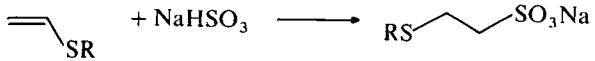
2-Mercaptothiophene (**337**), upon storage under nitrogen, transforms to 5-(2-thienylthio) tetrahydrothiophene-2-thione (**339**), apparently via the homolytic addition of **337** to its tautomer **338** (equation 245)[698].



(**337**) (**338**) (**339**) (245)

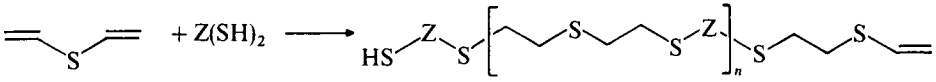
Alkyl vinyl sulfides (and less readily aryl vinyl sulfides) react with sodium bisulfite to form sodium β-(thioalkyl)sulfonates (equation 246)[123,124,126,131]. Judging from the relative positions of the two added groups, a free-radical mechanism took place.

Polyalkylene sulfides of various types and their heteroatomic analogs have been obtained in 70–90% yields by reaction of divinyl sulfide (**39**) with H_2S and dithiols (equations 247 and 248)[24].



(246)

(247)



$Z = (CH_2)_2, (CH_2)_2(OCH_2CH_2)_3$ (248)

The polyaddition follows a free-radical mechanism without the addition of either a catalyst or solvents at 40–55 °C.

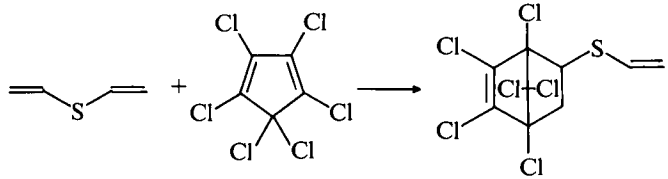
D. Cycloaddition

1. Diels–Alder reactions

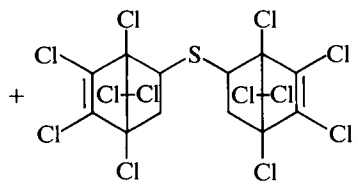
Vinyl sulfides undergo [2 + 4] cycloadditions with various 1,3-dienes[623,624,699–707], including cyclopentadiene (or dicyclopentadiene[699,700]), hexachlorocyclopentadiene[699,701], anthracene[704], acrolein[705] and isoprene[706,707].

For example, divinyl sulfide (**39**) reacts with cyclopentadiene at 180 °C to give di- (**341**, **342**) and triadducts (**343**, **344**), no monoadduct (**340**) being found (Scheme 20)[672].

Divinyl sulfide (**39**) reacts almost quantitatively with hexachlorocyclopentadiene to form mono- and diadducts (**345**, **346**) of an *endo*-form (equation 249)[708].



(**345**)



(249)

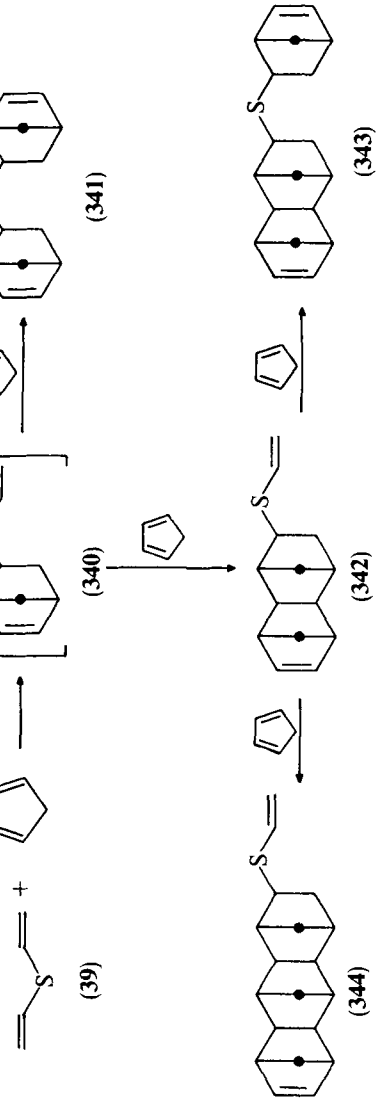
(**346**)

Thermal (50–165 °C) and catalytic ($ZnCl_2$, $SnCl_4 \cdot 5H_2O$)[709,710] Diels–Alder reactions of divinyl sulfide (**39**) with acrolein and crotonaldehyde give 2-vinylthio-3,4-dihydropyranes (**347**) and bis(3,4-dihydropyranyl-2) sulfide (**348**) in 44 and 58% yields, respectively (equation 250).

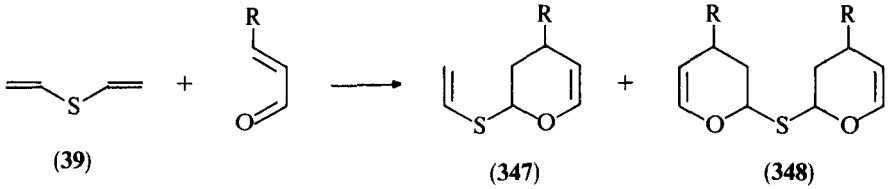
The reaction between **347** and hexachlorocyclopentadiene affords the adduct **349** in a 66% yield, thus demonstrating the possibility of a cross-Diels–Alder synthesis (equation 251)[710].

Vinyl sulfides cyclize with anils (**350**) in a Diels–Alder fashion to give the tetrahydroquinoline derivatives (**351**) (equation 252)[711].

6-Alkoxy-3,4-dihydro-2*H*-pyrans have been prepared from methyl vinyl sulfide and

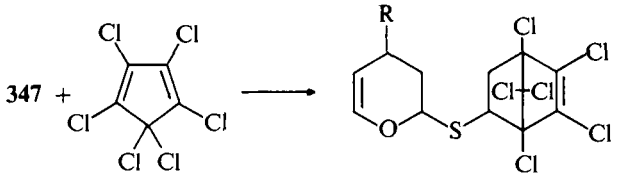


SCHEME 20

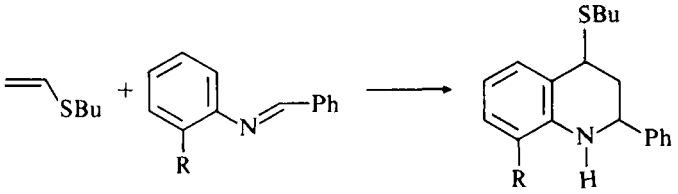


(39) (347) (348)

R = H, Me (250)



(349) (251)



(350) (351) (252)

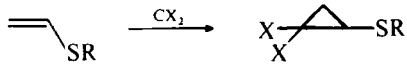
substituted α,β-unsaturated esters[712]. Intramolecular [4 + 2] cycloaddition of vinyl sulfide or ketene dithioacetals moieties to α,β-unsaturated esters or aldehydes have also been studied[713,714].

[2 + 2]-Cycloaddition of $(CF_3)_2C{=}C(CN)_2$ to vinyl sulfides and ketene *S,S*-acetals has been studied quantitatively[715]. It has been shown that the reactivity of alkyl vinyl sulfides is comparable to that of the corresponding alkyl vinyl ethers, while the reactivity of aryl vinyl sulfides is 2–3 orders of magnitude higher than that of aryl vinyl ethers.

The role of sulfur functionalities in activating and directing olefins in [4 + 2] cyclizations was discussed in a review[716]. Vinyl sulfide dienophiles were reported to undergo cycloaddition with isoquinolinium salts. Acidic hydrolysis of the cycloadduct results in cleavage, giving 1-naphthaldehydes or tetralins under different conditions[717]. Diels–Alder syntheses with 1,3-dienes containing the vinyl sulfide moiety are also known[718–720].

2. *Reactions with carbenes*

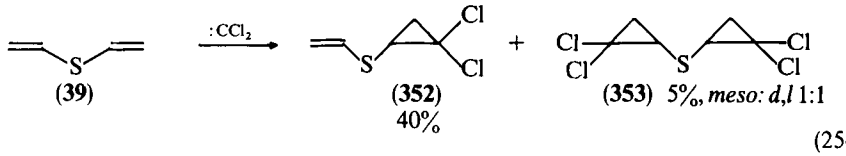
Vinyl sulfides add dihalocarbenes to form 2,2-dichlorocyclopropyl sulfides in satisfactory yields (equation 253)[721–723].



(253)

R = Et, Ph, $CH{=}CH_2$; X = Cl, Br

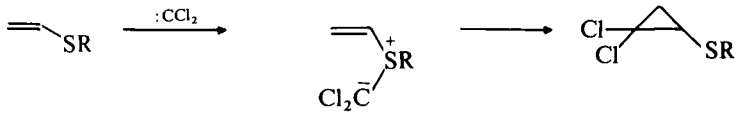
The reaction of divinyl sulfide (**39**) with dichlorocarbene obtained from $CHCl_3$ and *t*-BuOK leads to 2,2-dichloro-1-(vinylthio)cyclopropane (**352**) and bis(2,2-dichlorocyclopropyl) sulfide (**353**) (equation 254)[723].



(**39**) (**352**) 40% (**353**) 5%, *meso*: *d,l* 1:1

(254)

Dibromocarbene generated by phase transfer catalysis adds to **39** to form 2,2-dibromo 1-(vinylthio)cyclopropane in 30% yield[723]. The rate of the dichlorocarbene addition to vinyl sulfides is 5–6 times higher than that to vinyl ethers. The rates with vinyl sulfides decrease with the increase in the size of the alkyl substituent, whereas for vinyl ethers it increases[723]. This implies that the dichlorocarbene reacts with the sulfur atom rather than with the double bond to form the ylide **354** which further rearranges to the cyclopropane (equation 255)[723].

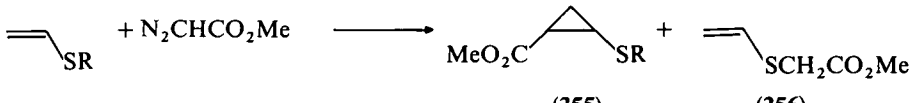


(**39**) (**354**)

R = Me, *n*-Bu, *i*-Bu, *t*-Bu, Ph, $CH{=}CH_2$

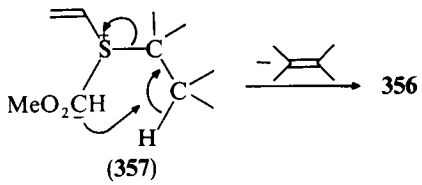
(255)

Thermal decomposition of methyl diazoacetate (or azidoformate) in vinyl sulfides yields the cyclopropanes **355** and the vinyl sulfides **356** (equation 256)[724]. The latter are formed via the ylid **357** (equation 257)[724].



(**355**) (**356**)

(256)



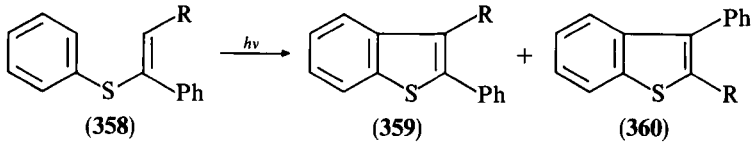
(**357**)

(257)

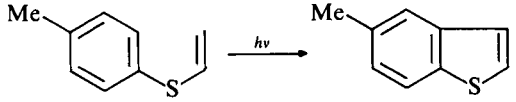
The reactions of vinyl sulfides with carbenes and the relative reactivities of reactions at sulfur *vs* the double bond to form vinyl sulfonium ylides such as **354** and **357** have further been reported in a series of papers (see, e.g., References 725 and 726 and references cited therein) and in a review[727].

3. Photocyclization

Upon UV irradiation, the aryl vinyl sulfides **358** and **361** yield the benzothiophenes **359**, **360** and **362**, respectively (equations 258 and 259), whereas di(1-propenyl) sulfide gives no detectable amounts of the cyclization products[728].

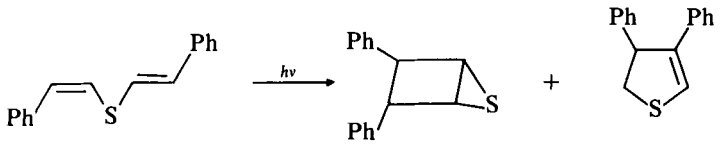


(358) (359) (360) (258)



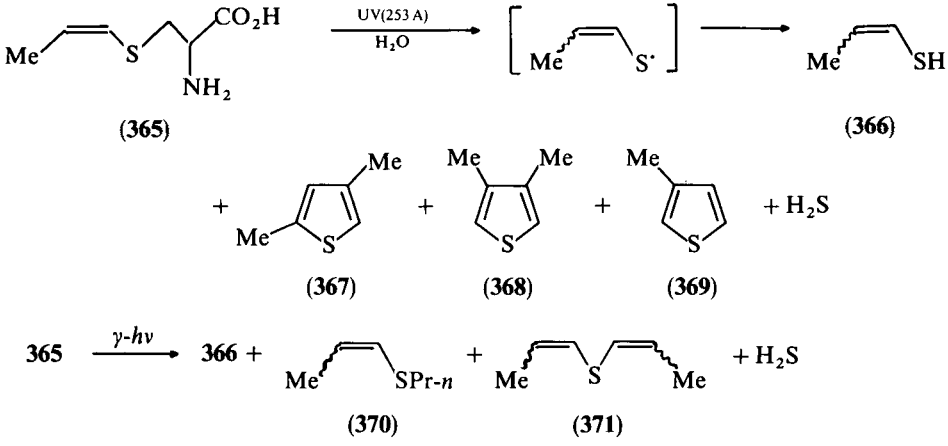
(361) (362) (259)

Di(2-phenylvinyl) sulfide undergoes photocyclization to afford *trans*-2,3-diphenyl-5-thiabicyclo[2.1.0]pentane (**363**) and 2,3-dihydro-3,4-diphenylthiophene (**364**) (equation 260)[729].



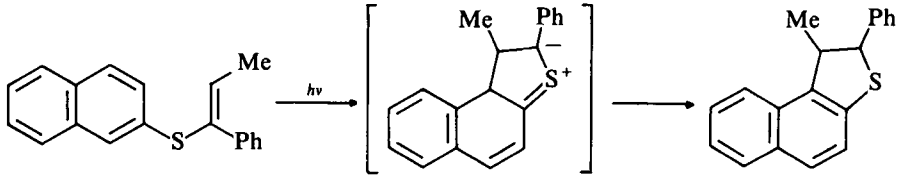
(363) (364) (260)

Irradiation of *S*-(*Z*-1-propenyl)-L-cysteine (**365**) by UV light in oxygen-free aqueous solutions produces 1-propenethiol (**366**) (via the 1-propenylthiyl radical), 2,4-dimethylthiophene (**367**), 3,4-dimethylthiophene (**368**) and 3-methylthiophene (**369**). On γ-radiolysis under the same conditions, **366**, *n*-propyl 1-propenyl sulfide (**370**) and di-1-propenyl sulfide (**371**) were formed (Scheme 21)[730].



SCHEME 21

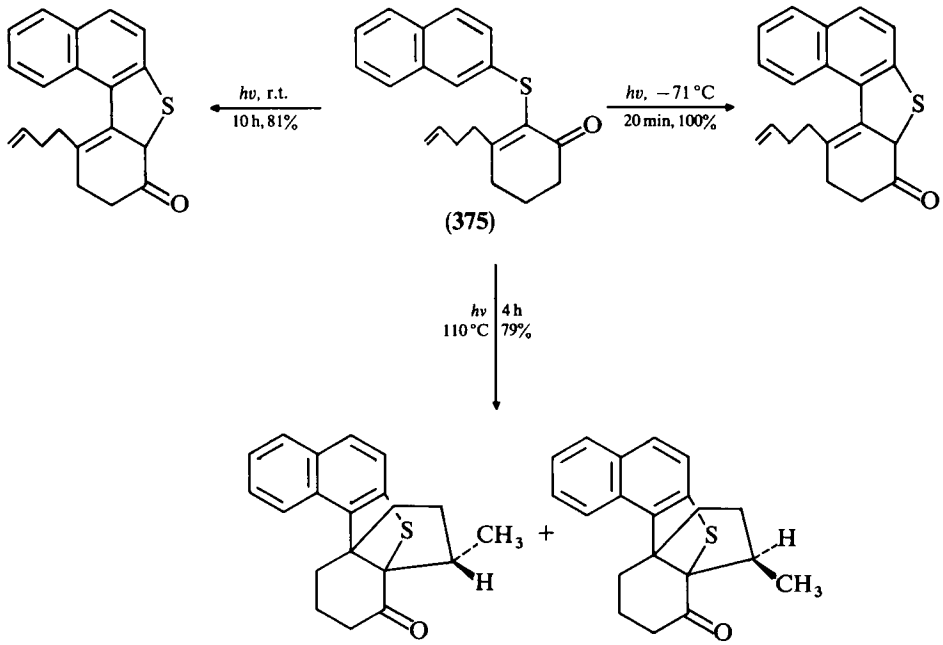
A detailed study of the photochemical ring closure of 2-naphthyl vinyl sulfides has been performed[731–733]. The major product from the irradiation of the vinyl sulfide (**372**) is the *trans*-dihydrothiophene (**374**). The thiocarbonyl ylide **373** was shown to be its precursor (equation 261)[731,733].



(**372**) (**373**) (**374**) 74%

(261)

Temperature-dependent photocyclization of 2-naphthyl vinyl sulfide (**375**) has been studied (Scheme 22)[734]. The reaction is more selective (at least, at room temperature) than that with the corresponding vinyl ether.



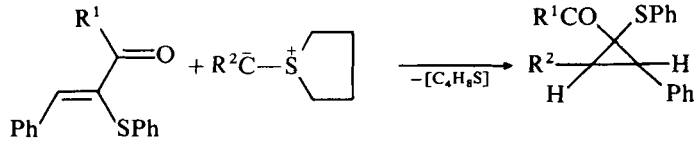
SCHEME 22

The photochemical reactions of vinyl sulfides with benzene[735] and that of 1,4-dithiine with tetracyanoethene, maleic anhydride, DMAD and acetylenes have also been studied[736]. Methyl vinyl sulfides, $R^1R^2C{=}CR^3SMe$, behave as traps of photochemically excited benzophenone in a stereoselective and regiospecific Paterno–Buchi reaction to produce oxetanes[737].

4. Other cyclizations

Cycloaddition of vinyl sulfides with sulfenes was reported[738,739]. Propyn-2-yl vinyl sulfide and its homologs undergo thermal rearrangement to 2*H*-thiopyranes and thiophenes[740]. 1-Alkyl- or 1-phenylthio-4-(methylthio)buta-1,3-dienes cyclize to thiophene derivatives[741]. In a number of diverse heterocyclization reactions, ketene *S,S*-diacetals and *S,N*-acetals and their derivatives served as the precursors[742–751].

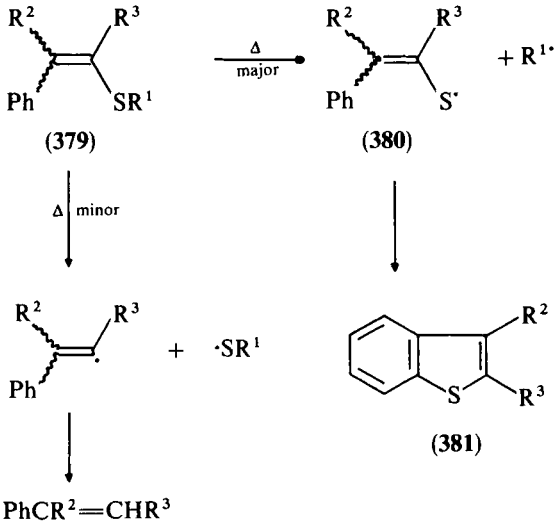
The activated vinyl sulfides (**376**) react with the ylides (**377**) to give stereospecifically cyclopropanes (**378**) (equation 262)[752].



(376) (377) (378) (262)

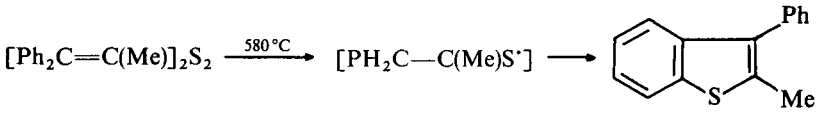
At 450–560 °C divinyl sulfide undergoes dehydrocyclization to form thiophene[753] and the thermolysis of di(1-propenyl)sulfide leads to 2-ethylthiophene[754].

An intramolecular addition of the thiyl radicals (**380**) occurs upon pyrolysis at 580 °C of alkyl styryl sulfides (**379**) with excess benzene to furnish benzothiophenes (**381**) in 50–70% yield and trace amounts of styrene derivatives (Scheme 23)[755].



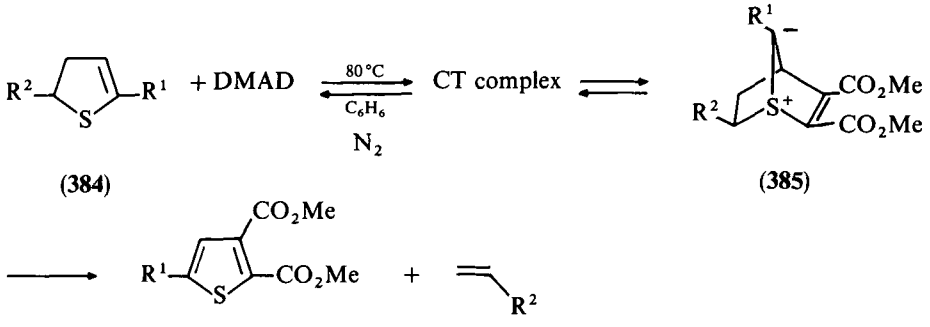
SCHEME 23

Under similar conditions the styryl disulfide (**382**) gives 2-methyl-3-phenylbenzothiophene (**383**) in 85% yield (equation 263)[755].



(382) (383) (263)

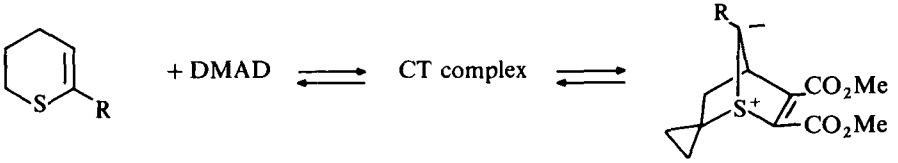
The cyclic vinyl sulfides, 2,3-dihydrothiophenes (**384**) and 3,4-dihydro-2*H*-thiopyranes (**387**) add DMAD reversibly to form initially yellow charge-transfer complexes and then the sulfonium ylides **385** and **388**, which in the former case give 2,3-di(methoxycarbonyl)thiophenes (**386**) and alkenes (Scheme 24)[756].



(**384**) (**385**)

(**386**)

R^1 = H, Me; R^2 = H, *i*-Pr;

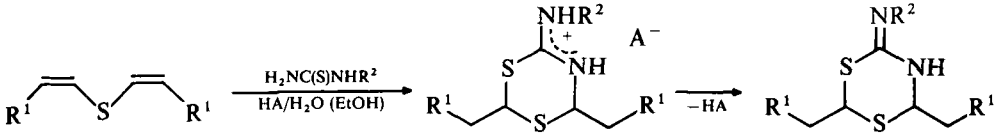


(**387**) (**388**)

R = H, Me

SCHEME 24

Cycloaddition of thiourea and its derivatives to divinyl sulfides in the presence of a strong acid results in 2*H*,6*H*-2,6-disubstituted 4-amino-1,3,5-dithiazinium salts (**389**) in 62–90% yield. The latter can be further converted to the free bases **390** (equation 264)[757–762].



(**389**) 62–90% (**390**)

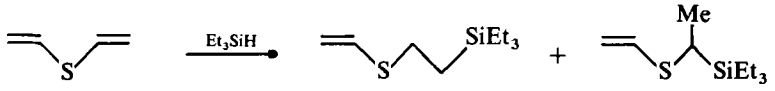
R^1 = H, Me, CO_2H; R^2 = Alk, Ar (264)

Many other annelations of vinyl sulfides (*e.g.* in References 763–769 and references cited therein) are also known.

E. Miscellaneous

1. Reactions with organometallics

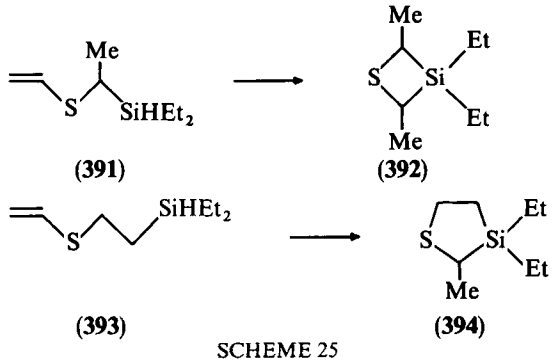
Regardless of a patent[770] claiming the hydrosilylation of vinyl sulfides in the presence of platinum catalysts to be impossible, the addition of trialkylsilanes to divinyl sulfide (**39**) has been performed. The silyl moiety is directed to both the α- and β-position to the vinylthio group (equation 265)[771,772].



(265)

(**39**)

Adducts **391** and **393** of dialkylsilanes to **39** form 1-thia-3-silacyclobutanes (**392**) and 1-thia-3-silacyclopentanes (**394**), respectively (Scheme 25)[772–774].



(**391**) (**392**)

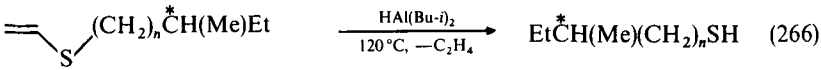
(**393**) (**394**)

SCHEME 25

The hydrosilylation of **39** in the presence of $(Ph_3P)_3RhCl$ and H_2PtCl_6 gives predominantly the β-adducts[775–777]. The process is complicated by a number of side-reactions including cleavage of the C—S bond by hydrosilane as the major one[771,775,778]. Dialkylfluorosilanes easily add to **39** in a similar manner[778], the yields of β-monoadducts spanning 35–50% and diadducts also being formed[779]. Trialkylsilanes and triethylgermanes react with aryl vinyl sulfides in the presence of H_2PtCl_6 to give the β-adducts[780]. The same vinyl sulfides give with tributylstannane, in the presence of AIBN at 65–70 °C for 12 h, the β-adducts in 72% yield[780]. The hydrosilylation of vinyl sulfides has also been reported in other works[698,781–783].

Dialkylaluminiums cleave optically active vinyl sulfides to form thiols (equation 266)[142,143].

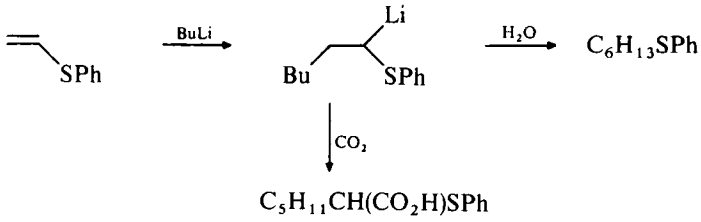
Application of the free-radical substitution reaction to interconversion of 1-alkenyl sulfides, -germanes and -stannanes has been published[784].



(266)

$n = 0, 1, 2$

Addition of butyllithium to phenyl vinyl sulfide gives an adduct which can be hydrolyzed or carboxylated (Scheme 26)[785].



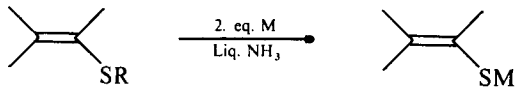
SCHEME 26

Lauryl vinyl sulfide with BuBr and lithium forms lauryl hexyl sulfide[786]. Additions, α-substitutions and related processes of vinyl sulfides with organolithium compounds are increasingly employed in organic synthesis (see, e.g., References 787–800 and references cited therein). These reactions were applied for the preparation of ketones[788], aldehydes[789], homologation of aldehydes and ketones to α,β-unsaturated ketones[790,792,793] (*via* metallated ketene thioacetals)[790,792,796] and synthesis of (±)-eldanolide *via* β-lithioacrylate equivalents derived from β-(phenylthio)acrylic acid[799].

Additions of Grignard reagents to ketene dithioacetals are also known[801].

2. *Other reactions*

Vinyl sulfides react vigorously with Li or Na in liquid ammonia to form vinylthiolates (**395**) which are versatile synthetic reagents (equation 267)[489,802,803].

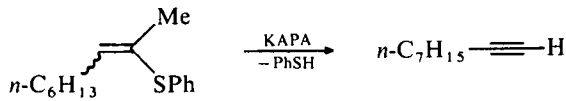


(267)

(**395**)

M = Li, Na

Under the action of potassium 3-aminopropylamide (KAPA) vinyl sulfides, *e.g.* **396**, undergo rapid elimination at room temperature to yield alkynes with a high degree of selectivity (*e.g.* equation 268)[804]. This reaction allows the C=C—SR unit to be considered as a convenient acetylene equivalent.

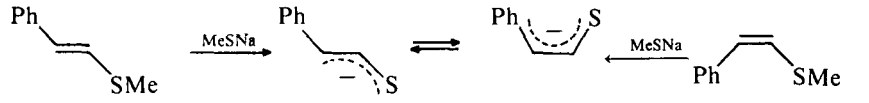


(268)

(**396**)

Vinyl methyl sulfides react with excess MeSNa to give a solution of the enethiolate anion as a result of nucleophilic aliphatic substitution[805]. When the demethylation reaction is applied to pure *E*- or *Z*-β-(methylthio)styrenes **397** and **398**, the same equilibrium mixture of *E* and *Z* anions **399** and **400** is formed (equation 269)[450].

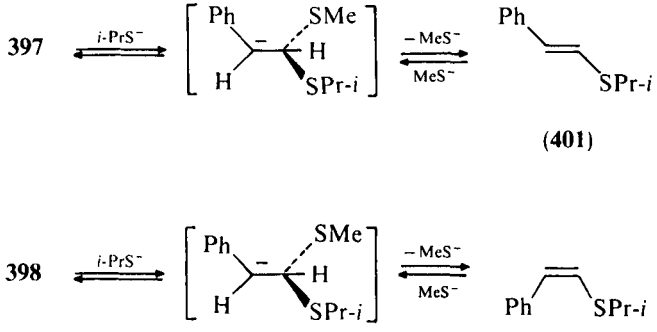
The reaction of the vinyl sulfides **397** and **398** with sodium 2-propanethiolate in DMF at 100 °C affords the corresponding substitution products **401** and **402** in 87 and



(269)

(397) (399) (400) (398)

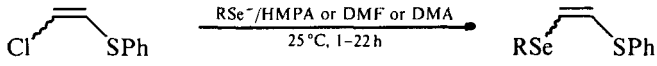
95% yields. These sulfides are converted again with sodium methanethiolate to the starting compounds **397** and **398** (Scheme 27)[805].



SCHEME 27

Likewise, lithium methyl selenide reacts with styryl alkyl sulfides in DMF at 100 °C to give the products of vinylic or aliphatic substitution[805].

2-Chlorovinyl phenyl sulfides undergo vinylic substitution with alkyl and aryl selenide anions in dipolar aprotic solvents. These reactions are stereospecific leading to products of retained configuration (equation 270)[806,807].



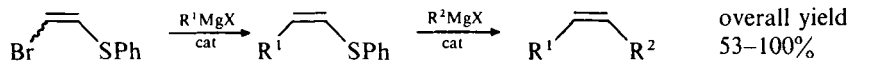
(270)

56–58%

R = Me, Et, *i*-Pr, CH_2=$CHCH_2$, Ph

The substitution of the methylthio group in (methylthio)ethenes by Grignard reagents has been carried out[808], and further relevant work was also reported[809,810].

The sequential formation of two C—C bonds at room temperature by reaction of aromatic or aliphatic Grignard reagents with *E*- or *Z*-1-bromo-2-(phenylthio)ethene (**403**) in the presence of nickel(II) or palladium(II) catalysts provides a novel stereospecific route to a variety of *E* or *Z* olefins of RCH=CHR and R^1CH=CHR^2 types. The stereoselectivity of these processes is > 99% for the *E* isomers and in the range of 95–98% for the *Z* isomers (equation 271)[605]. The leaving ability of the bromine is so much higher than that of the phenylthio group that formation of the symmetric final product is easily avoided[605].

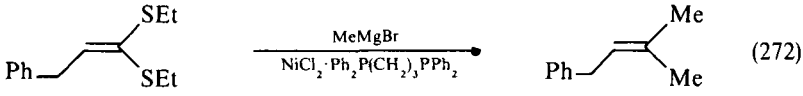


(403) (271)

R^1 = *n*-Bu, Me_3CCH_2, Ph, Ph(Me)CH
R^2 = Me, *n*-Bu, Ph, 1-naphthyl
cat = $NiCl_2 \cdot Ph_2P(CH_2)_nPPh_2$; $n = 2,3$;
$PdCl_2 \cdot PPh_3$

A series of insect sex pheromones and structurally related olefins have been synthesized with high stereoisomeric purity by the sequential cross-coupling reactions described above[16].

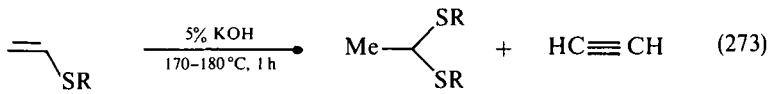
Another general alkene synthesis *via* similar substitution of vinyl sulfides (**404**) by Grignard reagents is exemplified by equation 272.



(272)

(404)

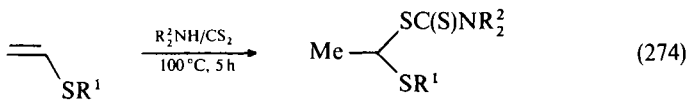
Upon heating vinyl sulfides in the presence of KOH in a steel autoclave, they rearrange into mercaptals in 22–40% yields, acetylene being detected in the reaction mixture (eqution 273)[811]. The rearrangement does not occur in a glass-sealed tube. Apparently the metallic wall has a catalytic effect in this reaction.



(273)

R = Et, *i*-Pr, *i*-Bu

Dithiocarbamic acids, generated *in situ* from secondary amines and CS_2, add to vinyl sulfides in a sealed ampoule, to afford the Markovnikov adducts **405** in essentially quantitative yield (equation 274)[812].

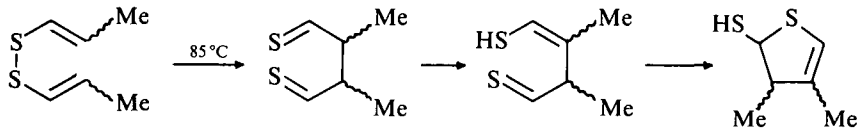


(274)

(405)

R^1 = Me, Et, *i*-Pr, *n*-Bu; R^2 = Me, Et;
R^2–R^2 = $(CH_2)_5$, $(CH_2)_2O(CH_2)_2$

Bis(1-propenyl) disulfides (**406**) containing two vinyl sulfide moieties undergo thermal dithio-Claisen [3,3]-sigmatropic rearrangement followed by an intramolecular addition to afford a 1:1 mixture of the *Z* and *E* isomers of 2-mercapto-3,4-dimethyl-2,3-dihydrothiophene (**407**) (equation 275)[813].



(406) (407) (275)

A [3,3]-sigmatropic rearrangement of 1-alkenyl allenyl sulfides leads to γ,δ-acetylenic aldehydes and ketones[814]. A number of other useful syntheses with vinyl sulfides are also known[815].

3. Polymerization

a. Radical polymerization. Vinyl sulfides are homo- and copolymerized readily with common vinyl and polyvinyl monomers in the presence of radical initiators (AIBN, dimethyl azodiisobutyrate, benzoyl peroxide, *t*-butyl peroxide and the like)[269,272,279,503,816]. The effects of *p*-substituents in aryl vinyl sulfides on their radical homo- and copolymerization[817,818] have been studied. These vinyl sulfides could easily be homopolymerized with a radical initiator and the Alfrey–Price *Q* values of these monomers are 0.45–0.47 from a study of the copolymerizations with methyl methacrylate. The copolymerization reactivities of these monomers toward polystyryl and poly(methyl methacrylate) radicals correlate linearly with Hammett σ constants of the *para* substituents[817,818].

The copolymerization of 1,2-di(phenylthio)ethene derivatives[819] and ketene diethylmercaptal[820] have also been investigated. Earlier, the radical copolymerization of methyl vinyl sulfide with styrene and methyl acrylate[821] as well as radical and ionic copolymerization of several alkyl vinyl sulfides[822–824] were investigated.

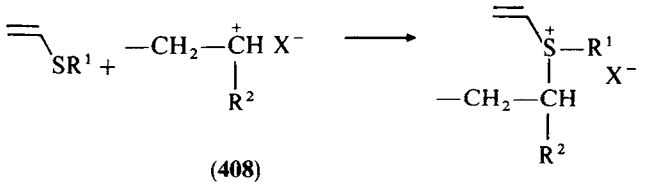
The radical copolymerizations of vinyl sulfides, CH_2=CHSR (R = Me, Et, *i*-Pr, *n*-Bu, *i*-Bu, *t*-Bu, $PhCH_2$, Ph), with styrene, methyl methacrylate and acrylonitrile were investigated at 60 °C and the copolymerization parameters (*Q*, *e*) were estimated to be 0.3–0.5 and (−1.1)–(−1.7), respectively, from copolymerization with styrene. These values were almost insensitive to the nature of R[825].

The copolymer composition varied widely with the comonomers used. The tendency for alternative copolymerization increased with an increase in the electron-withdrawing nature of the comonomer according to the order: styrene < methyl methacrylate < acrylonitrile[825].

The radical homopolymerization of divinyl sulfide to 50% conversion was first reported[826] to give a completely soluble polymer which was assigned a normal structure with a pendant SCH=CH_2 group at each unit. The fact that the remaining vinylthio groups do not polymerize further to form a cross-linked polymer points, in the author's opinion, to their lower reactivity compared to that of the same groups in the monomer activated by conjugation. However, judging from more recent reports, e.g. References 825, 827–829 on the ready polymerization of unconjugated alkyl vinyl sulfides including branched ones, upon radical initiation, the above rationalization is no longer acceptable. Later on, the divinyl sulfide polymers were shown to consist mainly of bicyclic and, to a less extent, monocyclic structural units[830].

A cross-linked granular polymer has been prepared by polymerization of divinyl sulfide in an aqueous emulsion ($NaNO_2$, starch, AIBN, 60–90 °C, 24–28 h)[831]. Diverse copolymers[23,24,80,832–838] of divinyl sulfide have also been obtained under radical conditions.

b. Cationic polymerization. In contrast to vinyl ethers, cationic homopolymerization of vinyl sulfides proceeds with a satisfactory rate mostly upon heating[836]. In the presence of $BF_3 \cdot Et_2O$, only the polymer of phenyl vinyl sulfide is formed at 0 °C[839]. The low reactivity is also peculiar to vinyl sulfides in cationic copolymerizaton. Thus, vinyl sulfides, $CH_2{=}CHSR$ (R = Me, Et, *i*-Bu, *t*-Bu, Ph, 4-MeC_6H_4), do not form copolymers with styrene and α-methylstyrene at 0 °C and the yield of the copolymer of ethyl vinyl sulfide with isobutyl vinyl ether drops sharply as the concentration of the former in the monomer mixture increases. Also, the reduced viscosity of the copolymers of vinyl sulfides with isobutyl vinyl ether decreases upon increasing the vinyl sulfide concentration in the monomer mixture[839]. On the other hand, the viscosity of copolymers of *para*-substituted aryl vinyl sulfides with isobutyl vinyl ether is practically independent of the composition of the monomer mixture. It follows that vinyl sulfides are the chain transfer agents. Actually, homopolymers of vinyl sulfides which were synthesized under the same conditions possess a very low polymerization degree, only 11–20[839]. A probable mechanism of the slowing down (the chain transfer) is as follows: the active cation **(408)** reacts with the sulfur of the vinyl sulfide to form the stable vinyl sulfonium salt **(409)** (equation 276)[839].



(276)

(408) **(409)**

$X^- = (e.g.)^- BF_3 \cdot OEt$

An NMR examination[839] does not confirm the formation of a stable complex between vinyl sulfides and $BF_3 \cdot Et_2O$ as was assumed earlier[840,841].

According to patent data[842] divinyl sulfide rapidly homo- and copolymerizes in the presence of $AlCl_3$ or gaseous BF_3 in MeCl or pentane. The homopolymerization of divinyl sulfide with $SnCl_2$, $FeCl_3$, $Al_2(SO_4)_3 \cdot H_2SO_4$ and $BF_3 \cdot Et_2O$ has been studied[843,844]. The cross-linked structure proposed[842] is not in agreement with the fusibility of the polymer. The copolymerization of divinyl sulfide with *n*-butyl vinyl ether in the presence of $FeCl_3$ or $BF_3 \cdot Et_2O$ was performed by introduction of the former monomer into partially polymerized vinyl ether, *i.e.* at the propagation step[845,846]. A method for the determination of vinylthio groups in the copolymers by UV and IR spectroscopy has been developed[847].

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CHAPTER 15

High-coordinated sulfur compounds*

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* Dedicated to Professor J. C. Martin on the occasion of his retirement from the Department of Chemistry, Vanderbilt University and in recognition of his contribution to the development of this field of organic sulfur chemistry.

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I. INTRODUCTION

The first question which should be answered in this chapter is the meaning of the term: high-coordinated sulfur species. At present a large number of stable organosulfur compounds with ligand number from 1 to 6 can be prepared and, after isolation, handled under typical laboratory conditions[1]. The high efficiency of SF_6 to form in the mass spectrometer SF_6^- (of unknown structure)[2] allows one to hope that some day organic sulfur derivatives

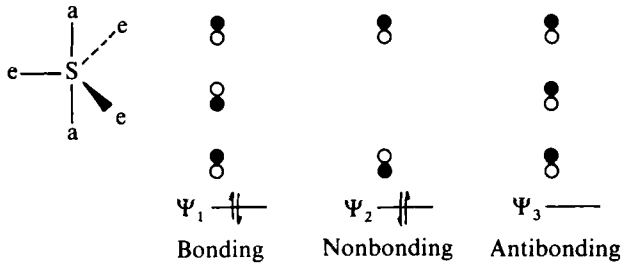
having more than six ligands bonded to the central sulfur will also be isolated as stable species. Therefore, it is obvious that the selection of a borderline between organosulfur compounds which may be considered as the low-coordinated derivatives and their high-coordinated analogues is to some extent a matter of formality and, as such, may always be considered as an arbitrary choice. At present, the generally accepted view locates the organosulfur compounds with $N \leqslant 4$ (including an electron pair as a ligand) in the family of the low-coordinated derivatives. Consequently, all organosulfur derivatives with the number of ligands N equal to 5 or 6 should be considered as high-coordinated sulfur species. This chapter will be devoted to the presentation of the chemistry of these two classes of organosulfur compounds in which the central sulfur expanded its valence shell from eight to ten or twelve electrons, respectively. The first group of compounds are commonly termed as sulfuranes and the second one as persulfuranes[3]. According to a general systematic classification scheme proposed by Martin and coworkers[4] sulfuranes are classified as 10-S-5 species and persulfuranes are designated as 12-S-6 species. It should be noted here that the contribution by Martin's group to the creation and development of this field of organic sulfur chemistry is of the utmost importance and cannot be overestimated.

A short discussion on the reactivity and properties of high-coordinated sulfur species may be found in many recent review articles[3,5-8] and books[1b,1a] devoted to sulfur chemistry. The present review is an attempt, perhaps the first, to summarize in a systematic and comprehensive way various aspects of the chemistry of both classes of high-coordinated organosulfur derivatives. Although this chemistry began in 1873 with the preparation of a highly unstable SCl_4[9], only the last two decades have witnessed real development in this field. Therefore, an effort has been made to cover results published after 1970 including very recent reports from 1991 and 1992.

II. THE NATURE OF BONDING AND MOLECULAR GEOMETRY OF HIGH-COORDINATED ORGANOSULFUR DERIVATIVES

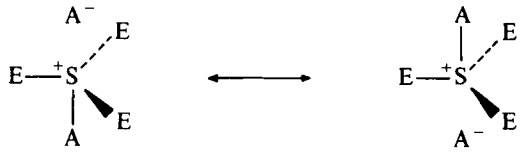
For a long time the sp^3d and sp^3d^2 hybridization scheme has been invoked to rationalize the nature of bonding in high-coordinated sulfur compounds such as SF_4 and SF_6. Though such a d-orbital hybridization scheme has long been criticized on the basis of the large promotion energies involved and poor overlap, these two models are still employed in many elementary valency courses[10-13]. In 1969 Musher described[14] an approximate bonding model for electron-rich three-centre four-electron bonds, without any significant d-orbital contribution, and named it a hypervalent bonding and applied it to both sulfuranes and persulfuranes. The Musher model is very similar to the scheme proposed earlier by Pimental[15], Rundle[16] and Pitzer[17] for the isoelectronic interhalogen compounds and xenon halides. More recently, Kutzelnigg[18] has reviewed the theory of hypervalency and concluded that a model of the excess-electron multicenter bonding is closer to reality than a hybridization model involving d-orbitals. The theory of Musher[14] when applied to high-coordinated sulfur compounds describes, for example, a three-center four-electron bond in sulfuranes by an approximate molecular orbital model (MO) shown in Scheme 1.

According to this model, of the four bonding electrons of the hypervalent bond, two electrons fill the lowest bonding MO(ψ_1) and the other two electrons are placed into the nonbonding MO(ψ_2) which has no contribution from the central atom. The third antibonding MO(ψ_3) remains empty. The delocalized σ bonds in such species are closely related to the delocalized π bonds in the allyl anion. In sulfuranes, the four equatorial C—S bonding electrons and the equatorial lone pair are placed on hybrid orbitals made up from 3s, $3p_x$ and $3p_y$ atomic sulfur orbitals. The four axial bonding electrons are in hybrid orbitals constructed only with the use of the sulfur $3p_z$ atomic orbitals. Because the



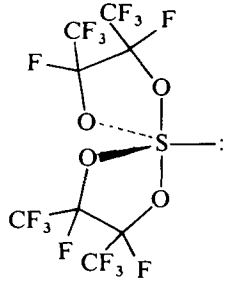
SCHEME 1. Approximate molecular orbital model of hypervalent bonding in sulfuranes

two axial bonding electrons involved in bonding are in a nonbonding molecular orbital, the apical bonds are expected to be weak and long since they contain only two electrons in the bonding molecular orbitals. The electron distribution in the nonbonding molecular orbitals predicts relative negative charges on the apical ligands and positive charge on the central sulfur atom. Therefore, the bonding in such a system can also be represented by a qualitative valence bond description involving a nonbond resonance structure shown in Scheme 2.



SCHEME 2

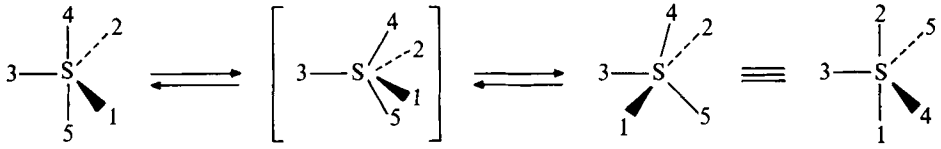
In molecules, in which the central atom participates in hypervalent bonding and forms simultaneously other σ bonds, there are two different types of single bonds connecting the central atom with substituents. Therefore, in the ^{19}F-NMR spectrum of the sulfurane **1** two sets of distinct resonances can be seen, one for the apical fluorines and the apical CF_3 groups and another for the equatorial fluorines and the equatorial CF_3 groups[19].



(**1**)

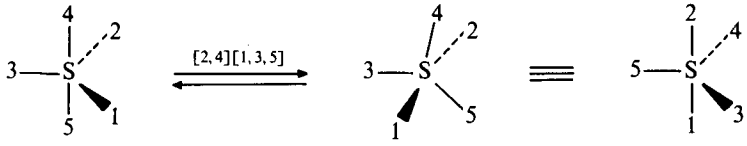
However, the apical and equatorial ligands can interchange with each other to form a special type of stereoisomers, the so-called permutational isomers. As early as 1960 Berry proposed[20] a mechanism called pseudorotation for nondissociative permutational

isomerism of such trigonal bipyramidal structures. A pairwise exchange of the two equatorial and two apical ligands results from a single pseudorotation step, via a square pyramidal structure. This mechanism is shown in Scheme 3.



SCHEME 3. Mechanism of Berry pseudorotation (BPR)

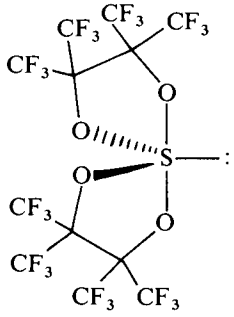
According to this mechanism isomerization takes place with the substituent 3 as stationary (pivot) while the angles between it and the two other equatorial substituents 1 and 2 decrease and the angles between it and the two apical substituents 4 and 5 increase until 1, 2, 4 and 5 form the corners of a square pyramidal intermediate. Further movement in this intermediate results in the formation of a new trigonal bipyramid in which the substituents 1 and 2 are apical and the substituents 3, 4 and 5 are equatorial. Soon thereafter, a closely related mechanism called the 'turnstile' rotation has been proposed by Ugi and Ramirez[21]. In this mechanism (see Scheme 4) isomerization results from the internal movement of one equatorial and one apical substituent against the remaining three substituents.



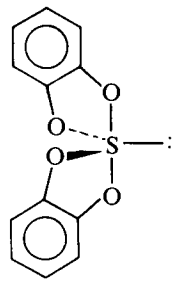
SCHEME 4. Permutational isomerization via the turnstile rotation (TR)

During isomerization the central atom, equatorial substituent 2 and axial substituent 4 are located in one plane and the remaining substituents 1, 3 and 5 are changing their positions until they lie in a plane which is perpendicular to the first plane. There is an internal rotation until substituents 1 and 2 are aligned and can become apical. The TR was shown to be a higher-energy process in comparison with the BPR. Far-infrared studies of SF_4 (**2**) showed that the permutational isomerization occurs via a transient structure having the C_{4v} symmetry which is in full accord with the BPR mechanism[22]. The ^{19}F-NMR studies established that the barrier to interchange of the apical and equatorial fluorines in SF_4 is 11–12 kcal mol^{-1} (46–50 kJ mol^{-1})[23]. The pseudorotation barriers for the tetraoxospirosulfuranes **3**[24] and **4**[25] have values about 7.5 and 9 kcal mol^{-1}, respectively.

It should be noted here that in the case of the bicyclic sulfuranes **3** and **4** the apical and equatorial ligands can interchange with each other in a single BPR step. This can be achieved by keeping the lone electron pair at the central sulfur atom in the equatorial position and therefore the barrier for pseudorotation via rectangular pyramidal structure is low. However, if a pseudorotation mechanism interconverting one sulfurane structure to another requires passing through a very unstable sulfurane with an apical lone pair, its probability becomes very small. This point and other ways of isomerization of sulfuranes will be discussed in Section VI of this chapter.



(3)



(4)

The sulfurane structures are best described as close to a trigonal bipyramidal geometry with an equatorial lone pair, and distinguishable apical and equatorial positions. In the case of the corresponding sulfurane oxides the equatorial lone pair is replaced by the oxygen atom. The structural data collected in Table 1 are in full agreement with theoretical predictions that electronegative substituents prefer the apical sites and that the apical bonds are weak[14,26,27].

Evidence for a weakening of these bonds comes from solid state structural studies. Thus, for all sulfuranes listed in Table 1 having symmetrical structure (acyclic and bicyclic) the apical S—O bonds are significantly longer than the sum of the sulfur and oxygen covalent radii (1.70 Å)[28]. The S—O bonds in the acyclic sulfurane **5**[29] are *ca* 1.90 Å in length, in the bicyclic sulfurane **6**[30] *ca* 1.82 Å and in the spirosulfurane oxide **7**[30] 1.78 Å. Bond orders, calculated from Pauling's equation[31] relating bond order and bond length, for the apical S—O bonds of **5**, **6** and **7** are 0.46, 0.62 and 0.74. The weakness of apical bonds in sulfuranes is evident from structural data of the spirosulfurane **1**[19] and sulfur tetrafluoride **2**. For SF_4 the apical S—F bonds are 0.1 Å longer than the equatorial ones[32-34]. For the sulfurane **1** the apical S—O bonds are 0.12 Å longer than the equatorial bonds[19]. The large difference in S—O bond lengths (1.955 Å vs 1.713 Å) seen for **8** stems from the polarization of the hypervalent O—S—O bonds, resulting from the unsymmetrical nature of the apical substituents.

The apical S—O (N, Cl, F) bonds of all sulfuranes and sulfurane oxides having equatorial aryl substituents collected in Table 1 are not exactly collinear. In each case, with the apparent exception of the dichlorosulfurane **9**[35], the X—S—X (X = O, N, Cl or F) angle is bent away from the lone pair (or equatorial oxygen) towards the equatorial phenyl rings. The magnitudes of deviations from linearity are in the order 7.7° for **6**, 4.9° for **5** and 1.8° for **7** (2.9° or 1.8°). These deviations can be rationalized by considering the repulsive interactions[36-40] between the π-donor ligands and the apical ligand bonding electrons in the spirosulfurane oxide **7** and between the sulfur lone pair and the apical ligand bonding electrons in the sulfuranes **6** and **5**, following the suggestions of Gillespie[41]. The apparent exception of the dichlorosulfurane **9**[35], which in the solid state has its Cl—S—Cl axis bent towards the lone electron pair, is caused most probably by weak intermolecular interactions between the sulfur atom and the chlorine atom in an adjacent molecule in the unit cell[30]. Intermolecular Cl—Cl interactions can also be considered as possible contributors to the anomalous geometry of **9** in the crystals[30]. Considering the S—O equatorial bond of the spirosulfurane oxide **7**, it should be noted that its length [1.439 (4) Å] is considerably shorter than the S—O bond lengths found in sulfoxides, for example in diphenyl sulfoxide (1.473 Å)[42], *cis*-9-methylthioxantene 10-oxide (1.492 Å)[43], *trans*-thioxanthen-9-ol oxide (1.484 Å)[44] and β-thianthrene dioxide (1.479 Å and 1.474 Å)[45]. The value is

TABLE 1. Structural data for sulfuranes and persulfuranes taken from X-ray analysis

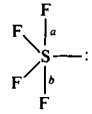
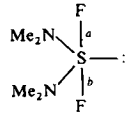
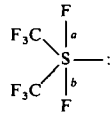
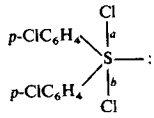
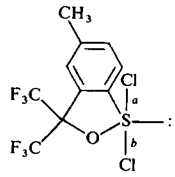
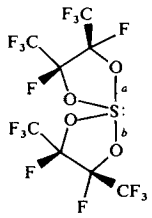
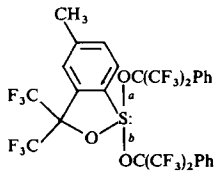
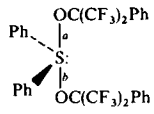
Compounds				
Structure No.	Formula	Bond distance	ab Angle	Reference
2		*a* 1.643 *b* 1.643	183.2	359
230		*a* 1.770 (2) *b* 1.770 (2)	174.7 (1)	360
208		*a* 1.681 (3) *b* 1.681 (3)	186.1 (8)	156c
9		*a* 2.259 (3) *b* 2.323 (3)	174.5 (1, 1)	35
238		*a* 2.551 (5) *b* 2.126 (5)	167.6 (2)	172
1		*a* 1.754 (3) *b* 1.756 (3)	188.5 (2)	19
298		*a* 1.829 (10) *b* 1.840 (10)	188.0 (4)	194
5		*a* 1.916 (4) *b* 1.889 (4)	184.9 (2)	29

TABLE 1. (*continued*)

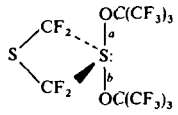
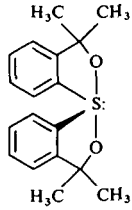
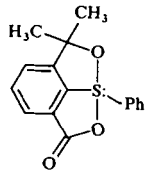
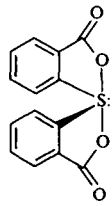
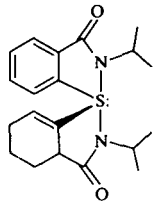
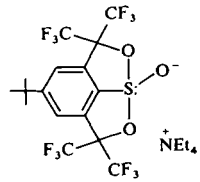
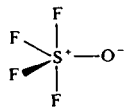
Compounds		Bond distance	ab Angle	Reference
Structure No.	Formula			
323		*a* 1.811 (7) *b* 1.816 (7)	191.2 (2)	187
263		*a* 1.787 (2) *b* 1.814 (2)	181.8 (1)	202
345		*a* 1.662 (2) *b* 2.248 (2)	189.5 (1)	202
355a		*a* 1.83 (1) *b* 1.83 (1)	181.5	57
265		*a* 1.899 (3) *b* 1.897 (3)	180.2 (2)	185
326		*a* 1.969 *b* 1.969	194.1	200
373		*a* 1.602 (5) *b* 1.602 (5)	182.8 (7)	33

TABLE 1. (*continued*)

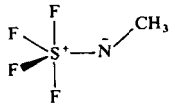
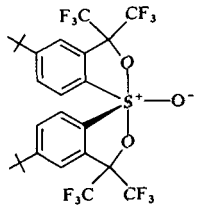
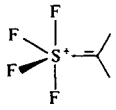
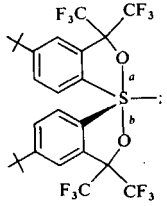
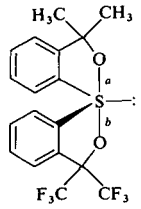
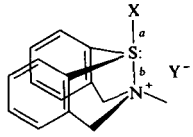
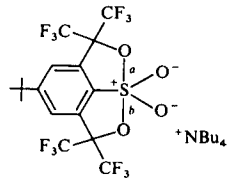
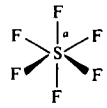
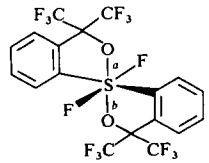
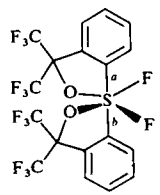
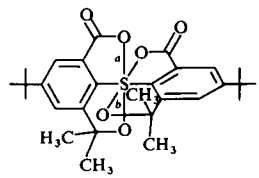
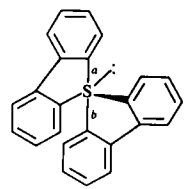
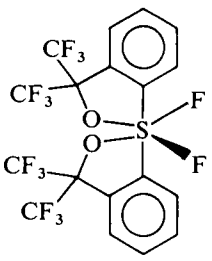
Compounds		Bond distance	ab Angle	Reference
Structure No.	Formula			
446b		*a* 1.622 (8) *b* 1.560 (15)	191.7 (3, 1)	235
7a		*a* 1.780 (5) *b* 1.777 (5)	187.7 (2)	30
416		*a* 1.592 *b* 1.594	189.56	226
6		*a* 1.819 (5) *b* 1.832 (5)	182.9 (2)	30
8		*a* 1.713 (2) *b* 1.955 (2)	182.7	183
365				206
	e X = OEt	*a* 1.501 *b* 2.609	179.4	
	b X = Me, Y = PF_6	*a* 1.804 *b* 2.447	176.9	
	d X = OMe, Y = $SbCl_6$	*a* 1.658 *b* 2.206	175.3	

TABLE 1. (*continued*)

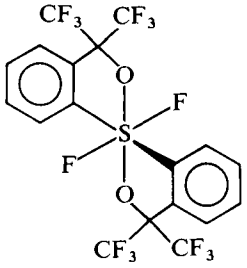
Compounds		Bond distance	ab Angle	Reference
Structure No.	Formula			
415		*a* 1.912 *b* 1.936	192.31	200
458		*a* 1.58		361
11		*a* 1.693 (2) *b* 1.817 (2)	180.00 (8)	52
12		*a* 1.804 (3) *b* 1.717 (2)	175.3 (1)	52
106		*a* 1.67 (1) *b* 1.91 (3)	173 (1)	202
370		*a* 1.926 (2) *b* 1.926 (2)	175.19 (9)	207

close to the S—O bond lengths in bis(*p*-chlorophenyl)sulfone (1.439 Å)[46], bis(*p*-aminophenyl)sulfone (1.440 Å)[47] and bis(*p*-iodophenyl)sulfone (1.43 Å)[48].

This similarity suggests a $p\pi-d\pi$ bonding between sulfur and oxygen analogous to that usually invoked for sulfones[49,50]. On the other hand, the change in hybridization in the σ bond from sulfur to oxygen from *ca* sp^3 in the sulfone to *ca* sp^2 in the spirosulfurane oxide **7** might have been expected to give some bond shortening. The X-ray structural analysis for the persulfurane **10** indicates the approximate octahedral geometry around sulfur[51]. The large differences in the S—O bond lengths (0.24 Å) observed in the crystals of **10** clearly indicate the polarization of the three-center four-electron hypervalent bond in this persulfurane derivative. The X-ray structural analysis[52] of the *trans*-persulfurane **11** indicates that the geometry about the central sulfur atom in this compound is essentially octahedral and all of the bond angles between *cis* bonds to sulfur are $90° \pm 1$. Each five-membered ring and the phenyl ring fused to it are planar. On the other hand, the geometry about the sulfur atom in the *cis*-persulfurane **12** is a slightly distorted octahedron. The largest deviation from octahedral geometry is in the O—S—O and F—S—F angles which are 93.91° and 86.48°, respectively. The five-membered rings of **12**, unlike those of the more symmetrical **11**, are not planar and the oxygen atom is the largest contributor to this deviation.



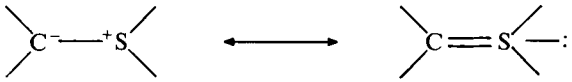
12 (*cis*)



11 (*trans*)

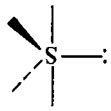
III. SULFURANES AND THEIR OXIDES

Accepting the definition of sulfuranes as a class of compounds in which sulfur expanded its formal valence shell from eight to ten electrons, two types of sulfuranes need to be considered. They are named π-sulfuranes and σ-sulfuranes[6]. Because π-sulfuranes, commonly known as ylides[53,54], possess only three σ bonds and one π bond, they should be regarded as a low-coordinated sulfur species (only three substituents are connected with the central sulfur atom); see Scheme 5.



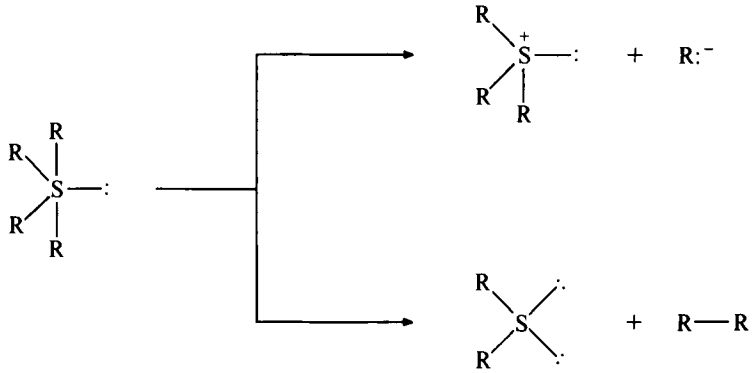
SCHEME 5. Resonance structure of π-sulfurane

On the other hand, σ-sulfuranes (Scheme 6) possess four σ bonds to sulfur in addition to the lone electron pair. Therefore, they belong to the family of high-coordinated organosulfur derivatives.



SCHEME 6. σ-Sulfurane

Normally, σ-sulfuranes (classified according to Martin as a 10—S—4 species[4]) have trigonal bipyramidal (TBP) structure in which lone pair electrons always occupy an equatorial position and, of the four ligands, the two most electronegative ones take the apical positions, whereas the other two are located at the remaining two equatorial positions. The most essential feature of sulfuranes as a species having an expanded valence shell is their relatively low stability caused by the tendency of the central sulfur atom to resume the normal valency by extruding a ligand bearing a pair of electrons or a pair of ligands affording stable compounds with an octet around the sulfur atom (Scheme 7).



SCHEME 7

Although SF_4[55] and some other stable perhalogenated sulfuranes[9] have been known for more than 100 years, considerable interest has focused on their chemistry since Martin and Arhart[56] and Kapovits and Kalman[57] described the synthesis of the first stable spirosulfuranes in 1971. Earlier, sulfuranes and their oxides have been often proposed as intermediates in various reactions of organosulfur compounds and in a few cases their formation as reactive intermediates has been supported by spectroscopic methods. Therefore, we will divide this discussion into three parts: The first will be devoted to presentation of the sulfurane structures proposed as reaction intermediates, the second will discuss the application of spectroscopic techniques to the detection of sulfuranes as reaction intermediates and the third will present the synthesis of stable sulfuranes and their oxides and discuss their reactivity and synthetic utility.

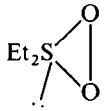
A. Sulfuranes and Their Oxides Proposed as Reaction Intermediates

Sulfuranes and their oxides seem to be involved in many reactions. The nonbonded atomic contacts of nucleophilic centers with divalent sulfur in X-ray structures indicate the possibility of forming sulfurane structures even in some reactions of divalent organosulfur compounds. Tri- and tetracoordinated sulfur compounds, such as sulfonium salts and sulfinic acid derivatives, undergo nucleophilic substitution upon treatment with nuc-

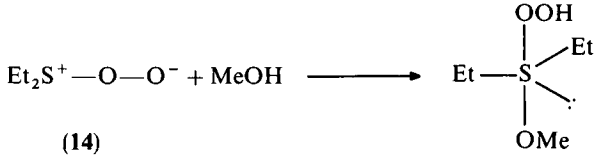
leophiles and such reactions have been thought to proceed via initial formation of a sulfurane. Nucleophilic substitution at the sulfonyl sulfur atom and a few reactions of hexavalent four-coordinate organosulfur compounds have been proposed to proceed with the transient formation of a sulfurane oxide intermediate. The decomposition of the transient sulfurane or sulfurane oxide via either ligand exchange or ligand coupling affords the final nucleophilic substitution products. In the following we will discuss the intermediary involvement of sulfuranes and their oxides in the reactions of organic sulfur compounds having different valencies and/or coordination numbers.

1. Sulfuranes as reactive intermediates in the reactions of divalent sulfur compounds

a. Photooxidation of sulfides. In 1983 Foote and coworkers[58] reported a detailed kinetic study on photooxidation of diethyl sulfide. To accommodate the kinetic results they proposed the formation of two sulfurane structures among other intermediates. The first is the cyclic sulfurane **13** named thiadioxirane, and the second is the peroxysulfurane **15**, formed by addition of methanol to a peroxy sulfoxide **14** (equation 1).

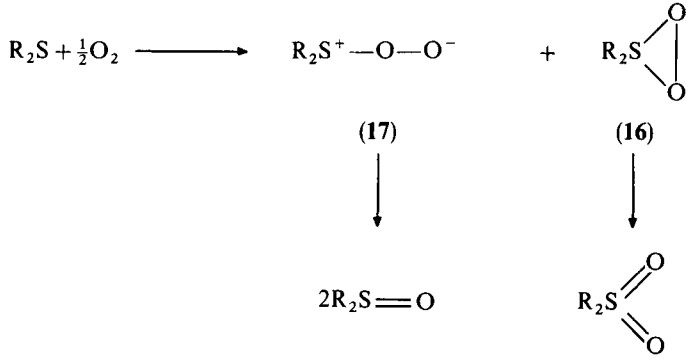


(13)



(14) **(15)** (1)

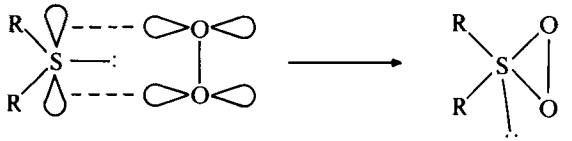
Very recently, the structures and reactivities of intermediates in the reaction of a variety of sulfides with singlet oxygen have been studied in aprotic solvents. It was shown[59] that sulfoxides and sulfones are formed as the major products. All observations, including kinetic data and ^{18}O-tracer experiments, show that both oxygen atoms in sulfones come



SCHEME 8

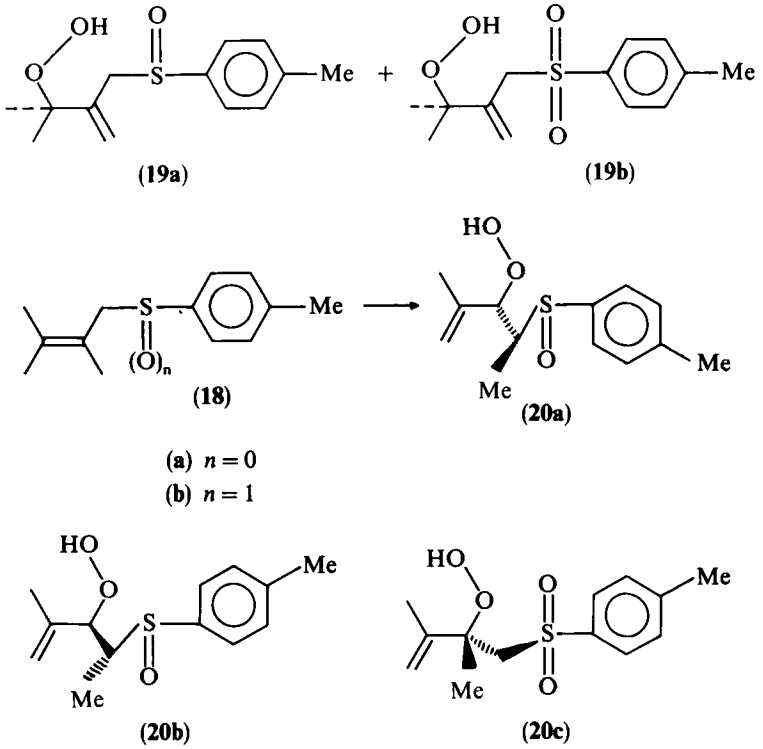
from one oxygen molecule, and suggest that thiadioxirane intermediates **16** are formed via a nonpolar reaction in competition with formation of the persulfoxide **17** (Scheme 8), which is based on the assumption that **16** and **17** are formed as independent intermediates, rationalizes the observed reaction course.

The formation of the cyclic sulfurane **16** could be considered as a concerted cycloaddition between a sulfur lone pair orbital and the π^* orbital of $^1O_2$ (equation 2).



(16) (2)

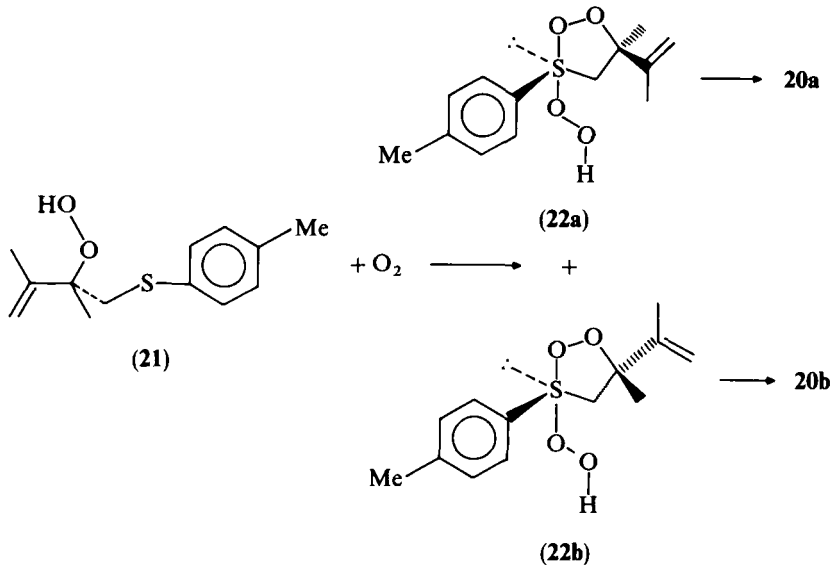
The reaction of singlet oxygen with 2, 3-dimethyl-2-butenyl *p*-methylphenyl sulfide **18a** was found[60] to afford a complex mixture of the products **19a**, **b** and **20a–c** (Scheme 9).



SCHEME 9

In contrast to the behavior observed in the reaction of the corresponding sulfoxide **18b**, which afforded a mixture of **20a** and **20b** in a ratio *ca* 1:1.3, the ratio of the diastereomeric hydroperoxides **20a** and **20b** formed in the singlet oxidation of **18a** was greater than 13:1 and decreased as the reaction proceeded. These results rule out a possibility that the allylic

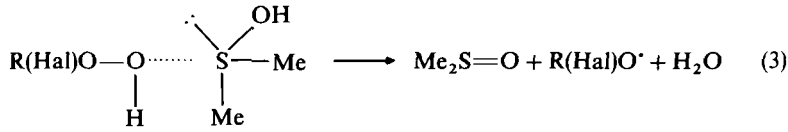
sulfoxide **18b** is the immediate precursor of **20a** and **20b**. They can be explained, however, if the hydroperoxy sulfide **21** rather than sulfoxide **18b** is the immediate precursor producing **20a** and **20b**. A large preference for the diastereomer **20a** in the photooxidation of **18a** reflects in fact the energy difference between the two sulfuranes **22a** and **22b** formed upon action of singlet oxygen on the hydroperoxy sulfide **21** as shown in Scheme 10.



SCHEME 10

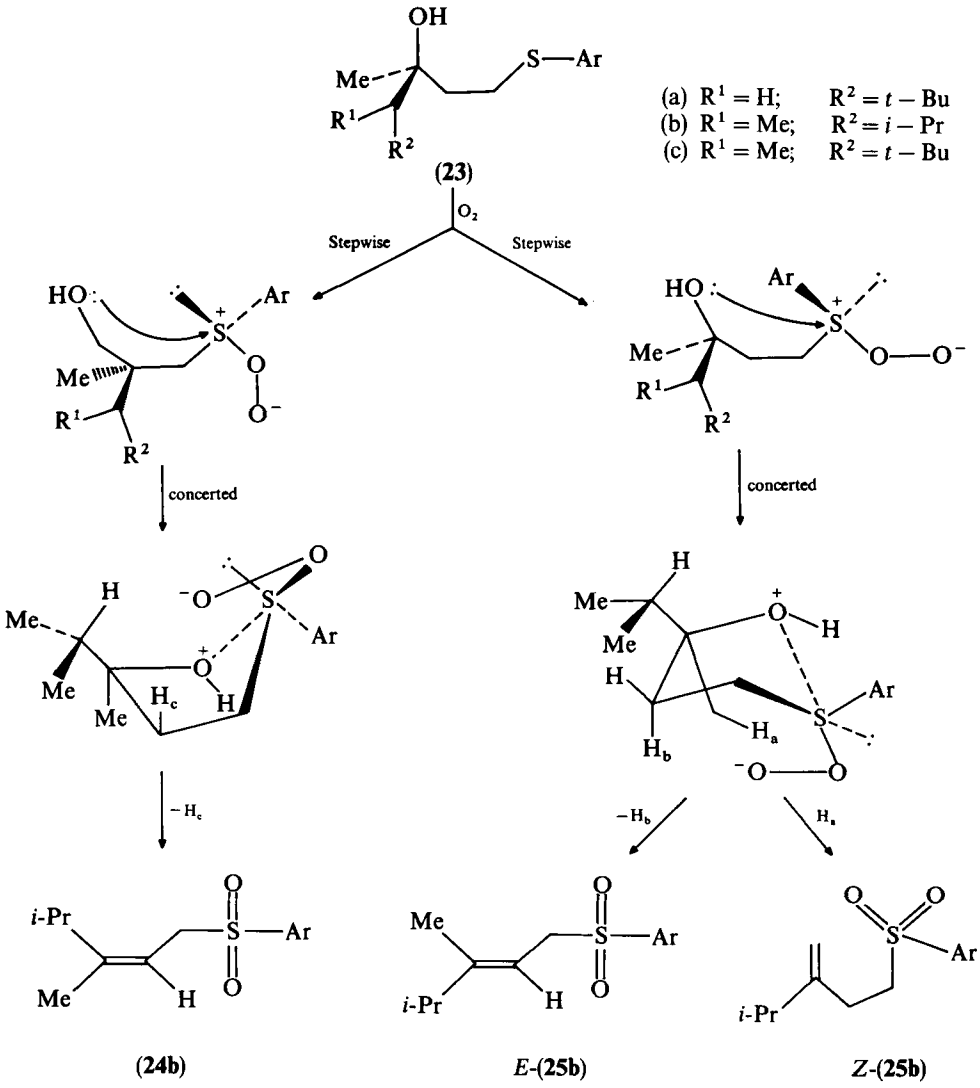
The formation of a sulfurane intermediate during photooxidation of γ-hydroxy sulfides **23a–c** has been suggested[61] to be responsible for the production of the sulfonoolefins **24a–c** and E-**25a–c** and Z-**25a–c**. The proposed mechanism of olefin formation during the photooxidation of **23b** is pictured in Scheme 11.

All observations concerning the dimethyl sulfide oxidation with a halogenated peroxy radical as a two-electron transfer agent have been accounted for by assuming that the sulfuranyl-type adduct **26** is formed in the first reaction step, and its decomposition yields DMSO (equation 3).



(26)

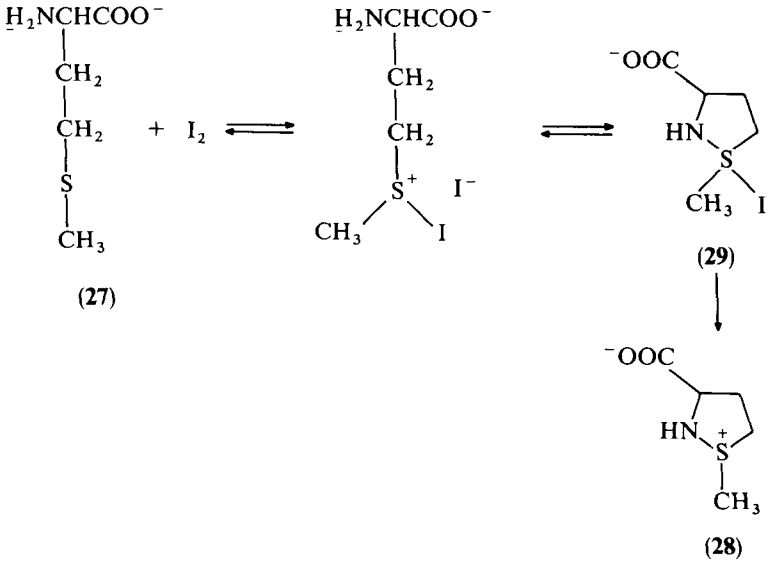
b. Chemical oxidation of sulfides. The iodine oxidation of methionine **27** to the cyclic sulfimine **28** is general base catalyzed and gives a nonlinear Bronsted plot which changes from a slope of *ca* 1 to a slope of zero at approximately $pK_a = 2$. This has been interpreted as evidence that the sulfurane **29** is involved as an intermediate and that the breakdown of this sulfurane has become rate-limiting (Scheme 12)[62].



SCHEME 11

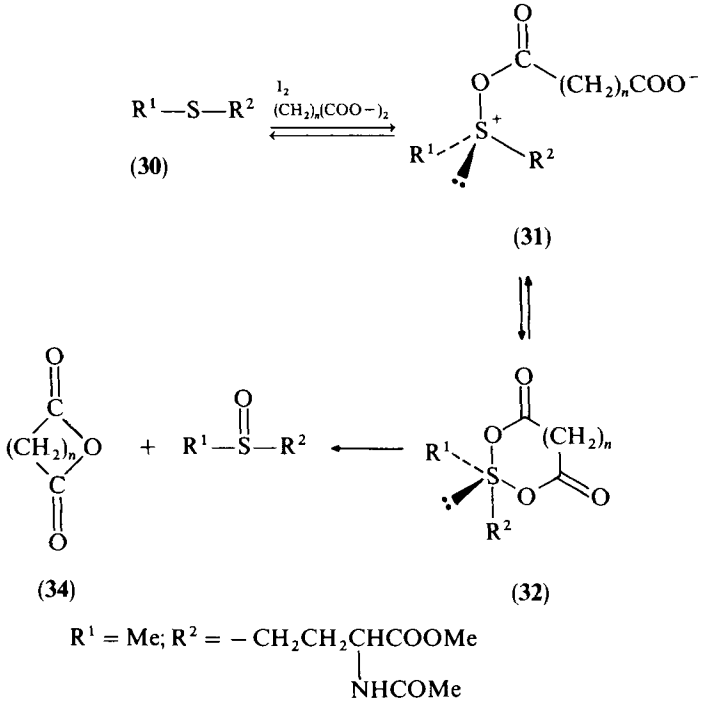
All the kinetic data on the dicarboxylate-catalyzed iodine oxidation of *N*-acetylmethionine methyl ester **30**, and particularly the unexpected low effective molarity, have suggested that the intermediate *O*-acyl sulfoxide **31** exists largely in the sulfurane structure **32**, the breakdown of which is rate-limiting and gives rise to the corresponding sulfoxide **33** and anhydride **34** (Scheme 13)[63].

It was shown[64] that, in *s*-methyl-1-thia-5-azacyclooctane **35**, the transannular tertiary amine group catalyzed better the aqueous iodine oxidation of the mesocyclic thioether by a factor of 10^5 relative to simple analogues. This was satisfactorily interpreted in terms of the facile formation of an intermediate sulfurane **36** or a dication **37** (Scheme 14).



(27) (29) (28)

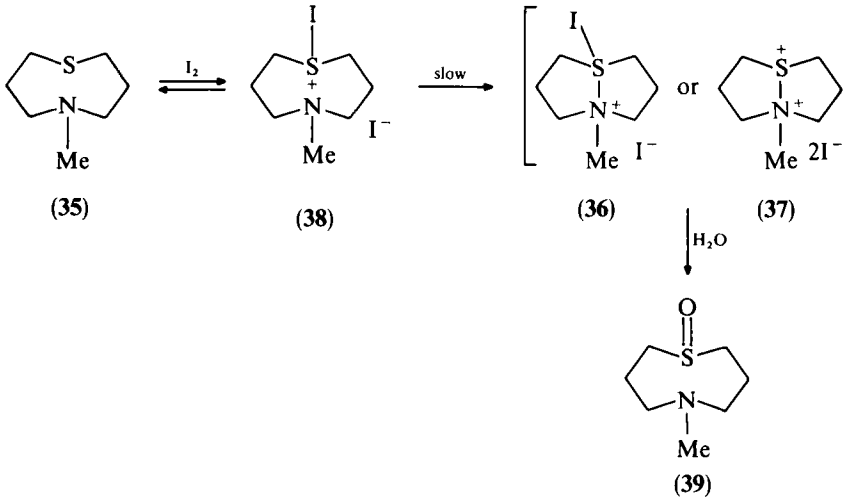
SCHEME 12



(30) (31) (34) (32)

R^1 = Me; R^2 = $-CH_2CH_2CHCOOMe$ (NHCOMe)

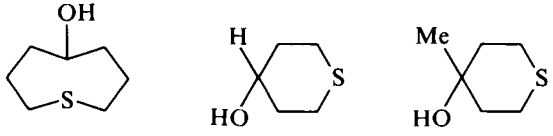
SCHEME 13



(35) (38) (36) (37) (39)

SCHEME 14

In contrast to the behavior of **35**, the aqueous iodine oxidations of 5-hydroxythiacyclooctane **40**, 4-hydroxythiacyclohexane **41** and 4-hydroxy-4-methylthiacyclohexane **42** are more susceptible to phosphate buffer mediation. The observed two-term rate law indicates that there are two major reaction pathways both involving hydroxyl group participation and sulfurane intermediates (Scheme 15).



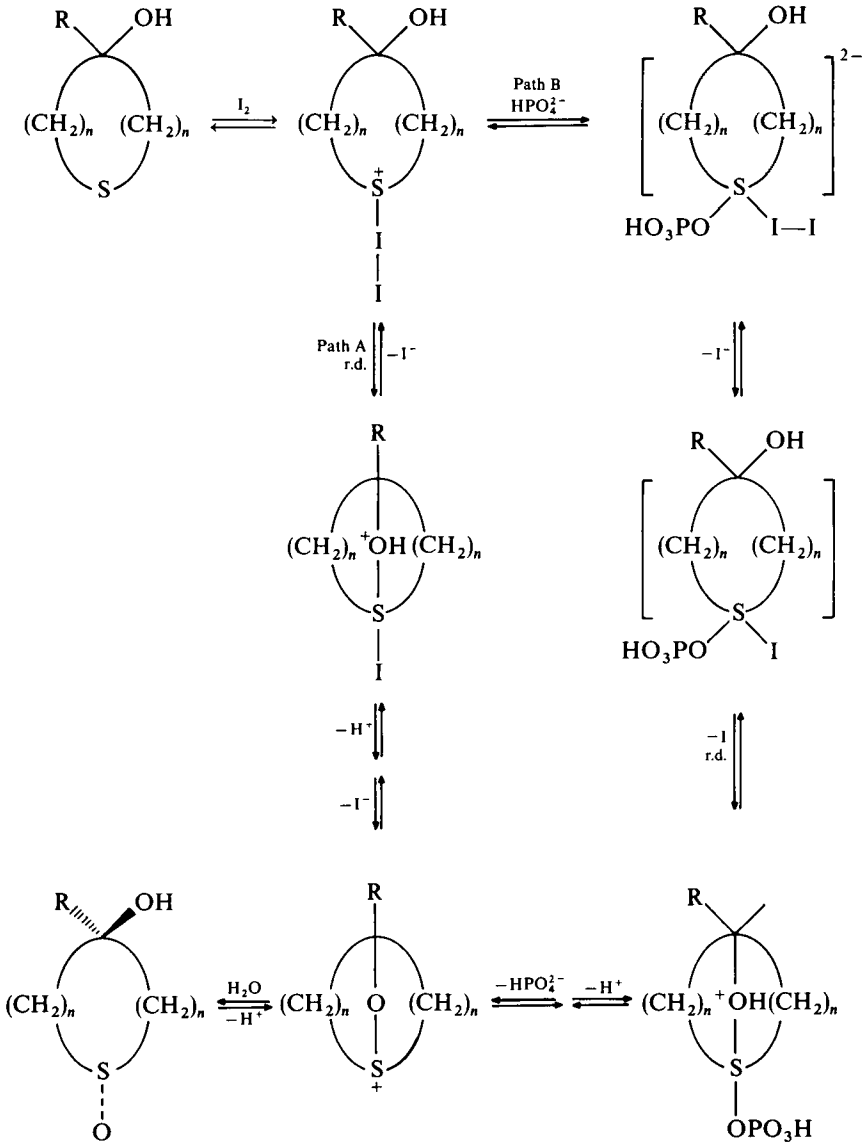
(40) **(41)** **(42)**

In a very detailed paper on the effect of the neighboring sulfide group in the decomposition of the *ortho*-S-phenyl substituted *t*-butyl perester of benzoic acid **43**, Bentrude and Martin[66] proposed a sulfurane intermediate **44** to explain the formation of diphenyl sulfoxide-2-carboxylic acid **45** and isobutylene. According to this proposal the perester **43** first yields an ion pair or a radical pair, which then recombines to form the sulfurane **44**. The final decomposition of the latter affords the products (Scheme 16).

c. Chlorination of sulfenyl chlorides. Early studies by Zincke and coworkers[67] on aromatic disulfides and more recent investigations of Douglass and coworkers[68,69] on aliphatic disulfides showed that equimolar ratios of a disulfide and chlorine give quantitatively the corresponding sulfenyl chloride **46** (equation 4). The latter on further addition of chlorine affords also in a quantitative way the corresponding sulfur trichloride **47** (equation 5).

$$\underset{}{RS-SR} + Cl_2 \longrightarrow \underset{(46)}{2RS-Cl} \qquad (4)$$

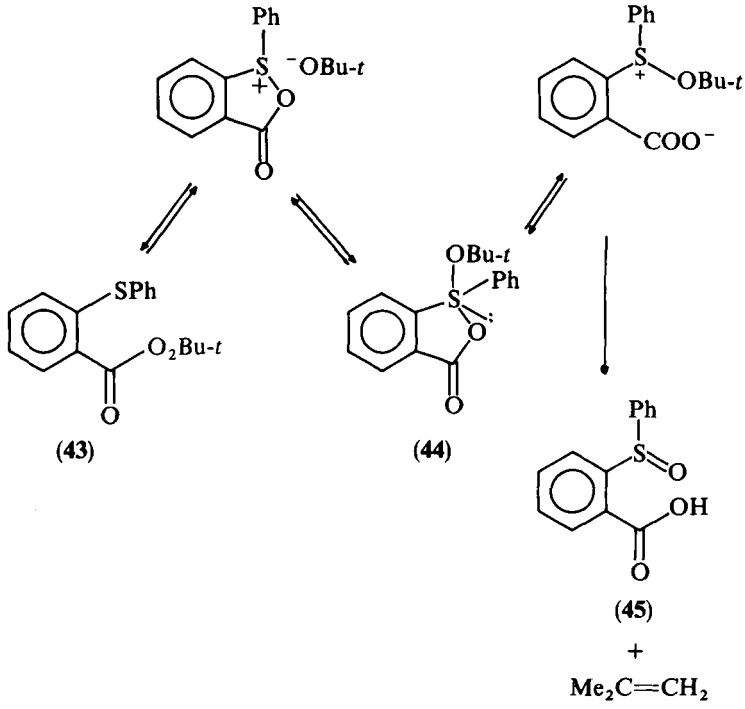
$$\underset{(46)}{RS-Cl} + Cl_2 \longrightarrow \underset{(47)}{R-SCl_3} \qquad (5)$$



SCHEME 15

Of several sulfur trichlorides prepared, the most stable, methylsulfur trichloride **47a**, has a decomposition temperature of 30 °C. Phenylsulfur trichloride **47b** decomposes below 10 °C. Later on, work of Givens and Kwart[70,71] showed that the reaction of sulfenyl chlorides with chlorine in hydroxylic solvents follows a rate equation having a first-order dependence on chlorine concentration (equation 6).

$$\text{rate} = k[\text{Cl}_2][\text{ROH}]^2[\text{RSCl}] \qquad (6)$$



SCHEME 16

This dependence suggests the existence of the sulfur trichloride species **47**, which after reaction with a solvent molecule is converted into another sulfurane structure **48** according to the general quation 7.

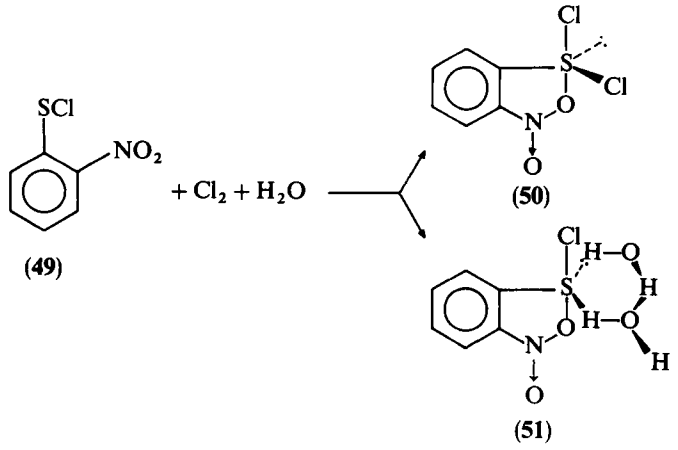
$$\underset{\textbf{(46)}}{RS-Cl} + Cl_2 \rightleftharpoons \underset{\textbf{(47)}}{RSCl_3} \overset{R^1OH}{\rightleftharpoons} \underset{\textbf{(48)}}{RSCl_2(OR^1)} \qquad (7)$$

a: R = Me
b: R = Ph

products

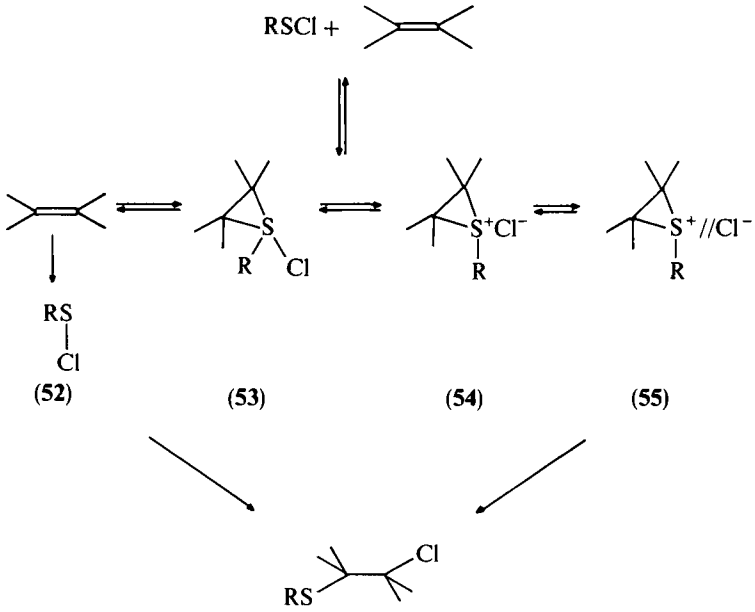
The above authors observed also the abnormal mechanism of the chlorination of *o*-nitro-substituted aromatic sulfenyl chlorides **49** (Scheme 17), for which the existence of the sulfuranes **50** and **51** has been proposed.

d. Addition of sulfenyl chlorides to unsaturated carbon–carbon bonds. In a recent excellent review on the chemistry of sulfenyl halides and sulfenamides, Capozzi, Modena and Pasquato[72] discussed the possible involvement of sulfuranes in the addition of sulfenyl chlorides to alkenes. In analogy with the mechanism proposed for bromine addition to alkenes, the sulfenyl chloride addition may be regarded as the equilibrium formation of a π-complex **52** which may change to the sulfurane **53** by simple strengthen-



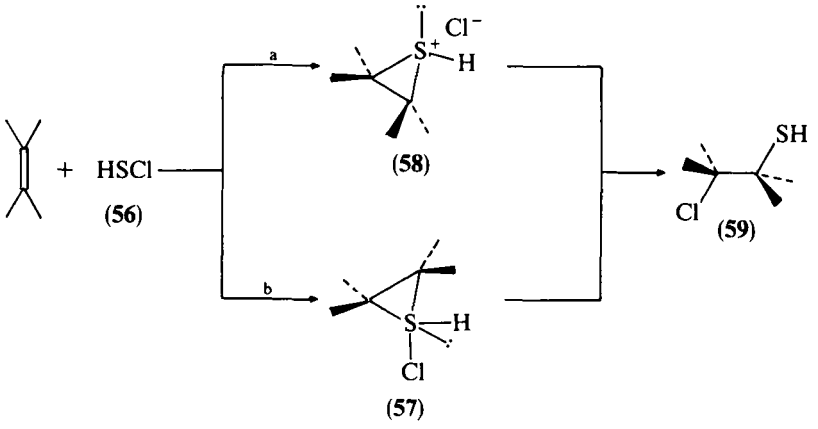
SCHEME 17

ing of the bonds. The conversion of the sulfurane **53** to the products may occur either via heterolysis to a thiiranium chloride tight ion pair **55** or a direct rearrangement (Scheme 18).



SCHEME 18

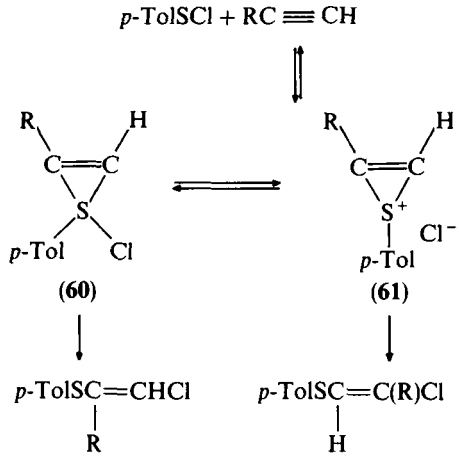
Considering the addition of sulfenyl halides to alkenes, it should be noted that non-empirical *ab initio* SCF-MO calculation of energies of the reaction intermediates formed by addition of thiohypochlorous acid **56** to ethylene indicated that in the gas phase the covalent cyclic sulfurane **57** is favored over the ionic species **58** (Scheme 19)[73].



SCHEME 19

The activation energy for the internal collapse of the cyclic sulfurane **57** to the product **59** was calculated to be 42 kcal mol^{-1}, well below the energy for the formation of the ion pair **58** (Scheme 19)[73].

Both Markovnikov and anti-Markovnikov orientations observed in the addition of *p*-toluenesulfenyl chloride to acetylenes have been explained in terms of a common intermediate which leads, via internal collapse, to the anti-Markovnikov products, or via dissociation into chloride and organic ions to the Markovnikov products[74]. Such a common intermediate may be formulated as an equilibrium mixture between a sulfurane structure **60** and a tight ion pair **61** (Scheme 20).



SCHEME 20

2. Sulfuranes as reactive intermediates in the reactions of tri-coordinated sulfur compounds

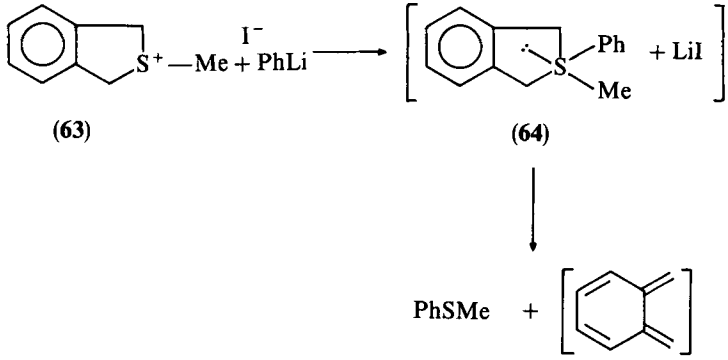
a. Reactions of sulfonium salts with organometallic reagents and other nucleophiles. The reaction of the triphenylsulfonium ion **62** with phenyllithium to form biphenyl and diphenyl sulfide (equation 8) reported by Wittig and Fritz as early as 1952

and the observation made 8 years later by Franzen and Mertz[77] that the phenyl – *n*-butyl exchange takes place when the salt **62** is treated with *n*-butyllithium (equation 9) constitute the first indications of a sulfurane involvement in the reaction of sulfonium salts with organometallics.

$$\underset{\textbf{(62)}}{Ph_3S^+X^-} + PhLi \longrightarrow Ph{-}Ph + Ph_2S \tag{8}$$

$$\underset{\textbf{(62)}}{Ph_3S^+X^-} + n\text{-}BuLi \longrightarrow Ph_2S^+BuX^- + PhLi \tag{9}$$

Bornstein and Supple[78,79] were the first who, in order to explain the results of the reaction of phenyllithium with the sulfonium salt **63**, proposed the formation of the intermediate **64** in which the sulfur atom has an expanded valence shell (equation 10).



(63) **(64)** (10)

The formation of methyl phenyl sulfide was believed to occur by collapse of the sulfurane **64** to give sulfide and *o*-quinodimethane. The latter product was not observed but was believed to have polymerized. Later on, a possibility that the reaction described by Wittig in 1952 proceeds via the tetraphenylsulfurane received support from isotopic tracer experiments of Mislow and coworkers[80]. These experiments demonstrated that all phenyl groups become equivalent on the way to the products described by equation 8. The formation of tetra-*p*-tolylsulfurane **65** in the reaction of tri-*p*-tolylsulfonium fluoroborate **66** with *p*-tolyllithium in THF at – 78 °C was indicated by the fact that the observed coupling products retained the methyl group exclusively in the *para* position (equation 11)[681].

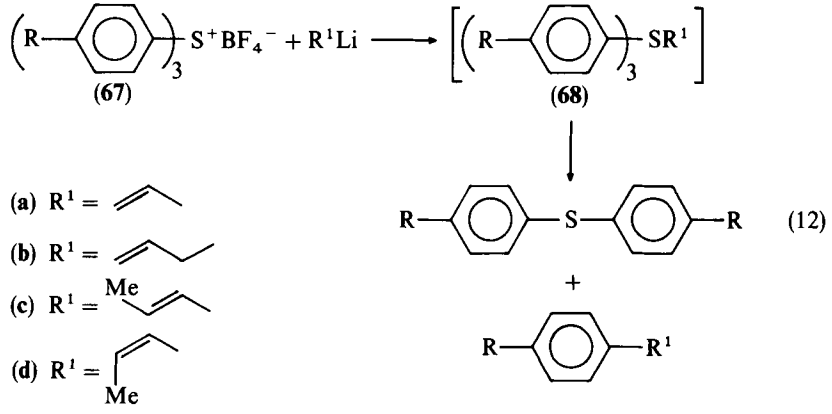
$$\underset{\textbf{(66)}}{(p\text{-Tol})_3S^+BF_4^-} + p\text{-Tol-Li} \longrightarrow \underset{\textbf{(65)}}{[p\text{-Tol}_4S{-}:]} \tag{11}$$

$$\downarrow$$

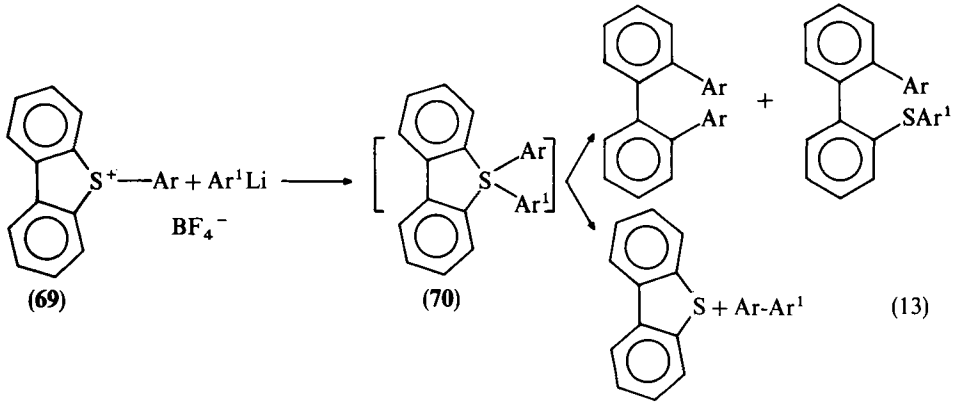
$$p\text{-Tol-S-Tol-}p + Me{-}C_6H_4{-}C_6H_4{-}Me$$

These results are not in full agreement with those of Khim and Oae[82], who found that both *p*, *p*′-ditolyl and *m*, *p*′-ditolyl were formed when the reaction of the sulfonium salt **66** with phenyllithium was carried out in refluxing ether. Many synthetically useful reactions

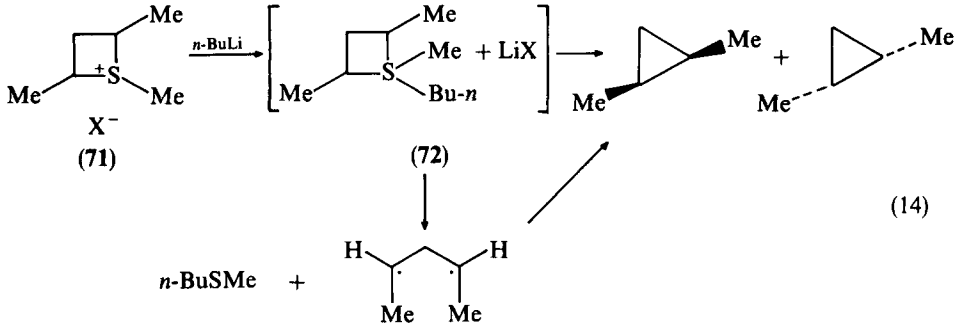
of sulfonium salts with organometallics, in which the formation of sulfuranes as reaction intermediates was proposed, have been discussed in detail in a review by Trost. A few of them are presented in equations 12–14.



(12)

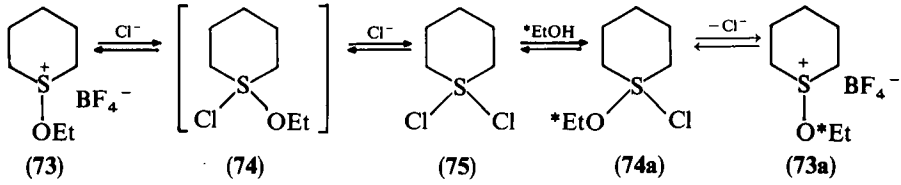


(13)



(14)

It was found[83] that alkoxy exchange in the ethoxysulfonium salt **73** was very slow in neutral ^{14}C-labeled ethanol, but becomes very rapid after addition of catalytic amounts of hydrogen chloride or tetrabutylammonium chloride. To explain this, the mechanism involving the formation of the sulfuranes **74** and **75** was proposed (Scheme 21).



(73) **(74)** **(75)** **(74a)** **(73a)**

SCHEME 21

b. Pyrolysis of sulfonium salts. Triarylsulfonium halides **76** undergo pyrolysis[84] at moderate temperatures to produce theoretical yields of diaryl sulfides and the corresponding aryl halides according to equation 15.

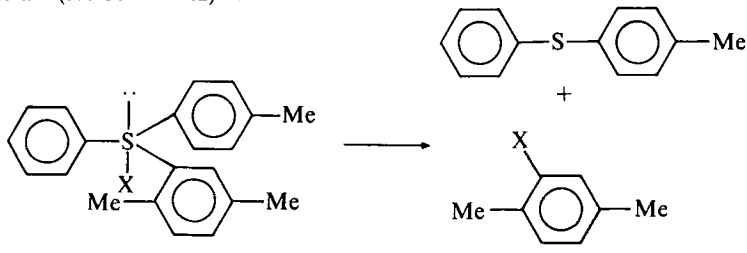
$$\underset{\textbf{(76)}}{Ar^1Ar^2Ar^3S^+X^-} \xrightarrow{250\,^\circ C} Ar^1{-}S{-}Ar^2 + Ar^3X \quad \text{(and other isomers)} \qquad (15)$$

Analysis of the product ratios observed in the pyrolysis of the sulfonium salts **76**, in which at least two different groups are present (see Table 2), clearly indicates that the reaction course cannot be explained on the basis of either an aromatic S_N1 mechanism or a bimolecular aromatic nucleophilic substitution process.

TABLE 2. Pyrolysis of triarylsulfonium halides **76** at 250 °C

	Sulfonium salt **76**				Molar ratio of aryl halides		
No.	Ar^1	Ar^2	Ar^3	X	Ar^1	Ar^2	Ar^3
76a	Ph	*p*-Tol	2,5-$Me_2C_6H_3$	Cl	Ph (1.63)	*p*-Tol (1.00)	2,5-$Me_2C_6H_3$ (5.00)
76b	Ph	*p*-Tol	2,5-$Me_2C_6H_3$	Br	Ph (1.91)	*p*-Tol (1.00)	2,5-$Me_2C_6H_3$ (11.6)
76c	Ph	*p*-Tol	2,5-$Me_2C_6H_3I$	I	Ph (3.40)	*p*-Tol (1.00)	2,5-$Me_2C_6H_3$ (12.4)

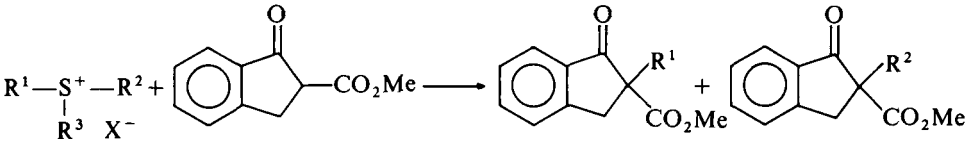
The results can be best explained in terms of the formation and decomposition of a sulfurane intermediate that decomposes preferentially so as to give maximum relief of a steric strain (see Scheme 22)[84].



(76) **(77)** major products

SCHEME 22

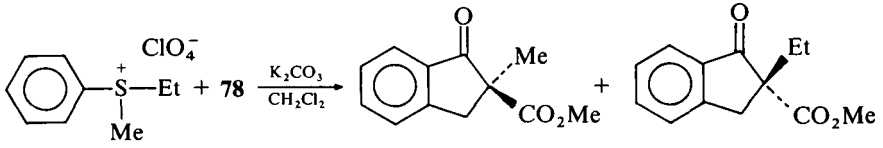
c. Alkylation of β-keto esters with sulfonium salts. Alkylation of the cyclic β-keto ester, 2-(methoxycarbonyl)-1-indanone **78**, with sulfonium salts **79** was found[85] to give a mixture of 2-alkylindanones **80** and **81** in 60–96% yield (Scheme 23). Small amounts of O-alkylation products were also formed.



79 **78** **80** **81**

SCHEME 23

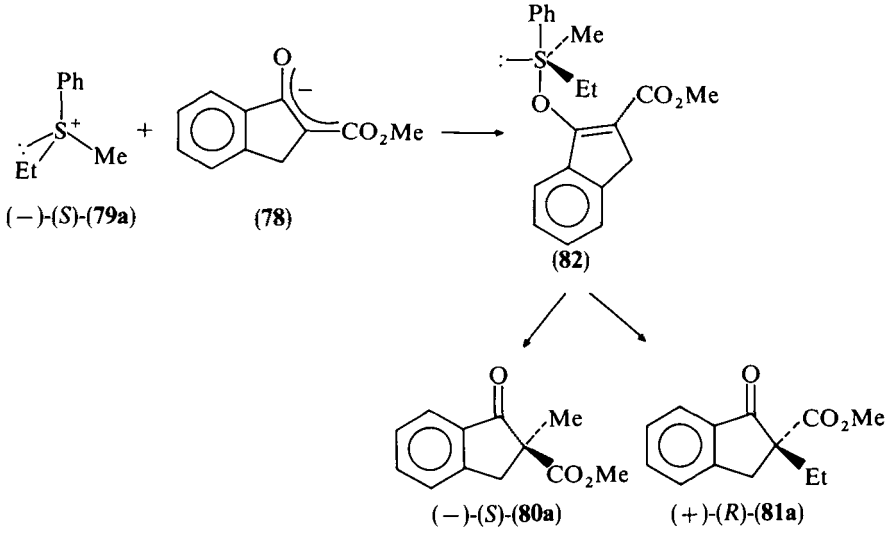
When optically active sulfonium salts **79a** have been used as the alkylation agent, a mixture of the optically active C-alkylation products (−)-**80a** (30%) and (+)-**81a** (44%) was isolated, accompanied by O-methylated products (Scheme 24).



(+)-(*S*)-(**79a**) (−)-(*S*)-(**80a**) (+)-(*R*)-(**81a**)

SCHEME 24

The authors proposed that the reaction proceeds via the sulfurane intermediate **82** (Scheme 25).



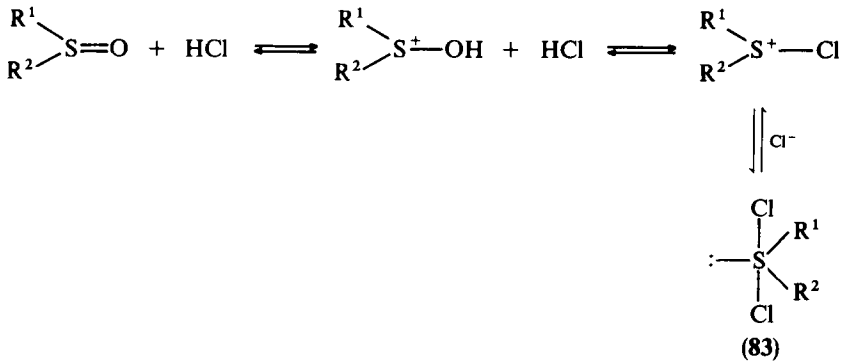
(−)-(*S*)-(**79a**) (**78**) (**82**) (−)-(*S*)-(**80a**) (+)-(*R*)-(**81a**)

SCHEME 25

In the first step the enolate ion derived from **78** attacks the sulfonium sulfur atom to form a sulfurane intermediate **82** in which the methyl group is located in the bottom (*re*) face of the enolate π face SO(=C), therefore C-methylation is taking place preferentially from the *re*face to give the C-methylated product (−)-(*S*)-**80a**. On the other hand C-ethylation takes place preferentially from the top (*si*) face of the sulfurane **82** to yield the C-ethylation product (+)-(*R*)-**81a** with the opposite absolute configuration on the newly created chiral carbon center.

3. Sulfuranes as reactive intermediates in the reactions of sulfinyl derivatives and other tetravalent organosulfur compounds

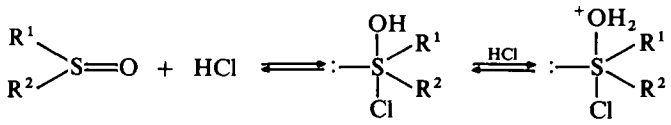
a. Racemization of sulfinyl derivatives. To explain the rapid racemization of optically active sulfoxides in the presence of hydrogen chloride, Mislow and coworkers[86] proposed the mechanism in which the reversible formation of the dichlorosulfurane **83** is the rate-determining step (Scheme 26).



(83)

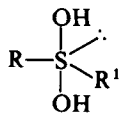
SCHEME 26

However, according to Oae and coworkers[87] the second protonation, which leads to the formation of the protonated hydroxysulfurane intermediate **84** via the hydroxysulfurane **85**, is the slowest step in the process (equation 16).



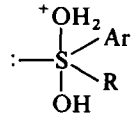
(85) **(84)** (16)

Kwart and Omura suggested[88] the formation of a dihydroxysulfurane intermediate **86** in the hydrochloric acid-catalyzed racemization of sulfoxides.



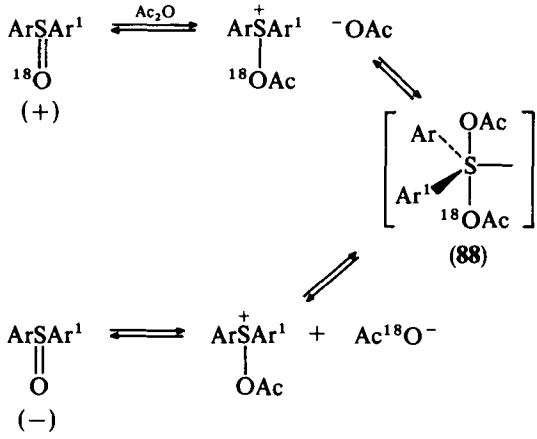
(86)

The involvement of the protonated dihydroxysulfurane intermediate **87** was assumed in the racemization of optically active diarylsulfoxides induced by low concentrations of sulfuric acid[89].



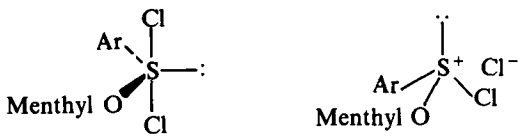
(87)

Detailed studies on the racemization of optically active sulfoxides containing ^{18}O induced by acetic anhydride indicated that the formation of a symmetrical diacyloxysulfurane **88** is responsible for the loss of optical activity and oxygen exchange (Scheme 27)[90,91].



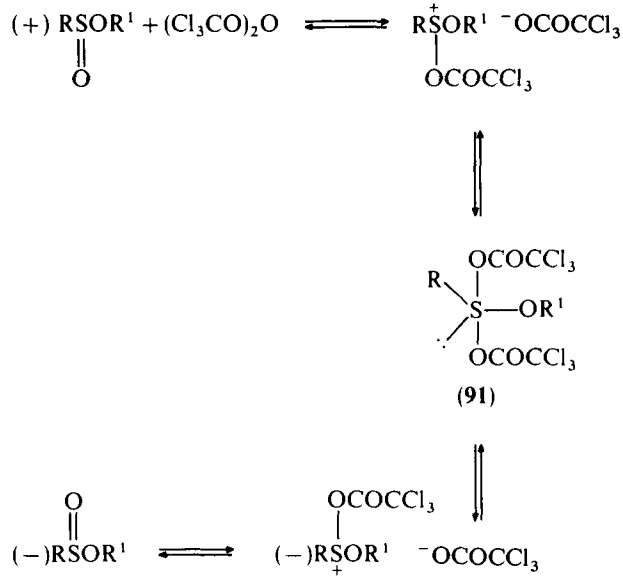
SCHEME 27

Mislow and coworkers[86] suggested that the hydrogen chloride induced epimerization of menthyl arenesulfinates occurs via either a sulfurane intermediate **89** or a sulfonium salt **90**.



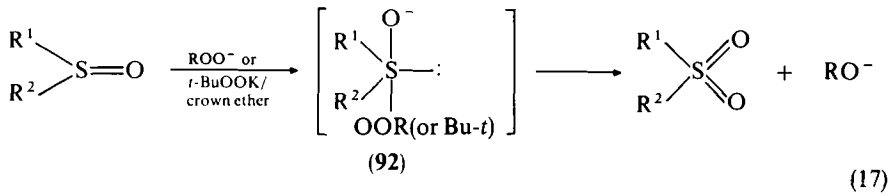
(89) **(90)**

The diacyloxyalkoxysulfurane **91** was proposed to participate in the racemization of optically active sulfinates induced by trichloroacetic acid anhydride (Scheme 28)[92].



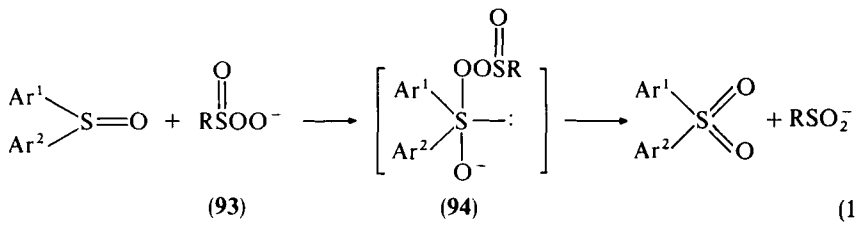
SCHEME 28

b. Oxidation of sulfinyl derivatives. A sulfurane intermediate **92** has been suggested[93] in the oxidation of sulfoxides both with a peroxide anion alone as well as with a potassium *t*-butyl peroxide – crown ether system (equation 17).



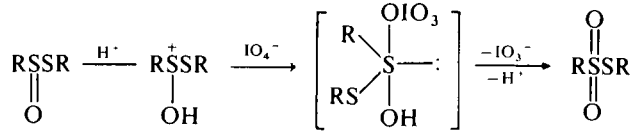
(17)

Oxidation of diaryl sulfoxides with the peroxysulfinate anion **93** most probably also involves a transient sulfurane **94** (equation 18)[94].



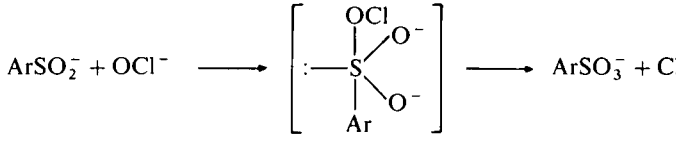
(18)

Similarly, the sulfurane **95** has been proposed as an intermediate in the acid catalyzed periodate oxidation of thiosulfinates **96** (equation 19)[95].



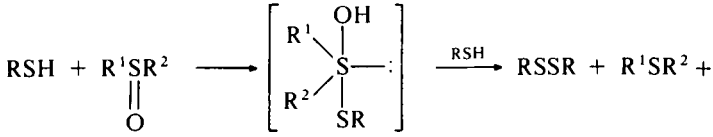
(96) (95) (19)

Arenesulfinates **97** are also oxidized to the corresponding arenesulfonates **98** by hypochlorite. Both HOCl and OCl^- can bring about this conversion, but OCl^- is about 300 times more reactive than HOCl. It has been suggested that the fast oxidation involves a nucleophilic attack by OCl^- on the sulfur of the arenesulfinate **97** to form the sulfurane **99**, which then decomposes rapidly to the arenesulfonate **98** and chloride anion (equation 20).[96]



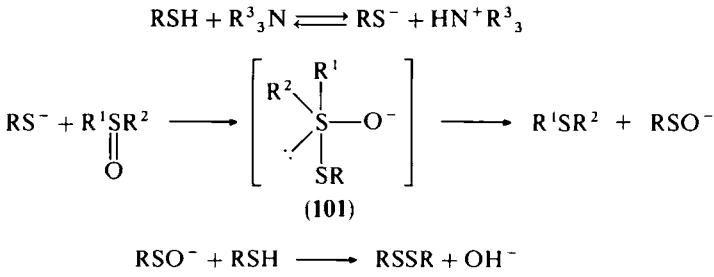
(97) (99) (98) (20)

c. Reduction of sulfinyl derivatives. Thiols are good reducing agents for sulfoxides and tertiary amines catalyze this reaction and increase the yields. According to the proposal of Wallace and Mahon[97], which is based on very detailed kinetic studies, these reactions proceed via the formation in the rate-determining step of a sulfurane **100**, which after reaction with the second molecule of a thiol affords the final products (equation 21).



(100) (21)

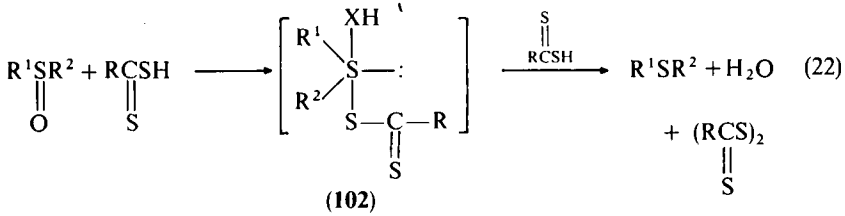
However, Oae pointed out recently[98] that all data on these conversions can be explained assuming the formation of a sulfurane intermediate **101** and its decomposition via ligand coupling (Scheme 29).



(101)

SCHEME 29

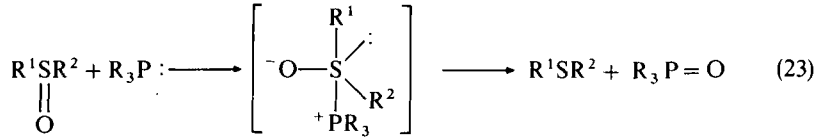
Reduction of sulfoxides and sulfimines by dithiocarboxylic acids was suggested to proceed through a mechanism, analogous to that proposed by Wallace and Mahon[97] involving the sulfurane **102** (equation 22)[99].



(22)

(102)

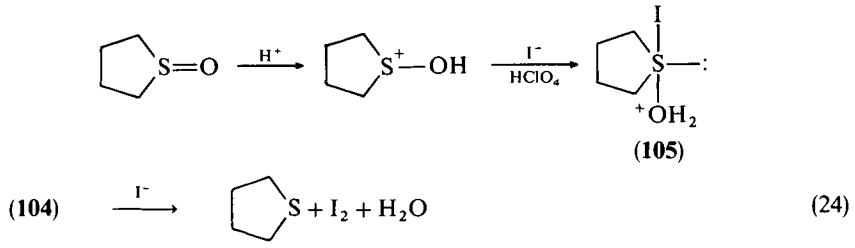
On the other hand, the ligand-coupling reaction mentioned above, which takes place in a sulfurane structure **103**, has been assumed to be responsible for the relatively fast reduction of some sulfoxides by a group of tricoordinate phosphorus compounds (equation 23)[100].



(23)

(103)

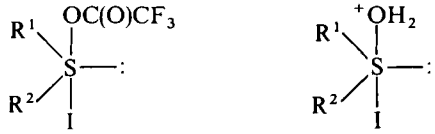
A high reactivity of the five-membered sulfoxide **104** in the reaction with I^- in acidic media (it is reduced 717 times faster than the six-membered analogues and *ca* 180 times faster than ethyl methyl sulfoxide) is believed to result from the formation of a transient sulfurane **105** (equation 24)[101].



(105)

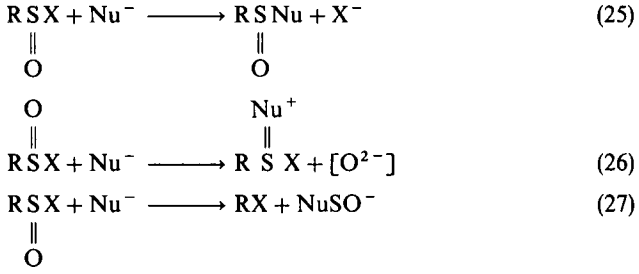
(24)

Formation of sulfuranes **106** and **107** has been suggested to explain the ease of reduction of a variety of sulfoxides with either $(CF_3CO)_2O/NaI$[102] or with RSO_3H/NaI[103].



(106) **(107)**

d. Nucleophilic exchange reactions of sulfinyl derivatives. Nucleophilic exchange reactions of sulfinyl derivatives can take place by three different reaction pathways (equations 25–27):

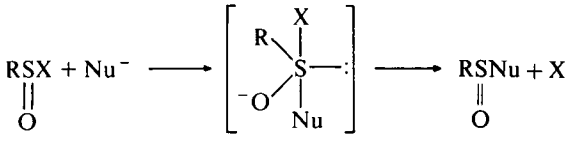


(25)

(26)

(27)

The first two conversions are typical ligand exchange processes and the third one is considered to be ligand coupling reaction. Only in the conversion presented by equation 25 can bond making and bond breaking be synchronous as in the S_N2-type reactions. However, here too, bond making may occur in advance of bond breaking, so that a sulfurane intermediate **108** is present on the route from the substrate to the product (equation 28).



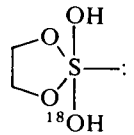
(28)

(108)

In equations 26 and 27 bond making may occur in advance of bond breaking. Therefore, all mechanistic considerations concerning these conversions should take into account the formation of the sulfurane intermediate **108**.

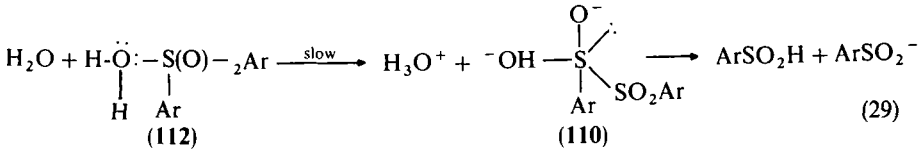
It has long been debated whether sulfuranes are actually formed in the nucleophilic substitution at the sulfinyl sulfur atom (equation 25). Detection of some sulfuranes by spectroscopic methods and especially the isolation of stable sulfuranes strongly supported a view that these conversions also occur with an intermediate **108** present on the reaction coordinate[1b,3,8,106].

The kinetic data, including the ^{18}O tracer experiments, on the S—O bond cleavage in the acid-catalyzed hydrolysis of ethylene sulfite also fit the formation of a sulfurane **109**. However, this could be so short-lived that there is no chance for ^{18}O exchange with water[104].

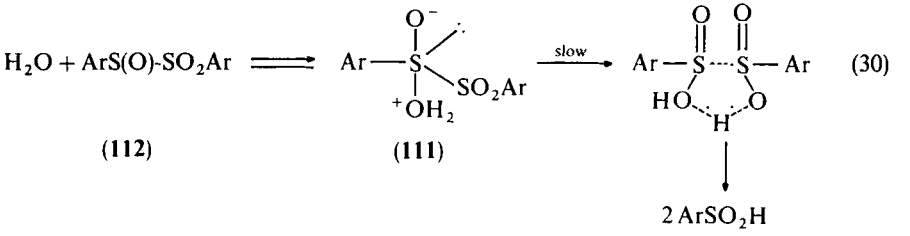


(109)

Formation of the sulfurane intermediates **110** and **111** was postulated in order to explain the fact that a proton transfer is part of the rate-determining step of the spontaneous hydrolysis of sulfinylsulfones **112** (equations 29 and 30).

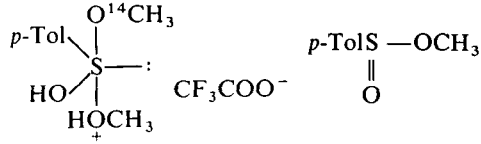


(112) (110) (29)



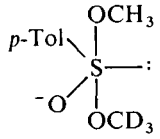
(112) (111) (30)

A mechanism involving a transient sulfurane intermediate **113** has been proposed[106] as an alternative explanation of the fact that optically active *O*-methyl *p*-toluenesulfinate **114** containing ^{14}C in the methoxy group loses its optical rotation practically twice as fast as it loses the radioactive methoxy group upon dissolving in methanol containing trifluoroacetic acid.



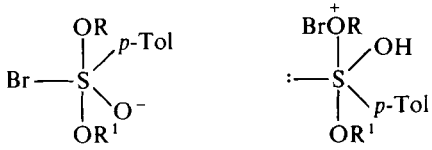
(113) (114)

An analogous sulfurane structure **115** was assumed to be formed during the acetate-catalyzed exchange of $[^2H_3]$ methanol in the sulfinate **114**[107].

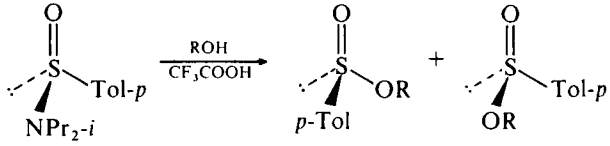


(115)

A completely nonstereoselective NBS-catalyzed isopropanolysis of optically active *O*-alkyl *p*-toluenesulfinates suggests that sulfuranes **116** and **117** are formed as intermediates in the exchange step of the reaction[108].

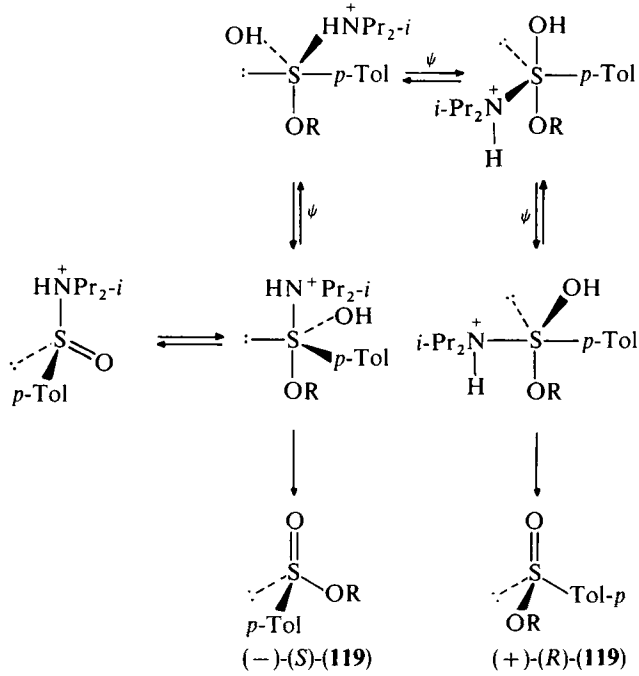


(116) (117)



(+)-(*S*)-(**118**) (−)-(*S*)-(**119**) (+)-(*R*)-(**119**) (31)

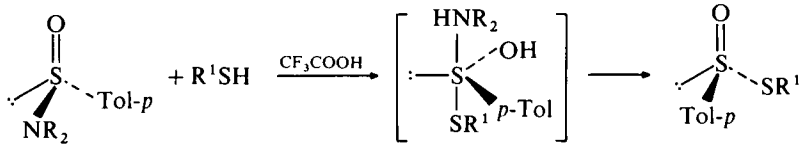
The retention of configuration, which is sometimes observed in the acid-catalyzed alcoholysis of optically active *N,N*-diisopropyl *p*-toluenesulfinamide **118** (equation 31), has been attributed to the formation of sulfurane intermediates that undergo rapid pseudorotation (Scheme 30)[109].



(−)-(*S*)-(**119**) (+)-(*R*)-(**119**)

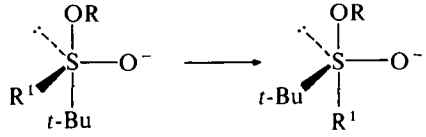
SCHEME 30

Similarly, formation of a sulfurane **120** and its pseudorotation have been proposed to explain the differences observed in stereoselectivity during the acid-catalyzed displacement of sulfinamides **118** by thiols (equation 32)[110].



(+)-(*S*)-(**118**) (**120**) (32)

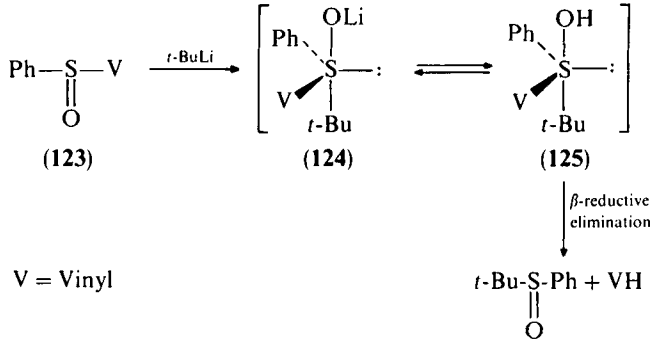
Retention of configuration observed in the reaction of either nonbranched alkanesulfinates with hindered organometallic reagents or sulfinates containing sterically demanding substituents at the sulfinyl sulfur atom with nonhindered organometallics can be most reasonably explained by assuming the formation of a sulfurane intermediate **121** directly or via pseudorotations of a sulfurane **122** (equation 33)[111].



(33)

(122) **(121)**

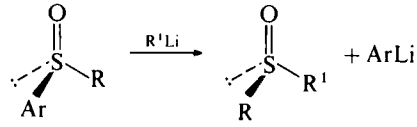
Stereospecific reductive desulfurization of vinyl sulfoxides **123** with *t*-butyllithium and an internal proton source has been suggested[112] to proceed through the direct protonation of a sulfurane intermediate **124** which affords a new sulfurane **125**. Decomposition of the latter gives the final products (Scheme 31).



(123) **(124)** **(125)**

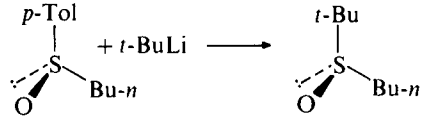
SCHEME 31

Aryl alkyl sulfoxides were found[113] to undergo facile ligand-exchange reactions upon treatment with organolithium reagents to give dialkyl sulfoxides with complete inversion of configuration at the sulfinyl sulfur atom (equation 34).



(34)

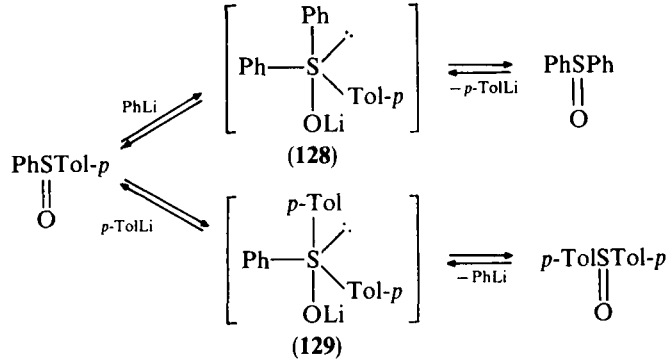
However, it was recently found[114] that the stereochemistry of this reaction is strongly dependent on the reaction conditions. Thus, for example, the reaction between *p*-tolyl *n*-butyl sulfoxide **126** and *t*-butyllithium afforded *n*-butyl *t*-butyl sulfoxide **127** with predominant retention of configuration at the sulfinyl sulfur atom (equation 35).



(35)

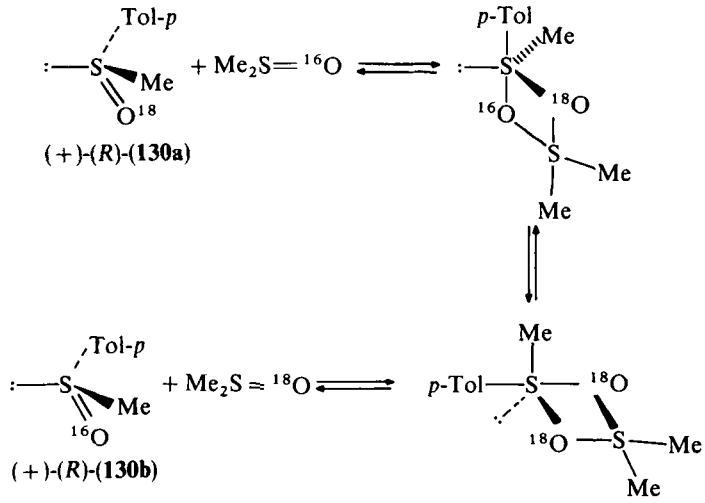
(+)-(*R*)-(**126**) (−)-(*R*)-(**127**)

It is obvious that such a stereochemical outcome requires the formation of a sulfurane intermediate. The mechanism involving formation of sulfuranes **128** and **129** has also been proposed[8] to explain the fact that diaryl sulfoxides undergo a facile ligand exchange and racemization upon treatment with organolithium reagents (Scheme 32).



SCHEME 32

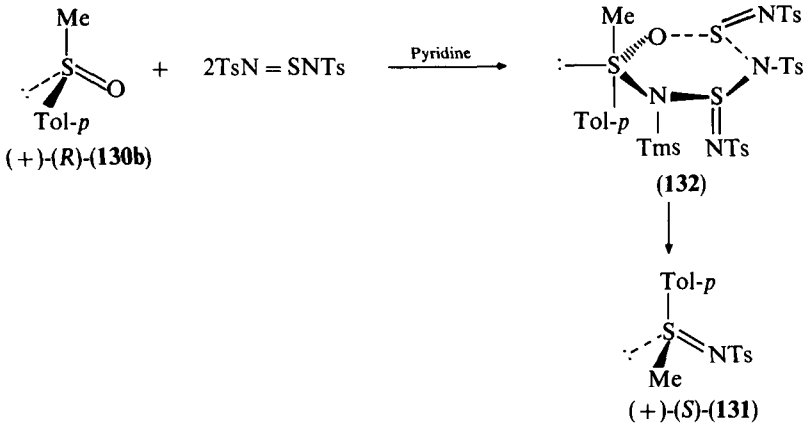
The first example of a nucleophilic exchange reaction, in which the sulfinyl oxygen is a leaving group and a sulfurane is formed as reaction intermediate, constitutes the oxygen exchange reaction between methyl *p*-tolyl sulfoxide labeled with ^{18}O **130** and DMSO (Scheme 33)[115].



SCHEME 33

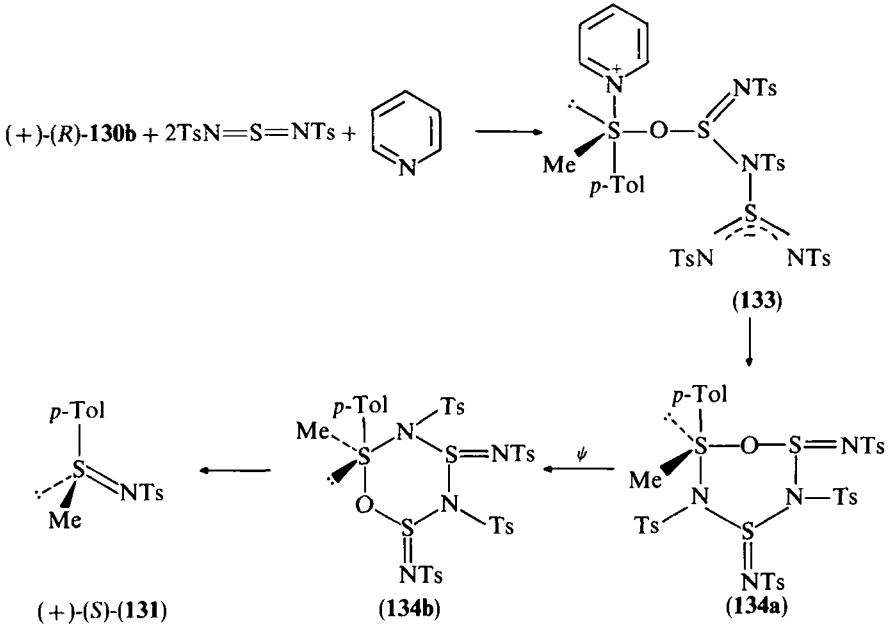
Formation of methyl *p*-tolyl *N*-*p*-tosylsulfimine **131** from the corresponding optically active sulfoxide **130b**, which is second order in the diimine and proceeds with 98%

inversion, was suggested[116] to involve a sulfurane intermediate **132**, in which the entering and leaving groups occupy equatorial positions (Scheme 34).



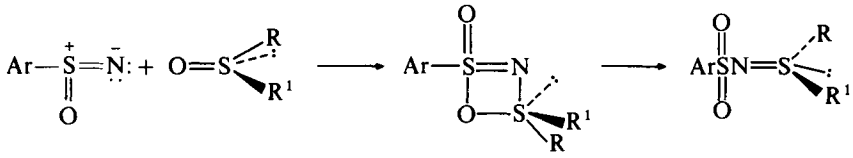
SCHEME 34

An alternative explanation for the observed stereochemical outcome of this reaction was suggested by Kwart and King[117]. According to their proposal, the primarily formed sulfurane intermediate **133**, having the pyridine in an apical position, is converted into the sulfurane structure **134a** with the entering group in an apical position. Pseudorotation in **134a** occurs to place this group in an equatorial position and the leaving group in an apical position before the breakdown of **134b** to the final products (Scheme 35).



SCHEME 35

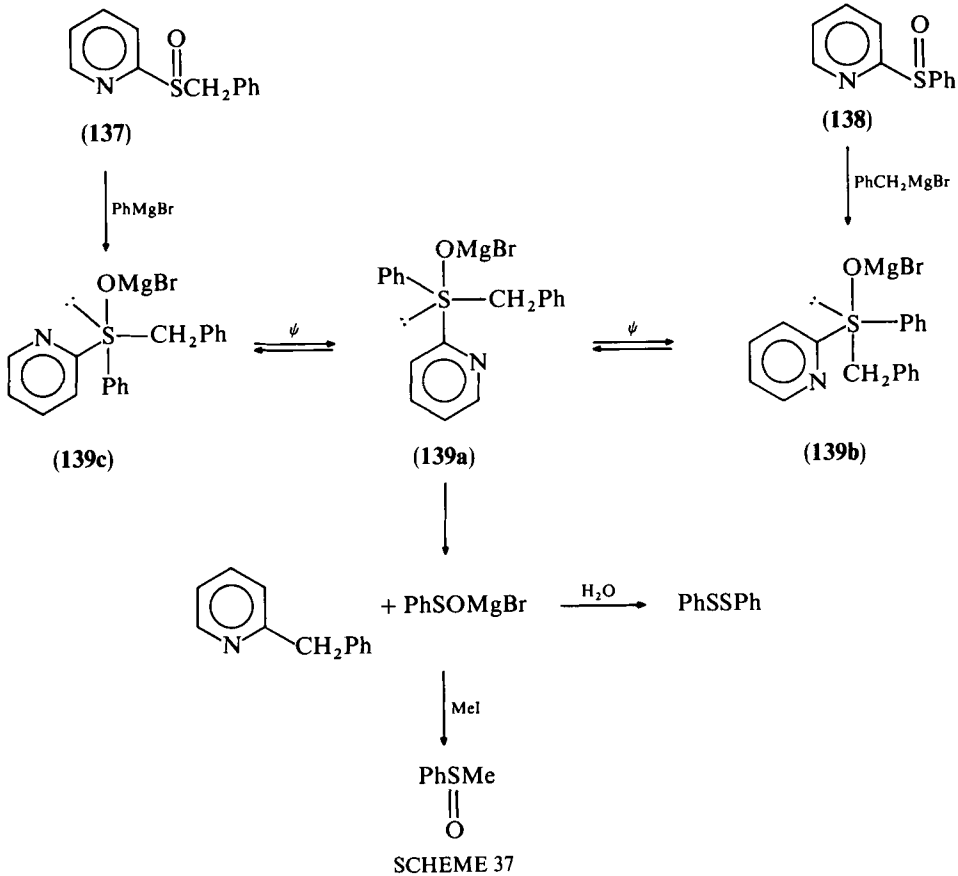
The mechanism shown in Scheme 36 has been proposed[118] for reaction of the sulfinyl nitrene **135** with sulfoxides. The formation of a transient sulfurane **136** accounts satisfactorily for the fact that *N*-arylsulfonylsulfimide has retained configuration with respect to the starting sulfoxide.



(135) **(136)**

SCHEME 36

The third pathway on which the nucleophilic exchange at the sulfinyl sulfur atom can occur and which requires the formation of a sulfurane intermediate is the ligand coupling reaction. The latter process is generally observed in the reactions of sulfoxides bearing heteroaryls with Grignard or organolithium reagents. In the past few years Oae,

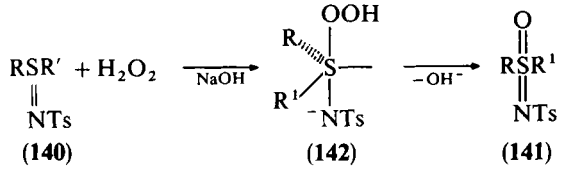


SCHEME 37

Furukawa and their coworkers have found numerous examples of such reactions and summarized their studies in recent excellent reviews[8,119]. Therefore, in this account we will limit our presentation of this reaction pathway to reactions of 2-pyridyl benzyl sulfoxide **137** with phenylmagnesium bromide and 2-pyridyl phenyl sulfoxide **139** with benzylmagnesium chloride (Scheme 37)[120].

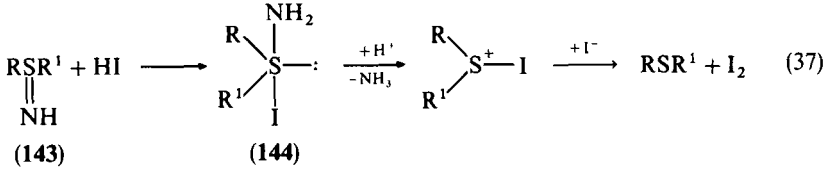
When the sulfoxide **137** was treated with phenylmagnesium bromide at room temperature, 2-benzylpyridine was formed in 98% yield. On the other hand, phenyl 2-pyridyl sulfoxide **138** also affords 2-benzylpyridine in a nearly identical yield upon treatment with benzylmagnesium bromide. These results indicate that both reactions proceed via a common intermediate, the sulfurane **139a**, which is formed via pseudorotation of the primarily formed sulfuranes **139b** and **139c**.

e. Reactions of sulfimines. Oxidation of a series of *N-p*-tosylsulfimines **140** to the corresponding sulfoximines **141** with H_2O_2 in alkaline medium is a nucleophilic oxidation via a sulfurane intermediate **142** (equation 36)[121].

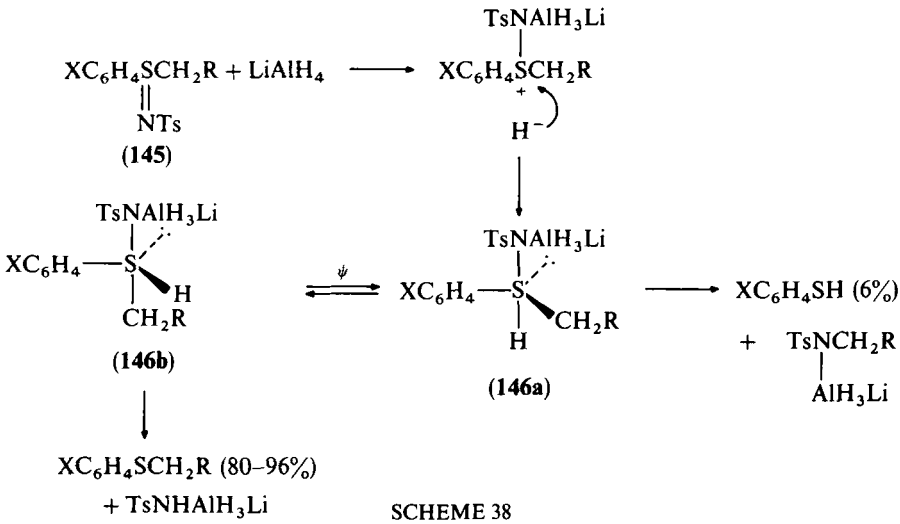


(36)

Acid-catalyzed reduction of the unsubstituted sulfimines **143** by iodide ion also involves a sulfurane intermediate **144** (equation 37)[122].



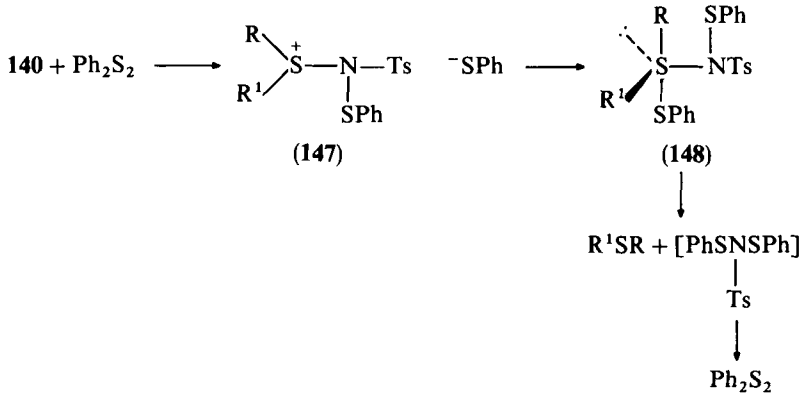
(37)



SCHEME 38

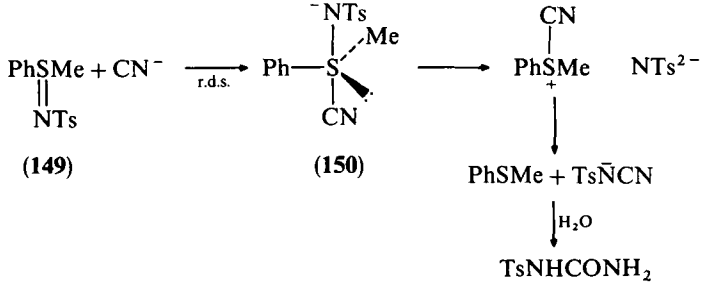
Based on the results of competitive reactivity of a series of aryl alkyl *N*-*p*-tolylsulfonylsulfimines **145** variously substituted in the aromatic ring towards LAH, a mechanism involving sulfurane intermediates **146a** and **146b** has been proposed (Scheme 38)[123].

Reduction of *N*-tosylsulfimines **140** by heating either with elemental sulfur or with diphenyl disulfide was suggested to proceed through initial nucleophilic attack on the azasulfonium salt **147**. This salt rearranges to the sulfurane **148**, which in turn decomposes to the final reaction products (Scheme 39)[119].



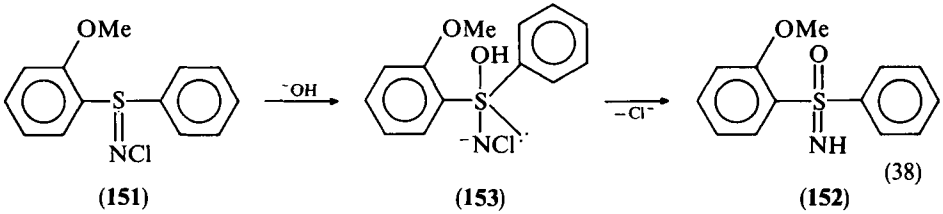
SCHEME 39

Analysis of the kinetic data indicates that the reaction of *N*-*p*-tosyl phenyl methyl sulfimine **149** with cyanide ion in DMSO proceeds by the mechanism shown in Scheme 40, in which the formation of the sulfurane **150** constituted the slowest reaction step[124].



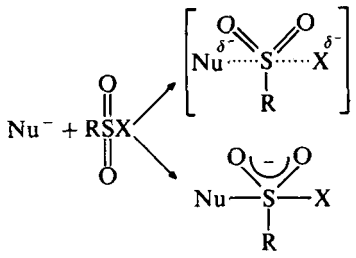
SCHEME 40

Alkaline hydrolysis of *N*-chlorosulfimine **151** formed *in situ* by treatment of the parent unsubstituted sulfimine with NaOCl leads to the quantitative formation of the sulfoximine **152** with retention of configuration at the chiral sulfur atom, with the sulfurane **153** as an intermediate (equation 38).



4. Sulfurane oxides as reactive intermediates

a. Nucleophilic substitution at sulfonyl sulfur. The main question in mechanistic studies on a direct nucleophilic substitution at the sulfonyl center is the timing of bond breaking and bond making. In other words, one should establish whether such reactions are concerted (equation 39a) or stepwise (equation 39b) with a sulfurane oxide **154** present on the reaction pathway.

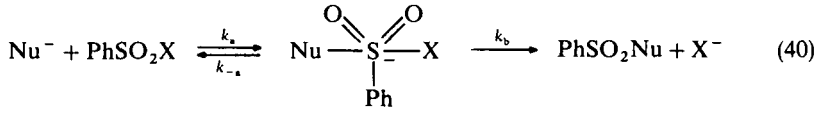


$$Nu^- + RSX \longrightarrow RSO_2Nu + X^- \qquad (39a)$$

$$Nu^- + RSX \longrightarrow RSO_2Nu + X^- \qquad (39b)$$

(154)

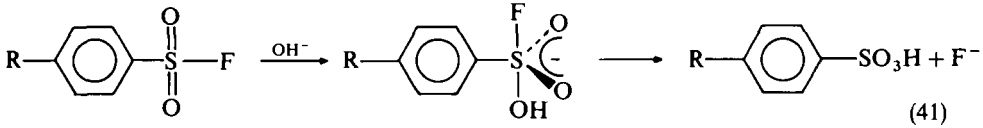
Ciuffarin and coworkers[126], after examination of the effect of a change in the leaving group X (X = F, Cl, Br, I) on the rate of the reaction of $PhSO_2X$ with several nucleophiles, came to the conclusion that the results obtained and especially the fact that K_{PhSO_2F}/K_{PhSO_2Cl} changes dramatically, being 0.22 for OH^- as a nucleophile and 6×10^{-6} for $PhNH_2$, can be most satisfactorily explained by a mechanism involving the sulfurane oxide **154a** as the reaction intermediate (equation 40).



$$Nu^- + PhSO_2X \underset{k_{-a}}{\overset{k_a}{\rightleftharpoons}} Nu{-}S(O)_2{-}X \xrightarrow{k_b} PhSO_2Nu + X^- \qquad (40)$$

(154a)

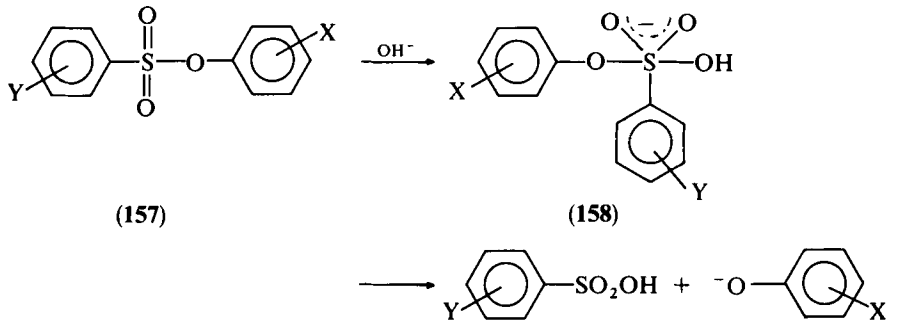
Hydrolysis of arenesulfonyl fluorides **155** (equation 41), studied by the same authors, had a Hammett ρ value of 2.8. This value is very similar to that observed in the nucleophilic substitution at silicon, which is also believed to proceed through the formation of a closely related five-coordinated Si intermediate[126,127].



(155) **(156)** (41)

The large ρ values observed in the hydrolysis of substituted aryl arenesulfonates **157** ($\rho_x = 3.0$ and $\rho_y = 2.4$) also point to the formation of a sulfurane intermediate **158** (equation 42)[128].

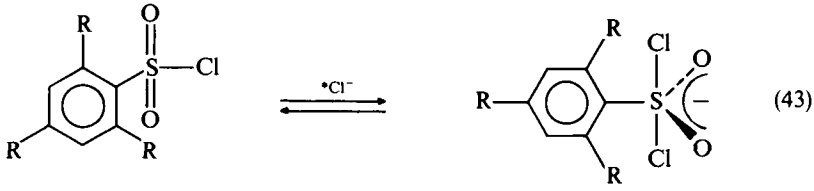
The large α-effect observed in the nucleophilic substitution at the sulfonyl sulfur atom with hydroperoxide anion[129] or with hydrazine[130] can be considered as a strong argument for the transient formation of a sulfurane oxide intermediate in both reactions.



(157) (158)

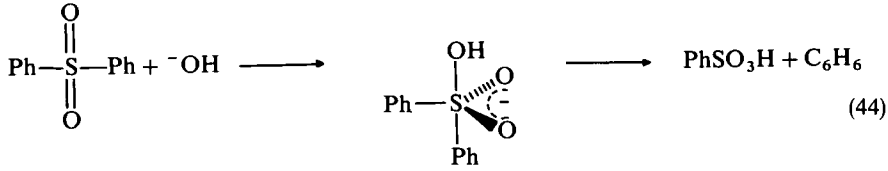
(42)

It was found[131] that the Cl/Cl* exchange in *o,p*-substituted sulfonyl chlorides was accelerated by bulky substituents in the *ortho* position. This was attributed to relief of steric interactions between alkyl groups and the sulfonyl oxygen atoms upon transformation of a tetravalent sulfonyl structure **159** into a trigonal bipyramidal sulfurane oxide intermediate **160** (equation 43).



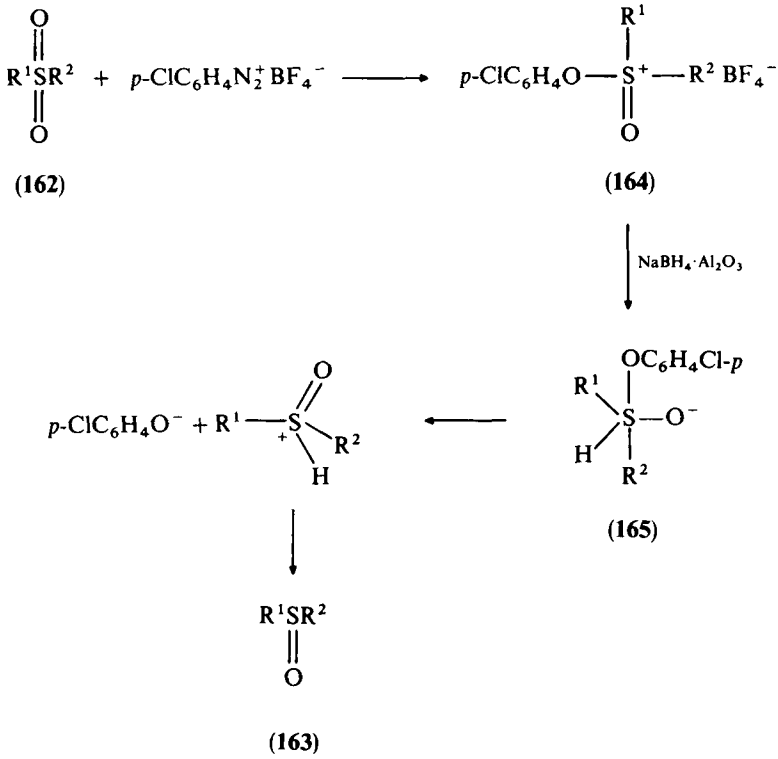
(159) (160) (43)

b. Decomposition of sulfones in the presence of strong inorganic base. Decomposition of diphenyl sulfone by potassium hydroxide was reported[132] as early as 1886 to give biphenyl and phenol. However, Ingold and Jessop[133] showed later that the main initial products of this reaction are benzene and benzenesulfonic acid. To explain this observation, they suggested a mechanism involving the primary attack of hydroxide anion on the sulfonyl sulfur atom to form a sulfurane oxide **161**, which in turn yields the products shown in equation 44.



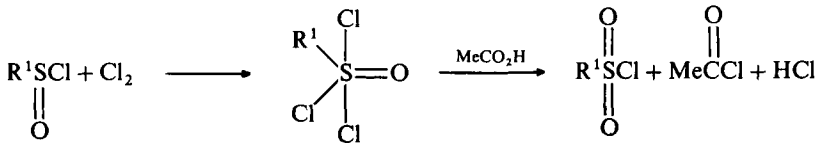
(161) (44)

c. Hydride reduction of arylsulfoxonium salts. A very interesting conversion of sulfones **162** into sulfoxides **163** may occur by a two-state procedure[134]. The first step involves the reaction of a sulfone with 4-chlorobenzenediazonium tetrafluoroborate affording the corresponding aryloxysulfoxonium salt **164**, which upon subsequent reduction with $NaBH_4 \cdot Al_2O_3$ gives the desired sulfoxide. The sulfurane oxide intermediate **165** (Scheme 41) was proposed to be formed in the reduction step.



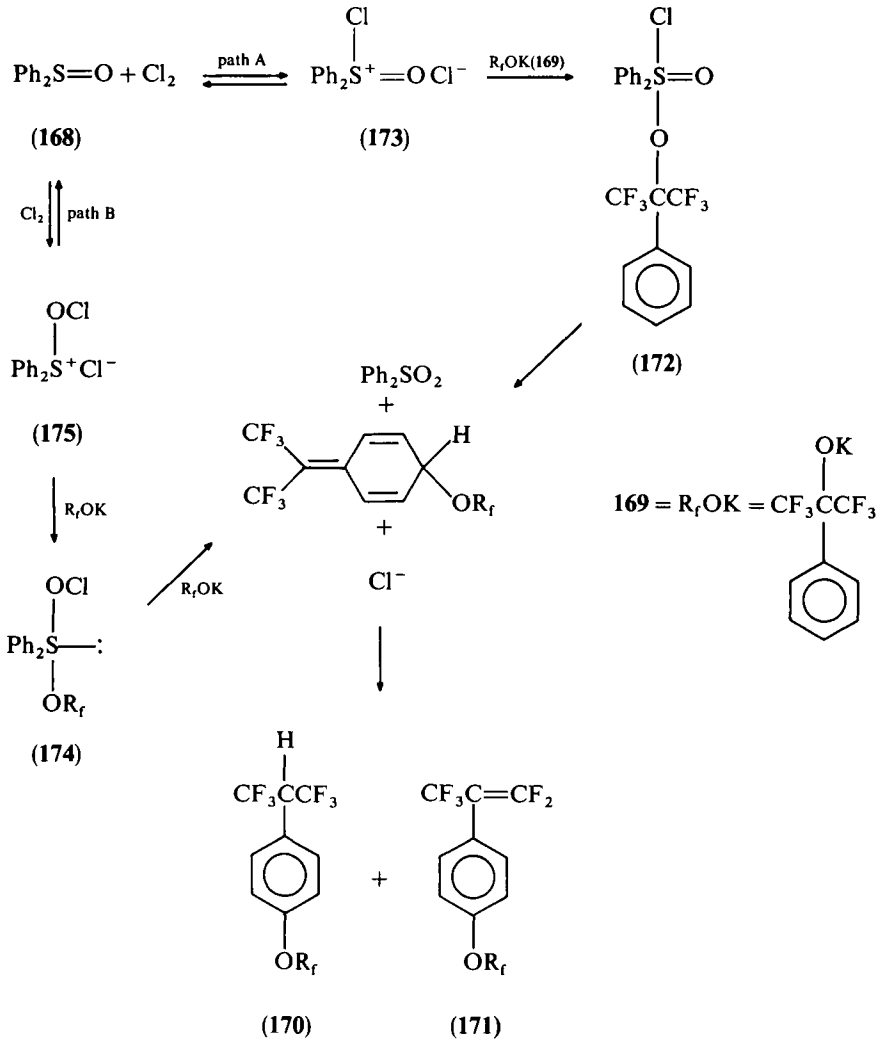
SCHEME 41

d. Chlorine oxidation of sulfinyl derivatives. Douglass and collaborators[135] considered the possibility that sulfinyl chlorides **166** may form a trichlorosulfurane oxide intermediate **167** upon treatment with chlorine in acetic acid. In the second step this intermediate undergoes solvolysis to give sulfonyl chloride as shown in equation 45.



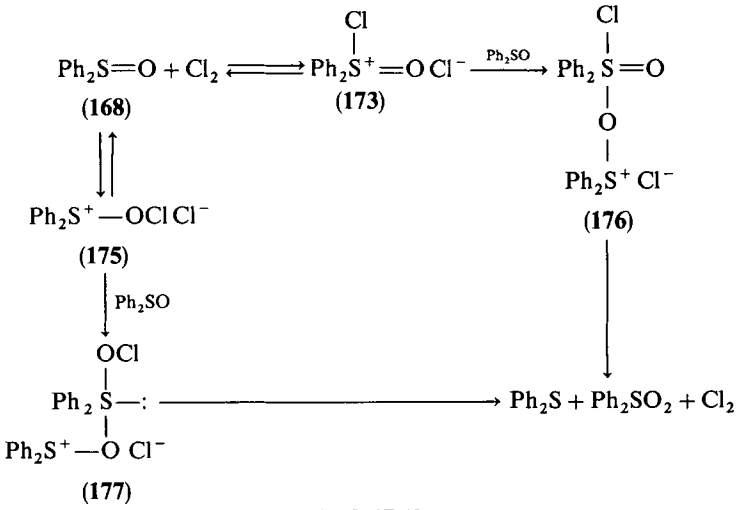
(45)

The chlorine oxidation of diphenyl sulfoxide **168** in the presence of potassium hexafluoro-2-phenylpropoxide-2 **169** to form diphenyl sulfone and ethers **170** and **171** was considered[136] to proceed either through a sulfurane oxide intermediate **172** (Scheme 42) resulting from initial attack of chlorine at the sulfinyl sulfur atom to form a chlorosulfoxonium salt **173** (path A) or through a sulfuranyl hypochlorite intermediate **174** resulting from initial attack of chlorine at the sulfoxide oxygen to form a sulfonium salt **175** (path B)[136].



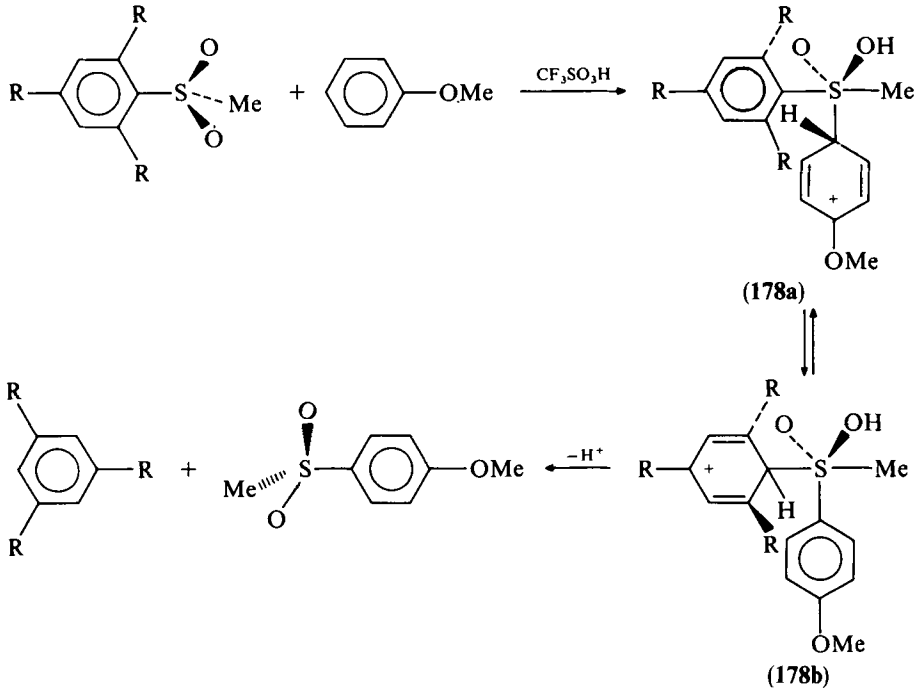
SCHEME 42

Similarly, the chlorine-catalyzed disproportionation of diphenyl sulfoxide **168** was proposed to occur by either of the pathways showed in Scheme 43 involving sulfurane oxide **176** or sulfurane **177** as intermediates.



SCHEME 43

e. Transsulfonylation between aromatic sulfones and arenes. Thermal transsulfonylation between various aromatic sulfones and arenes catalyzed by triflic acid was rationalized[137] in terms of the formation of the sulfurane oxide intermediates **178a** and **178b** (Scheme 44).

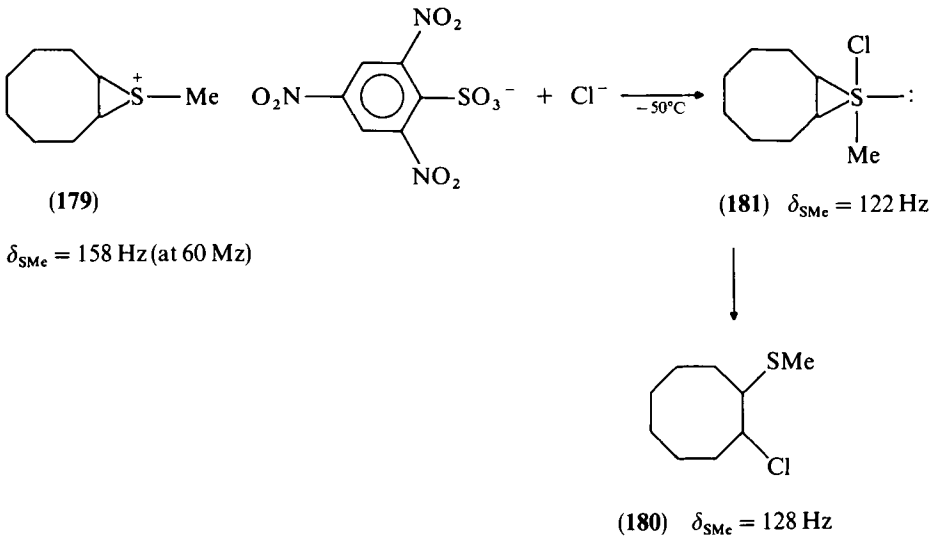


SCHEME 44

B. Sulfuranes Detected by Spectroscopic Methods

Until now only a few reports describing spectroscopic evidence for the formation of sulfurane intermediates have been published. This is mainly due to the fact that the sulfuranes and their oxides formed in various reactions are very reactive species. Therefore, the experiments aimed to detect them have to be carried out at very low temperatures. Because the sulfurane structures are usually generated from strongly polar precursors such as sulfonium salts or sulfoxides, measurements at such low temperatures generate many technical problem connected, for example, with a rapidly decreasing solubility, which in turn leads to a decrease in the observed resolution.

The first ^{1}H-NMR evidence for a distinct sulfurane intermediate was provided in 1969 by Owsley and coworkers[138]. They followed the course of the reaction of cyclooctene-*S*-methylepisulfonium 2,4,6-trinitrobenzenesulfonate **179** with tetraphenylarsonium chloride by the ^{1}H-NMR technique. The position of the *S*-methyl absorption was observed 7 minutes after mixing the substrates at -5 °C. The absorption corresponding to the *S*-methyl group of the substrate **179** at 158 Hz was no longer present and two new singlets (at 122 and 128 Hz) appeared, the second of which was ascribed to the product **180**. Over the next few minutes the product absorption increased while the other peak attributed to the sulfurane intermediate **181** decreased (Scheme 45).



(**179**) $\delta_{SMe} = 158$ Hz (at 60 Mz)

(**181**) $\delta_{SMe} = 122$ Hz

(**180**) $\delta_{SMe} = 128$ Hz

SCHEME 45

The ^{1}H-NMR spectrum of the product of the reaction between methyl phenyl sulfide and *t*-butyl hypochlorite differs significantly from the spectrum of methylphenyl-*t*-butoxysulfonium fluoroborate **182** (Scheme 46)[139]. According to the authors these differences could not be accounted for by ion-pairing phenomena and strongly suggest the formation of a stable sulfurane intermediate **183**.

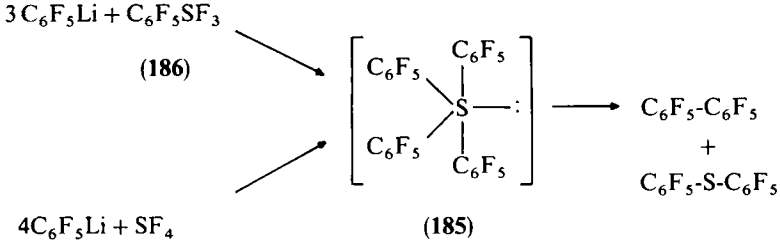
The complexation of chlorine by bis(*p*-fluorophenyl) sulfide in methylene chloride and acetonitrile studied by ^{19}F-NMR and UV spectroscopy indicated clearly that the system is best described as a rapid equilibrium almost completely shifted towards the covalent sulfurane structure **184** (equation 46)[140].

	δ [ppm]		
	Aryl	S—Me	*t*—Bu
(**182**)	8.05 (2H, m) 7.75 (3H, m)	3.42	1.54
(**183**)	8.25 (2H, m) 7.70 (3H, m)	3.78	1.49

SCHEME 46

$$p\text{-}FC_6H_4SC_6H_4F\text{-}p + Cl_2 \rightleftharpoons \underset{(\mathbf{184})}{p\text{-}FC_6H_4(Cl)S(p\text{-}FC_6H_4)Cl} \qquad (46)$$

Sheppard has described[141] the ^{19}F-NMR evidence for the formation of tetra(pentafluorophenyl)sulfurane **185**. This compound can be prepared *in situ* either by the reaction of pentafluorophenyllithium with pentafluorophenylsulfur trifluoride **186** at − 80 °C or from pentafluorophenyllithium with SF_4 at the same temperature (Scheme 47).

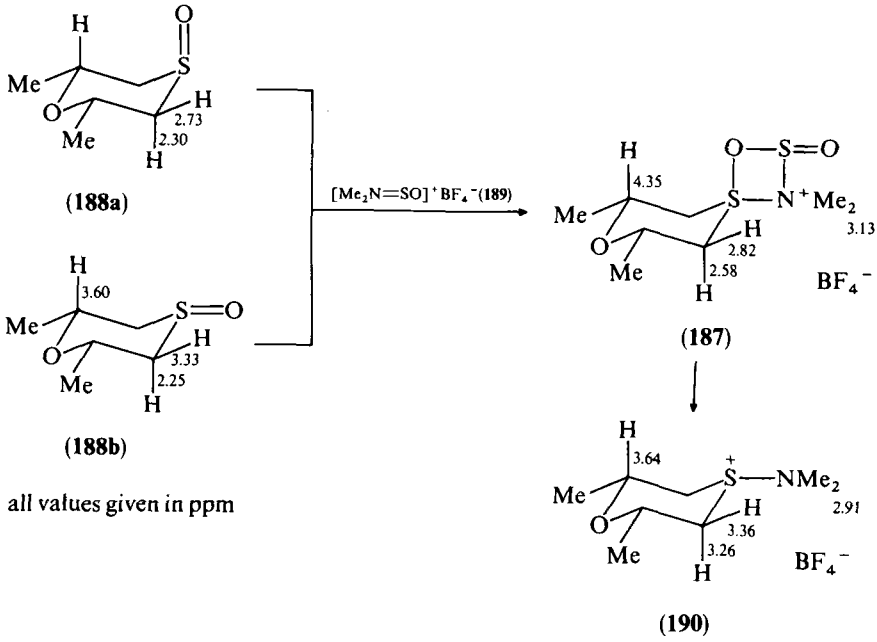


SCHEME 47

When both reactions were followed by the ^{19}F-NMR spectra at about − 40 °C, the ^{19}F resonance corresponding to the S—F fluorines disappeared and a single new set of the pentafluorophenyl resonances was only observed at − 159.1, − 151.9 and − 140.1 ppm in the ratio of 2:1:2 corresponding to the expected pattern for *ortho*, *para* and *meta* fluorines. When the solution was warmed to about 0 °C, peaks at − 161.8, − 151.6 to − 151.0, − 138.3 and − 132.6 to − 132.2 appeared at the expense of the old ones. The new spectrum corresponds exactly to that of a 1:1 mixture of decafluorobiphenyl and bis(pentafluorophenyl)sulfide. Further evidence for the presence of the sulfurane **185** was provided by the UV spectra. The UV absorption at 258 nm (ε ~ 77 000) was ascribed to **185** and was

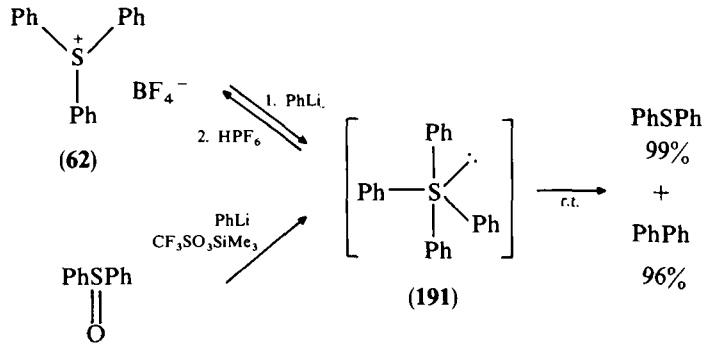
found to be different from those of $(C_6F_5)_2$ (265 and 230 nm) and $(C_6F_5)_2S$ (265, 243 and 231 nm).

The formation of the sulfurane **187** has been detected in the reaction of isomeric 2,6-dimethyl-1,4-oxathiane-4-oxides **188a** and **b** with *N,N*-dimethyl *N*-sulfinyl tetrafluoroborate **189** (Scheme 48). The ^{1}H-NMR spectra showed the presence of the same bicyclic sulfurane intermediate **187** formed from both isomers[142].



SCHEME 48

Very recently, the formation of tetraphenyl sulfurane **191** was detected both in the reaction of triphenylsulfonium tetrafluoroborate **62** with phenyllithium and diphenyl sulfoxide with phenyllithium by a combination of ^{1}H, ^{13}C (at − 105 °C) and of CH-COSY NMR techniques (Scheme 49)[143].



SCHEME 49

TABLE 3. ^{1}H and ^{13}C chemical shifts of **191** at $-105\,^{\circ}C$ (THF-d_8)

Nuclei	Chemical shift, δ		
	ortho	*meta*	*para*
^{1}H	7.27 (d, $J = 7.3$ Hz)	7.13 (d, $J = 7.3$ Hz)	7.05 (t, $J = 7.3$ Hz)
^{13}C	130.1	128.9	127.5

The ^{1}H- and ^{13}C-NMR chemical shifts which can be ascribed to the corresponding *ortho*, *meta* and *para* hydrogens and carbons of the phenyl group in the sulfurane **191** are shown in Table 3[143].

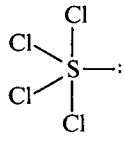
C. Sulfuranes Isolated as Stable Compounds

The last two decades have witnessed growing interest in a search for synthetic procedures which allow preparation and isolation of stable sulfuranes. As a consequence, this class of organosulfur compounds, which for almost eighty years was limited to a few perhalogenated members, has been growing rapidly. At present, the class of stable sulfuranes consists not only of those prepared in order to support theoretical considerations of the nature of bonding and structure, but also of compounds having interesting synthetic applications. In the following section we will describe all the synthetic procedures commonly applied for the preparation of stable sulfuranes and discuss their versatile reactivity.

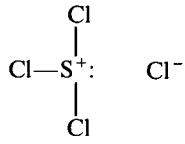
1. Halogenosulfuranes

Halogenosulfuranes constitute the oldest group of hypervalent organosulfur derivatives in which the relatively high chemical stability results from the presence of one or more halogen atoms bonded to the central sulfur atom.

Perhalides of tetravalent sulfur are known only for chlorine and fluorine and, of these, only the fluorine derivatives are stable at room temperature[144]. When sulfur is bonded to another element such as carbon, the compounds of the type RSX_3 (X = Cl or F) exhibit somewhat higher stability. Sulfur dichloride reacts with chlorine in the liquid phase at $-75\,^{\circ}C$ to form the white solid sulfur tetrachloride which starts to decompose at $-30\,^{\circ}C$. Although it is generally accepted that the sulfur dichloride–chlorine adduct is sulfur tetrachloride, its structure was not determined. Most probably, it has a covalent sulfurane structure **192**, however, an ionic form **193** cannot be excluded.



(192)



(193)

Reports concerning sulfur tetrafluoride have appeared since 1905[55,145]. The early literature concerning this compound has been summarized by Brown and Robinson[146] in their paper in which they reported the first unambiguous synthesis and full characterization of sulfur tetrafluoride. Their procedure is based on the direct fluorination of a thin

film of sulfur on a cooled surface (equation 47).

$$S + 2F_2 \longrightarrow SF_4 \tag{47}$$

The most convenient laboratory preparation of sulfur tetrafluoride involves the reaction of sulfur dichloride with dry, finely divided sodium fluoride in acetonitrile (equation 48)[147].

$$3SCl_2 + 4NaF \longrightarrow S_2Cl_2 + SF_4 + 4NaCl \tag{48}$$

By this procedure hundreds of grams of sulfur tetrafluoride can be prepared safely and without the extensive rapid and exothermal hydrolysis by aqueous media at all pH values according to equation 49.

$$SF_4 + H_2O \longrightarrow SOF_2 + 2HF \tag{49}$$

Organic sulfur trichlorides **194** can be obtained by the reaction of chlorine with sulfenyl chlorides (equation 50). They decompose on heating at the temperatures given in Table 4[145,148].

$$RS{-}SR \xrightarrow{Cl_2} 2\,RSCl + Cl_2 \longrightarrow R{-}SCl_3 \tag{50}$$

(194)

TABLE 4. Decomposition temperatures of trichloro sulfuranes $RSCl_3$ **194**

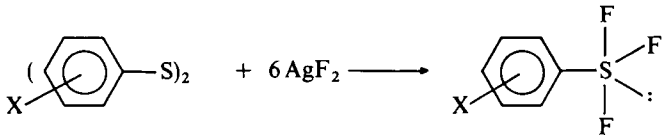
R	Decomposition temperature (°C)
Me	30
Et	11–13
n-Pr	9
i-Pr	< 9
n-Bu	5–10
n-C_5H_{11}	5–8
$ClCH_2$	20–25
Ph	<10

On the other hand, organic sulfur trifluorides are much more stable and can be handled at room temperature without any decomposition for unlimited periods of time in containers made of an inert material such as teflon. Prior to 1960 only CF_3SF_3 (**195**) and $F_3SCF_2SF_3$ (**196**) (isolated as minor products in fluorination reactions of organic sulfides,[149] (and 2, 4-dinitrophenyl sulfur trifluoride **197** prepared from hydrogen fluoride) fluorine and the corresponding disulfide (equation 51)[150] were known.

$$[(2,4\text{-}((NO_2)_2C_6H_3)_2S] \xrightarrow[F_2]{HF} O_2N{-}C_6H_3(NO_2){-}SF_3 \tag{51}$$

(197)

In 1962 Sheppard reported[151] the first general synthesis of arylsulfur trifluorides **198** from aryl disulfides **199** and silver difluoride in 1,1,2-trichloro-1,2,2-trifluoroethane (equation 52).

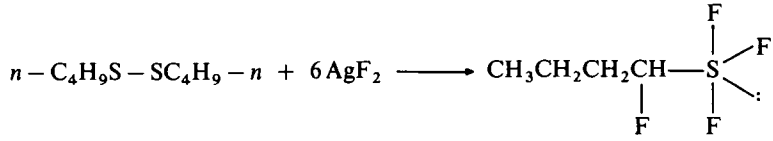


(52)

(199) **(198)**

X	Yield (%)
H	60
p-Me	57
p-NO_2	22
o-NO_2	25

When this procedure was applied for di-*n*-butyl disulfide, α-fluorobutylsulfur trifluoride **200** was isolated in 50% yield (equation 53)[151].



(53)

(200)

In the reaction of carbon disulfide with silver difluoride, trifluoromethyl sulfur trifluoride **195** was formed in 28% yield, together with SF_4, SF_6 and CF_3SF_5 (equation 54)[151].

$$CS_2 + 12AgF_2 \longrightarrow \underset{\textbf{(195)}}{CF_3SF_3} + CF_3SF_5 + SF_4 + SF_6 \qquad (54)$$

When bis-trifluoromethyl-trithiocarbonate **201** was treated with silver fluoride, sulfur trifluoride **195** was produced in much higher yield (47%) and as a sole reaction product (equation 55)[151].

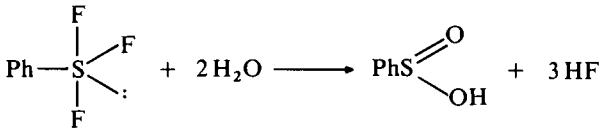
$$\underset{\textbf{(201)}}{CF_3S-\overset{\overset{S}{\|}}{C}-SCF_3} + 7AgF_2 \longrightarrow \underset{\textbf{(195)}}{CF_3SF_3} \qquad (55)$$

Perfluoroisopropylsulfur trifluoride **202** was prepared by addition of sulfur tetrafluoride to hexafluoropropene **203** in the presence of cesium fluoride as a catalyst (equation 56)[152].

$$\underset{\textbf{(203)}}{CF_3CF{=}CF_2} + SF_4 \longrightarrow \underset{\textbf{(202)}}{(CF_3)_2CF{-}SF_3} \qquad (56)$$

The reactions of alkyl and arylsulfur trifluorides were found to be analogous to those of sulfur tetrafluoride. Thus, hydrolysis of phenylsulfur trifluoride **198** (X = H) to benzenesul-

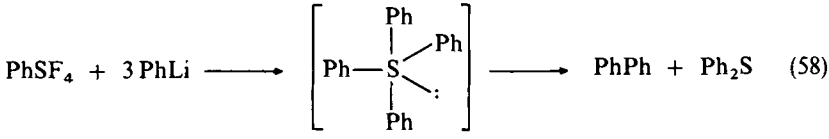
finic acid **204** occurs with almost explosive violence and affords direct chemical proof for its structure (equation 57)[152].



(57)

(198) **(204)**

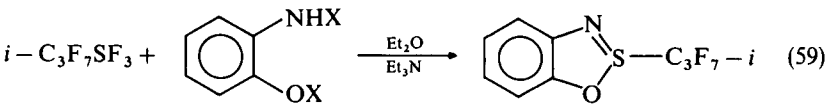
The reaction of this trifluorosulfurane with phenyllithium in ether at − 80°C gives only biphenyl and diphenyl sulfide and none of the products expected from stepwise replacement of the fluorines by phenyl could be detected. There is no doubt that both reaction products arise from the decomposition of tetraphenylsulfurane **191** (equation 58)[153].



(58)

(191)

The reaction of perfluoroisopropylsulfur trifluoride **202** with *o*-aminophenol **205a** in diethyl ether in the presence of triethylamine results in the formation of thioxazole **206** in up to 83% yield (equation 59)[154]. When silylated *o*-aminophenol **205b** in the presence of sodium fluoride was used in this reaction, **206** was obtained in 24% yield only[154].



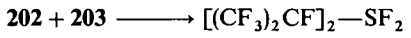
(59)

(202) **(205)** **(206)**

(a) X = H

(b) X = $SiMe_3$

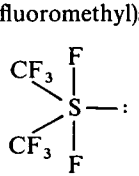
The reaction of **202** with perfluoropropene-1 (**203**) affords the corresponding diperfluoroisopropylsulfur difluoride **207** (equation 60)[155].



(60)

(207)

Another stable compound is di-(trifluoromethyl)sulfur difluoride) **208**[156].



(208)

It has been suggested[157] that an alkoxysulfur trifluoride is an intermediate in the reaction between hydroxylic compounds and SF_4[157a]. This suggestion has later found strong support when α, α, ω-trihydroperfluoroalkoxysulfur trifluorides **209** have been

isolated from the reaction of α, α, ω-trihydroperfluoroalkanols **210** with sulfur tetrafluoride in the presence of alkali metal fluorides at − 60 to 20 °C (equation 61)[157b].

$$H(CF_2)_nCH_2OH + SF_4 \longrightarrow H(CF_2)_nCH_2O-S(F)(F)(:)F \quad (61)$$

(210) **(209)**

(a) $n = 2$, **(b)** $n = 4$, **(c)** $n = 6$

Alkoxysulfur trifluorides **209** are colorless liquids that are readily hydrolyzed by atmospheric moisture to the starting alcohols, hydrogen fluoride and sulfur dioxide (equation 62)[157].

$$\underset{\textbf{(209)}}{H(CF_2)_nCH_2OSF_3} + 2H_2O \longrightarrow \underset{\textbf{(210)}}{H(CF_2)_nCH_2OH} + SO_2 + 3HF \quad (62)$$

The sulfuranes having four (**209b**) and six (**209c**) difluoromethylene groups may be quantitatively converted into fluorides of α, α, ω-trihydroperfluorosulfurous acids (equation 63)[157].

$$\textbf{209b, c} + H_2O \longrightarrow H(CF_2)_nO\overset{\overset{O}{\|}}{S}F + 2HF \quad (63)$$

1, 1, 3-Trihydroperfluoroxysulfur trifluoride **209a** at 20 °C decomposes after a few minutes to unidentified mixtures of products. On the other hand, fluorosulfuranes **209b** and **209c** ($n = 4$ or 6) gradually disproportionate into SF_4 and tetrakis (α, α, ω-trihydroperfluoroalkoxy)sulfuranes **211** via the transient formation of the unstable difluorosulfurane **212** (equations 64 and 65)[157].

$$\textbf{209} \xrightarrow[-SF_4]{} \underset{\textbf{(212)}}{[H(CF_2)_nCH_2O]_2SF_2} \quad (64)$$

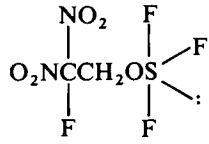
$$2\,\textbf{212} \longrightarrow S(OR)_4(:) \quad R = H(CF_2)_nCH_2- \quad (65)$$

(211)

Lithium 1, 1, 1, 3, 3, 3-hexafluoro-2-propoxide reacts with an excess of sulfur tetrafluoride in 1, 3-dimethoxybenzene to give 1, 1, 1, 3, 3, 3-hexafluoro-2-propoxysulfur trifluoride **213** in 54% yield (equation 66)[158].

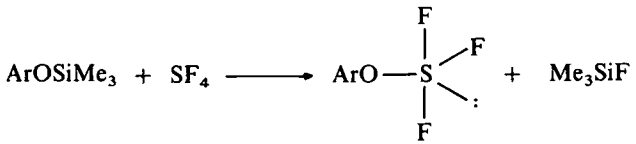
$$(CF_3)_2CHOLi + SF_4 \longrightarrow \underset{\textbf{(213)}}{(CF_3)_2CHO-S(F)(F)(:)F} + LiF \quad (66)$$

It should be noted that 2-fluoro-2,2-dinitroethyoxysulfur trifluoride **214** is also known[159].



(214)

The preparation of phenoxysulfur trifluorides **215** was reported by Sharp and coworkers[160] in 1970. Later they[161] reported properties of these compounds and discussed their structures based on spectroscopic measurements. In all cases, for aryloxysulfur trifluorides **215** prepared according to equation 67 and listed in Table 5, the structure appears to be based on trigonal bipyramidal arrangements about sulfur with the lone electron-pair equational and the fluorines apical.



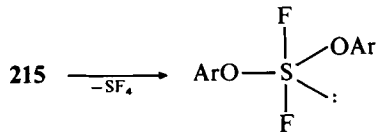
(216) **(215)** (67)

TABLE 5. Aryloxysulfur trifluorides, ArO—SF_3 **215**, prepared in the reaction between aryltrimethylsilyl ether **216** and sulfur tetrafluoride

	Reactions		Products[a]
216	Ar in $ArOSiMe_3$ (mmol)	SF_4 (mmol)	Me_3SiF (mmol)
a	Ph (11)	(13)	(9)
b	*o*-Tol (12)	(16)	(12)
c	*m*-Tol (15.5)	(17)	(16)
d	*p*-Tol (16)	(18)	(16)
e	*o*-FC_6H_4 (16.5)	(20)	(16)
f	*m*-FC_6H_4 (16)	(21)	(16)
g	*p*-FC_6H_4 (17)	(21)	(17)
h	*m*-ClC_6H_6 (15)	(18)	(14)
i	*p*-ClC_6H_4 (13.5)	(16)	(13.5)

a Yields of the $ArOSF_3$ products (**215** a–i) are not given

In some reactions the sulfurane products **215** are too unstable to allow satisfactory analysis and therefore their characterization is based on mass spectroscopic and/or NMR methods. All the aryloxysulfur trifluorides **215** except *o*-$FC_6H_4OSF_3$ (**215e**) and *o*-Tol-OSF_3 (**215b**) slowly disproportionate at room temperature to give bis(aryloxy)sulfur difluorides **217** and SF_4 (equation 68)[161].



(217) (68)

The rate of this reaction increases markedly with temperature. On hydrolysis the aryloxysulfur trifluorides (with the exception of **215b**) give *O*-aryl fluorosulfite **218** (equation 69)[161].

$$\mathbf{215} + H_2O \longrightarrow ArO\underset{\underset{O}{\|}}{S}F + 2HF \qquad (69)$$

(218)

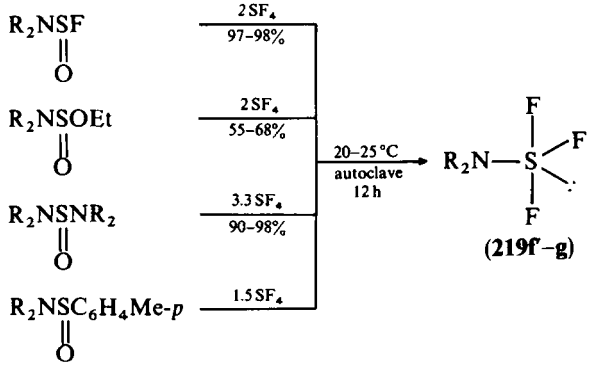
The first aminotrifluorosulfurane, namely dimethylaminosulfur trifluoride **219a**, was prepared in 1964 by treatment of dimethylaminotrimethylsilane **220a** with sulfur tetrafluoride (equation 70)[162,163].

$$R_2NSiMe_3 + SF_4 \longrightarrow R_2N{-}S(F)_3 + FSiMe_3 \qquad (70)$$

(220) **(219)**

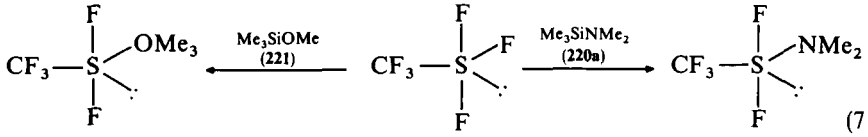
(a) R = Me
(b) R = Et
(c) R = i-Pr
(d) R = Ph
(e) R_2 =
(f) R_2 =
(g) R =
(h) R_2 =
(i) R_2 =
(j) R_2 =
(k) R_2 = Ph—
(l) R_2 =
(m) R_2 =

This reaction allowed the preparation of acyclic[163,166] and cyclic[167,168] analogues of **219a** in high yields. The cyclic aminosulfuranes **219f** and **219g** were also prepared from sulfur tetrafluoride with the appropriate sulfurous acid amides or sulfinamides (Scheme 50)[169].



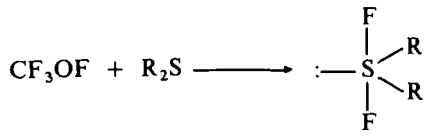
SCHEME 50

Treatment of trifluoromethylsulfur trifluoride **195** with either trimethylmethoxysilane **221** or *N*-trimethylsilyl —*N*,*N*-dimethylamine **220a** yielded, the difluorosulfuranes **222** and **223**, respectively (equation 71)[170].



(223) (195) (222) (71)

A series of alkyl- and aryldifluorosulfuranes **224** was prepared upon treatment of trifluoromethyl hypofluorite **225** with sulfides at low temperatures (equation 72)[171].



(225) (224) (72)

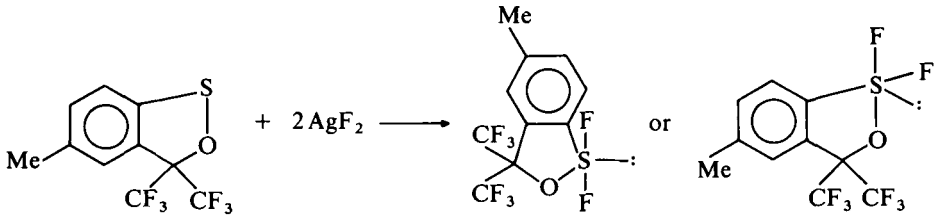
(a) R_2 =  (d) R = C_6F_5

(b) R_2 =  (e) R = *n*-Pr

(c) R_2 =  (f) R = Ph

The sulfuranes **224c** and **224d** are thermally much less stable than **224a** and **224b**. As expected, the sulfuranes **224e** and **224f** are relatively stable[171].

A very stable difluorosulfurane **226** was prepared in 96% yield as shown in equation 73[172].



(227) (226a) (226b) (73)

Since its ^{19}F-NMR spectrum shows nonequivalent trifluoromethyl groups and nonequivalent fluorines bonded to sulfur, the structure **226b** with an apical alkoxy and an equatorial fluorine ligands rather than **226a** was proposed[172].

The reaction of perhalogenoalkanesulfenyl chlorides **228** with HgF_2 or AgF_2 results in a mixture of sulfenyl fluorides and product for which a sulfurane structure **229** was assigned (equation 74)[173].

$$R_fSCl + HgF_2 \text{ or } AgF_2 \longrightarrow \underset{\textbf{(229)}}{R_fS(F)SF_2} + R_fSF \qquad (74)$$

(228)

A number of stable bis(dialkylamino)sulfur difluorides **230a–k** were prepared from dialkylaminotrimethylsilanes **220** and dialkylaminosulfur trifluorides **219** (equation 75)[174–176].

$$R_2NSiMe_3 + R_2^1NSF_3 \longrightarrow \underset{\textbf{(230)}}{(R_2^1N)(R_2N)SF_2} \qquad (75)$$

(220) **(219)**

(a) $R = R^1 = Me$
(b) $R = Me; R^1 = Et$
(c) $R = R^1 = Et$
(d) $R = R^1 = Bu\text{-}n$
(e) $R = R^1 = c\text{-}C_6H_{13}$
(f) $R_2 = R_2^1 =$ 
(g) $R = Et, R_2^1 =$ 
(h) $R_2 =$  $R_2^1 =$ O 
(i) $R_2 = R_2^1 =$ O
(j) $R_2 = Et; R_2^1 =$ O 
(k) $R_2 = Me; R_2^1 =$

Two stable difluorosulfuranes **231** and **232** were prepared starting from trifluoromethylsulfur trifluoride **195** and trimethylsilylated derivatives of methanol or dimethylamine as substrates (equation 76)[170].

$$\underset{\textbf{(195)}}{CF_3SF_3} \xrightarrow[\textbf{221}]{Me_3SiOMe} \underset{\textbf{(231)}}{CF_3S(F)(OMe)} \qquad (76)$$

$$\underset{\textbf{(195)}}{CF_3SF_3} \xrightarrow[\textbf{220a}]{Me_3SiNMe_2} \underset{\textbf{(232)}}{CF_3S(F)(NMe_2)}$$

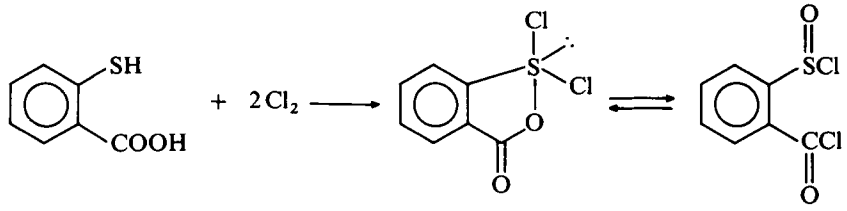
Similarly, some diaryloxysulfur difluorides **217** were isolated from the reaction between sulfur tetrafluoride and aryl trimethylsilyl ethers **216** used in excess (equation 77)[161].

$$SF_4 + 2ArOSiMe_3 \longrightarrow \mathbf{217} \qquad (77)$$

(216)

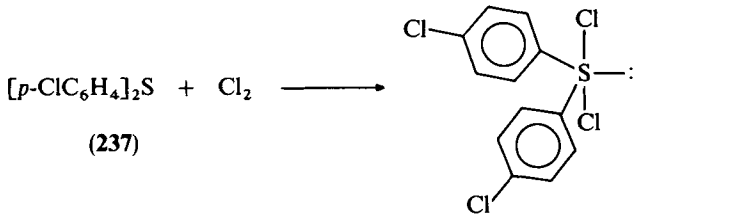
It should be mentioned that the same compounds can be obtained by disproportionation of aryloxysulfur trifluorides **215** (see equation 68)[161].

Dichlorosulfuranes, like sulfur tetrachloride and bisalkyl(or aryl)sulfur dichlorides, are unstable and eliminate chlorine at room temperature in solution. The first report on a dichlorosulfurane **234** appeared as early as 1928[176]. However, some workers questioned these results and proposed the structure **235**, for the product of chlorination of *ortho*-mercaptobenzoic acid **236**[177-179]. A careful analysis of the IR spectrum of the reaction product led Livant and Martin[180] to the conclusion that an equilibrium exists between **234** and **235** (equation 78).



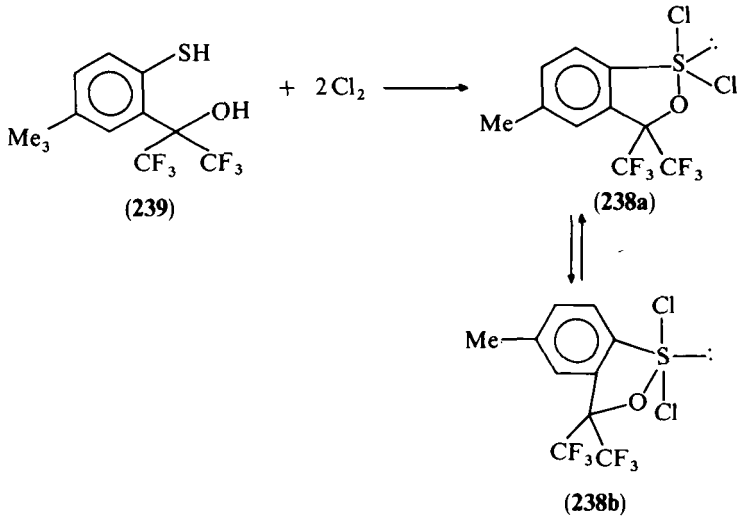
(236) **(234)** **(235)** (78)

In this context it is interesting to note that the crystal structure determination of a chlorine complex (**9**) of bis-(*p*-chlorophenyl)sulfide **237** indicated that it has a trigonal bipyramidal configuration around the sulfur atom (equation 79)[35]. However, the crystals of this sulfurane were quite unstable even in solution, being decomposed by traces of moisture and by lowering the partial pressure of chlorine. In contrast, the dichlorosulfurane **238** is very stable and can be stored as the solid for several months before any appreciable decomposition is observed[172]. It is easily prepared from the mercapto-alcohol **239** in carbon tetrachloride by bubbling chlorine into the solution until no further precipitation of **238** occurs (equation 80)[172]. The X-ray crystal structure determination revealed that in the crystalline form **238** exists as a tetramer with bridging chlorine ligands and an octahedral arrangement of ligands around sulfur. In a solution, based on the ^{1}H-NMR spectrum, a structure **238a** with an apical alkoxy ligand and an equatorial chlorine atom was postulated[172].



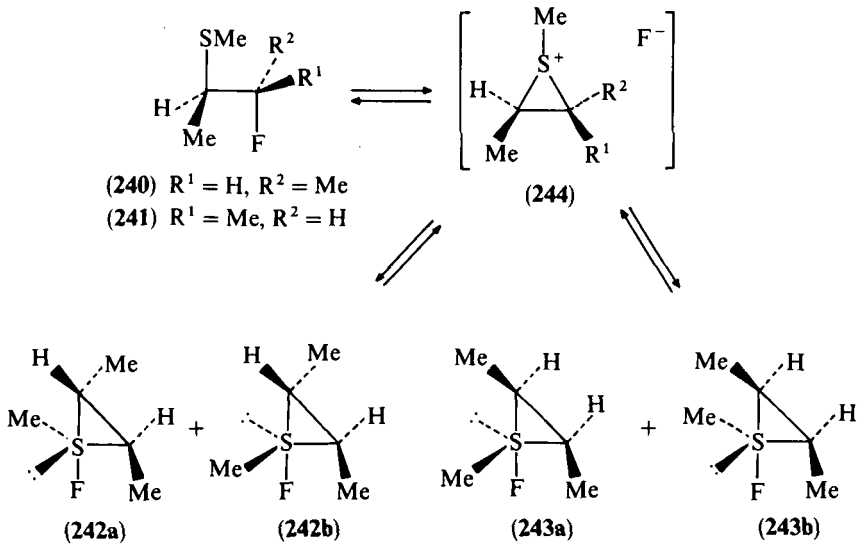
(237) **(9)** (79)

There is only a single report on the isolation of a monofluorosulfurane[181]. This paper described a slow isomerization of *threo*-**240** and *erytheo*-**241** isomers of 2-fluoro-3-methylthiobutane to the corresponding *trans*- and *cis*-1-fluoro-1,2,3-trimethylcyclopropylsulfuranes **242** and **243**, respectively. These conversions occur when chloroform or methylene chloride solutions of either **240** or **241** are kept at room temperature for 3 to 7 days. The



(239) (238a) (238b) (80)

formation of sulfuranes **242** and **243** was considered to be the result of a slow equilibration of the latter with the episulfonium salt **244** (Scheme 51)[181].



(240) $R^1 = H$, $R^2 = Me$
(241) $R^1 = Me$, $R^2 = H$

(244)

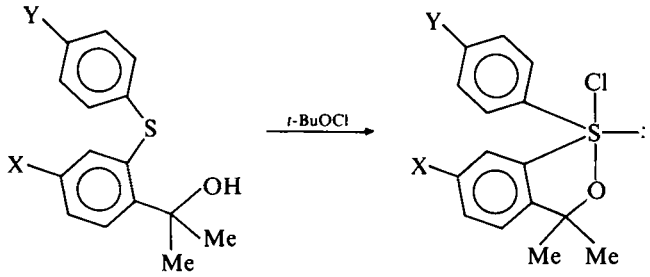
(242a) (242b) (243a) (243b)

SCHEME 51

The fact that both compounds **242** and **243** exhibit two sets of signals in their ^1H- and ^{13}C-NMR spectra was attributed to the formation of a nearly equimolar mixture of the two possible diastereoisomers, epimeric at sulfur. These two epimers could not be separated by preparative GC. However, the mixture of epimers of **242** or **243** analyzed by a GC/MS coupled system gave two separate peaks, both showing m/z 122 (M^+). The two fluorosulfuranes did not show epimerization at sulfur from $-80\,^\circ C$ to $+55\,^\circ C$ in $CDCl_3$.

This fact may be considered as evidence for the proposed structures, since the epimers designated a and b in Scheme 51 differ only in the relative arrangement of the two equatorial substituents and their interchange by a Berry pseudorotation mechanism is thus not possible[181].

Among a few synthetic procedures leading to monochlorosulfuranes, the most general is the oxidation of the appropriate sulfide-alcohols **245** with one equivalent of *t*-butyl hypochlorite[182]. By this procedure the diarylalkoxychlorosulfuranes **246** were obtained in a quantitative yield at room temperature (equation 81).

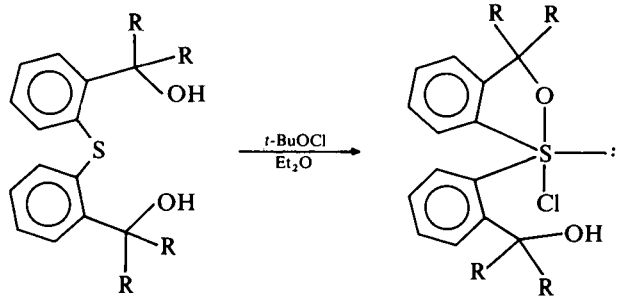


(81)

(245)
(a) X = Y = H
(b) X = Y = Me
(c) X = Cl, Y = H

(246)
(d) X = H, Y = Cl
(e) X = NO_2, Y = H
(f) X = H, Y = NO_2

Chlorosulfuranes **247** and **248** were isolated in yields approaching 90% when the symmetrical sulfide-alcohols **249** and **250** were treated with *t*-butyl hypochlorite in ether (equation 82)[183].



(82)

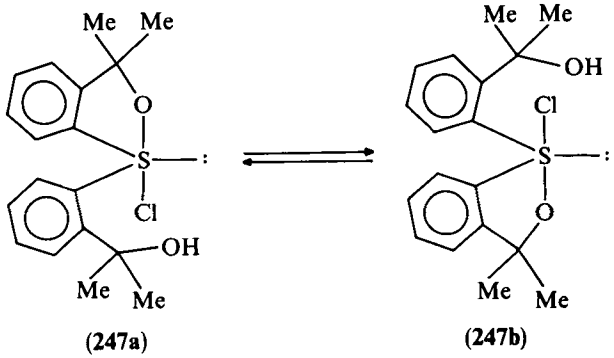
(249) R = Me
(250) R = H

(247) R = Me
(248) R = H

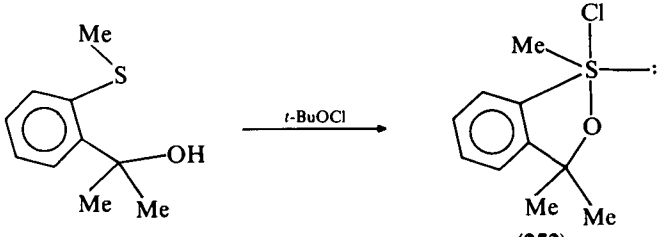
The ^{1}H-NMR spectrum of **247** points to a rapid degenerate intramolecular ligand exchange interconverting **247a** and **247b** (equation 83)[183].

t-Butyl hypochlorite was also effective in the conversion of sulfide-alchohols **251** and **252** to the corresponding chlorosulfuranes **253** and **254** (equation 84 and 85)[182,184].

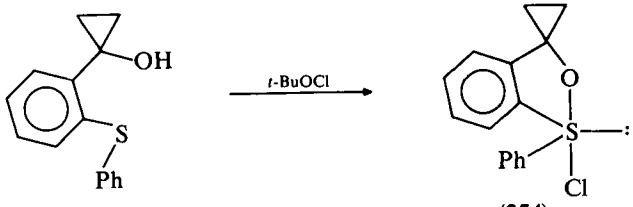
Chlorosulfurane **255** was prepared from a suspension of the potassium salt of *o*-(phenylthio)benzoic acid **256** with an excess of chlorine in carbon tetrachloride (equation 86)[185].



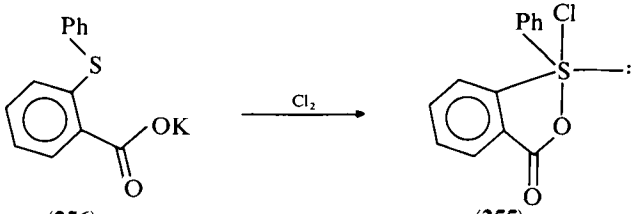
(247a) (247b) (83)



(251) (253) (84)

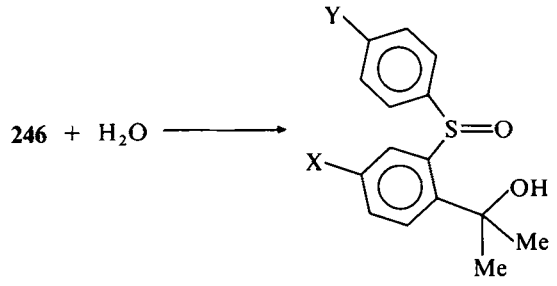


(252) (254) (85)



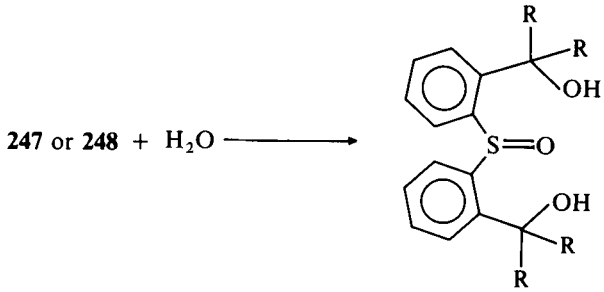
(256) (255) (86)

All monochlorosulfuranes mentioned above can be very easily hydrolyzed to give the corresponding hydroxy-sulfoxides. Thus, the chlorosulfuranes **246** afford quantitatively the corresponding sulfoxides **257** (equation 87), whereas hydrolysis of the chlorosulfuranes **247** and **248** gives the hydroxy-sulfoxides **258** and **259**, respectively (equation 88)[182].



(87)

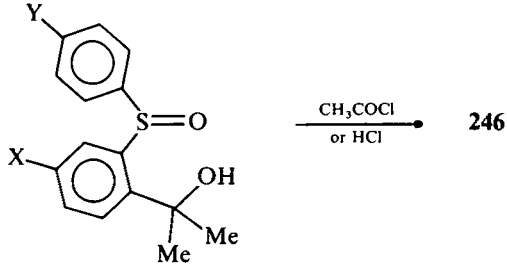
(257)



(88)

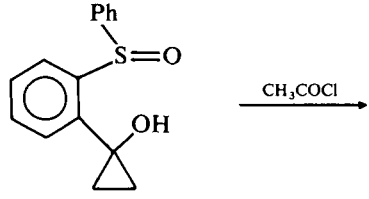
(258) R = Me
(259) R = H

Since the reverse reaction, i.e., elimination of water from the above shown hydroxysulfoxides, is a very clean and fast reaction, the conversion of the appropriately constructed sulfoxide-diols occurring upon treatment with either acetyl chloride or gaseous hydrogen chloride constitutes the second general procedure commonly used for the preparation of monochlorosulfuranes[182,184] as described in equations 89–91.



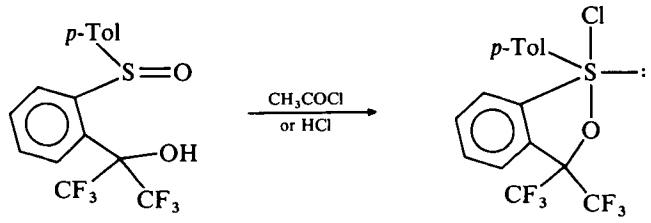
(89)

(257)



(90)

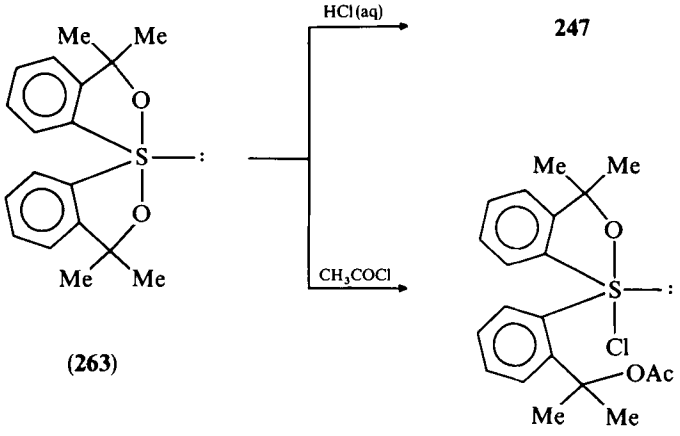
(260)



(91)

(261) (262)

Chlorosulfurane **247** was prepared in 76% yield by shaking a solution of symmetrical spirosulfurane **263** in methylene chloride with concentrated hydrochloric acid while in the reaction with acetyl chloride *O*-acylchlorosulfurane **264** was formed (equation 92)[183].

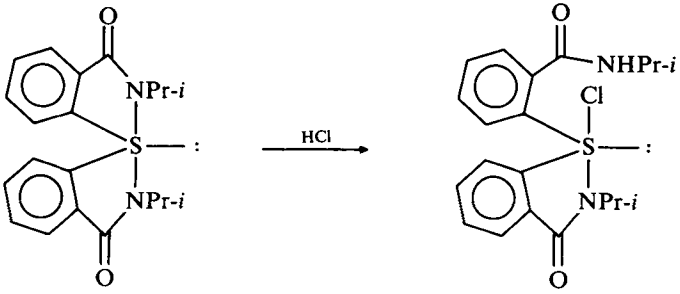


(92)

(263)

(264)

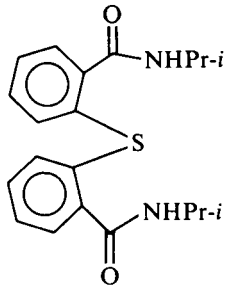
The reaction of diazasulfurane **265** with hydrogen chloride produces the air-stable chloroazasulfurane **266** (equation 93)[186]. Alternatively, this azasulfurane can be prepared by reacting diamide sulfide **267** with *t*-butyl hypochlorite (equation 94) or by treatment of



(93)

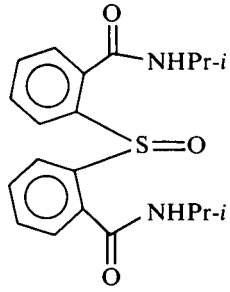
(265) (266)

diamide-sulfoxide **268** with an excess of thionyl chloride (equation 95). In a similar way chloroazasulfurane **269** is produced by the reaction of sulfoxide **270** with thionyl chloride (equation 96). Hydrolysis back to the sulfoxides **268** and **270** is easily accomplished (equations 95 and 96)[186].



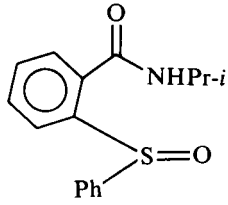
t-BuOCl → **266** (94)

(267)

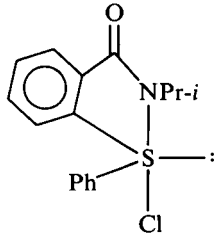


$SOCl_2$ ⇌ aq NaOH **266** (95)

(268)



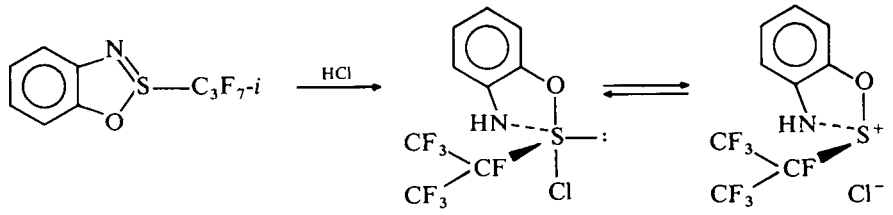
$SOCl_2$ ⇌ aq NaOH



(96)

(270) **(269)**

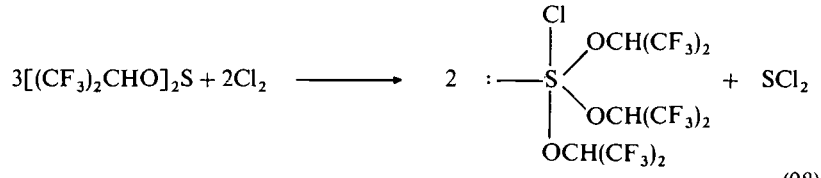
The reaction of thioxazole **206** with an excess of hydrogen chloride at room temperature in ether yielded the chlorosulfurane **271** in equilibrium with an ionic structure **272** (equation 97)[154].



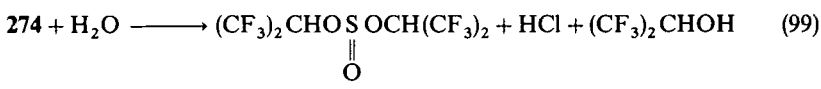
(206) (271) (272)

(97)

The acyclic trialkoxychlorosulfurane **274** has been prepared by the action of elemental chlorine on bis(hexafluoroisopropyl) sulfoxylate **273** in 85% yield as shown in equation 98[187]. This chlorosulfurane is extremely sensitive to moisture and is rapidly hydrolyzed by water (equation 99)[187].



(273) (274) (98)



(275) (99)

It is stable for several days at room temperature but melts with decomposition at 78 °C to form sulfite **275** and hexafluoroisopropyl chloride (equation 100)[187].

$$2(\mathbf{274}) \xrightarrow{\Delta} 2(\mathbf{275}) + (CF_3)_2CHCl \qquad (100)$$

A very interesting reaction of the chlorosulfurane **274** is the transfer of the $(CF_3)_2CHO$ group into a phosphite according to equation 101[187].

$$2(\mathbf{274}) + 2P[OCH(CF_3)_2]_3 \longrightarrow \mathbf{275} + SCl_2 + 2P[OCH(CF_3)_2]_5 \qquad (101)$$

A stable chloro perfluoro sulfurane **276** results from the reaction of $(CF_3)_3COCl$ with trifluoromethanesulfenyl chloride (equation 102)[188].

(276) (102)

276 is hydrolyzed rapidly in the presence of traces of water to give perfluoro *t*-butyl alcohol and trifluoromethanesulfinyl chloride. At room temperature this decomposition is slow, but after 2 h at 80 °C the products shown in equation 103 are formed quantitatively[188].

$$\mathbf{276} \xrightarrow{80\,^{\circ}C} 2CF_3C(=O)CF_3 + CF_3SCF_3 + CF_3Cl \qquad (103)$$

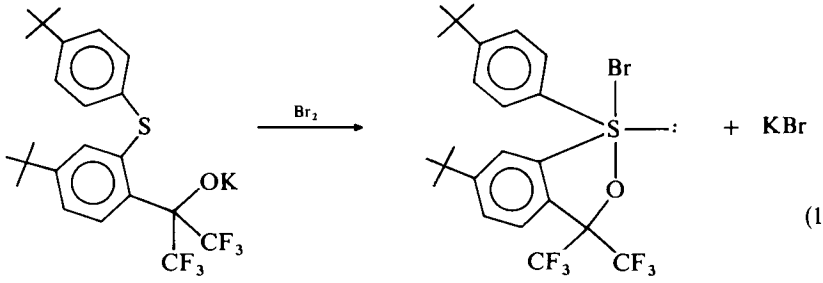
Relatively stable chlorosulfuranes **277** and **278** were isolated from the reaction between CF_3SF_4Cl **279** and silylated *N*,*N*-dimethyl or *N*,*N*-diethylamine **220**. The reaction, in which a reduction of sulfur(VI) to sulfur(IV) occurs, is shown in equation 104[189].

$$CF_3SF_4Cl + 3R_2NSiMe_3 \longrightarrow \underset{\mathbf{(277)}\ R = Me;\ \mathbf{(278)}\ R = Et}{\text{Cl}(CF_3)(NR_2)(R_2N)S{:}} + 3Me_3SiF + [R_2NF] \qquad (104)$$

(279) **(220a,b)**

Both sulfuranes are slowly hydrolyzed to form the corresponding sulfinamides, $CF_3S(O)NR_2$[189].

Till now only three stable bromosulfuranes have been described. Thus, the diarylalkoxybromosulfurane **280** formed in the reaction of the potassium salt of hydroxy-sulfide **281** with bromine was isolated in 13.4% yield (equation 105)[190].



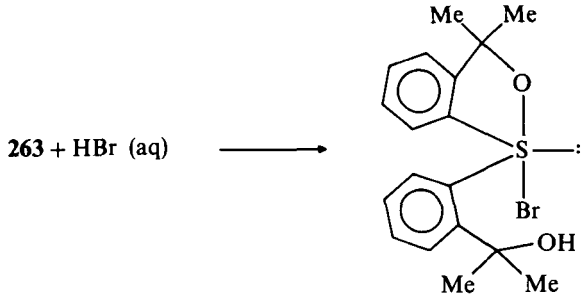
(105)

(281) **(280)**

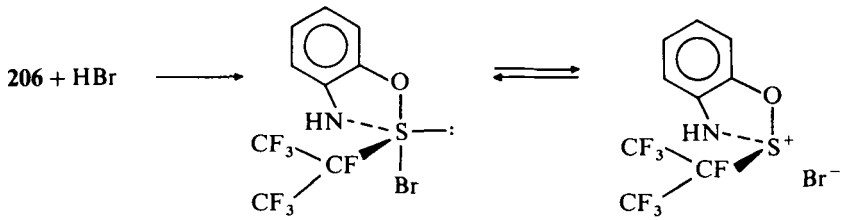
Interestingly, this very stable compound can be easily reduced to the starting sulfide **281** by treatment with bromine in diethyl ether which had been exposed to the air for a period of time. Because the bromosulfurane **280** is considerably more stable in freshly prepared dry ether, it was suggested that traces of peroxides initiate this conversion.

The monocyclic bromosulfurane **282** was prepared from the sulfurane **263** with 16% aqueous hydrobromic acid (equation 106)[190].

The reaction of thioxazole **206** with hydrogen bromide, which proceeds smoothly in diethyl ether even at − 78 °C, gives a mixture consisting of the bromosulfurane **283** and its isomer having probably an ion pair structure **284** (equation 107)[154].



(282) (106)



(283) (284) (107)

2. Alkoxysulfuranes

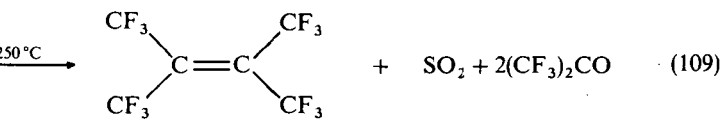
Due to the fact that the electronegativities of oxygen and of chlorine or bromine are very close, sulfurane structures having several alkoxy substituents connected to the central sulfur atom constitute another group of relatively stable species.

The first tetraalkoxysulfurane, namely perfluoropinacol *ortho*-sulfite **3**, was reported as early as 1968[191]. It was formed in the reaction of sulfur dichloride with the disodium derivative of perfluoropinacol **285** in less than 10% yield (equation 108). The formation of **3** in this reaction most probably results from disproportionation of the sulfur(II) to sulfur(IV) and to elementary sulfur.

$$2\ \begin{matrix}(CF_3)_2CO^-Na^+\\ |\\ (CF_3)_2CO^-Na^+\end{matrix} + 2SCl_2 \longrightarrow \mathbf{3} + S + 4NaCl \qquad (108)$$

(285)

Later, the reaction of **285** with an excess of sulfur dichloride and pyridine in ether was found to give **3** in almost 50% yield[24]. **3** has an approximate trigonal–bipyramidal structure. Evidence for an intramolecular ligand exchange process having a $\Delta G^{\#}$ of *ca* 7.5 kcal mol^{-1} at $-100\,^{\circ}C$ has been found in a variable-temperature ^{19}F-NMR study of this compound. The complete pyrolysis of **3** was accomplished by heating it in a sealed tube at 250 °C, according to equation 109[24].



(109)

The perfluorospirosulfurane **1** was obtained as the single reaction product when SF_4 and perfluorobiacetyl were allowed to react in a 1:2 molar ratio during a period of several days at room temperature (equation 110)[19]. Its formation results from the transfer of fluoride from sulfur to carbon.

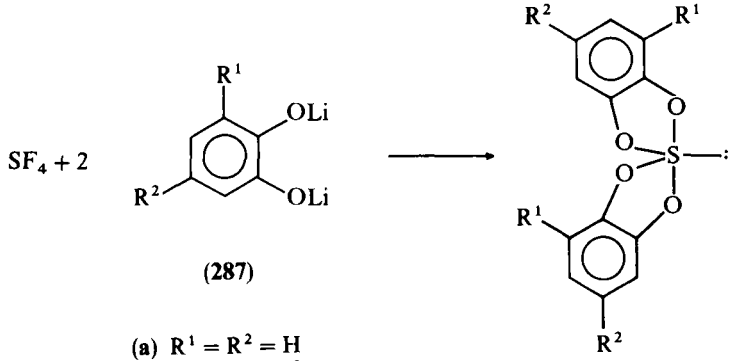
$$SF_4 + 2CF_3C(=O)C(=O)CF_3 \longrightarrow \mathbf{1} \qquad (110)$$

Treatment of more than three moles of phenoxytrimethylsilane with one mole of sulfur tetrafluoride results in the formation of tetraphenyl *ortho*-sulfite **286** (equation 111)[160].

$$SF_4 + 3.4\,PhOSiMe_3 \longrightarrow \mathbf{286} \qquad (111)$$

(286)

By reacting lithium salts of *ortho*-bishydroxyphenols **287** with SF_4 several stable symmetrical tetraoxysulfuranes **288** have been prepared (equation 112)[192].



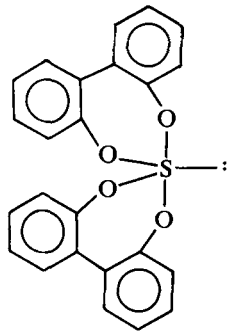
(112)

(287)

(a) $R^1 = R^2 = H$
(b) $R^1 = Me$, $R^2 = H$
(c) $R^1 = R^2 = t\text{-Bu}$

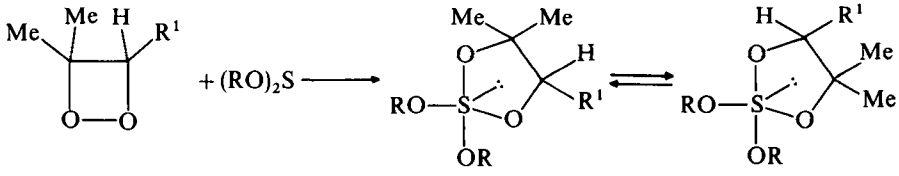
(288)

The sulfurane **289** was also prepared in this way[192].



(289)

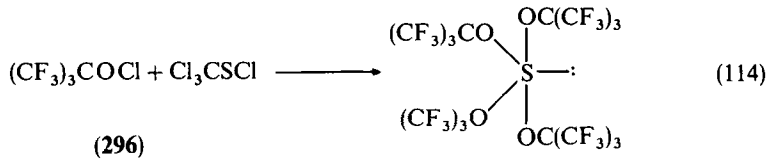
Two tetraalkoxysulfuranes **290** and **291** were synthesized via insertion reaction of the sulfoxylic esters **292** and **293** into the oxygen–oxygen bond in dioxetanes **294** and **295** (equation 113)[193].



(113)

(**294**) $R^1 = H$ (**292**) R = Me (**290**) R = Me, $R^1 = H$
(**295**) R^1 = Me (**293**) R = *n*-Pr (**291**) R = *n*-Pr, $R^1 = H$

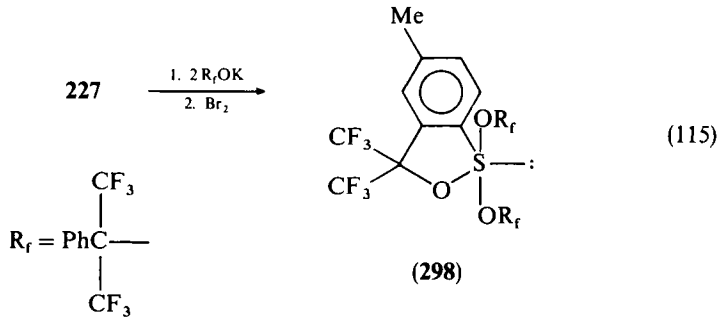
When perfluoro-*t*-butyl hypochlorite **296** was allowed to react with trichloromethanesulfenyl chloride, a white solid melting very sharply at 112 °C was obtained as a sole reaction product. Based on spectroscopic and analytical data the structure of tetraperfluoro-*t*-butoxysulfurane **297** was proposed for the isolated product (equation 114)[187].



(**296**) (**297**) (114)

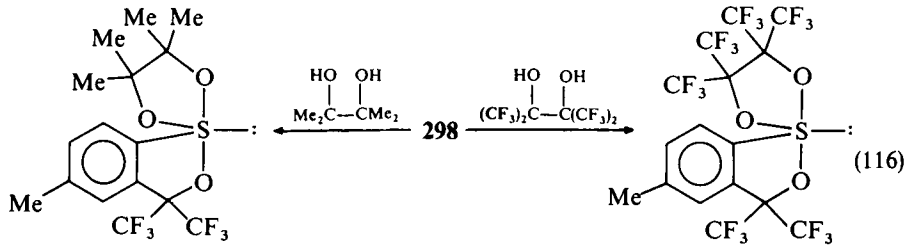
In sharp contrast to other acyclic tetraalkoxysulfuranes, this tetraalkoxysulfurane is very resistant to hydrolysis, most probably due to the steric hindrance around the central sulfur atom[187].

A cyclic sulfenic ester **227** upon treatment with one equivalent of bromine and two equivalents of the potassium salt of hexafluoro-2-phenyl-2-propanol (KOR_F) gives the crystalline sulfurane **298** (equation 115) which appears to exist in a structure with the five-membered ring occupying equatorial positions of a trigonal bypyramid[194].



(**298**) (115)

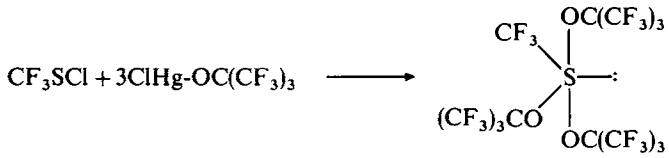
The sulfurane **298** reacts with pinacol to give the spirosulfurane **299** in 63% yield while with perfluoropinacol it affords the spirosulfurane **300** (equation 116)[194].



(116)

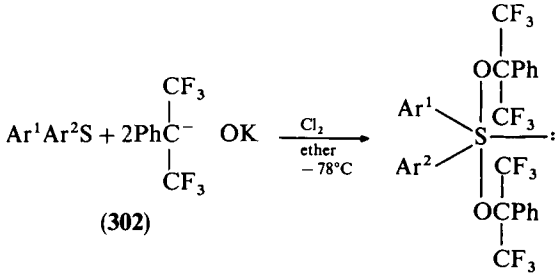
(299) (300)

A different route to tri-perfluoro-*t*-butoxysulfurane **301** involves the reaction of perfluoro-*t*-butoxymercury chloride with trifluoromethanesulfenyl chloride[195].



(301)

Of the many known dialkoxysulfuranes, usually two alkoxy substituents occupy apical positions in a trigonal bypiramidal structure. The first member of this group of sulfuranes, the dialkoxydiphenylsulfurane **5a**, was prepared by treatment of an ethereal solution of the potassium salt of hexafluoro-2-phenyl-2-propanol (R_fOH) and diphenyl sulfide **302a** with chlorine at $-78\,^{\circ}C$ (equation 117)[194]. Later, this procedure was found to be general and improved by the use of bromine instead of chlorine[197].



(117)

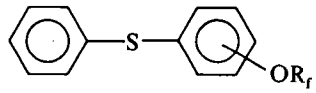
(302)

(5)

(a) $Ar^1 = Ar^2 = Ph$
(b) $Ar^1 = p\text{-}FC_6H_4$, $Ar^2 = Ph$
(c) $Ar^1 = m\text{-}FC_6H_4$, $Ar^2 = Ph$
(d) $Ar^1 = Ar^2 = p\text{-}t\text{-}BuC_6H_4$
(e) $Ar^1 = Ar^2 = p\text{-}MeOC_6H_4$

The crystalline **5a** is stable indefinitely at room temperature. However, it is hydrolyzed very rapidly to give diphenyl sulfoxide and R_fOH. The replacement of alkoxy ligands in **5** by other alcohols, acid and other active hydrogen compounds is also rapid, providing a basis for several synthetic applications. Some of them will be described in another part of this chapter. Upon boiling an ethereal solution of **5a** for several days or heating molten **5a**

at 120 °C for a few hours, the formation of one equivalent of R_fOH and one equivalent of a mixture of the alkoxylation products **303** is observed.

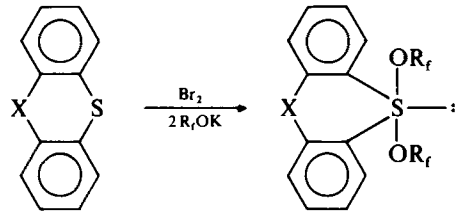


(303) (a) *ortho*
(b) *meta*
(c) *para*

When the sulfurane **5a** is boiled in ether for several days in the presence of phenyl trifluoromethyl sulfide, the products shown in equation 118 are detected[197].

$$\mathbf{5a} + Et_2O \xrightarrow{PhSCF_3} MeCH(OEt)(OR_f) + R_fOH + Ph_2S \qquad (118)$$

Bromination of thianthrene **304**, *N*-phenylphenothiazine **305** and phenoxathiin **306** in the presence of R_fOK results in the formation of dialkoxysulfuranes **307–309** (equation 119)[198].

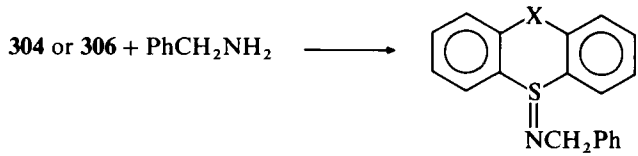


(119)

(304) X = S
(305) X = NPh
(306) X = O

(307) X = S
(308) X = O
(309) X = O

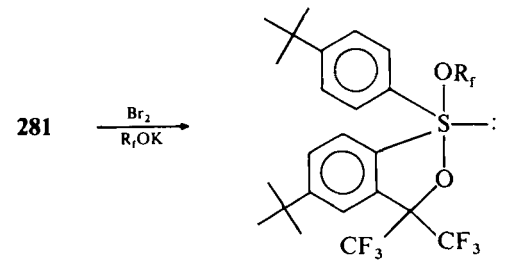
The sulfuranes **307** and **309** are stable at ambient temperatures. However, the sulfurane **308** is unstable under these conditions and is partially destroyed in CCl_4 solution after 2 days at room temperature. The reaction of sulfuranes **307** or **309** with benzylamine gives the corresponding sulfimine **310** or **311** (equation 120).



(120)

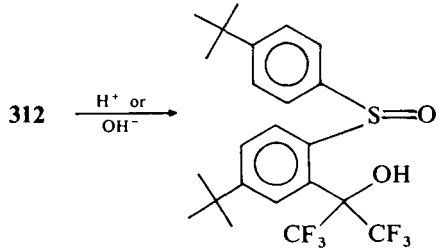
(310) X = S
(311) X = O

Treatment of the sulfide **281** with bromine and potassium hexafluoro-2-phenyl-2-propoxide (KOR_f) in THF gives the hexafluorocumyloxysulfurane **312** in 75% yield (by ^{19}F NMR; 46% isolated) (equation 121)[189].



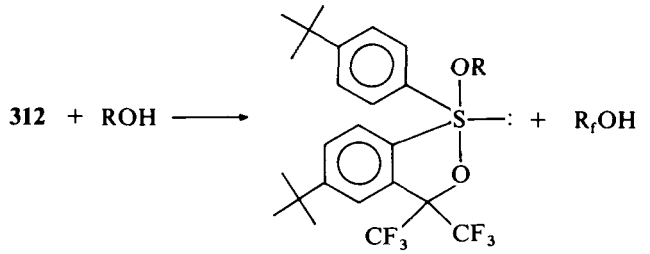
(312) (121)

As expected, rapid hydrolysis of this sulfurane occurs in a chloroform solution upon treatment with either aqueous base or acid and gives the sulfoxide-alcohol **313** (equation 122)[189].



(313) (122)

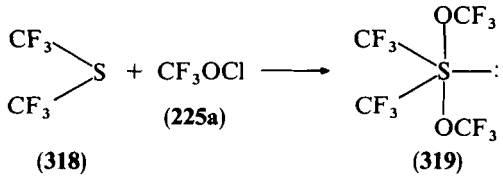
When alcohols are added to the sulfurane **312**, alkoxyperfluorocumyloxysulfuranes **314–317** are formed quantitatively (^{19}F–NMR assay). The crystalline *t*-butoxysulfurane **317** was isolated in 56% yield. However, the methoxy, benzyloxy and cyclohexyl analogues were not isolated (equation 123)[189].



(123)

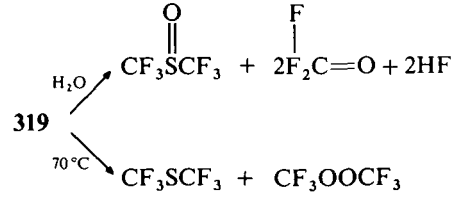
(**314**) R = Me (**316**) R = *c*-C_6H_{11}
(**315**) R = $PhCH_2$ (**317**) R = *t*-Bu

A series of acyclic and cyclic di-perfluoroalkoxysulfuranes was prepared by the reaction of perfluoromethyl (or *t*-butyl) hypochlorites with acyclic and cyclic sulfur(II) compounds. For example, photolysis of a mixture of bis(trifluoromethyl) sulfide **318** and trifluoromethyl hypochlorite **225a** was found to afford dialkoxysulfurane **319** (equation 124)[199].



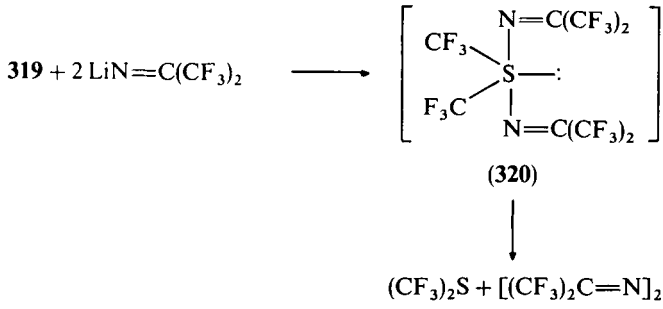
(124)

This sulfurane is stable in a Pyrex glass at 25 °C for a few days. However, in the presence of water, a facile hydrolysis occurs to afford bis(trifluoromethyl)sulfoxide (85%) and carbonyl fluoride (85%). After 1 h heating at 70 °C bis(trifluoromethyl)sulfide and bis(trifluoromethyl)peroxide are formed as the final decomposition products of **319** (equation 125)[199].



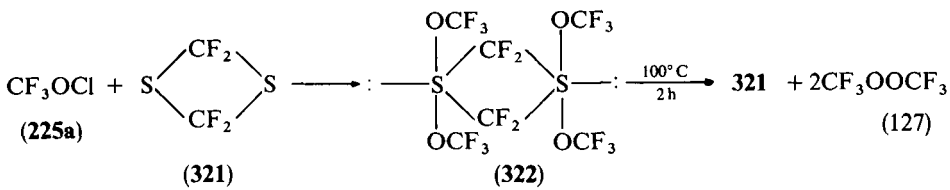
(125)

This sulfurane apparently undergoes a ligand exchange reaction when treated with lithium hexafluoroisopropylideneimine to form a new diaza sulfurane **320**. However, the latter is unstable and decomposes to bis(trifluoromethyl)sulfide (85%) and hexafluoroacetone azine (equation 126)[199].



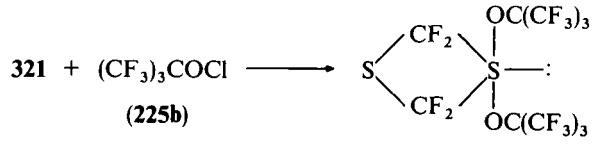
(126)

Tetrafluoro-1, 3-dithiane **321** and **225a** yield on photolysis the bis-sulfurane **322** which is stable in the absence of moisture, but decomposes to **321** and bis(trifluoromethyl)peroxide quantitatively after 1 h heating at 110 °C (equation 127)[188].



(127)

When the reaction of **321** and perfluoro *t*-butylhypochlorite (**225b**) was carried out at 0 °C without irradiation, the monosulfurane **323** was formed as the single reaction product (equation 128)[188].



(128)

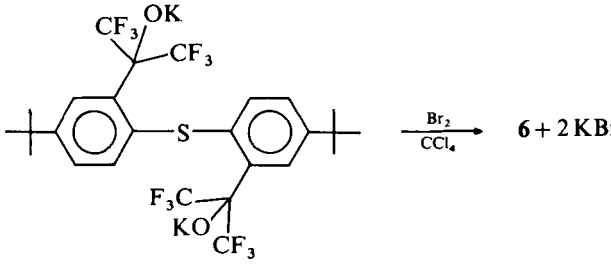
(**323**)

Similarly, **225b** and bis-trifluoromethyl disulfide yielded a stable thiasulfurane **324** in which the central tetravalent sulfur atom is connected with a substituent containing a bivalent sulfur (equation 129)[187].

(129)

(**324**)

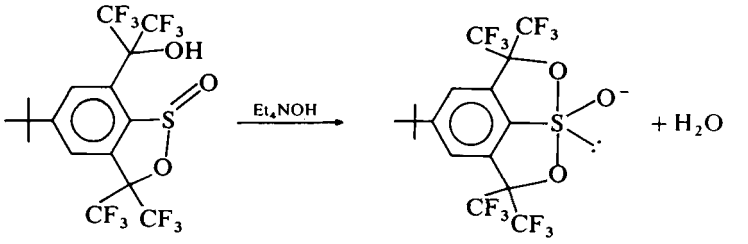
The bicyclodialkoxysulfurane **6** (see Table 1) was prepared by the bromine oxidation of the dipotassium salt of bis-perfluorocumyl sulfide **325** (equation 130)[136].



(130)

(**325**)

In contrast to the acyclic sulfurane **5** (Table 1), the sulfurane **6** does not react with alcohols and is resistant to treatment with a boiling 9:1 THF–water solution, even in the presence of hydrochloric acid or sodium hydroxide[136].

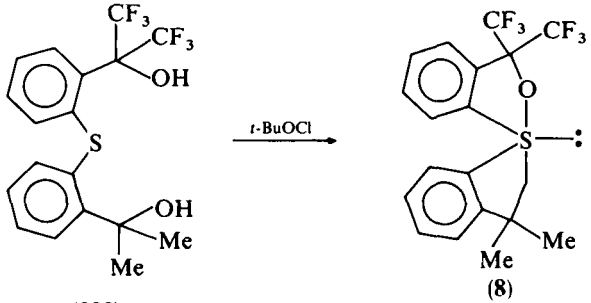


(131)

(**327**) (**326**)

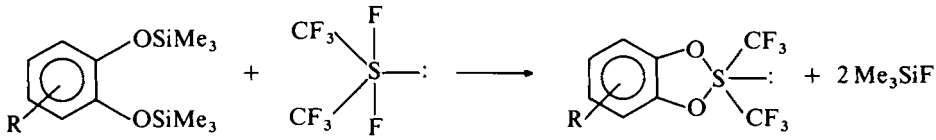
Taking into account our definition of the term 'high-coordinate sulfur compound' it is desirable to mention here a sulfurane oxide salt **326** obtained in 99% yield from the sultine alcohol **327** upon treatment with tetraethylammonium hydroxide (equation 131)[200]. This sulfuranoxide anion constitutes the first example of an observable analogue of the intermediate proposed to be formed during nucleophilic alkoxy exchange at the sulfinyl sulfur atom. Undoubtedly, the stability of **326** results from the presence of the two perfluorocumyloxy substituents included in the five-membered rings[200].

The unsymmetrical bicyclic spirosulfurane **8** was prepared by the *t*-butyl hypochlorite oxidation of the appropriate dihydroxy sulfide **328** (equation 132)[182].



(328) (8) (132)

Due to the presence of the two trifluoromethyl groups and the five-membered ring, which stabilize sulfurane structures, it was possible to obtain monocyclic diaryloxy sulfuranes **329**, **330** and **331** in the reaction of difluorosulfurane **208** with silylated *o*-catechols **332** (equation 133)[156a].

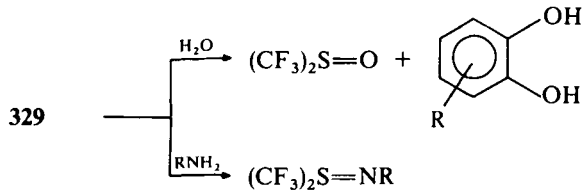


(332) (208)

(329) R = H
(330) R = 3-Me
(331) R = 3,5-di-*t*-Bu

(133)

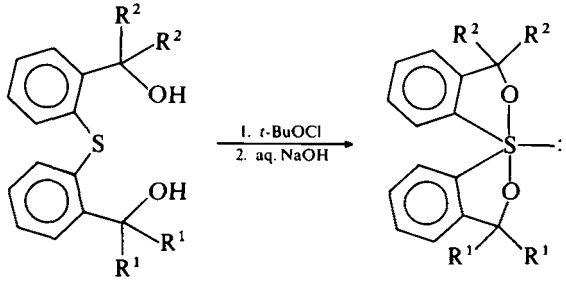
Although these sulfuranes were stable enough to be characterized at room temperature, they were hydrolyzed rapidly to bis(trifluoromethyl)sulfoxide and the corresponding catechols. Primary amines and **329** gave the corresponding *s*,*s*-bis(trifluoromethyl) *N*-alkyl(or aryl)sulfimines **333** (equation 134)[156a].



(134)

(333)
R = Me (56%)
R = PhCO (67%)

Additional three stable bicyclosulfuranes **263**, **334** and **335** without the perfluoroalkoxy ligands were prepared by the *t*-butyl hypochlorite induced oxidative ring closure of the sulfides **249**, **250** and **336** (equation 135)[190].



(135)

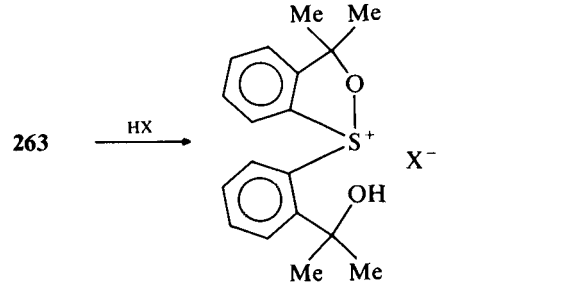
(**250**) $R^1 = R^2 = H$
(**249**) $R = R^2 = Me$
(**336**) $R^1 = Me; R^2 = Et$

(**334**) $R^1 = R^2 = H$
(**263**) $R^1 = R^2 = Me$
(**335**) $R^1 = Me; R^2 = Et$

The sulfurane **263** can be exposed to air without hydrolysis. It can, however, be converted to sulfoxide-diol **258** upon boiling for 2 h in 10% aqueous methanol (equation 136)[190].

$$\mathbf{263} \xrightarrow{10\%\ \text{eq. MeOH}} \mathbf{258} \qquad (136)$$

The unsubstituted sulfurane **334** is more easily hydrolyzed than **263**. For instance, additon of D_2O to a chloroform solution of **334** in an NMR tube resulted in 94% hydrolysis to the sulfoxide-diol **259** after 220 min at 25 °C. Upon treatment with HBF_4, CF_3SO_3H and d-camphorsulfonic acid the sulfurane **263** forms the corresponding sulfonium salts **337**–**339** (equation 137)[190].



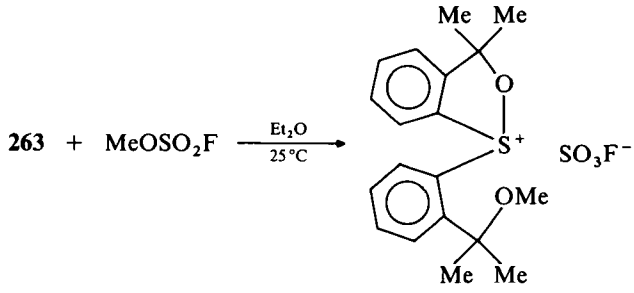
(137)

(**337**) $X = BF_4$
(**338**) $X = OSO_2CF_3$
(**339**) X = d-10-camphorsulfonate

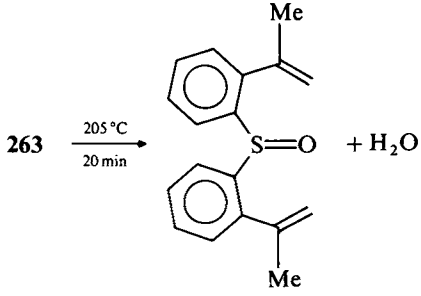
263 with methyl fluorosulfonate at 25 °C gives the salt **340** via methylation of one of the two apical oxygens (equation 138)[190]. When heated to 205 °C for 20 min, it loses one molecule of water and forms the sulfoxide diene **341** (equation 139)[190].

Pyrolysis of the sulfurane **334** at 182 °C gives the sulfide **342** most probably by disproportionation of the apical alkoxy ligands (equation 140)[190].

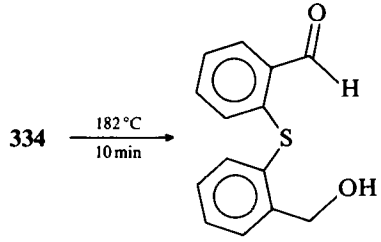
Oxidation of the sulfide-diol **343** allowed isolation of a very stable dialkoxysulfurane **344** (equation 141)[201].



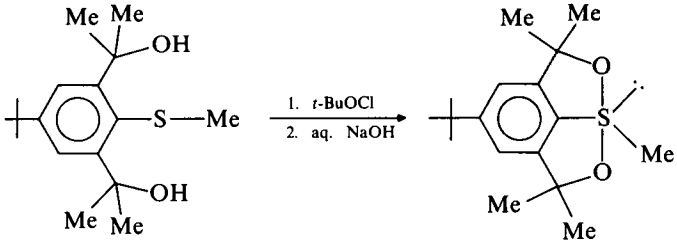
(340) (138)



(341) (139)



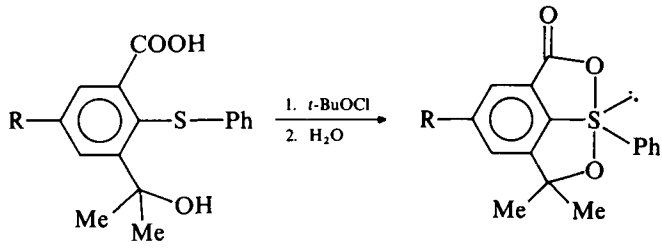
(342) (140)



(343) (344) (141)

3. Alkoxyacyloxysulfuranes

Only a few sulfuranes of this type have been described. Sulfuranes **345** and **346**, in which the presence of a tridentate ligand stabilizes the structures, were prepared by oxidative conversion of the corresponding carboxylic acids **347** and **348** substituted by the *S*-phenyl and 2-(2-hydroxy)-propyl groups (equation 142)[202].

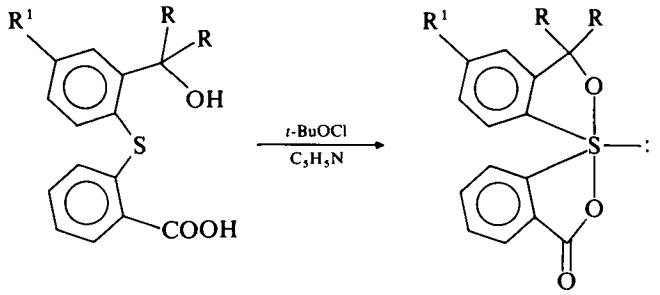


(142)

(**347**) R = H (**345**) R = H

(**348**) R = *t*-Bu (**346**) R = *t*-Bu

The same procedure was applied for the preparation of spirosulfuranes **349** and **350** starting from the corresponding sulfides **351** and **352** (equation 143)[184].



(143)

(**351**) R = Me; R^1 = H (**349**) R = Me; R^1 = H

(**352**) R = CF_3; R^1 = Me (**350**) R = CF_3; R^1 = Me

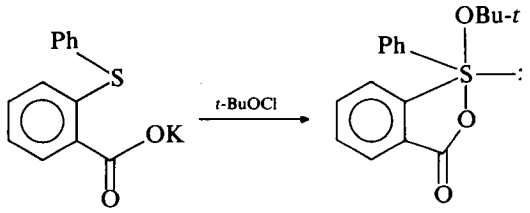
A monocyclic sulfurane **353** was also prepared by reacting the sulfide **354** with one mole of *t*-butyl hypochlorite (equation 144)[184].

4. Diacyloxysulfuranes

Two syntheses, the first of a spirodiacyloxy sulfurane **355a**[57] and the second of an acyclic sulfurane **302**[56], reported two decades ago stimulated an interest in the chemistry of hypervalent organic sulfur compounds. Since that time many of this class of sulfuranes have been prepared. The most general synthesis is based on the oxidation of bis-(2-carboxyaryl)sulfides **356a–k** with different halogenating agents (A – G) (equation 145)[203].

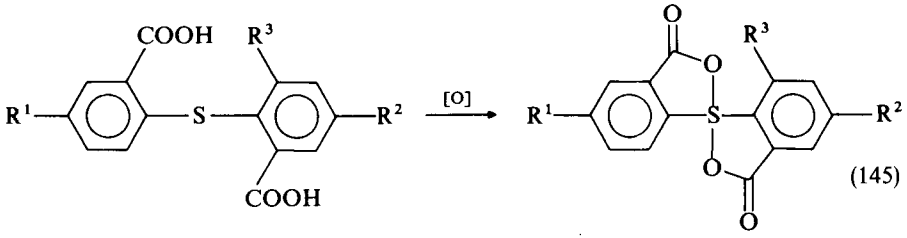
Oxidation of the sulfide **357** leads to the bis-spirosulfurane **358** (equation 146)[203].

All the spirosulfuranes mentioned above were also obtained by dehydration of the corresponding sulfoxides **359** and **360** (equations 147 and 148)[203].



(144)

(354) (353)



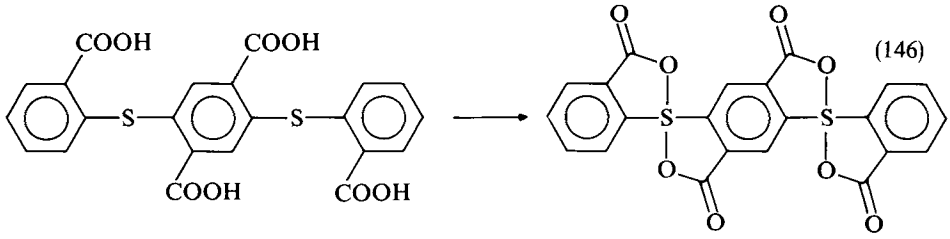
(145)

(356) (355)

a	b	c	d	e	f	g	h	i	j	k
$R^1 = H$	NO_2	Cl	NHAc	OMe	NO_2	Cl	NHAc	OMe	H	H
$R^2 = H$	H	H	H	H	NO_2	Cl	NHAc	OMe	Cl	N
$R^3 = H$	H	H	H	H	H	H	H	H	Cl	N

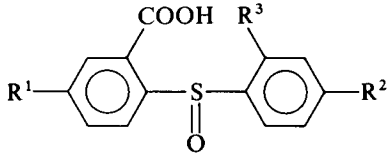
[O]

A TsNClNa/dioxane
B $TsNCl_2$/AcOH
C $TsNCl_2$/pyridine
D *t*-BuOCl/pyridine
E Cl_2/pyridine
F NBS/pyridine
G $PhI(OAc)_2$/pyridine



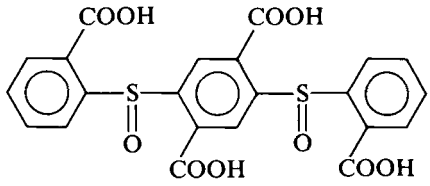
(146)

(357) (358)



355 (147)

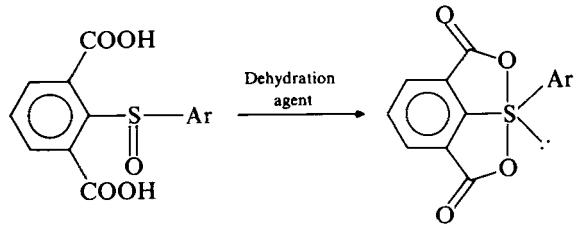
(359)



(148)

(360)

A series of diacyloxysulfuranes **361a–f** differing in the aromatic ligand were prepared through dehydration of the corresponding 2-(arylsulfinyl)isophthalic acids **362a–f** (equation 149)[204].

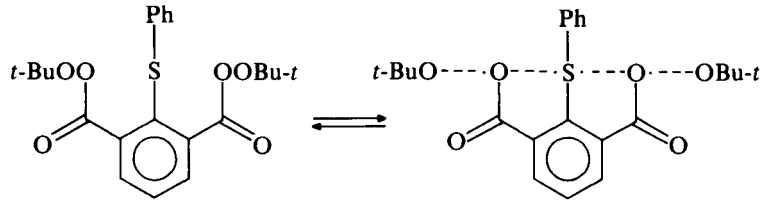


(149)

(362) (361)

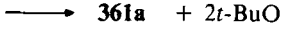
(a) Ar = Ph
(b) Ar = 4-MeC_6H_4
(c) Ar = 4-$MeOC_6H_4$
(d) Ar = 4-ClC_6H_4
(e) Ar = 4-FC_6H_4
(f) Ar = 4-$NO_2C_6H_4$

The unsubstituted parent sulfurane **361a** was earlier isolated in *ca* 48% yield by the decomposition of the bis-perester **363**. Detailed kinetic data provided evidence for a highly concerted reaction of **363**, simultaneously involving three neighboring groups in a reaction leading through the transition state **364** directly to the sulfurane **361a** (equation 150).



(150)

(363) (364)



In addition, this sulfurane was also prepared by pyrolysis of the sulfoxide **362a**[205].

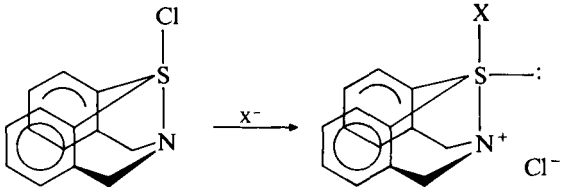
5. Azasulfuranes

A very limited number of azasulfuranes have been prepared and isolated as stable chemical species. The first example of a sulfurane with two apical nitrogen ligands, the spirodiaryldiamidosulfurane **265**, was prepared by treatment of a monocyclic chloroazasulfurane **266** with potassium hydride (equation 151)[185].

$$\mathbf{266} \xrightarrow{KH} \mathbf{265} \tag{151}$$

Hydrolysis of **265** is rapid in wet chloroform at 25 °C and the corresponding sulfoxide **268** is formed almost instantaneously. Even so, the crystals of **265** were sufficiently unreactive towards atmospheric moisture to allow an X-ray crystal structure determination to be carried out on a crystal exposed to the atmosphere[185]. The reaction of **265** with hydrogen chloride to form **266** has already been noted in this chapter (equation 93).

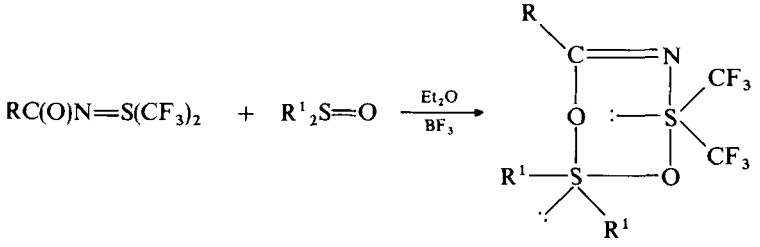
A few monoazasulfuranes **365b–e** differing only in the apical ligand were prepared from the chloroazasulfurane **365a** by nucleophilic displacement of the chloride anion by various nucleophiles (equation 152)[206].



(152)

(365a) **(365b–e)**

(b) X = Me
(c) X = Et
(d) X = MeO
(e) X = EtO



(153)

(367)

(a) R = Ph
(b) R = $PhCH_2$

(368)

(a) R^1 = Me
(b) R^1 = OMe

(366)

(a) R = Ph; R^1 = Me
(b) R = $PhCH_2$; R^1 = Me
(c) R = Ph; R^1 = OMe
(d) R = $PhCH_2$; R^1 = OMe

X-ray crystallographic analysis established the proposed structures of **365b** and **365d**. Since the geometry around the sulfur atom is essentially trigonal bipyramidal, **365b** constitutes the first example of a stable alkylsulfurane with an apical alkyl group[206].

Another group of stable monoazasulfuranes **366** with two tetracoordinate sulfur(IV) atoms bonded to carbon, oxygen and/or nitrogen per molecule has been prepared by cycloaddition of *S*, *S*-bis(trifluoromethyl)-*N*-benzoyl (or 2-phenylacetyl)sulfimide **367** with sulfoxides or sulfites **368** (equation 153)[156a].

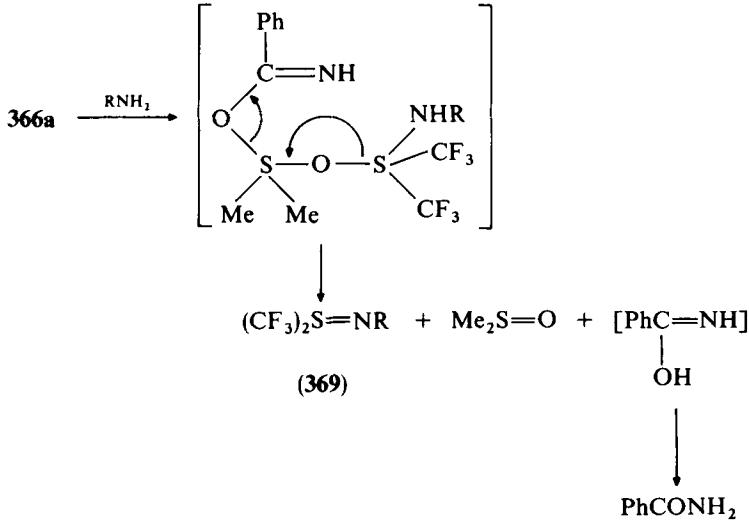
The sulfurane **366a** is hydrolyzed slowly to bis(trifluoromethyl)sulfoxide, dimethyl sulfoxide and benzamide (equation 154)[156a].

$$\mathbf{366a} + H_2O \longrightarrow (CF_3)_2S{=}O + Me_2S{=}O + PhCONH_2 \qquad (154)$$

When heated at 150 °C for 3 h in a stainless steel vessel, bis(trifluoromethyl)sulfoxide, DMSO, and benzonitrile were formed quantitatively (equation 155)[156a].

$$\mathbf{366a} \longrightarrow (CF_3)_2S{=}O + Me_2S{=}O + PhCN \qquad (155)$$

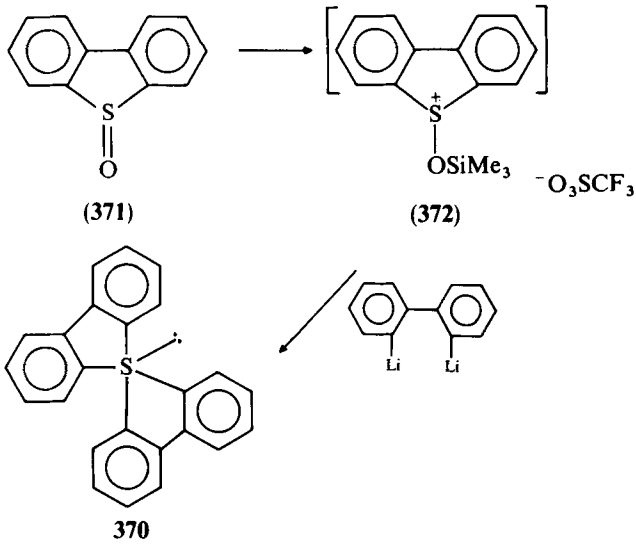
In the reaction of the bis-sulfurane **366a** with primary amines, the formation of bis-(trifluoromethyl)-*N*-alkyl sulfimines **369** was observed. This suggests that the reaction was initiated by attack on the more electropositive sulfurane sulfur atom to which the two trifluoromethyl groups are bonded (Scheme 52)[156a].



SCHEME 52

6. *Tetracarbosulfuranes*

Sulfuranes with four carbon ligands were early postulated as intermediates in substitutions at sulfur in sulfonium salts or in sulfoxides with organometallic reagents. However only very recently was the first synthesis and structural characterization of a stable sulfurane with four carbon–sulfur bonds, namely bis(2,2′-phenylene)sulfurane **370** (Table 1) reported. It was synthesized from dibenzothiophene s-oxide **371**, which was converted to the sulfonium salt **372** upon treatment with trimethylsilyl trifluoromethanesulfonate. Then, the salt was reacted with 2,2′-dilithiobiphenyl to form the sulfurane **370** in almost quantitative yield (Scheme 53)[207].



(371) (372)

370

SCHEME 53

D. Sulfurane Oxides and Their Analogues Isolated as Stable Species

1. Sulfurane oxides

Sulfurane oxides and their analogues, in which the sulfur–oxygen bond is replaced by a sulfur–carbon or sulfur–heteroatom bond, belong to a second group of high-coordinated sulfur compounds. The chemistry of sulfurane oxides began in 1937 with a patent [208] describing the preparation of sulfur oxytetrafluoride **373** from thionyl fluoride and elemental fluorine. Later, the full details of this procedure were disclosed (equation 156)[209].

$$SOF_2 + F_2 \longrightarrow \underset{\textbf{(373)}}{F_4SO} \qquad (156)$$

SOF_4 was more efficiently synthesized by oxidation of sulfur tetrafluoride with oxygen in the presence of catalytic amounts of nitrogen oxides[210]. The best oxidizing agents were found to be those in which the nitrogen atom has a tripositive or higher oxidation state. Nitrogen dioxide, sodium nitrite and nitrate were effective at 300 °C, but little or no oxidation occurred when SF_4 was heated with nitrous oxide or nitric oxide at this temperature. The formation of SOF_4 is favored at low temperatures and lower SF_4 concentrations, while sulfur hexafluoride is the primary oxidation product at higher temperatures and with higher SF_4 concentration. The effect of the SF_4 concentration is evident in the idealized equations describing the two conversions (equations 157 and 158).

$$2NaNO_3 + 6SF_4 \longrightarrow 5SOF_4 + SOF_2 + 2NaF + N_2 \qquad (157)$$

$$2NaNO_3 + 11SF_4 \longrightarrow 5SF_6 + 6SOF_2 + 2NaF + N_2 \qquad (158)$$

A few trifluoro oxa- or azasulfurane oxides **374** were prepared from sulfur oxytetrafluoride and the appropriate silanes (equation 159)[211,212].

$$OSF_4 + Me_3SiX \longrightarrow O{=}S(F)(F)(X)(F) + Me_3SiF \qquad (159)$$

(373) (374)

(a) X = NMe_2
(b) X = NEt_2
(c) X = OPh

The observed and calculated ^{19}F-NMR spectra of these compounds suggest that they adopt a trigonal bipyramidal structure. On reaction with bis(trimethylsilyl)carbodiimide **375** they give the corresponding fluoro imides **376** (equation 160)[212].

$$374 + Me_3SiN{=}C{=}NSiMe_3 \xrightarrow{0\,^\circ C} N{\equiv}C{-}N{=}S(F)(=O)(R) \qquad (160)$$

(375) (376)

(a) R = Me
(b) R = Et
(c) R = OPh

A replacement of the two fluorine atoms in **374** by the imino group is illustrated by equation 161[212].

$$O{=}S(F)(F)(OPh)(F) + (Me_3Si)_2NMe \longrightarrow MeN{=}S(F)(OPh){=}O + 2FSiMe_3 \qquad (161)$$

(374c) (377) (378)

$$\downarrow\ CF_3C[OSiMe_3]{=}NSiMe_3$$

(379)

$$CF_3CON{=}S(F)(OPh){=}O$$

(380)

The reaction of sulfur oxytetrafluoride with silyl ethers **381** was found to proceed easily, but more than one fluorine is substituted (equation 162)[213]. The relatively stable aryloxy derivatives of sulfur oxyfluoride are collected in Table 6. It should be noted that alkoxy derivatives are unstable and that previous attempts to effect substitution of sulfuroxytetrafluoride by the use of phenols were unsuccessful[214].

$$OSF_4 + n\,Me_3SiO{-}C_6H_4{-}X \longrightarrow O{=}SF_n(O{-}C_6H_4{-}X)_{4-n} \qquad (162)$$

(373) (381) (382)

TABLE 6. Aryloxy derivatives **382** from silyl ethers **381** and sulfur oxytetrafluoride **373**[a]

381	Structure of **382**	δ_F (ppm from CCl_3F) eq	ax
a	$PhOS(O)F_3$	−67.6	−89.1
b	p-$TolOS(O)F_3$	−67.2	−88.4
c	m-$TolOS(O)F_3$	−67.0	−88.2
d	o-$TolOS(O)F_3$	−67.4	−86.4
e	p-$ClC_6H_4OS(O)F_3$	−68.1	−89.7
f	m-$ClC_6H_4OS(O)F_3$	−68.4	−89.5
g	p-$FC_6H_4OS(O)F_3$	−67.4	−88.2
h	m-$FC_6H_4OS(O)F_3$	−67.6	−88.9
i	o-$FC_6H_4OS(O)F_3$	−69.8	−86.1
j	$(PhO)_2S(O)F_2$		−89.0
k	$(p$-$TolO)_2S(O)F_2$		−86.0
l	$(p$-$ClC_6H_4O)_2S(O)F_2$		−87.1
m	$(PhO)_3S(O)F$		−68.4
n	$(p$-$TolO)_3S(O)F$		−67.0
o	$(p$-$ClC_6H_4O)_3S(O)F$		−69.9
p	$(C_6F_5O)_3S(O)F$		−68.1

[a] Taken from Reference 213.

The ^{19}F-NMR spectra of aryloxytrifluorosulfurane oxides **382a–i** show an AB_2 system which indicates that they have trigonal bipyramidal structure with the oxygen occupying an equatorial position. The bisaryloxysulfurane oxides **382j–l** show only one ^{19}F signal which occurs at almost the same position as the signals for the axial fluorines of the trifluorides. The chemical shifts of the compounds formulated as tri(aryloxy) derivatives **382m–p** indicate that the fluorine atom can also be located in an equatorial position[213].

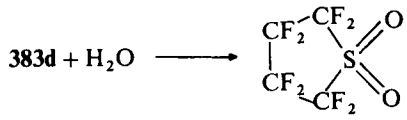
The first bis(perfluoroalkyl)sulfur oxydifluorides **383** were synthesized by the reaction of chlorine monofluoride with bis(perfluoroalkyl) sulfoxides **384** at −78 °C. At temperatures higher than −78 °C, yields of the oxydifluorides decrease and amounts of products resulting from C—S bond cleavage increase (equation 163)[215].

$$R_f\text{—}S(=O)\text{—}R_f^1 + ClF \xrightarrow[3\,h]{-78\,^\circ C} R_f\text{—}S(=O)(F)\text{—}F \quad (163)$$

(384) **(383)**

(**a**) $R_f = R_f^1 = CF_3$ (82%)
(**b**) $R_f = CF_3$; $R_f^1 = C_2F_5$ (75%)
(**c**) $R_f = R_f^1 = C_2F_5$ (75%)
(**d**) $R_f = R_f^1 = CF_2CF_2CF_2CF_2$ (99%)

All of the acyclic isolated oxysulfuranes **383** are moderately stable to hydrolysis and may be stored in Pyrex glass vessels at −78 °C indefinitely. In contrast, the cyclic analogue **383d** is extremely reactive to glass and is easily hydrolyzed by water to the sulfone **385** (equation 164)[215].



(164)

(385)

While the oxysulfurane **383a** does not react with hydrogen chloride, it gives with perfluorocarboxylic acids a variety of products, including perfluoroesters (equation 165).

$$\mathbf{383a} + R_fCO_2H \longrightarrow R_fCO_2CF_3 + CF_3S(O)F + (CF_3)_2SO + (CF_3)_2SO_2 \quad (165)$$

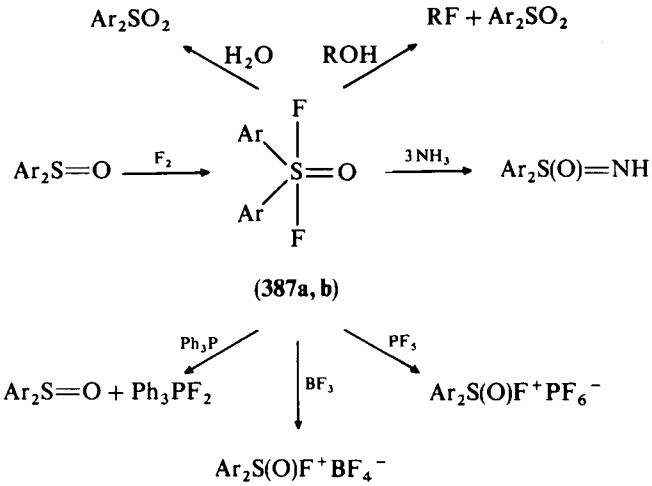
$$R_f = CF_3 \text{ or } CF_2Cl$$

In contrast to difluorosulfuranes, the oxydifluorides **383** react smoothly with ammonia to give bis(perfluoroalkyl) sulfoxyimines **386a–c** (equation 166)[216].

$$\mathbf{383a\text{–}c} + 3NH_3 \xrightarrow{25\,^\circ C} R_f\text{—}\underset{\underset{NH}{\|}}{\overset{\overset{O}{\|}}{S}}\text{—}R_f^1 + 2NH_4F \quad (166)$$

(386a–c)

Direct fluorination of diaryl sulfoxides with elemental fluorine also gave in 80–90% yields the corresponding diaryloxosulfur difluorides **387**[217]. Some of their reactions are shown in Scheme 54.



(387a, b)

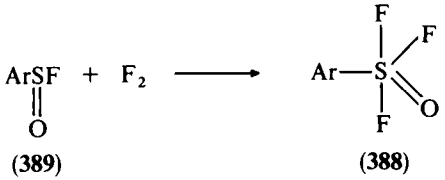
(a) Ar = Ph
(b) Ar = *p*-FC_6H_4

SCHEME 54

Fluorination of diphenyl sulfoxide with one mole of xenon difluoride resulted in the formation of diphenyl sulfone[218]. However, difluorosulfurane oxide **387a** was suggested to

be an intermediate in this reaction. In a similar way, arylsulfur trifluoride oxides **388** were obtained by direct addition of fluorine to sulfinyl fluorides **389** (equation 167)[219].

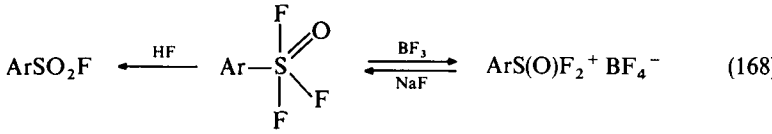
The fixed trigonal bipyramidal ligand arrangement in **388** was supported by ^{19}F- and ^{13}C-NMR data. In glass vessels **388a** and **b** readily undergo decomposition catalyzed by HF to give the corresponding sulfinyl fluorides **389**. On the other hand, action of BF_3 on **388a** yields the difluorophenylsulfonium salt **391a**, which on dry distillation with NaF reliberates **388a** (equation 168)[219].



(167)

(389) **(388)**

(a) Ar = Ph
(b) Ar = *p*-FC_6H_4

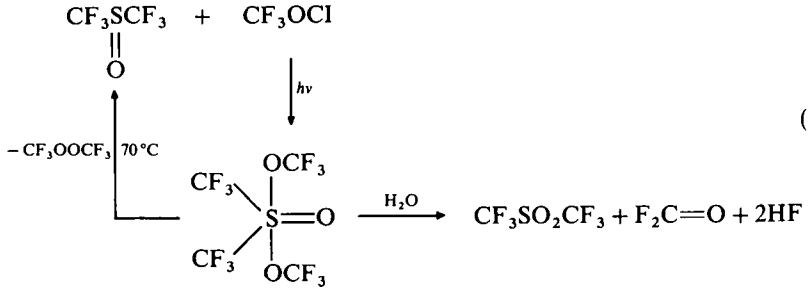


(168)

(390a, b) **(388a, b)** **(391a)**

When a mixture of bis(trifluoromethyl)sulfoxide and trifluoromethyl hypochlorite is photolyzed, the sulfurane oxide **392** is formed (equation 169)[220]. The latter is stable in Pyrex vessels at 25 °C for days. However, it hydrolyzes rapidly to give bis(trifluoromethyl)sulfone, carbonyl fluoride and HF. Its pyrolysis at 70 °C in a stainless steel vessel affords bis(trifluoromethyl)sulfoxide and bis(trifluoromethyl)peroxide quantitatively[220].

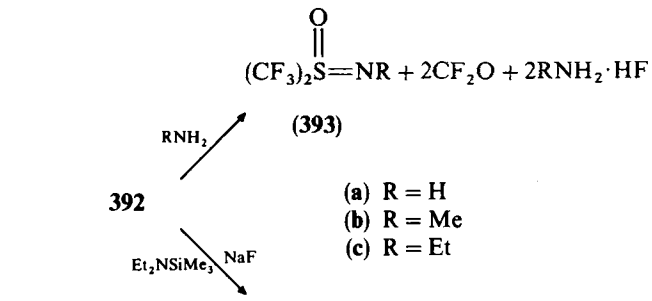
With primary amines **392** affords *N*-alkyl bis(trifluoromethyl) sulfoxyimines **393**, while on treatment with *N*,*N*'-diethylaminotrimethylsilane in the presence of sodium fluoride the corresponding imine **394** is formed (equation 170)[220].



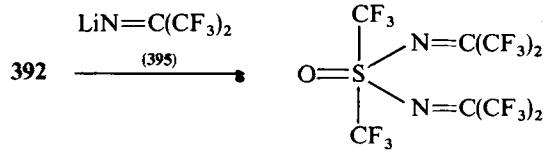
(169)

(392)

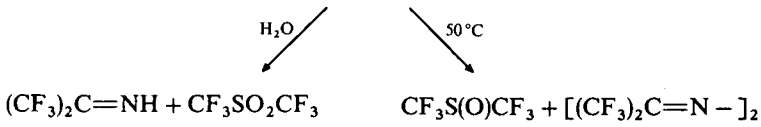
A ligand exchange reaction is observed on treatment of **392** with lithium hexafluoroisopropylideneimine **395**. The newly formed sulfurane oxide **396** is hydrolyzed slowly and decomposed at 50 °C to give the products shown in equation 171[220].



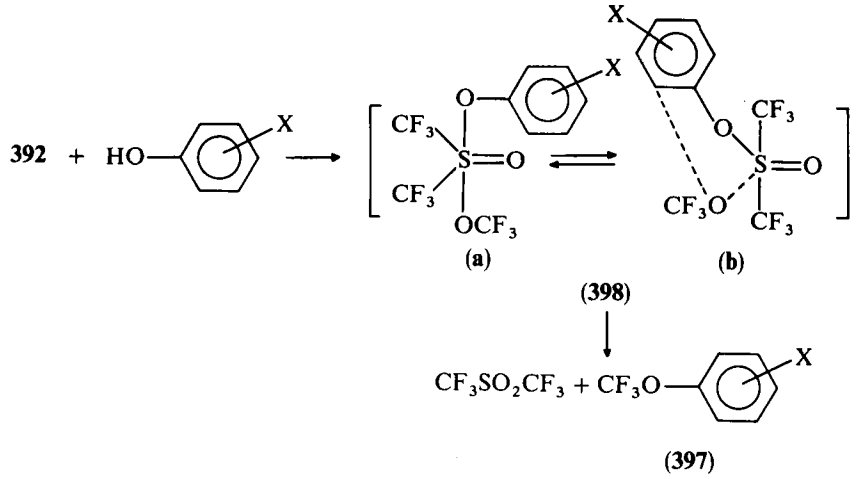
(170)



(171)

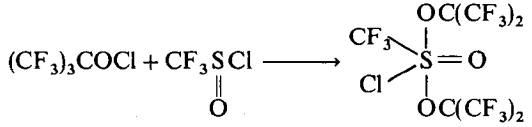


When **392** reacts with phenols, α,α-(trifluoromethyl)anisole derivatives **397** are formed, most probably by an intramolecular decomposition of the transient sulfurane oxide **398** via an electrocyclic mechanism (Scheme 55)[220].



SCHEME 55

In the reaction between trifluoromethanesulfinyl chloride and perfluoro *t*-butyl hypochlorite the oxidative displacement of chlorine leads to sulfurane oxide **399** (equation 172)[220].

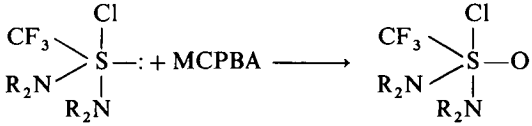


(172)

(399)

Oxidation of sulfuranes **400a, b** produces sulfurane oxides **401**, which are stable at room temperature (equation 173)[221].

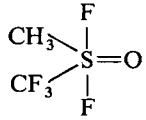
Methyl(trifluoromethyl)difluorosulfurane oxide **402** was also isolated and fully characterized by spectroscopic and analytical methods[170].



(173)

(400a, b) **(401a, b)**

(a) R = Me
(b) R = Et



(402)

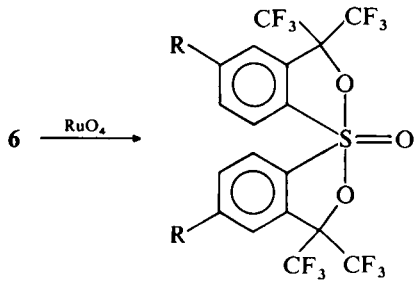
In addition to sulfurane oxides containing halogens, a few compounds with the alkoxy substituents in the apical position of a trigonal bipyramidal structure have been isolated and fully characterized as stable species. Of these, two structures are stabilized by the presence of the perfluorocumyloxy group. The first one, a symmetrical spirodisulfurane oxide **7a**, was prepared by oxidation of the parent sulfurane **6** with ruthenium tetroxide[136]. The yield of this conversion was found by ^{19}F NMR to be nearly quantitative (equation 174).

Its analogue **7b** was prepared by the acid – catalyzed hydrolysis of difluoropersulfuranes **11** and **12**[52].

The nonequivalence of the geminal CF_3 groups seen in the ^{19}F-NMR spectra of **7** is consistent with a trigonal bipyramidal geometry with apical alkoxy ligands and equatorial aryl and oxide ligands. Like the sulfuranes **6** the sulfurane oxides **7** are completely resistant to hydrolysis, even under forced conditions[136].

A similar oxidation was attempted on the acyclic sulfurane **5**, but no sulfurane oxide analogous to **7** could be detected[136]. On the other hand, the sulfurane oxide **403** was formed in 70% when the sulfurane **263** was allowed to react with an excess of ozone (equation 175)[222].

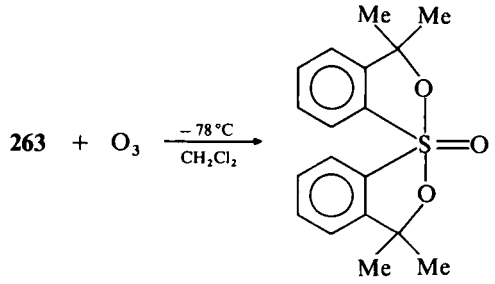
403 is very easily transformed to the sulfon-ene-ol **404**. It is obvious that the formation of a very stable sulfone function in **404** is a driving force for this reaction. This quantitative and irreversible fragmentation occurs very rapidly under acidic conditions and is much slower under basic conditions. Thus, a sample of **403** in dry chloroform at 44 °C was



(174)

(7)

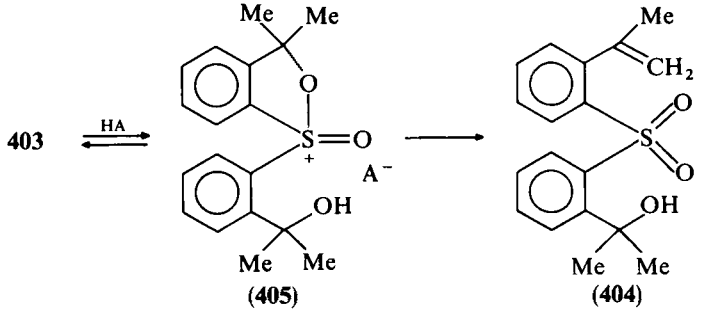
(a) R = *t*-Bu
(b) R = H



(175)

(403)

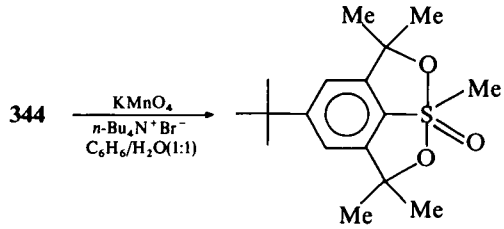
completely converted within seconds to **404** when one drop of chloroform saturated with HCl was added. However, in a 15% aqueous pyridine solution containing equimolar amounts of **403** and KOH the extent of fragmentation was only 14% after 88 h at 86 °C. The acid-catalyzed fragmentation of **403** (Scheme 56) is initiated by a reversible protonation of an apical oxygen giving the oxysulfonium salt **405**, which is very reactive and rapidly loses a proton to give the final product **404**[222].



(405) (404)

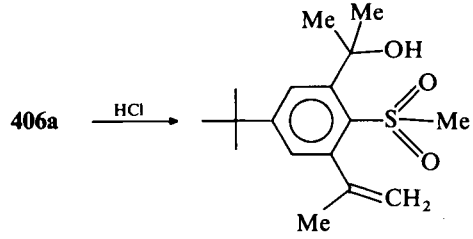
SCHEME 56

A more stable sulfurane oxide **406a** containing a tridentate ligand was prepared[201] by oxidation with potassium permanganate of the sulfurane **344** (equation 176).



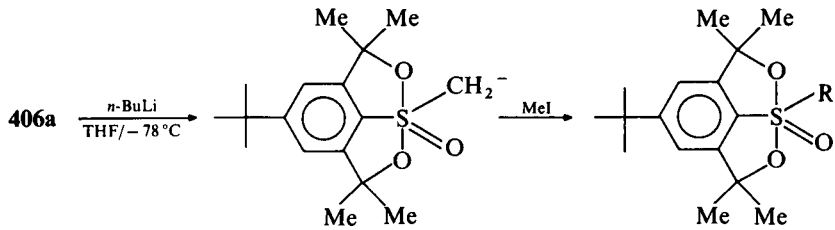
(406a) (176)

This sulfurane oxide, like **403**, is sensitive to acids and gives the sulfone-ene-ol **407** (equation 177) in chloroform solution containing a trace of hydrogen chloride[201].



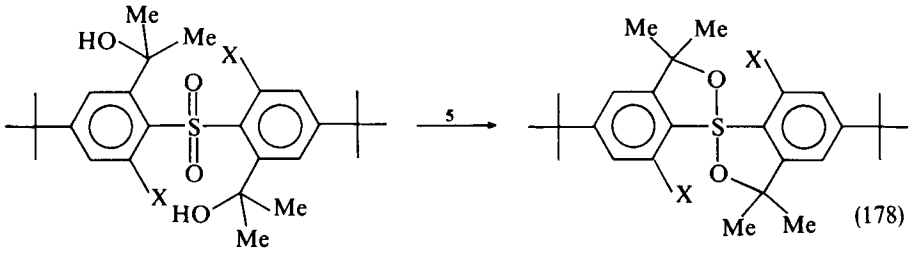
(407) (177)

However, **406a** is stable under basic conditions and can be kept without any change in a pyridine solution for at least three months. An interesting chemical property of **406** is the remarkable lability of the *S*-methyl protons. Thus deprotonation of **406a** by a base leads to a pentacoordinate sulfur ylide **408**. As a consequence of this, deuterium exchange of the methyl protons is complete within minutes at room temperature, even in the absence of a base, when an excess of D_2O is added to its solution in acetone. In pyridine-d_5 this exchange is complete within seconds. This high lability of the α protons allowed the preparation of a stable solution of **408** in THF upon treatment of **406a** with *n*-butyllithium and trapping by the addition of a large excess of methyl iodide to form the monoalkylated product—the spirosulfurane oxide **406b**. A mixture of **406b** and **406c** was observed by NMR when a slight excess of methyl iodide was added under the same reaction conditions (Scheme 57)[201].



SCHEME 57

A cyclodehydration of the dihydroxy sulfones **409** and **410** occurred on treatment with the dialkoxy sulfurane **5**, giving the corresponding sulfurane oxides **411** and **412** in 70% and 40% yield, respectively (equation 178)[223,224].

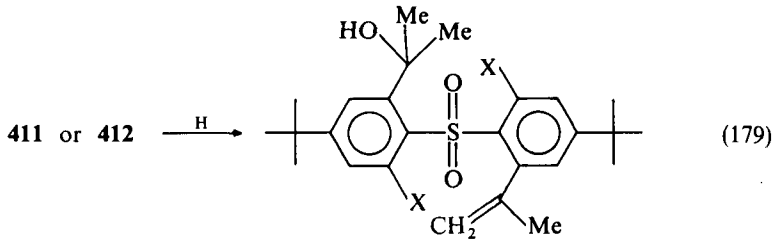


(178)

(**409**) X = CO_2Et
(**410**) X = CH_2OH

(**411**) X = CO_2Et
(**412**) X = CH_2OH

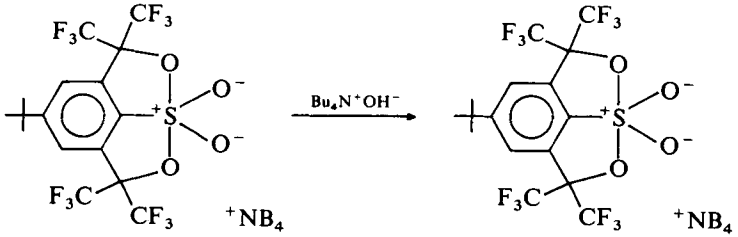
Under acidic conditions they also undergo fragmentation to the isomeric sulfone olefins **413** and **414** (equation 179)[223,224].



(179)

(**413**) X = CO_2Et
(**414**) X = CH_2OH

A special type of sulfurane oxide is the dioxide salt **415**, the first example of an isolable intermediate postulated to explain an associative nucleophilic attack at the sulfonyl sulfur atom. It was isolated in an almost quantitative yield on reacting the hydroxy sulfone in equation 180 with tetra-*n*-butylammonium hydroxide[200].



(180)

(**415**) (**415**)

2. Sulfurane oxide analogues

All stable sulfurane oxide analogues contain four halogen atoms (usually fluorine) bonded to the central sulfur atom. One group of these compounds are sulfurane oxide analogues in which the equatorial sulfur–oxygen bond is replaced by a sulfur–carbon bond, while the second group has a sulfur–nitrogen bond.

The parent member of the first group is methylenesulfur tetrafluoride **416**. It was obtained from bromomethylsulfur pentafluoride **417** by lithium–bromide exchange followed by elimination of lithium fluoride (equation 181)[225].

$$F_5S{-}CH_2Br \xrightarrow[-110\text{ to }-70\,^\circ C]{n\text{-BuLi}} \underset{\textbf{(416)}}{\begin{matrix} & F & \\ F & | & \\ & S{=}CH_2 & \\ F & | & \\ & F & \end{matrix}} \qquad (181)$$

(417)

The sulfur atom in this molecule is approximately the center of a trigonal bipyramid. The methylene group occupies an equatorial position, with the hydrogen atoms located in the plane of the S, C and axial fluorine atoms. The carbon–sulfur bond is best described as a strong double bond with only little ylidic polarity. Addition reactions with polar species yield hexa-coordinated sulfur structures with *cis*-geometry (equations 182 and 183)[226].

$$CH_2{=}SF_4 + HX \longrightarrow \begin{matrix} & F & \\ CH_3 & | & F \\ & S & \\ X & | & F \\ & F & \end{matrix} \qquad (182)$$

(418) X = F
cis-**(419)** X = Cl
cis-**(420)** X = Br

$$\textbf{416} + XY \longrightarrow \begin{matrix} & F & \\ XCH_2 & | & F \\ & S & \\ Y & | & F \\ & F & \end{matrix} \qquad (183)$$

(421) X = I; Y = Cl
(422) X = Hg/2; Y = F
(423) X = AsF_4; Y = F
(424) X = Br ; Y = F

The reaction course with nonpolar reagents is completely different and some examples are shown in equation 184[226].

$$\textbf{416} + X_2 \xrightarrow{0\,^\circ C} SF_4 + X_2CH_2 \qquad (184)$$

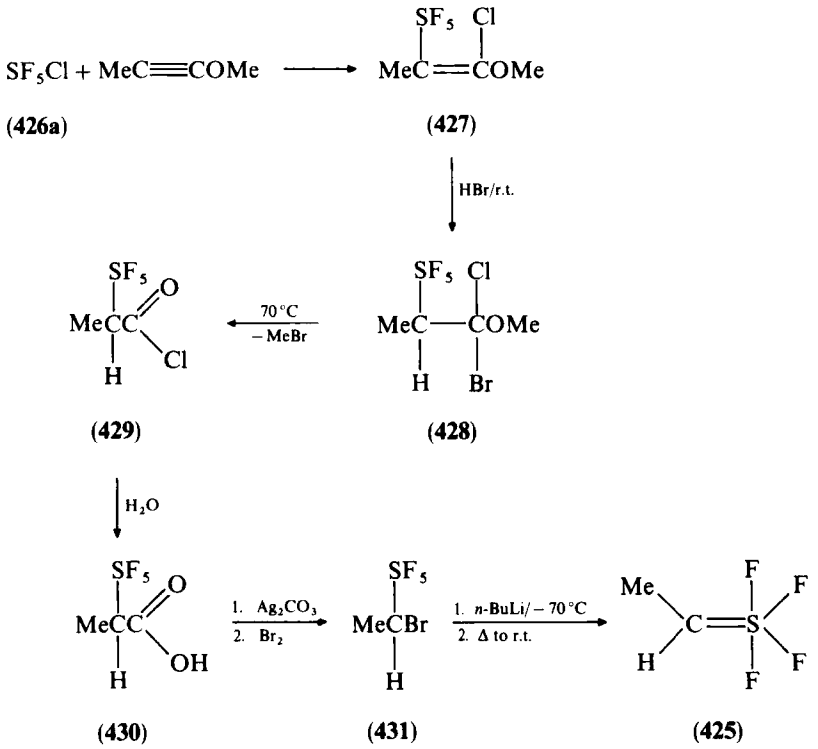
(a) X = Cl
(b) X = Br
(c) X = I

The reaction of **416** with chlorine at a lower temperature (− 78 °C) affords a complex mixture of products (equation 185)[227].

$$\textbf{416} + Cl_2 \xrightarrow{-78\,^\circ C} MeSF_5 + ClCH_2SF_5 + \textit{cis}\text{-}ClCH_2SF_4Cl + SF_4 + CH_2Cl_2 \qquad (185)$$

Some α-substituted derivatives have been also isolated. A multistep preparation of ethylidenesulfur tetrafluoride **425** is shown in Scheme 58[228].

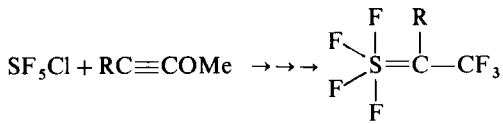
The structure of **425**, deduced mainly from its NMR spectra, is a trigonal bipyramid around the sulfur with two axial and two equatorial fluorine atoms, and the ethylidene



SCHEME 58

ligand in an equatorial position. The methyl group is located in the plane formed by the axial fluorine atoms and sulfur.

Two (2,2,2-trifluoroethylidene)sulfur tetrafluorides **432** and **433** were prepared from methoxyacetylene **434a** and 1-methoxypropyne **434b** and SF_3Cl (**426a**) in a multistep procedure somewhat analogous to that presented in Scheme 58 (equation 186)[229].

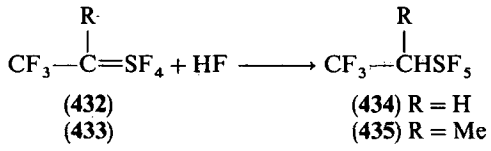


(186)

(**434**) (**a**) R = H (**432**) R = H
(**b**) R = Me (**433**) R = Me

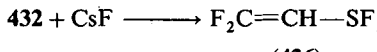
These compounds also adopt a trigonal bipyramidal geometry. Their reactions with hydrogen fluoride, cesium fluoride and potassium hydroxide are shown in equations 187–190[229].

The thermal isomerization of the ketene **439** at 270–290 °C affords the corresponding (α-fluoroacetylmethylidene)sulfurtetrafluoride **440** (equation 191)[230].



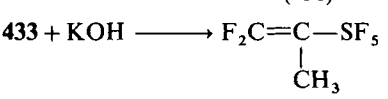
(187)

(432) (433) (434) R = H (435) R = Me



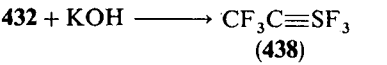
(188)

(436)



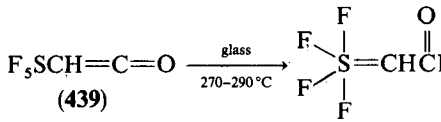
(189)

(437)



(190)

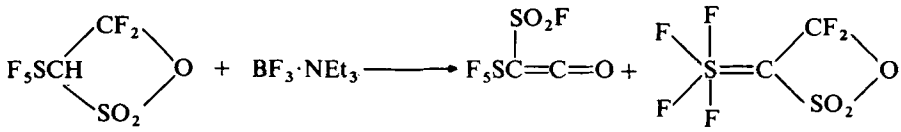
(438)



(191)

(439) (440)

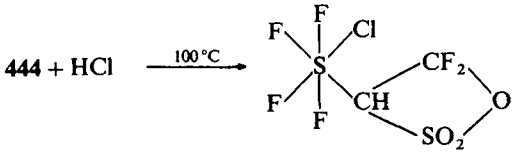
Dehydrohalogenation of the sultone **441** with a complex of boron trifluoride and triethylamine **442** as a base gives a mixture of the ketene **443** and its isomer **444**. The latter is the first example of a cyclic alkylidenesulfur tetrafluoride (equation 192)[231].



(192)

(441) (442) (443) (444)

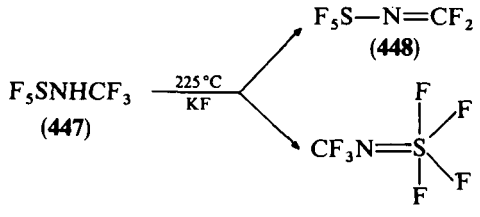
Of interest is that the four *S*-fluorine atoms in **444** are rigidly bound: no evidence for exchange is observed in its ^{19}F spectrum. This compound is relatively stable and can be exposed to air for a short time without decomposition. Hydrogen fluoride adds to **444** giving back the sultone **441** in a high yield. However, with hydrogen chloride no reaction occurs at room temperature and it can be completed only after several hours of heating with an excess of gaseous HCl at 100 °C (equation 193). This contrasts very strongly with the ease of the hydrogen chloride addition to **416**. It was suggested that the large sultone ring slows down the rate of the attack of HCl at the sulfur and also at the neighboring carbon atom[231].



(193)

(445)

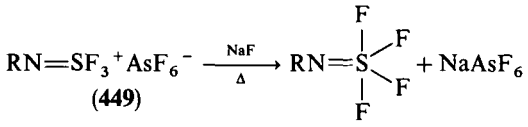
The first member of the family of nitrogen analogues of sulfurane oxides, *N*-trifluoromethyliminosulfur tetrafluoride **446a**, was formed as a byproduct on heating the amine **447** with potassium fluoride at 225 °C (equation 194)[232].



(194)

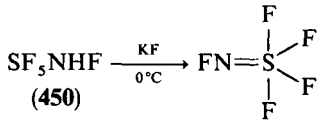
(446a)

Later on, a few analogues of **446a** were prepared by different approaches shown in equations 195–198[233–236].



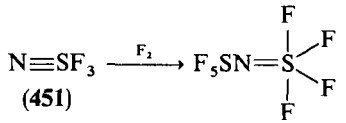
(195)

(446b) R = Me
(446c) R = Et



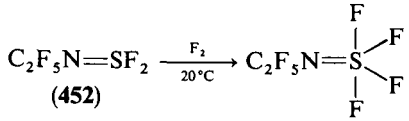
(196)

(446d)



(197)

(446e)



(198)

(446f)

All of the above compounds, except the fluoroiminosulfur tetrafluoride **446d**, exhibit equivalence of the sulfur fluorines in the ^{19}F-NMR spectra at ambient temperatures. In the case of **446d** the spectrum does not coalesce up to 100 °C. The apparent lack of fluxionality in **446d** is similar to $CH_2{=}SF_4$ **416**.

Carbamoyliminosulfur tetrafluorides **453** were also reported to be formed in the reaction of pentafluorosulfanyl isocyanate **454** with (dialkylamino)trimethylsilanes (equation 199)[237–239].

$$F_5SNC{=}O + R_2NSiMe_3 \longrightarrow \underset{F}{\overset{F}{\overset{|}{F{-}S{=}NCNR_2}}}{}_{F}^{\|O} + FSiMe_3 \qquad (199)$$

(454) (453)

(a) R = Me
(b) R = Et

Further reaction with an excess of the nucleophile gives the compounds **455** (equation 200)[237,238].

$$\mathbf{453} + R_2NSiMe_3 \longrightarrow \underset{R_2N}{\overset{F}{\overset{|}{F{-}S{=}NCNR_2}}}{}_{F}^{\|O} \qquad (200)$$

(455)

The reaction of the lithioimine **395** with SF_5Cl or SF_5Br occurred without reduction of S(VI) to S(IV) and in each case the corresponding *N*-perfluoroisopropyliminesulfur trifluorides **456a, b** were formed as a result of the breaking of the S—F bonds, while the S—Cl or S—Br bonds were unchanged (equation 201)[188].

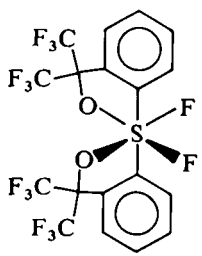
$$SF_5X + LiN{=}C(CF_3)_2 \longrightarrow \underset{X}{\overset{F}{\overset{|}{F{-}S{=}N{-}CF}}}{}_{F}^{CF_3} \qquad (201)$$

(426) (395) (456)

(a) X = Cl
(b) X = Br

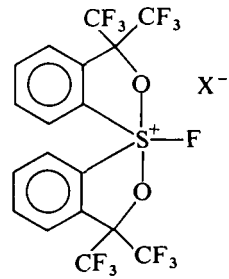
(a) X = Cl
(b) X = Br

The persulfonium cation **457** may be considered as a special sulfurane oxide analogue. With very nonnucleophilic counterions, such as SbF_6^-, PF_6^- and $CF_3SO_3^-$ this persulfonium cation, formed from the difluoropersulfurane **12**, was unambiguously characterized by NMR spectroscopy (equation 202)[52,240].



(12)

$$+ SbF_5 \text{ or } PF_5 \longrightarrow \qquad (202)$$



(457)

(a) X = SbF_6
(b) X = PF_6

IV. PERSULFURANES

Hexacoordinate, hexavalent sulfur compounds, for which the name 'persulfuranes' was introduced by Musher in 1969[14], can be classified as 12-S-6 hypervalent species according to the scheme of Martin and coworkers[4]. The chemistry of persulfuranes, which began almost at the same time as the chemistry of sulfuranes (the parent member of this family, sulfur hexafluoride was prepared five years earlier than sulfur tetrafluoride), has not been as extensively studied as that of tetracoordinate sulfuranes. The chemistry of persulfuranes containing at least five halogen atoms gained momentum in the sixties. There is a substantial difference in the reactivity of these two groups of high-coordinated sulfur species. While SF_4 is extremely reactive towards water, sulfur hexafluoride **458** is very inert. The latter is not hydrolyzed by water vapors up to 500 °C and it does not react with halogens, HCl, NH_3 or molten KOH. This lack of reactivity is similar to CF_4 and to saturated fluorocarbons, and is kinetic rather than thermodynamic in origin. The best support of this explanation is the fact that the free energy of hydrolysis of sulfur hexafluoride is favorable (equation 203) and the average S—F bond energy of SF_4 (*ca* 78 kcal mol^{-1}) is slightly higher than that of SF_6 (72 kcal mol^{-1})[241].

$$\underset{\textbf{(458)}}{SF_6(g)} + 3H_2O(g) \longrightarrow SO_3(g) + 6HF(g) \qquad (203)$$

$$\Delta G^\circ = -48 \text{ kcal mol}^{-1}$$

Various explanations have been proposed for the lack of reactivity of **458** particularly towards nucleophiles. Direct attack of nucleophiles (such as hydroxyl ion) on the sulfur atom could only take place by extensive electronic rearrangement and, as such, may be expected to be difficult. Another factor may be the reluctance of combined fluorine atoms to interact with nucleophiles. This explanation is strongly supported by the fact that when one fluorine is replaced by chlorine, hydrolysis under basic conditions is rapid and replacement by bromine makes hydrolysis possible even in acidic media. In the following sections, the first (IV.A) will cover sulfur hexafluoride and its inorganic derivatives, the second (IV.B) will discuss the organic derivatives of sulfur hexafluoride and the final part (IV.C) will deal with persulfuranes in which the number of halogen ligands is two or less.

A. Sulfur Hexafluoride and Its Inorganic Derivatives

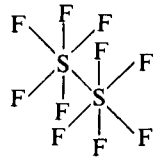
Sulfur hexafluoride was first isolated and characterized in 1900 by Moissan and Lebeau[242]. They prepared it by burning sulfur in an atmosphere of fluorine. This method is still used as a commercial synthesis. **458** can also be prepared according to the patent literature by heating a mixture of sulfur and chlorine in the presence of salts such as NaF, PbF_2 or HgF_2 at 400–1000 °C. Sulfur hexafluoride has the expected octahedral structure for sp^3d^2 hybridization. In contrast to its inertness towards nucleophiles, it shows appreciable reactivity towards electrophiles. Thus, at 225 °C it reacts with aluminum chloride to give sulfur chlorides and chlorine. It also reacts with sulfur trioxide to form sulfuryl fluoride (equation 204)[243].

$$\underset{\textbf{(458)}}{SF_6} + 2SO_3 \longrightarrow 3SO_2F_2 \qquad (204)$$

Although it does not react appreciably with sodium below 200 °C, it undergoes a rapid reaction with a solution of sodium in a diphenylethyleneglycol dimethyl ether even at −64 °C. At room temperature, quantitative reaction occurred within a few minutes according to equation 205[244].

$$8Na + SF_6 \longrightarrow Na_2S + 6NaF \qquad (205)$$

Disulfur decafluoride **459** was first isolated in a pure state from a mixture of gases formed during fluorination of sulfur to produce sulfur hexafluoride[245]. A convenient laboratory preparation is based on the photochemical reduction of sulfur chloride pentafluoride **426a** with hydrogen (equation 206)[246].

$$2\,SF_5Cl + H_2 \longrightarrow \underset{\textbf{(459)}}{\text{  }} \qquad (206)$$

(426a)

Although **459** like sulfur hexafluoride is resistant to hydrolysis by aqueous acid and bases, it reacts with many other reagents. For instance, it liberates iodine from potassium iodide and reacts rapidly with ammonia[247]. The last reaction under carefully controlled conditions can be used to obtain NSF_3. On heating, **459** starts to decompose rapidly at 150 °C to give sulfur hexafluoride and sulfur tetrafluoride (equation 207)[248].

$$\textbf{459} \xrightarrow{150\,^\circ C} SF_6 + SF_4 \qquad (207)$$

Chlorine and bromine react with **459** to form SF_5Cl (**426a**)[249] and SF_5Br (**426b**)[247], respectively, while sulfur dioxide affords SF_5OSO_2F (**460**)[250].

426a was first isolated and characterized as a minor by-product in the reaction of fluorine with sulfur dichloride[251]. The following two reactions are of synthetic value (equations 208 and 209)[252,232]:

$$SF_4 + ClF \xrightarrow{380\,^\circ C} SF_5Cl \qquad (208)$$

$$SF_4 + CsF + Cl_2 \xrightarrow{110\,^\circ C} SF_5Cl + CsCl \qquad (209)$$

After slight modification both reactions were applied also for the preparation of sulfur bromopentafluoride **426b**. In contrast to SF_5Cl, which is stable up to 400 °C, SF_5Br starts to decompose at 150 °C (equation 210).

$$2SF_5Br \longrightarrow SF_6 + SF_4 + Br_2 \qquad (210)$$

The decompositions of **426a** and **b** are much faster under UV radiation and their ability to give SF_5 radicals constitutes an important features of their chemistry.

In contrast to sulfur hexafluoride, these mixed halogenopersulfuranes are hydrolyzed by aqueous alkali and the bromide **426b** even by water. **426b** can be used to prepare a few other inorganic sulfur pentafluorides. Generally, the bromide reacts in the same way as the chloride **426a**, but usually at lower temperatures. Thus, photochemical reaction of **426a** with oxygen gives the peroxide **461** as the primary product, which is converted to SF_5OSF_5 (**462**) if **461** is allowed to reach appreciable concentrations in the reactor (equation 211)[253].

In the reaction with tetrafluorohydrazine the chloride **426a** gives the aminopersulfurane **463** (equation 212)[254].

$$\underset{\textbf{(426a)}}{SF_5Cl} + O_2 \xrightarrow{h\nu} \underset{\textbf{(461)}}{SF_5{-}O{-}O{-}SF_5} \longrightarrow \underset{\textbf{(462)}}{SF_5OSF_5} \qquad (211)$$

$$\textbf{426a} + F_2NNF_2 \longrightarrow \underset{\textbf{(463)}}{SF_5{-}NF_2} \qquad (212)$$

The preparation of aminosulfur pentafluoride **464** is based on the addition of two molecules of HF across the sulfur–nitrogen triple bond in thiazyl trifluoride NSF_3 (**451**) (equation 213)[255].

$$N{\equiv}S(F)(F)F + 2HF \longrightarrow SF_5NH_2 \qquad (213)$$

(**451**) (**464**)

The amine **464** dissociates slowly to NSF_3 and HF at room temperature and rapidly around 45 °C in the presence of moisture. It can, however, be handled in a dry vacuum system if transfers are made rapidly, and is stable when kept at − 78 °C. Hydrolysis of **464** occurs rapidly by aqueous base (equation 214).

$$SF_5NH_2 + 6OH^- \longrightarrow SO_3NH_2^- + 3H_2O \qquad (214)$$

(**464**)

The utility of **464** for the synthesis of a variety of organic derivatives will be presented in Section IV.B. Among other nitrogen-containing inorganic derivatives of sulfur hexafluoride, the [(pentafluorosulfanyl)imino]difluorosulfane, $SF_5N{=}SF_2$[256], the dichloro analogue $SF_5N{=}SCl_2$[257] and [(pentafluorosulfanyl)imino]chlorofluorosulfane $SF_5N{=}SClF$[258] are worthy of mention.

Pentafluorosulfur hypofluorite **465a** was obtained by fluorination of sulfur oxytetrafluoride over a silver difluoride or cesium fluoride catalyst (equation 215)[259,260].

$$SOF_4 + F_2 \xrightarrow[CsF \text{ or } AgF_2]{F_2} SF_5OF \qquad (215)$$

(**465a**)

The corresponding hypochlorite **465b** was obtained in a similar way by the alkali metal fluoride catalyzed addition of ClF to SOF_4 (equation 216)[261].

$$SOF_4 + ClF \xrightarrow{MF} SF_5OCl \qquad (216)$$

(**465b**)

The product reacts photochemically with tetrafluorohydrazine according to equation 217[261].

$$F_2NNF_2 + 2F_5SOCl \longrightarrow 2F_5SONF_2 + Cl_2 \qquad (217)$$

The formation of bis(pentafluorosulfur)peroxide **461** has already been mentioned in this section. As could be expected the chemistry of both, peroxide **461** and hypofluorite **465** is dominated by their facile decomposition into radicals (equations 218 and 219).

$$SF_5OF \rightleftharpoons SF_5O\cdot + F\cdot \qquad (218)$$

$$SF_5OSF_5 \rightleftharpoons 2SF_5O\cdot \qquad (219)$$

This property was used, for example, to synthesize bis(pentafluorosulfur)sulfate **466** by reacting the peroxide **461** with sulfur dioxide (equation 220)[262].

$$SF_5{-}O{-}O{-}SF_5 + SO_2 \longrightarrow SF_5O{-}\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}{-}OSF_5 \qquad (220)$$

(**461**) (**466**)

B. Organic Derivatives of Sulfur Hexafluoride

1. Organic derivatives of sulfur hexafluoride containing a sulfur–carbon bond

This type of persulfuranes can be prepared according to three general methods. The first is based on fluorination of various organosulfur derivatives with a lower oxidation state. The second group of methods utilize the addition of pentafluorosulfur halogenides to unsaturated hydrocarbons. The third approach involves the addition to organosulfur compounds in a lower oxidation state and of lower coordination number.

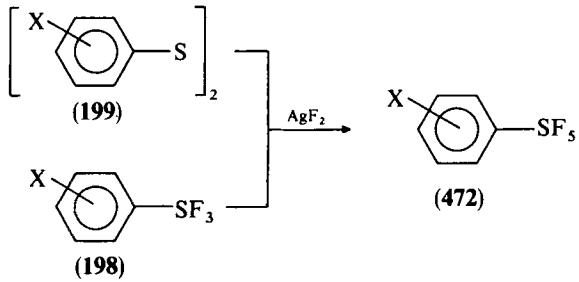
a. Fluorination of organosulfur compounds with a lower oxidation state. The first report on such a procedure appeared as early as 1950 when Silvey and Cady reported[263] the isolation and full characteristics of trifluoromethylsulfur pentafluoride **467** formed by fluorination of methyl mercaptan or of CS_2 with either cobalt trifluoride at 250 °C or with elemental fluorine (equation 221).

$$CH_3SH \text{ or } CS_2 \xrightarrow[\text{or } F_2]{CoF_3,\,250°C} \underset{\textbf{(467)}}{CF_3SF_5} \qquad (221)$$

Three years later it was reported[264] that interaction of carbon disulfide with fluorine gives, among other products, two persulfuranes **468** and **469** (equation 222).

$$CS_2 + F_2 \longrightarrow \underset{\textbf{(468)}}{CF_3CF_2SF_5} + \underset{\textbf{(469)}}{SF_5CH_2SF_5} + \text{other products} \qquad (222)$$

In 1959 it was found that electrolytic fluorination of dimethyl disulfide gives in a low yield a mixture of methylsulfur pentafluoride (**470**) and $CF_3SF_4CH_2F$ (**471**)[265]. The first general synthesis of arylsulfur pentafluorides **472** was accomplished by the reaction of diaryl disulfides **199** or arylsulfur trifluorides **198**[199] with silver difluoride at 120 °C (equation 223)[266].



(223)

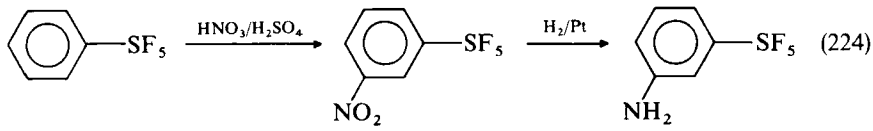
Arylsulfur pentafluorides prepared by the above procedures are listed in Table 7.

The stability of the parent phenylsulfur pentafluoride **472a** is similar to that of sulfur hexafluoride. Thus, it is recovered unchanged from refluxing solutions of sodium hydroxide in aqueous ethanol. It is also inert to concentrated sulfuric acid at moderate temperatures, and only a small amount of degradation occurs on heating a sample at 400 °C for several hours in a sealed glass tube. Phenylsulfur pentafluoride could be nitrated with nitric acid in concentrated sulfuric acid to afford **472b** in over 80% yield, suggesting that the pentafluorosulfur group has electron-withdrawing properties. The high stability of this group was further demonstrated when **472b** was catalytically hydrogenated to **472d** (equation 224).

TABLE 7. Arylsulfur pentafluorides, $XC_6H_4SF_5$ (**472**) prepared by fluorination of the disulfides **199** or the arylsulfur trifluorides **198**[a]

No	X	bp (°C) [mp °C]
a	H	72.0/48 mmHg
b	*m*-NO_2	85.5/2.6 mmHg
c	*p*-NO_2	[37.5–38.5]
d	*m*-NH_2	[37]
e	*p*-NH_2	[67.5–68.0]
f	*m*-NHC(O)Ph	[166–167]
g	*p*-N_3	57.5/1.0 mmHg
h	*m*-OH	[66.5]
i	*p*-OH	[104–105]
j	*p*-Cl	77/17 mmHg
k	*m*-Br	82.0/12 mmHg
l	*p*-Br	77.2/10 mmHg
m	*m*-CO_2H	[153.0–155.2]
n	*p*-CO_2H	[191.5–192.5]
o	*m*-$CH{=}CH_2$	74.5/10 mmHg
p	*m*-C_6H_5	[20.5–21.5]
q	*m*-(4-$NO_2C_6H_4$)	[128.6–129.0]
s	*m*-(2-$NO_2C_6H_4$)	[81.0–81.7]

[a] Taken from Reference 266.



(224)

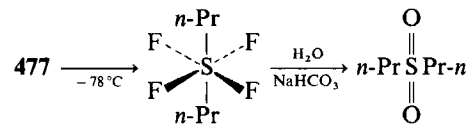
(472a) **(472b)** **(472d)**

The stability of the pentafluorosulfur group in arylsulfur pentafluorides allowed one to carry out some other conversions collected in Scheme 59.

Fluorination of cyclic and acyclic sulfides with trifluoromethyl hypofluorite gave dialkyl and diaryl tetrafluoropersulfuranes. Thus, treatment of di-*n*-propyl sulfide with an excess of CF_3OF at -80 °C gave di-*n*-propyl trifluoromethoxy trifluoropersulfurane **477** with unknown geometry (equation 225)[267].

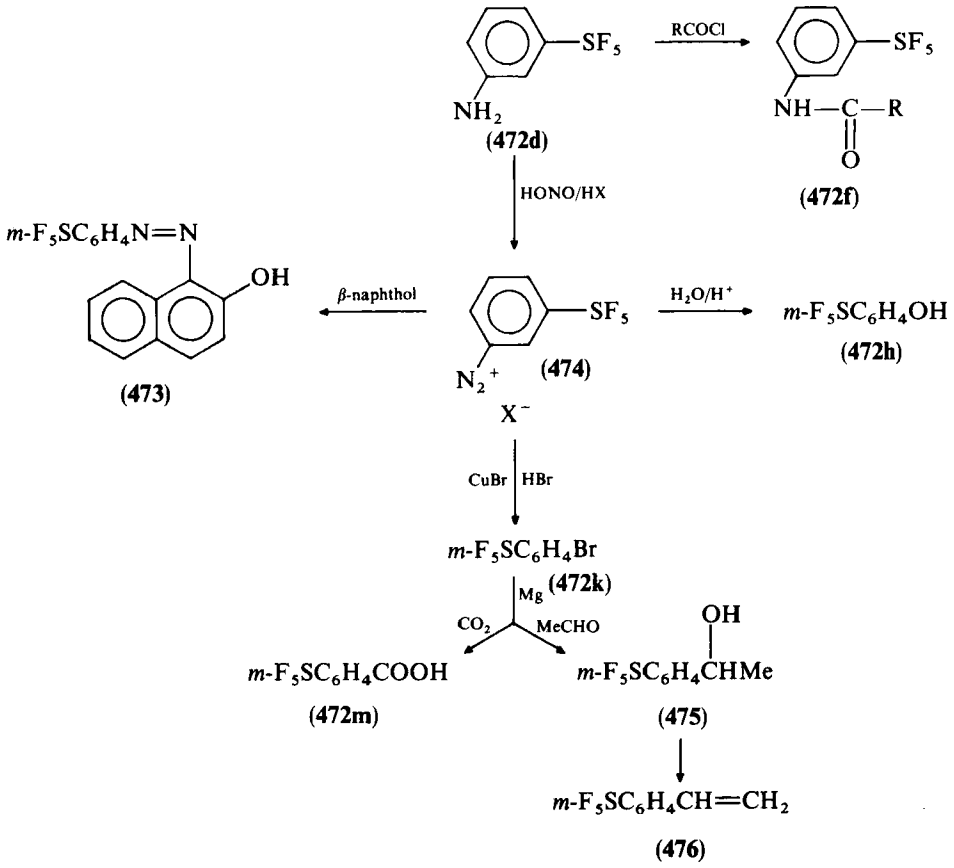
$$n\text{-PrSPr-}n + CF_3OF \longrightarrow (n\text{-Pr})_2SF_2OCF_3 \quad (225)$$

(477)



(226)

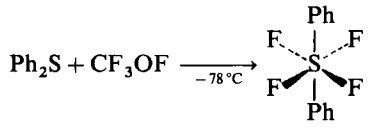
(478)



SCHEME 59

Since **477** with aqueous sodium bicarbonate at − 78 °C gave di-*n*-propyl sulfone, it was suggested that the alkoxypersulfurane **477** is converted to the corresponding tetrafluoropersulfurane **478** with the propyl groups *trans* to each other (equation 226).

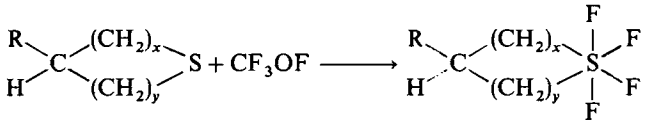
Treatment of diphenyl sulfide with CF_3OF at − 78 °C gave a product which had a single signal at − 64.5 ppm in the ^{19}F-NMR spectrum. It was assumed that this product was *trans*-diphenyl tetrafluoropersulfurane **479** (equation 227)[267].



(227)

(479)

Formation of the tetrafluorosulfur persulfurane structures was also observed in the reactions of the cyclic sulfides **480** with an excess of CF_3OF at − 78 °C (equation 228)[267].



(228)

(480) (481)

(a) $x = y = 1$; R = H
(b) $x = y = 2$; R = Me
(c) $x = 1$; $y = 2$; R = H
(d) $x = y = 2$; R = H

In general, warming solutions of the persulfuranes prepared in this way to room temperature is accompanied by extensive decomposition leading to unidentified products. Interestingly, decomposition of **481** was inhibited by adding trimethylsilyl *N,N*-diethylamine and such solutions of the persulfuranes **481a–d** were stable for several weeks[267].

Electrochemical fluorination (e.f.) of divalent organosulfur compounds to obtain high-coordinated sulfur derivatives was first applied in 1957 for dimethyl sulfide[268]. This reaction, carried out in anhydrous hydrogen fluoride, gave a mixture of the corresponding perfluorosulfurane **467** and persulfurane **195**, formed in a ratio of 10:1 (equation 229).

$$CH_3—S—CH_3 \xrightarrow[HF]{\text{e.f.}} \underset{\textbf{(467)}\ 20\%}{CF_3—SF_5} + \underset{\textbf{(195)}\ 2\%}{CF_3—SF_3} \qquad (229)$$

Under similar conditions carbons disulfide affords the persulfurane **467** in a yield above 90%, accompanied by small amounts of the persulfurane **482** and sulfurane **482a**[268].

$F_5SCF_2SF_5$ (**482**) $F_3SCF_2SF_3$ (**482a**)

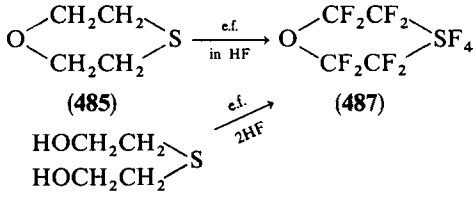
When electrochemical fluorination was extended to other dialkyl sulfides and disulfides, mixtures of the corresponding perfluoroalkylsulfuranes **483** and perfluorodialkylpersulfuranes **484** (equation 230) were obtained. However, yields of the isolated products were as a rule very low[268].

$$\begin{matrix} R^1SR^1 \\ \text{or} \\ R^1S—SR^1 \end{matrix} \xrightarrow[HF]{\text{e.f.}} \underset{\textbf{(483)}}{R_fSF_5} + \underset{\textbf{(484)}}{(R_f^1)_2SF_4} \qquad (230)$$

(a) $R^1 = C_2H_5$ (a) $R^1 = C_2F_5$
(b) $R^1 = C_3H_7$ (b) $R^1 = C_3F_7$
(c) $R^1 = C_4H_9$ (c) $R^1 = C_4F_9$

The ^{19}F-NMR spectra of the diperfluoroalkylsulfuranes **484** prepared in this way clearly indicated the *trans* relationship of the perfluoroalkyl substituents[269].

Electrofluorination of the cyclic sulfide **485** or bis(2-hydroxyethyl)sulfide **486** afford the tetrafluoropersulfurane **487** (equation 231)[270].



(231)

(485) (487)

$HOCH_2CH_2$
$HOCH_2CH_2$ S

(486)

Similarly, bis(2-diethylaminoethyl) disulfide **488** gives the corresponding sulfur tetrafluoride **489** (equation 232)[270].

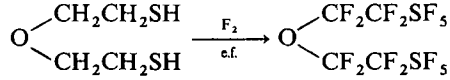
$$[Et_2NCH_2CH_2S]_2 \xrightarrow[\text{in HF}]{\text{e.f.}} (C_2F_5)_2NCF_2CF_2SF_4 \qquad (232)$$

(488) **(489)**

The same methodology applied to 1,4-butanedithiol **490**, 1,5-pentanedithiol **491** and 3-oxapentane-1,5-dithiol **492** and to the cyclic sulfides, tetrahydrothiophene **493**, 2-methyltetrahydrothiophene **494**, 3-methylthiophene **495** and tetrahydrothiopyran **496**, afforded the corresponding fully fluorinated tetrafluoro persulfuranes **497–502** and **487** (equations 233–237)[271].

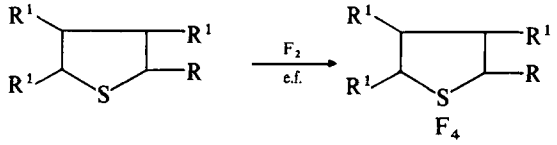
$$HS(CH_2)_nSH \xrightarrow[\text{e.f.}]{F_2} F_5S(CF_2)_nSF_5 \qquad (233)$$

(490) $n = 4$ **(497)** $n = 4$
(491) $n = 5$ **(498)** $n = 5$

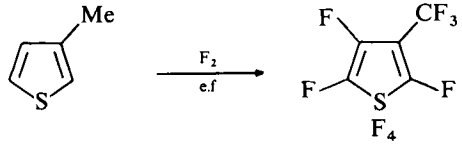


(492) **(499)** (234)

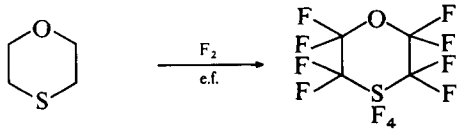
However, these products were generally formed in very low yields and contaminated by many fluorine-containing by-products, among them perfluorinated *n*-alkylsulfur persulfuranes such as **503–507**[271].



493 $R = R^1 = H$ **500** $R = R^1 = F$
494 $R = Me$, $R^1 = H$ **501** $R = CF_3$, $R^1 = F$ (235)



(495) **(502)** (236)



(496) **(487)** (237)

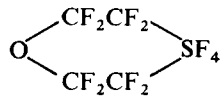
n-$C_4F_9SF_5$ (503)

n-$C_5F_{11}SF_5$ (504)

$C_2F_5OC_2F_4SF_5$ (505)

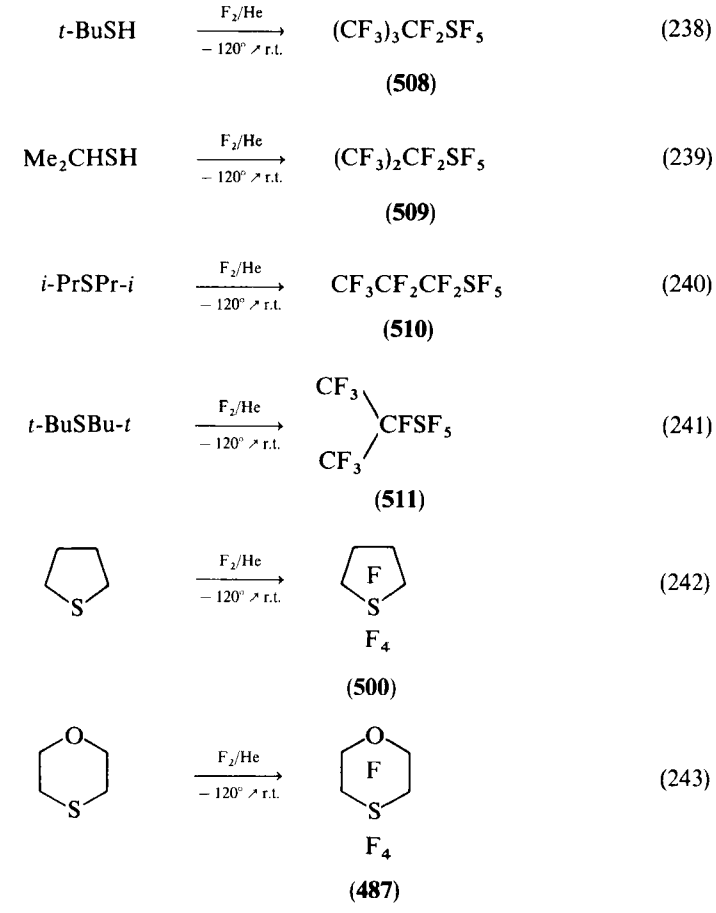
$SF_5CF_2CF_2SF_5$ (506)

$(C_2F_5)_2SF_4$ (507)



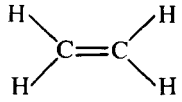
(487)

Very recently, combination of low temperature and helium dilution made it possible to eliminate structural rearrangements occurring in the cobalt trifluoride or electrochemical fluorination processes of highly branched alkyl mercaptans and sulfides as well as of cyclic sulfides. Under such conditions a series of pentafluoro and tetrafluoro persulfuranes was produced in relatively high yields (equations 238–243)[272].



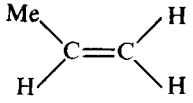
b. Addition of pentafluorosulfur halides to unsaturated hydrocarbons. Addition of pentafluorosulfur halides, such as the chloride **426a** and the bromide **426b**, to unsaturated hydrocarbons has been proven to be a general and useful methodology for the preparation of pentafluoro persulfuranes containing one sulfur–carbon bond. This reaction can be executed under thermal conditions as well as by irradiation with visible or UV light. The reaction course depends on both reaction partners, however, the primary factor is the structure of the unsaturated compound.

The first report on this reaction was published, in 1961[273]. This shows that **426a** adds to certain olefins and chloroolefins to give 2-chloroalkylsulfur pentafluorides. The scope of the reaction is rather wide and it was performed with ethylene, propene, butadiene, vinyl chloride and cyclohexene, giving the corresponding persulfuranes shown in equations 244–248.

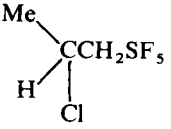


+ **426a** ⟶ $ClCH_2H_2SF_5$ (244)

(512) (47%)

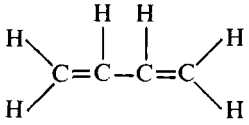


+ **426a** ⟶

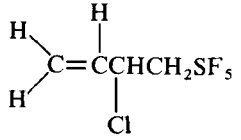


(245)

(513) (78%)

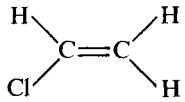


+ **426a** ⟶

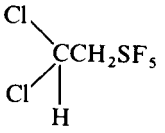


(246)

(514) (15%)



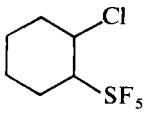
+ **426a** ⟶



(247)

(515) (25%)

+ **426a** ⟶



(248)

(516) (~ 15%)

The reaction failed with isobutene and styrene because these olefins polymerized very rapidly in the presence of **426a**. Ethylene and vinyl chloride also showed a tendency to polymerization as indicated by the fact that the simple addition products (**512** or **515**) were accompanied by small amounts of higher-boiling fractions from which telomers containing two molecules of the olefin were isolated. For instance, from **426a** and ethylene 4-chlorobutylsulfur pentafluoride $ClCH_2CH_2CH_2CH_2—SF_5$ (**517**) was isolated in *ca* 8% yield. The reactions could be carried out in an autoclave, or at atmospheric pressure with UV irradiation. The structures of the isolated products may be easily rationalized in terms of a free radical mechanism shown in Scheme 60.

$$R^{\cdot} + SF_5Cl \longrightarrow RCl + SF_5^{\cdot}$$

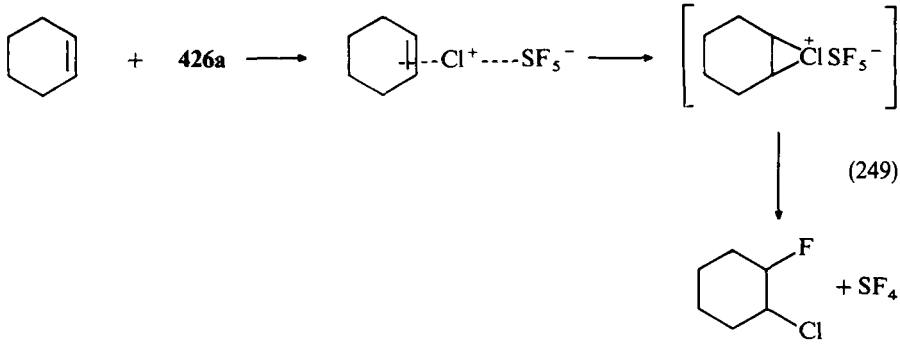
$$SF_5^{\cdot} + RCH{=}CH_2 \longrightarrow R\dot{C}HCH_2SF_5$$

$$R\dot{C}HCH_2SF_5 + SF_5Cl \longrightarrow \underset{\displaystyle Cl}{\underset{|}{RCHCH_2SF_5}}$$

SCHEME 60

This proposal was supported by the isolation of telomers from the reactions of **426a** with ethylene and vinyl chloride. However, the very rapid polymerization of isobutene and styrene by **426a** suggests that it can sometimes react ionically, and the formation of chlorofluorocyclohexane **518** (equation 249) from cyclohexene strengthens this assumption.

The β-chloroalkyl(or cycloalkyl)sulfur pentafluorides prepared as shown above eliminate hydrogen chloride on treatment with potassium hydroxide and give pentafluorosulfur substituted olefins **519–521** (equation 250).



(518)

$$\underset{\displaystyle Cl}{\underset{|}{RCHCH_2SF_5}} \xrightarrow{KOH} \underset{}{\overset{R}{\overset{|}{HC{=}CHSF_5}}} \qquad (250)$$

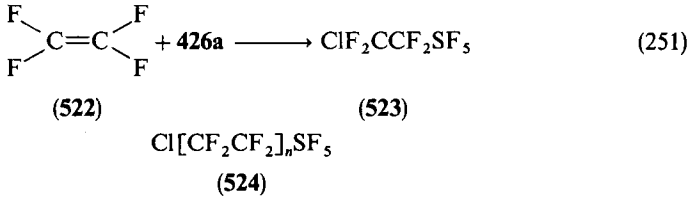
(512) R = H	**(519)** R = H
(513) R = Me	**(520)** R = Me
(515) R = Cl	**(521)** R = Cl

With fluoroolefins, the title addition does not take place readily and a free radical initiator was used to promote it in the liquid phase. When the reaction was carried out in

the gas phase, the expected chlorofluoroalkyl sulfur pentafluorides were contaminated with other products[273].

With tetrafluoroethylene, addition of **426a** proceeds smoothly in the presence of dibenzoyl peroxide as a catalyst at 100 °C to give 2-chlorotetrafluoroethylsulfur pentafluoride **523** as the major product (equation 251)[274].

However, telomers **524** were also obtained depending on the molar ratios of the reactants.



(251)

(522) **(523)**

$Cl[CF_2CF_2]_nSF_5$

(524)

Trifluoroethylene reacts under similar conditions to give mainly the product of a 1:1 addition, i.e. the persulfurane **525**[274]:

$$CHF{=}CF_2 + \mathbf{426a} \longrightarrow ClCF_2CHFSF_5$$

(525)

It is interesting to mention that this compound, in sharp contrast to other pentafluoro sulfuranes, is unstable in aqueous alkali solutions and decomposes, giving sulfide ions. However, with powdered potassium hydroxide in light petroleum it undergoes β-elimination to afford perfluorovinylsulfur pentafluoride **526** (equation 252)[274].

$$\mathbf{525} \xrightarrow{KOH} CF_2{=}CFSF_5 \qquad (252)$$

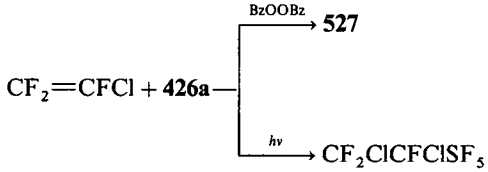
(526)

Addition of **426a** to chlorotrifluoroethylene gives small amounts of 2,2-dichlorotrifluoroethylsulfur pentafluoride **527** (equation 253) and much high-boiling material, probably telomers[274].

$$CF_2{=}CFCl + \mathbf{426a} \longrightarrow CFCl_2CF_2SF_5 \qquad (253)$$

(527)

In contrast to the olefins discussed above, hexafluoropropene does not react with **426a** even in the presence of benzoyl peroxide at 150 °C. By UV irradiation a complex mixture of products was obtained. The same results were obtained with tetrafluoroethylene and chlorotrifluoroethylene. Among the products of the reaction with chlorotrifluoroethylene, compound **528** was isolated, which is the isomer of **527** obtained in the benzoyl peroxide catalyzed reaction (equation 254)[274].



(254)

(528)

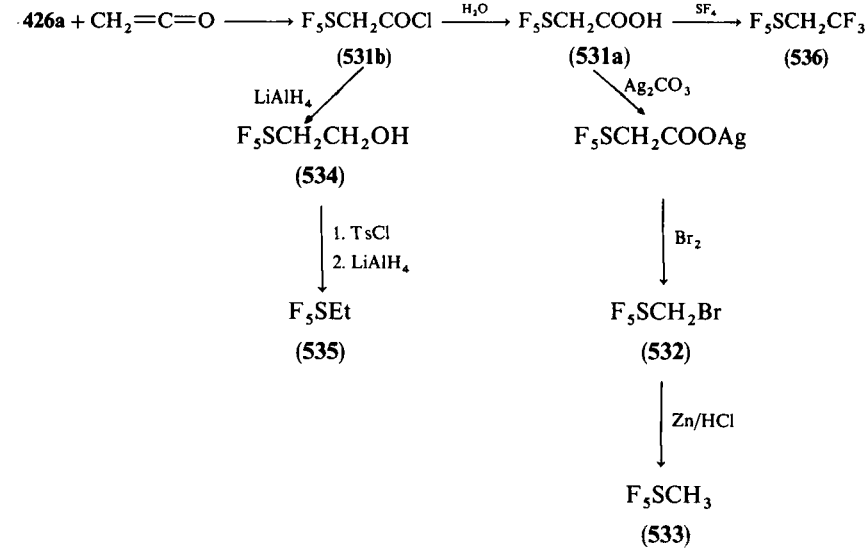
The UV-initiated addition of **426a** to fluoroethylene yields 2-chloro-2-fluoroethylsulfur pentafluoride (**529**). The latter, by elimination, gives the unsaturated persulfurane **530** (equation 255)[275].

$$CH_2{=}CHF + \textbf{426a} \longrightarrow CHFClCH_2SF_5 \quad \textbf{(529)}\ (76\%) \qquad (255)$$

$$\downarrow \text{NaOH}$$

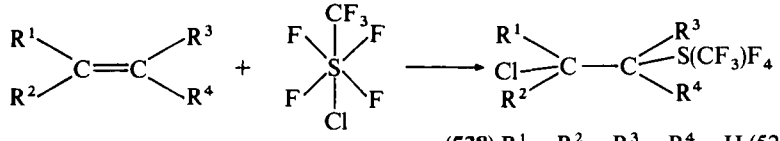
$$FCH{=}CHSF_5 \quad \textbf{(530)}$$

Addition of **426a** to ketene is a key step in the synthesis of α-pentafluorosulfur substituted acetic acid **531a**. This acid as well as its chloride (**531b**) were used as substrates for the preparation of various alkylsulfur pentafluorides. Some examples are shown in Scheme 61[276,277].



SCHEME 61

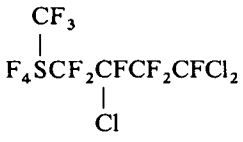
trans-Trifluoromethylsulfur chloride tetrafluoride **537** was found to react in a Pyrex apparatus with various olefins forming the normal addition products **538–543** (equation 256)[278].



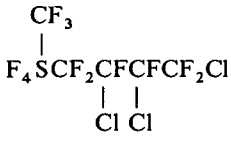
(526)

(**538**) $R^1 = R^2 = R^3 = R^4 = H$ (52%)
(**539**) $R^1 = Me$; $R^2 = R^3 = R^4 = H$ (59%)
(**540**) $R^1 = R^2 = R^3 = R^4 = F$ (85%)
(**541**) $R^1 = CF_3$; $R^2 = R^3 = R^4 = F$ (44%)
(**542**) $R^1 = R^2 = F$; $R^3 = R^4 = H$ (57%)
(**543**) $R^1 = R^2 = R^3 = F$; $R^4 = H$ (47%)
(**544**) $R^1 = R^1 = R^3 = F$; $R^4 = Cl$ (23%)

However, equimolar quantities of **537** and $CF_2{=}CFCl$ gave both the 1:1 adduct **543** and two isomeric 1:2 adducts **545** and **546**.

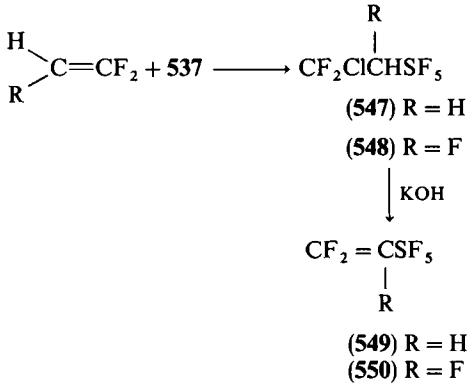


(545)



(546)

Photolysis of **537** with $CH_2{=}CF_2$ and $CHF{=}CF_2$ gave rise to anti-Markovnikow-type products **547** and **548**, which were readily dehydrochlorinated with powdered KOH to form the unsaturated persulfuranes **549** and **550** (equation 257)[278].



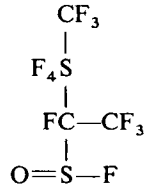
(257)

(547) R = H
(548) R = F

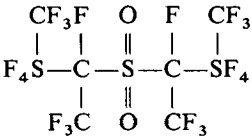
KOH

(549) R = H (57%)
(550) R = F (47%)

Upon treatment of **550** with SF_4 or SOF_2 and SO_2F_2 in the presence of cesium fluoride, new sulfuranes **551** and **552** were formed.

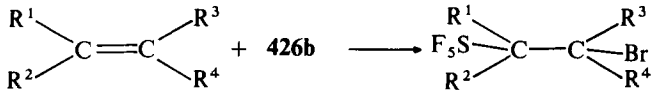


(551)



(552)

The reaction of pentafluorosulfur bromide **436b** with fluoroolefins was reported in 1968 by Steward and coworkers[279], who found that the reaction at room temperature in a Pyrex glass vessel gives an addition across the double bond (equation 258).



(258)

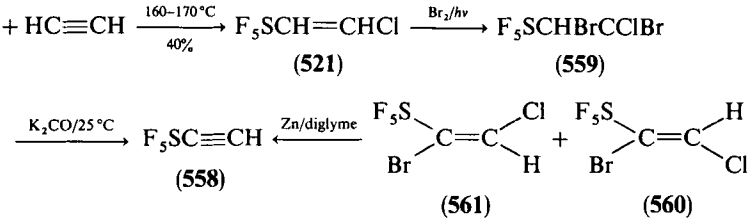
(553) $R^1 = R^2 = R^3 = H$; $R^4 = F$ (70%)
(554) $R^1 = R^2 = H$; $R^3 = R^4 = F$ (70%)
(555) $R^1 = H$; $R^2 = R^3 = R^4 = F$ (46%)
(556) $R^1 = Cl$; $R^2 = R^3 = R^4 = F$ (60%)

All reactions proceeded smoothly at room temperature and only in the case of fluoroethylene was some decomposition observed. The proposed structure for the addition products was supported by the NMR data that showed the SF_5 group to be attached to the carbon carrying more hydrogens. This assignment further substantiated the result of the dehydrobromination of **555** leading to perfluoroethylene persulfurane **550** (equation 259)[279].

$$\mathbf{555} + KOH \xrightarrow[\text{p. ether}]{} F_5SCF{=}CF_2 \quad (259)$$
$$\mathbf{(550)}$$

Pentafluorosulfur halogenides also add to carbon–carbon triple bonds. Such an addition of **426a** to acetylene is the key step in the first synthesis of acetylenesulfur pentafluoride **558** presented in Scheme 62[280].

As shown below, thermal addition of **426a** to acetylene affords 2-chlorovinylsulfur pentafluoride **521**. The other reactions presented in Scheme 62 lead to new saturated and unsaturated persulfuranes **559–561**. The dehalogenations of the bromochloropersulfuranes **560** and **561** gave the desired acetylenic persulfurane **558**, which undergoes some



(426a) **(521)** **(559)** **(558)** **(561)** **(560)**

SCHEME 62

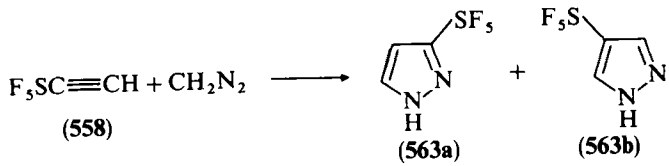
very interesting reactions. Thus the base-catalyzed addition of methanol to **558** gave *cis*-2-methoxyvinylsulfur pentafluoride **562a** (equation 260)[280].

$$\mathbf{558} + MeOH \xrightarrow{OH^-} \underset{H}{\overset{F_5S}{\diagdown}}C{=}C\underset{H}{\overset{OMe}{\diagup}} \quad (260)$$
$$\mathbf{(562a)}$$

Its *trans*-isomer **562b** was prepared by treatment of 2-chlorovinylsulfur pentafluoride (**521**) with methanolic potassium hydroxide (equation 261)[280].

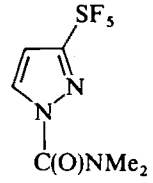
$$F_5SCH{=}CHCl + MeOH \xrightarrow{OH^-} \underset{H}{\overset{F_5S}{\diagdown}}C{=}C\underset{OMe}{\overset{H}{\diagup}} \quad (261)$$
$$\mathbf{(521)} \qquad \mathbf{(562b)}$$

The well-known addition of diazomethane to multiple bonds when applied to the persulfurane **558** gives a mixture of the isomeric pyrazoles **563a** and **563b** (equation 262) in a 4:6 ratio[280].

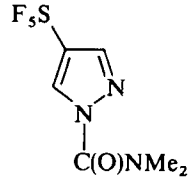


(558) **(563a)** **(563b)** (262)

Dimethylcarbamylation of this isomeric mixture gave products **564a** and **564b**, evidently derived from **563a** and **563b**, respectively[280].

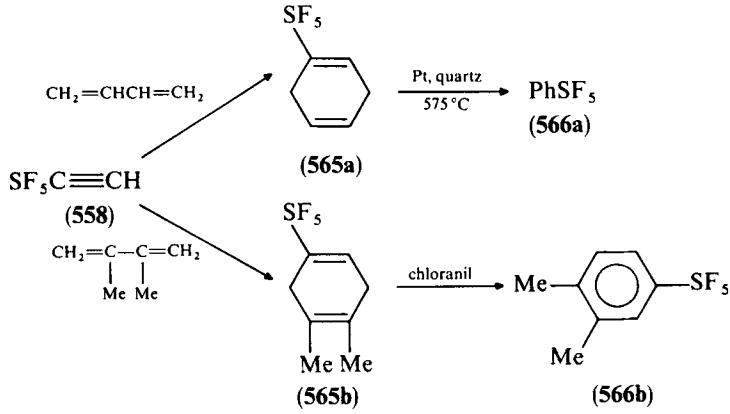


(564a)



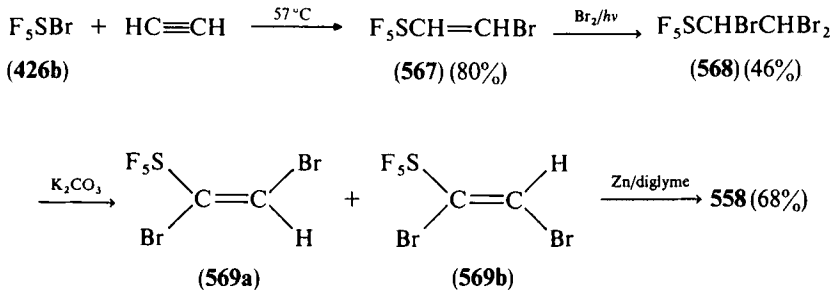
(564b)

A simple two-step synthesis of SF_5-substituted benzenes was developed in which the Diels-Alder reaction of **558** with 1,3-butadienes gives the key intermediate **565a** and **565b** the dehydrogenation of which yields alkyl-substituted phenylsulfur pentafluorides **566a** and **566b**[280] (Scheme 63).



SCHEME 63

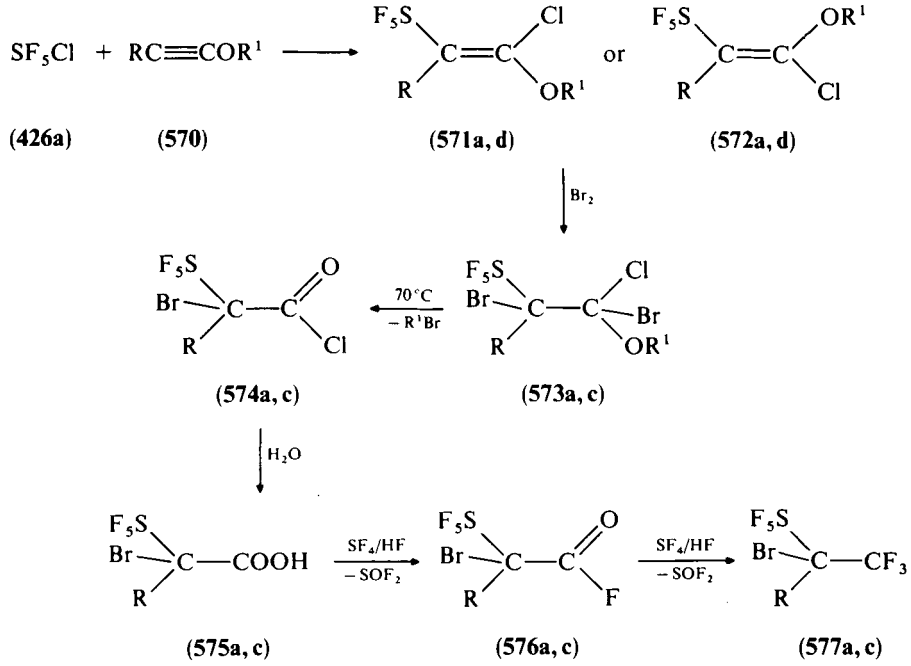
Recently, starting from **426b** a similar approach for the ethynylsulfur pentafluoride **558** presented in Scheme 64 was described[281]. Because of the unexpected low yields of the bromine addition to 2-bromovinylsulfur pentafluoride **567**, the overall yield of **558** was only 9% (Scheme 64). However, direct dehydrobromination of **567** gave the acetylene **558** in *ca* 50% yield (equation 263).



SCHEME 64

$$\mathbf{567} \xrightarrow[\text{petroleum ether}]{\text{KOH}} \mathbf{558} \qquad (263)$$

The addition of **426a** to 1-methoxy-2-methylacetylene and isolation of the persulfuranes **428–431** has already been mentioned in Section III.C2. The addition of this chloride to alkoxyacetylenes **570** and some other reactions, leading to the formation of modified persulfuranes, are presented in Scheme 65[229].

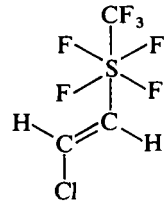


(a) R = H; R^1 = Me
(b) R = H; R^1 = Et
(c) R = R^1 = Me
(d) R = Me; R^1 = Et

SCHEME 65

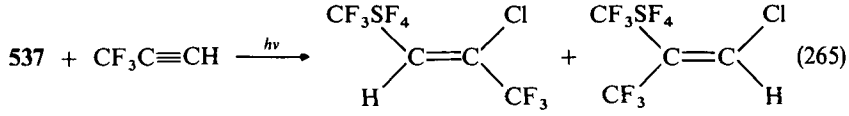
Addition of *trans*-trifluoromethylsulfur tetrafluoride chloride **537** to acetylene was found to give the *trans, trans*-persulfurane **578** (equation 264)[282,283].

$$\mathbf{537} + \text{HC}{\equiv}\text{CH} \longrightarrow \qquad (264)$$



(578)

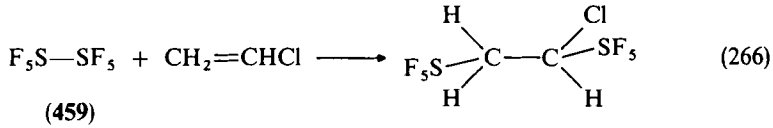
Two isomeric olefins, **579** and **580**, that contain the CF_3SF_4 group, were obtained when the chloride **537** and trifluoromethylacetylene were photolyzed. These isomers were separated by gas chromatography and identified as *Z* isomers based on the analysis of their respective ^{19}F- and ^{1}H-NMR spectra (equation 265)[283].



(265)

(579) **(580)**

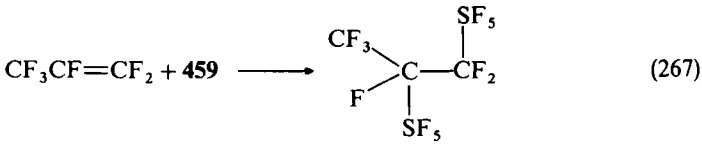
Disulfur decafluoride (**459**) also adds to olefins and fluoroolefins under pressure and elevated temperatures to give small amounts of the SF_5 addition products. Thus with vinyl chloride, chloro-1,2-bis(pentafluorothio)ethane **581** is formed in less than 10% yield (equation 266)[284].



(266)

(459) **(581)**

In a similar way, heating a mixture of hexafluoropropene with **459** in an autoclave at 200 °C for 15 h produces perfluoro-1,2-bis(pentafluorothio)propane **582** (equation 267)[284].



(267)

(582)

When **459**, benzene and trichlorofluoromethane were heated at 180 °C for 10 h, a fraction containing minute amounts of phenylsulfur pentafluoride was isolated (equation 268)[284].

$$\mathbf{459} + Cl_3CF \longrightarrow PhSF_5 \qquad (268)$$

Tremblay reported[285] that the formation of persulfuranes **583–589** was detected in the reaction of **459** with olefins, dienes and acetylenes carried out under pressure at 125–140 °C.

$CH_2FCHClSF_5$ $CH_2FCHBrSF_5$ $CFH_2CHBrCH_2CHBrSF_5$ $CFH_2CHFCH_2CHFSF_5$

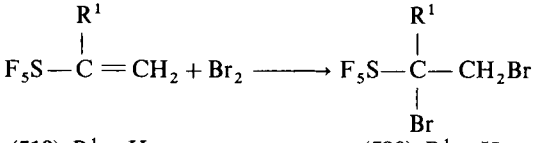
(583) **(584)** **(585)** **(586)**

$CH_2{=}CHCHFCH_2SF_5$ $FCH_2CF_2CH_2SF_5$ $EtCF_2CHFSF_5$

(587) **(588)** **(589)**

Modification of the addition products of pentafluorosulfur halides to unsaturated hydrocarbons leads to new persulfuranes in which the carbon-containing ligand under-

goes further functionalization. Some selected examples are presented below. Although bromine was found to react very slowly with vinylsulfur pentafluoride **519** at room temperature, the reaction became rapid by exposing the reaction mixture to a 275–W sun lamp for 37 min, when 1,2-dibromoethylsulfur pentafluoride (**590**) was formed in 82% yield. Under similar conditions 1-bromovinylsulfur pentafluoride (**591**) adds bromine giving 88% of 1,1,2-tribromoethylsulfur pentafluoride **592** (equation 269)[286].

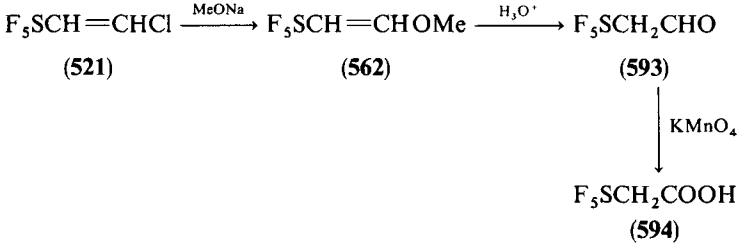


(269)

(**519**) $R^1 = H$ (**590**) $R^1 = H$
(**591**) $R^1 = Br$ (**592**) $R^1 = Br$

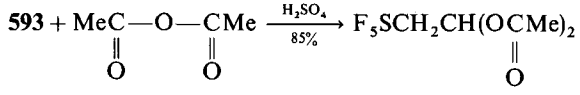
Debromination of **590** to **591** occurs easily upon treatment with powdered K_2CO_3 in acetone solution for 75 min[286].

Pentafluorothioacetaldehyde **593** was prepared by acid hydrolysis of 2-methoxyvinylsulfur pentafluoride (**562**), which was formed *in situ* by treatment of **521** with finely-powdered sodium methoxide. Oxidation of the aldehyde **593** afforded the corresponding acid **594**. Its dissociation constant in aqueous solution is 3.9×10^{-3}, i.e. its acidity is between that of monofluoroacetic acid and of difluoroacetic acid (Scheme 66)[286].



SCHEME 66

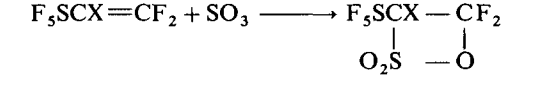
Bis(acetoxy)ethylsulfur pentafluoride **595** was obtained when **593** was added to an excess of acetic anhydride containing one drop of concentrated sulfuric acid and the resulting mixture was kept for 4 h at a temperature below 40 °C (equation 270)[280].



(270)

(**595**)

Addition of sulfur trioxide to 2,2-difluorovinylsulfur pentafluorides **549a** gave the already mentioned pentafluorothiosultone **441a**, when heated in a Carius tube at 100 °C (equation 271). The same reaction with **549b** gave the fluoro-analogue **441b**[287,288].



(271)

(**549**) (**441**)
(**a**) X = H (**a**) X = H
(**b**) X = F (**b**) X = F

These sultones undergo rearrangement in the presence of NaX (X = I, F) or Et_3N, giving the isomeric bifunctional fluorides **596** (equation 272[287-291].

$$\mathbf{441a,b} \xrightarrow[Et_3N \text{ for b}]{NaX \text{ for a}} F_5SCX(SO_2F)-C(=O)F \qquad (272)$$

(596)
(a) X = H
(b) X = F

In the presence of water both **596a** and **b** so obtained are hydrolyzed and decarboxylated to form the SF_5-containing sulfonyl fluorides **597a, b** (equation 273)[287,288,290].

$$\mathbf{596a,b} + H_2O \longrightarrow \left[F_5SCXCOOH(SO_2F)\right] + HF \longrightarrow F_5SCHXSO_2F + CO_2 \qquad (273)$$

(597)
(a) X = H
(b) X = F

Treatment of the latter with an aqueous hydroxide solution gives the corresponding sodium salts **598a, b** from which, upon passing gaseous hydrogen chloride, the free sulfonic acids **599a, b** were isolated (equation 274)[292].

$$\mathbf{597a,b} \xrightarrow[2.\,HCl]{1.\,NaOH} F_5SCHXSO_3Y \qquad (274)$$

(a) X = H **(598)** Y = Na
(b) X = F **(599)** Y = H

Interaction of the sultone **441** with fluoroalcohols produces new bifunctional SF_5-containing derivatives **600** and **601** (equation 275)[292].

$$\mathbf{441} + R_FOH + NaF \longrightarrow F_5SCH(SO_2F)-C(=O)OR_f \qquad (275)$$

(600) $R_f = CF_3CH_2$
(601) $R_f = (CF_3)_2CH$

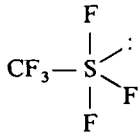
With a fluorinated diol the diester **602** was formed (equation 276)[292].

$$\mathbf{441} + HOCH_2(CF_2)_3CH_2OH \xrightarrow{2\,NaF} [F_5SCH(SO_2F)-C(O)O-CH_2CF_2]_2CF_2 + 2NaHF_2 \qquad (276)$$

(602)

The base-induced rearrangement of **441** to form a new ketenopersulfurane structure **443** has already been discussed (see equation 192).

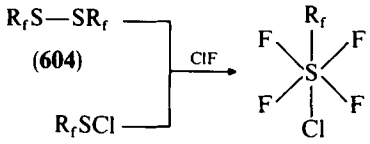
c. Addition to derivatives having a lower oxidation or coordination number. Only a limited number of such reactions is described in the literature. One procedure is a nucleophilic addition of the fluoride anion to trifluoromethylsulfur trifluoride **195** occuring when the sulfurane is treated with elemental chlorine in the presence of cesium fluoride. This reaction results in the formation of *trans*-trifluoromethylsulfur tetrafluoride chloride (**537**) (equation 277)[293].



$$+ \ Cl_2 \xrightarrow{CsF} \mathbf{537} \qquad (277)$$

(195)

The *trans* isomers of persulfuranes **603** were formed during oxidative addition of chlorine fluoride to perfluoroalkyl disulfides **604** or perfluoralkylsulfenyl chlorides **605** (equation 278)[294].



(278)

(604) **(605)** **(603)**

(a) $R_f = CF_3$
(b) $R_f = C_2F_5$
(c) $R_f = n\text{-}C_3F_7$
(d) $R_f = n\text{-}C_4F_9$

In contrast, the reaction of chlorine fluoride with bis(perfluoroalkyl) sulfides **606** affords mixtures of *cis* and *trans* isomers, the latter being a major product (equation 279)[294].

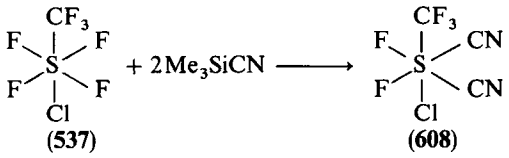
$$\underset{\mathbf{(606)}}{R_fSR_f} + 4ClF \longrightarrow \underset{\mathbf{(607)}}{cis/trans\ (R_f)_2SF_4} \qquad (279)$$

(a) $R_f = CF_3$
(b) $R_f = C_2F_5$

On the other hand, alkyl perfluoroalkyl sulfides and $CF_3SCH_2SCF_3$ form exclusively the *trans* adducts under the same reaction conditions[295].

Several addition reactions leading from the carbon analogues of sulfurane oxides to organic derivatives of sulfur hexafluoride have already been discussed in this review (see equations 182, 184 and 193).

d. Mutual interconversion among persulfuranes via a nucleophilic exchange or a free radical reaction. In the only known reaction of this type, a moderately stable hexacoordinate persulfurane **608** with four different ligands is formed when trifluoromethylsulfur tetrafluoride chloride **537** reacts with trimethylsilyl cyanide (equation 280)[296].



(537) (608) (280)

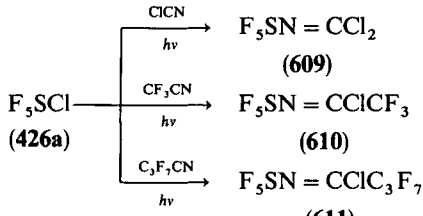
2. Organic derivatives of sulfur hexafluoride containing a sulfur–nitrogen bond

Organic persulfuranes, which posses a sulfur–nitrogen bond, can be prepared by two general methods and a few special procedures. The oldest and still most common approach to the title compounds is based on the addition of pentafluorosulfur chloride **426a** to the carbon–nitrogen triple bond[232] (equation 281). The second general method utilizes aminosulfur pentafluoride (pentafluorosulfanylamide) **464** as a starting material which is further functionalized.

$$F_5SCl + X{-}C{\equiv}N \xrightarrow{h\nu} F_5SN{=}CXCl \qquad (281)$$

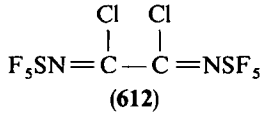
(426a)

The first method involves the photolytically induced free-radical reaction between **426a** and a cyano component. Although its scope is limited and yields are low, these imines can be further modified increasing substantially the synthetic utility of the method. Addition of SF_5Cl to cyanogen chloride and perfluoronitriles is illustrated in Scheme 67.



SCHEME 67

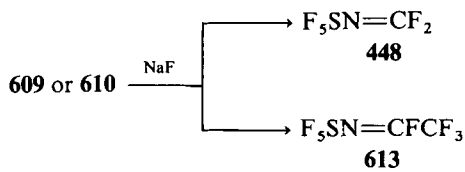
Under the same reaction conditions, cyanogen chloride undergoes a double addition of SF_5Cl to form the bis-adduct **612**[232].



(612)

All of the above-described perfluorosulfur imines are stable on storage in glass and moderately resistant to hydrolysis at 25 °C. In aqueous alkali solutions they decompose quickly and all the fluorine atoms attached to sulfur appear in the water phase as fluoride anions[232].

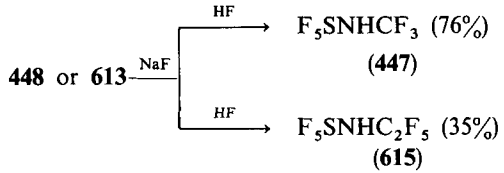
The chlorine atoms in these imines readily undergo exchange with fluoride ion to form the corresponding difluoroimines **448** and **613** (equation 282)[232].



(282)

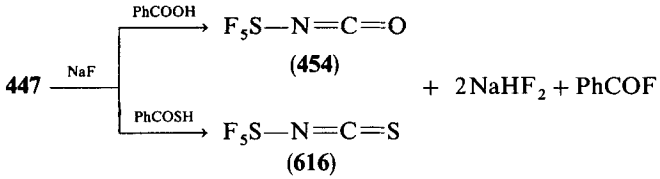
Hydrogen fluoride adds to both the above azomethines to give amines **447** and **615** (equation 283)[232].

These amines are thermally stable and do not attack glass, but they are completely hydrolyzed by aqueous alkali. The amine **615** tends to dissociate on heating. When the amine **447** was allowed to react either with benzoic acid or thiobenzoic acid in the presence



(283)

of sodium fluoride, the first isocyanate **454** and isothiocyanate **616** derivatives of sulfur hexafluoride were formed, respectively (equation 284)[232].



(284)

An alternative preparation of the isothiocyanate **616** involves thiolysis of the dichloroimine **609** with hydrogen sulfide in the presence of sodium fluoride as a hydrogen chloride acceptor[232].

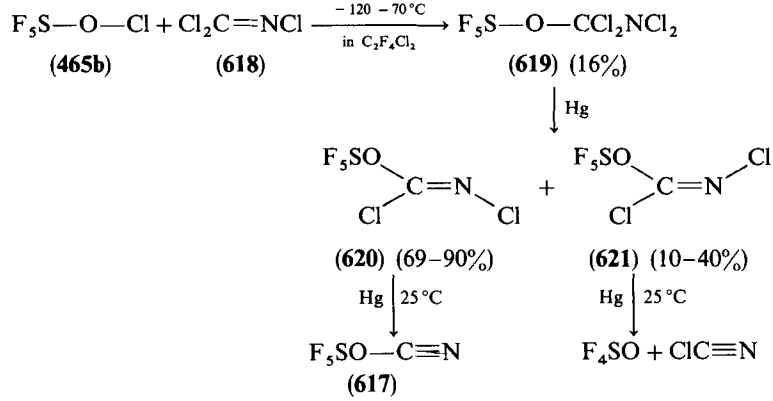
616 can also be prepared in very high yield from **609** and phosphorus pentasulfide in boiling toluene (equation 285)[297].

$$\mathbf{609} + P_2S_5 \longrightarrow \underset{(\mathbf{616})}{F_5S{-}N{=}C{=}S} \tag{285}$$

A recent synthesis of the isocyanate **454** is based on the dehydration of aminosulfur pentafluoride (**464**) with carbonyl difluoride (equation 286)[298].

$$\underset{(\mathbf{464})}{F_5SNH_2} + COF_2 \longrightarrow \mathbf{454} + 2HF \tag{286}$$

The pentafluoride **617**, which is an isomeric form of **454**, was recently isolated in 10% yield in the sequence of reactions shown in Scheme 68[299,300].



SCHEME 68

The above-mentioned isocyanate and isothiocyanate derivatives are rapidly decomposed by aqueous alkali and react easily with alcohols to give urethanes **622** (equation 287) and thiourethane **623** (equation 288), respectively. With thiols they give thiolurethanes **624** (equation 289) and dithiourethane **625** (equation 290). Their reaction with amines leads to a variety of substituted ureas **626** and **627** and thiourea **628** (equations 291–293)[297].

$$F_5S{-}N{=}C{=}O + ROH \longrightarrow F_5SNHCOOR \quad (287)$$

(**454**) (**622**)

(**a**) R = Me
(**b**) R = $CH_2CH_2OC(O)NHSF_5$
(**c**) R = Ph
(**d**) R = 4-$C_6H_4OC(O)NHSF_5$
(**e**) R = 4-C_6H_4OH

$$\mathbf{616} + CH_3OH \longrightarrow F_5SNHC(S)OMe \quad (288)$$

(**623**)

$$\mathbf{454} + RSH \longrightarrow F_5SNHC(O)SR \quad (289)$$

(**624**)

(**a**) R = Me
(**b**) R = Ph

$$\mathbf{616} + MeSH \longrightarrow F_5SNHC(S)SMe \quad (290)$$

(**625**)

$$\mathbf{454} + RNH_2 \longrightarrow F_5SNHC(O)NHR \quad (291)$$

(**626**)

(**a**) R = H
(**b**) R = Me
(**c**) R = $CH_2CH_2NHC(O)NHSF_5$
(**d**) R = Ph
(**e**) R = 4-$C_6H_4NHC(O)NHSF_5$
(**f**) R = 4-$C_6H_4CH_2C_6H_4NHC(O)NHSF_5$

$$\mathbf{454} + R^1R^2NH \longrightarrow F_5SNHC(O)NR^1R^2 \quad (292)$$

(**627**)

(**a**) $R^1 = R^2 = Et$
(**b**) $R^1, R^2 = -(CH_2)_5-$
(**c**) $R^1 = R^2 = Ph$

$$\mathbf{616} + PhNH_2 \longrightarrow F_5SNHC(S)NHPh \quad (293)$$

(**628**)

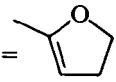
Treatment of **454** with tertiary amines leads to the zwitterionic thiourea **629** (equation 294).

$$\mathbf{454} + R_3N \longrightarrow F_5SN^-{-}C(O)NR_3^+ \quad (294)$$

(**629**)

Isocyanate **454** reacts also with aldehydes **630** to form a series of iminopersulfuranes **631** (equation 295)[297].

$$\underset{\textbf{(630)}}{\textbf{454} + RC(O)H} \longrightarrow \underset{\textbf{(631)}}{F_5SN{=}CHR} + CO_2 \qquad (295)$$

(a) R = Ph
(b) R = *p*-Tol
(c) R = *p*-An
(d) R = 

In a similar way *N,N*-disubstituted formamides give with **454** the persulfuranes **631** (equation 296)[297].

$$\textbf{454} + RR^1N{-}C(O)H \longrightarrow \underset{\textbf{(632)}}{F_5SN{=}CHNRR^1} + CO_2 \qquad (296)$$

(a) R = R¹ = Me
(b) R = Me; R¹ = Ph

The reaction of the isothiocyanate **616** with *N,N*-dimethylacetamide occurs with elimination of the COS molecule and simultaneous formation of the persulfurane **632a**[297].

A closely related reaction of **454** with DMSO affords the persulfurane **633** (equation 297)[297].

$$\underset{\textbf{(633)}}{\textbf{454} + DMSO \longrightarrow F_5SN{=}SMe_2} + CO_2 \qquad (297)$$

The reaction of **454** with trimethyl orthoformate follows the two pathways shown in equation 298[297].

$$\textbf{454} + HC(OMe)_3 \longrightarrow \underset{\textbf{(634)}}{F_5SNH{-}C(O)C(OMe)_3} \qquad (298)$$

$$\underset{\textbf{(634)}}{F_5SNH{-}C(O)C(OMe)_3} \longrightarrow \left[F_5SN(HC(OMe)_2){-}C(O)OMe\right] \longrightarrow \underset{\textbf{(635)}}{F_5SN(Me){-}C(O)OMe} + HCO_2Me$$

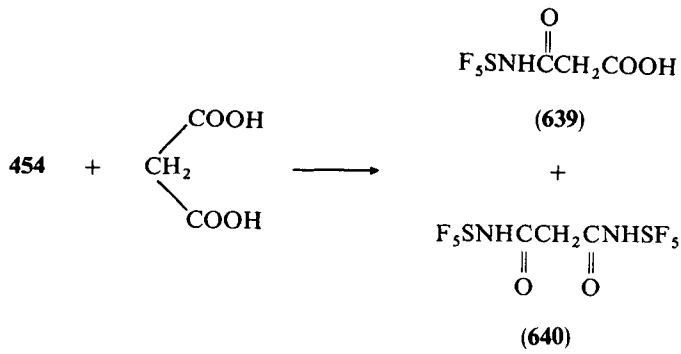
The reaction of FS_5NCO with certain carboxylic acids **636** provides a synthetic approach to the *N*-acylsulfur pentafluoride derivatives **637**. It was suggested that a mixed acid anhydride **638** is an intermediate which loses CO_2 to give the corresponding *N*-pentafluorosulfenamide according to equation 299[255,298].

$$\underset{\textbf{(636)}}{\textbf{454} + RCOOH} \longrightarrow \underset{\textbf{(638)}}{[F_5SNHC(O){-}O{-}C(O)R]} \longrightarrow \underset{\textbf{(637)}}{F_5SNHCOR} \qquad (299)$$

(a) R = Me
(b) R = $CH_2{=}CH$

(a) R = Me (98%)
(b) R = $CH_2{=}CH$ (35%)

At 60 °C **454** reacts also with malonic acid, and both the amido acid **639** and diamide **640** were isolated from the product mixture (equation 300)[298].



(300)

However, the isocyanate **454** failed to react with carboxylic acids, in which the carboxylate group is electron deficient, including perhalogenoacetic acids and even benzoic acid.

The amides **637** discussed above were found to give, upon treatment with phosphorus pentachloride, the corresponding alkyl-substituted iminosulfur pentafluorides **641** which are not available by the photolytic method of Tullock and coworkers[232] (equation 301)[255,297,298].

$$F_5SNH{-}\underset{\underset{O}{\|}}{C}{-}R + PCl_5 \xrightarrow[60\text{–}100\,^\circ C]{CCl_4} F_5SN{=}\underset{\underset{Cl}{|}}{C}{-}R + POCl_3 + HCl \qquad (301)$$

(637) **(641)** (**a**) R = Me (**b**) R = $CH_2{=}CH$

In a similar way, the bis-amide **642** reacts with PCl_5 producing the carbodiimide **643** (equation 302), which can also be prepared according to equation 303[232].

$$F_5SNH{-}\underset{\underset{O}{\|}}{C}{-}NHSF_5 + PCl_5 \longrightarrow F_5SN{=}C{=}NSF_5 + POCl_3 + 2HCl \qquad (302)$$

(642) **(643)**

$$F_5SNH_2 + F_5SN{=}CCl_2 \longrightarrow F_5SN{=}C{=}NSF_5 \qquad (303)$$

(464) **(609)** **(643)**

Difluoroiminosulfur pentafluoride **448** in the presence of pyridine dimerizes to the persulfurane **644** below room temperature. The dimer **644** is also formed when the azomethine **609** is heated to 225 °C, in the presence of potassium fluoride (equations 304 and 304a[232].

$$F_5SN{=}CF_2 \xrightarrow{C_5H_5N < 20\,^\circ C} F_5SN{=}\underset{\underset{CF_3}{|}}{\overset{\overset{F}{|}}{C}}{-}NSF_5 \qquad (304)$$

(448) **(644)**

$$F_5SN{=}CCl_2 \xrightarrow[KF]{\Delta(225\,^\circ C)} \mathbf{644} \qquad (304a)$$

(609)

Mercury fluoride adds to the azometine **448** at 125 °C to give the reactive mercurial **645**. The latter is hydrolyzed rapidly in moist air to mercuric oxide and reacts with benzoyl chloride, giving the persulfurane **646** (equation 305)[234].

$$\underset{\textbf{(448)}}{2F_5S{-}N{=}CF_2} + HgF_2 \longrightarrow \underset{\textbf{(645)}}{Hg[N(CF_3){-}SF_5]} \qquad (305)$$

$$\xrightarrow{2PhCOCl} 2F_5SN(CF_3){-}C(=O)Ph + HgCl_2$$

(646)

The hydrazosulfurane **647** was prepared by the reaction of the amine **447** with sliver(II) fluoride at 100 °C (equation 306)[232].

$$\underset{\textbf{(447)}}{2F_5SNHCF_3} + AgF_2 \longrightarrow \underset{\textbf{(647)}}{F_5SN(CF_3){-}NSF_5} + 2AgF + 2HF \qquad (306)$$

Among perfluorosulfuranes containing a sulfur–nitrogen bond, **647** is the most hydrolytically stable and is not attacked by aqueous alkali, even at 100 °C[232].

Addition of chlorine to a mixture of AgF_2 and amine **447** gives the corresponding chloroamine **648** (equation 307)[232].

$$\textbf{447} + AgF_2 \xrightarrow{Cl_2} \underset{\textbf{(648)}}{F_5SNCl(CF_3)} + AgCl + HCl \qquad (307)$$

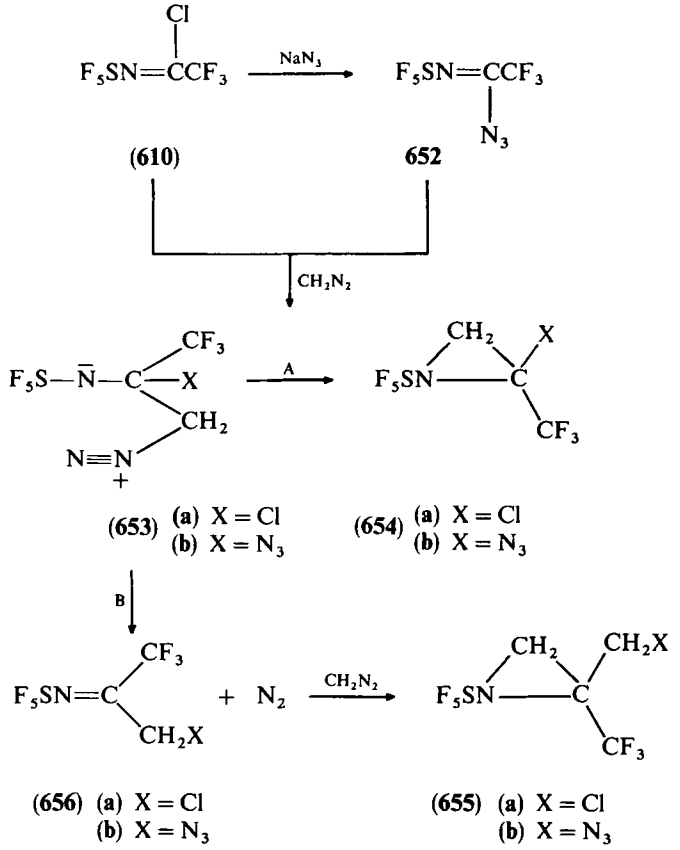
The addition of trifluoroacetic acid to difluoroiminosulfur pentafluoride **448** occurs readily below room temperature to afford a new aminopersulfurane **649** (equation 308)[301].

$$\underset{\textbf{(448)}}{F_5SN{=}CF_2} + CF_3COOH \longrightarrow \underset{\textbf{(649)}}{F_5SN(H){-}CF_2{-}OC(=O)CF_3} \qquad (308)$$

This persulfurane showed no tendency to decompose at 25 °C in glass when kept at its equilibrium vapor pressure for 1 day. Its dehydrofluorination in the presence of sodium fluoride leads to the oxaziridine **650** in a high yield accompanied by the persulfurane **651** as a by-product (equation 309)[301].

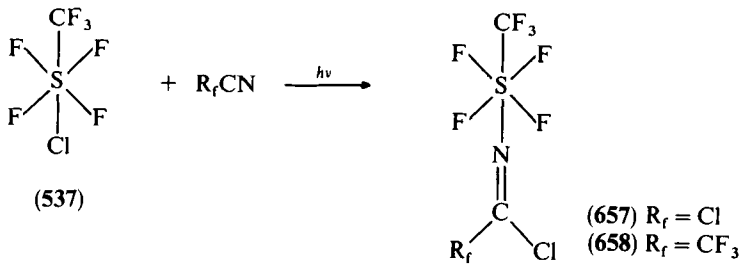
$$\textbf{649} \xrightarrow{NaF} \underset{\textbf{(650)}}{F_5S{-}N(\text{O}){-}CF_2} + NaF\cdot HF + \underset{\textbf{(651)}}{F_5S{-}N(CF_3){-}C(=O){-}F} \qquad (309)$$

The chloroimine **610** was converted to the corresponding azido derivative **652**. Both **652** and **610** add diazomethane by nucleophilic attack to form an intermediate **653**, which loses nitrogen followed either by a ring closure to give the aziridinepersulfuranes **654a, b** (pathway A) or by a shift of X (X = Cl or N_3) to form the persulfuranes **656a, b** (pathway B) (Scheme 69)[302].



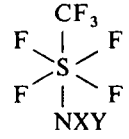
SCHEME 69

The addition of **537** to carbon–nitrogen triple bonds affords the corresponding iminosulfur tetrafluorides **657** and **658** (equation 310)[303].



(310)

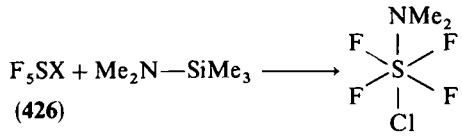
The reactivity of **657** and **658** resembles that of **609** and **610**. Thus, reactions similar to those shown in Scheme 67 allowed one to synthesize the following trifluoromethylsulfur tetrafluoro substituted persulfuranes **659**[294]:



(659)

(**a**) X = H; Y = CF_3
(**b**) X = Cl; Y = CF_3
(**c**) X = H; Y = CF_2CF_3
(**d**) X = Cl; Y = CF_2CF_3

In addition to the two general approaches to persulfuranes with the S—N bond discussed above, some such compounds have been prepared by specific procedures. Thus, it was found that *N,N*-dimethylaminotrimethylsilane reacts with **426a** and **426b** at −78 °C by replacement of the axial fluorine atom and formation of stable disubstituted sulfur tetrafluoride derivatives **660a** and **660b** (equation 311)[304].



(426)

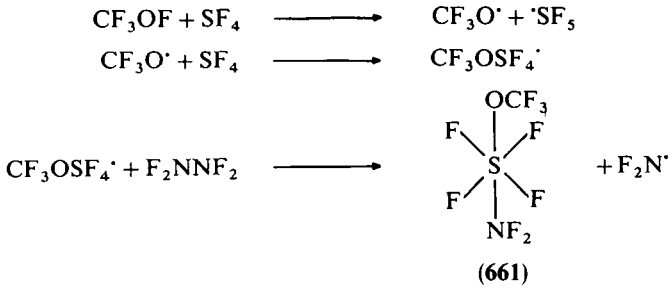
(**a**) X = Cl
(**b**) X = Br

(660)

(**a**) X = Cl
(**b**) X = Br

(311)

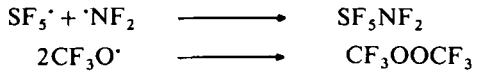
Difluoro(aminotrifluoromethoxy)sulfur tetrafluoride **661** is formed from trifluoromethyl hypofluorite and sulfur tetrafluoride in the presence of N_2F_4. The reaction was suggested to proceed by the steps shown in Scheme 70[305].



(661)

SCHEME 70

Termination of this chain reaction occurs by the reactions shown in equations 312 and 313



(312)

(313)

Irradiation of **426a** or sulfur tetrafluoride with *N*-chlorobis(trifluoromethyl)amine **662** gave bis(trifluoromethyl)aminosulfur pentafluoride **663** in low yields (10–15%) (equation 314)[306].

$$\underset{\textbf{(426a)}}{SF_5Cl} + \underset{\textbf{(662)}}{(CF_3)_2NCl} \xrightarrow{h\nu} \underset{\textbf{(663)}}{F_5SN(CF_3)_2} \qquad (314)$$

3. Organic derivatives of sulfur hexafluoride containing a sulfur–oxygen bond

The title compounds have been prepared essentially by two approaches. The first is based on oxidative addition to organosulfur compounds having a lower oxidation state and the second utilized the addition of pentafluorosulfur hypofluorites to unsaturated carbon–carbon systems.

Trifluoromethyl hypofluorite with sulfur tetrafluoride yielded trifluoromethoxysulfur pentafluoride **664** as the only product at room temperature (equation 315)[307].

$$SF_4 + CF_3OF \longrightarrow \underset{\textbf{(664)}}{F_5SOCF_3} \qquad (315)$$

The same reaction carried out in the presence of oxygen affords two additional persulfuranes, each having also a sulfur–oxygen bond such as **665** and **666**.

$$\underset{\textbf{(665)}}{CF_3OSF_4OSF_5} \qquad \underset{\textbf{(666)}}{CF_3OSF_4OOSF_5}$$

Ultraviolet irradiation of gaseous mixtures of sulfur tetrafluoride and either trifluoromethyl hypofluorite or di-trifluoromethyl peroxide leads to **664** and to *cis*-bis(trifluoromethoxy)sulfur tetrafluoride **667** (equation 316)[308].

$$SF_4 \xrightarrow[CF_3OOCF_3]{CF_3OF\ or} \underset{\textbf{(664)}}{CF_3OSF_5} + \underset{\textbf{(667)}}{\begin{array}{c} F \\ | \\ F\!-\!S\!-\!OCF_3 \\ | \\ F \end{array}\!\!\begin{array}{c} \\ \\ OCF_3 \\ \\ \end{array}} \qquad (316)$$

When the two reactants were photolyzed in the liquid state for 24 h with an ultraviolet quartz lamp, the *cis*-persulfurane **667** was formed almost quantitatively[309]. The reaction of SF_4 with bis(trifluoromethyl)trioxide afforded, in addition to **664** and **667**, two new persulfuranes containing the trifluoromethylperoxy group bonded to the central sulfur atom (equation 317)[310].

$$SF_4 + CF_3OOOCF_3 \longrightarrow \textbf{664} + \textbf{667} + \underset{\textbf{(668)}}{CF_3OOSF_5} + \underset{\textbf{(669)}}{CF_3OOSF_4OSF_3} \qquad (317)$$

Treatment of chlorine(I) trifluoromethanesulfonate **670** with SF_4 gave a mixture of *cis* and *trans* persulfuranes **671a** and **671b** in 45% yield (equation 318)[311].

$$\underset{\textbf{(670)}}{SF_4 + ClO\!-\!\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}\!-\!CF_3} \longrightarrow \underset{\textbf{(671a)}}{\begin{array}{c} F \\ | \\ F\!-\!S\!-\!OSO_2CF_3 \\ | \\ F \end{array}\!\!\begin{array}{c} \\ \\ Cl \\ \\ \end{array}} + \underset{\textbf{(671b)}}{\begin{array}{c} OSO_2CF_3 \\ | \\ F\!-\!S\!-\!F \\ | \\ Cl \end{array}\!\!\begin{array}{c} \\ \\ F \\ \\ \end{array}} \qquad (318)$$

The hypochlorite **465b** and carbon monooxide form, upon photolysis, the chloroformate derivative **672a** in 97% yield (equation 319)[261,312].

$$F_5SOCl + CO \longrightarrow F_5SOCX \quad (319)$$

(465b) (672)

(a) X = Cl
(b) X = F

Similarly, the hypofluorite **465a** afforded the fluoroformate derivative **672b** with oxalyl fluoride[313].

The oxidative addition reaction between chlorine fluoride and (trifluoromethyl) imidosulfites **673** results in the formation of a separable mixture of *cis* and *trans* bis-(polyfluoroalkoxy)sulfur tetrafluoride isomers **674** and **675**, the latter being predominant (equation 320)[314].

$$R_fO{-}S(=NCF_3){-}OR \xrightarrow[-78\,^\circ C/10\,h]{5\,ClF} \mathbf{674} + \mathbf{675} + Cl_2 \quad (320)$$

(673)

(674) (675)

(a) $R_f = CF_3CH_2$
(b) $R_f = CF_3CF_2CH_2$
(c) $R_f = CF_3CF_2CF_2CH_2$

Treatment of bis (2,2,2-trifluoroethyl)*N*-[(2,2,2-trifluoroethoxy)carbonyl] imidosulfite **676** with ClF gave the *cis* and *trans* isomers **674a** and **675a** with concomitant loss of nitrogen, chlorine and 1,1,1-trifluoroethyl fluoroformate (equation 321)[214].

$$(CF_3CH_2O)_2S{=}N{-}C(=O)OCH_2CF_3 \xrightarrow[10\,h/-78\,^\circ C]{ClF} \mathbf{674a} + \mathbf{675a} + Cl_2 + N_2 + FCOCH_2CF_3 \quad (321)$$

(676)

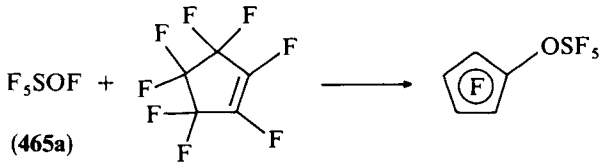
In both reactions the yield (*ca* 70%) as well as the ratio of the *cis–trans* isomers were approximately the same. All of these persulfuranes were thermally and hydrolytically stable and unreactive towards a variety of nucleophiles.[19] F-NMR analysis indicated that the *cis* and *trans* isomers were not interconvertible when kept at room temperature in a Pyrex vessel for a number of months[314].

A mixture of **674** and **675** was also obtained by a two-step procedure in which the first reaction involves a nucleophilic exchange in sulfur tetrafluoride (equation 322)[314].

$$2\,R_fOLi + SF_4 \xrightarrow{-78\text{ to }-60\,^\circ C} [(R_fO)_2SF_2] + 2\,LiF$$

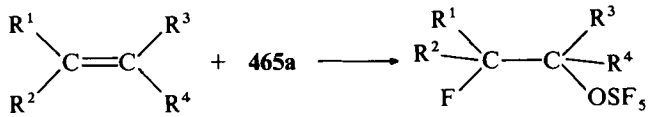
$$[(R_fO)_2SF_2] \xrightarrow[-90\text{ to }+25\,^\circ C]{ClF} \mathbf{674a{-}c} + \mathbf{675a{-}c} \quad (322)$$

The second general method consists in the reaction of **465a** with unsaturated compounds. Addition occurred quantitatively between **465a** and perfluorocyclopentene **676** and various other ethylene derivatives **678**. The addition of **465a** to unsymmetrical alkenes, where one sp^2 carbon is an unsubstituted methylene-type carbon atom, occurs in such a way that the F_5SO group is bonded to the methylene-type carbon (equations 323 and 324)[315,316].



F_5SOF + (**676**) → (**677**) (323)

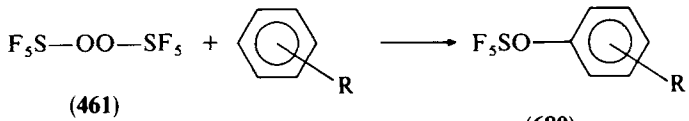
(**465a**)



(**678**) + **465a** → (**679**) (324)

(**a**) $R^1 = R^2 = R^3 = R^4 = H$
(**b**) $R^1 = R^2 = F$; $R^3 = R^4 = H$
(**c**) $R^1 = F$; $R^2 = R^3 = R^4 = H$
(**d**) $R^1 = Cl$; $R^2 = R^3 = R^4 = H$
(**e**) $R^1 = R^2 = R^3 = R^4 = Cl$
(**f**) $R^1 = R^2 = R^3 = R^4 = F$

Aryloxysulfur pentafluorides **680** were obtained in *ca* 50% yield when bispentafluorosulfur peroxide **461** was reacted with benzene, toluene or chlorobenzene at 150 °C (equation 325)[317].



$F_5S—OO—SF_5$ + → F_5SO— (325)

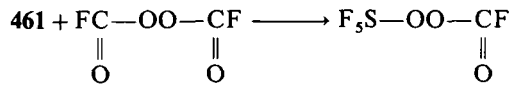
(**461**)

(**680**)

(**a**) R = H
(**b**) R = *p*-Me
(**c**) R = Cl

The reduction of the parent compound **680a** with sodium in ethanol gave phenol, and this reaction was used to establish the structure of the products **680b** and **680c**. Thus, **680b** gave on reduction *p*-cresol and must therefore be *p*-pentafluoropersulfuroxy toluene. The product from the reaction with chlorobenzene contained two isomers, which were shown to be the *o*- and *p*-chlorophenoxysulfur pentafluorides in a 1:10 ratio[317].

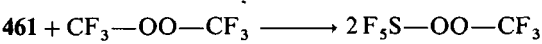
The reaction of **461** with fluorocarbonyl peroxide **681** afforded the corresponding peroxy persulfurane **682** (equation 326)[313].



(326)

(681) (682)

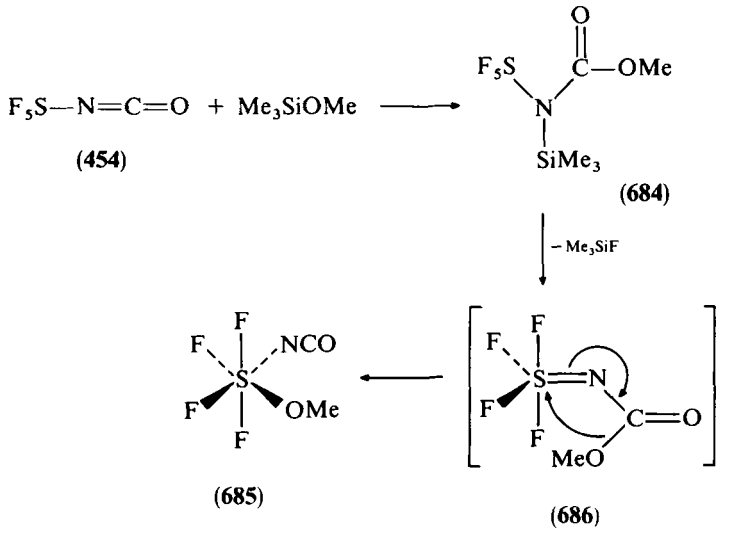
The photolytically induced reaction between **461** and bis(trifluoromethyl) peroxide gives the peroxy persulfurane **683** (equation 327)[313].



(327)

(683)

An interesting example of the synthesis of a persulfurane with a sulfur–oxygen bond is the reaction of pentafluorosulfur isocyanate **454** with trimethylmethoxysilane leading to *cis*-methoxy isocyanosulfur tetrafluoride **685**. It was proved that **685** is formed in this reaction via an unusual methoxy group migration in the reaction intermediate **686** as shown in Scheme 71[238].



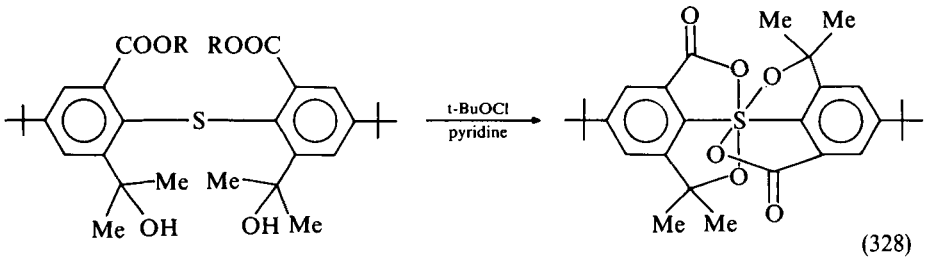
SCHEME 71

C. Persulfuranes With Only Two or Without Fluorine Atoms as Ligands

Only four such structures have been as yet described in the literature by Lam and Martin. The first persulfurane lacking fluorine ligands, diaryldiacyloxydialkoxypersulfurane **10** was prepared by the oxidative cyclization of bis[2-(1-hydroxy-2-methylethyl)-4-(1, 1-dimethylethyl)-6-carboxyphenyl]sulfide **688b** with *t*-butyl hypochlorite in the presence of pyridine at 0 °C (equation 328)[223,224].

This crystalline persulfurane is thermally stable and unreactive towards atmospheric moisture. However, in the presence of traces of acids it decomposed very rapidly to form the isomeric sulfone diacid diolefin **689**. In dry pyridine its decomposition is slower and affords after 8–10 days a 1:1 mixture of **689** and sulfone lactone **690**. The latter is another isomeric structure of **686** (equation 329).

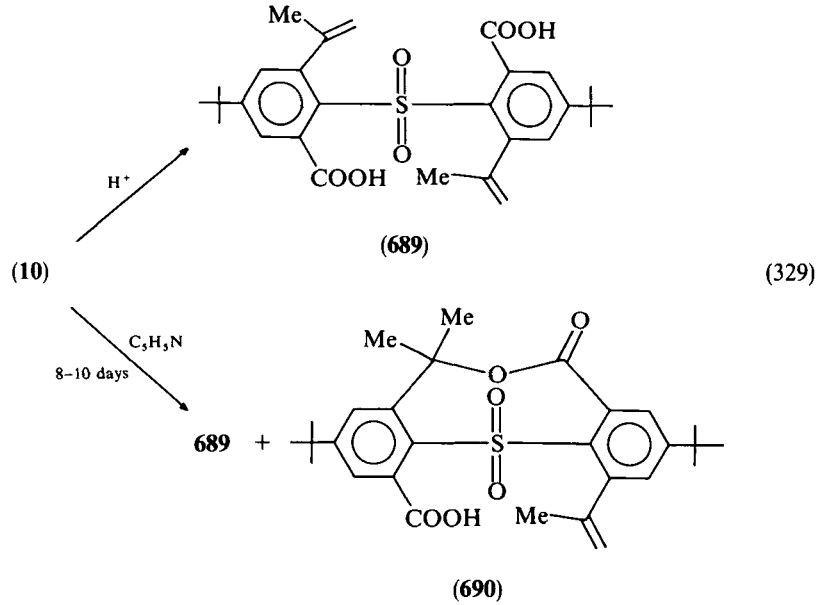
The symmetrical tetraalkoxy persulfurane **691** was prepared by treatment of the sulfurane oxide **692** [synthesized from the sulfide **687** with potassium hydride in THF and



(687) R = Et
(688) R = H

10

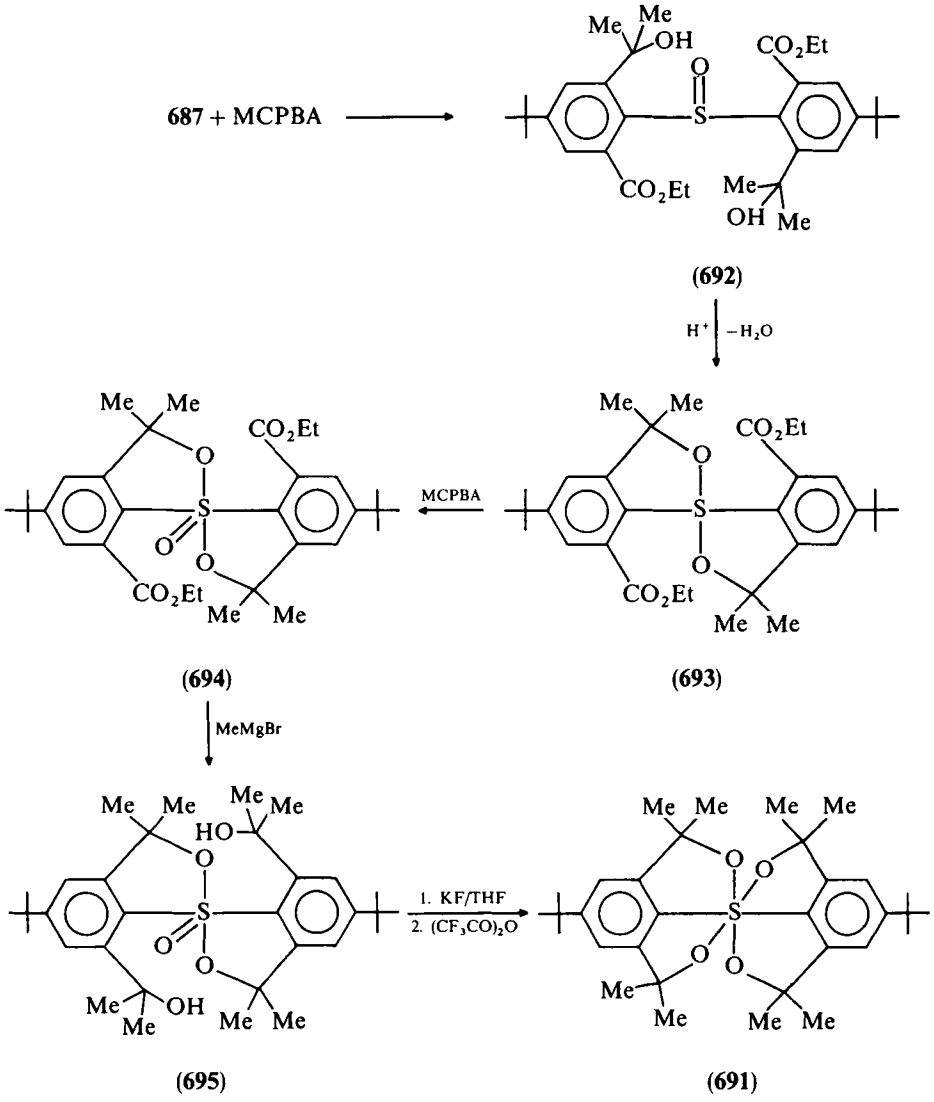
(328)



(329)

then with trifluoroacetic anhydride (Scheme 72). Although **691** was not isolated in the analytically pure state, its structure was fully supported by the ^{1}H-NMR and field-desorption mass spectra. The persulfurane **691** is stable for hours in chloroform (in which the sulfurane **10** was decomposed in less than 30 min). After longer periods it decomposed completely to unidentified products[223,224].

The reaction of bromine trifluoride with the sulfurane **6** was found to give the *cis*- and *trans*-difluoroalkoxydiaryl persulfuranes **11** and **12** (equation 330) depending on the amount of the fluorination agent used[52]. The fluorination of **6** using 0.667 mol of bromine trifluoride per mol of **6** proceeds smoothly below − 20 °C to give the difluoropersulfurane **11** for which an all-*trans* geometry was postulated on the basis of the ^{19}F-NMR spectrum and fully supported by the results of an X-ray crystallographic structure determination. Using an order of priority for the substituents about the sulfur atom based on atomic number, the structure **11** was later designated as the *trans*-F, *trans*-O, *trans*-C or (t, c, t) isomer[52].

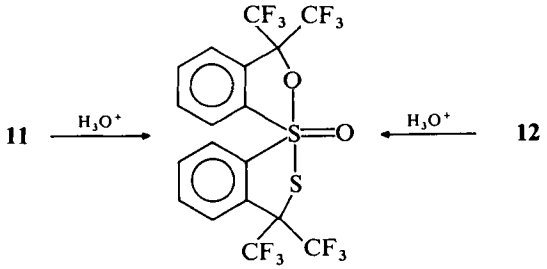


SCHEME 72

$$\mathbf{11}\,(t,t,t) \xleftarrow[CH_2Cl_2\ -80\,^\circ C]{\substack{2/3\ BrF_3\\ Freon\ -20\,^\circ C\\ or\ CF_3OF}} \mathbf{6} \xrightarrow[Freon\ -20\,^\circ C]{>2/3\ BrF_3} \mathbf{12}\,(c,c,t) \qquad (330)$$

When more than 0.67 mol of bromine fluoride per mol of sulfurane **6** was used, the product was found to be an isomer of **11** to which the (c, c, t) geometry **12** was assigned based on an X-ray crystallographic structure determination[52]. The persulfurane **11** was

found to be indefinitely stable under basic conditions and no reaction was observed with hydroxide ion or with any of several amines. On the other hand, acid-catalyzed hydrolysis of **11** and **12** proceeded rapidly with the formation of a common product, the sulfurane oxide **7b** (equation 331)[52].



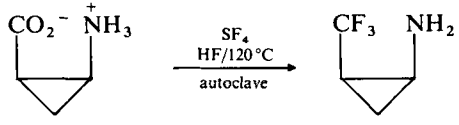
(7b) (331)

When a catalytic amount of antimony pentafluoride was added to a solution of **11** in methylene chloride, rapid isomerization occurred to the thermodynamically more stable *cis*-persulfurane **12** which constitutes 94 ± 1% of the equilibrium mixture. To explain the rapid hydrolysis of both isomers **11** and **12** under acidic conditions and their inertness to water, a dissociative mechanism involving a persulfonium ion intermediate was postulated. This suggestion was fully supported, when this persulfonium ion was subsequently isolated[52] as its hexafluorophosphate salt **457b** (see equation 202).

V. SYNTHETIC UTILITY OF HIGH-COORDINATED SULFUR COMPOUNDS

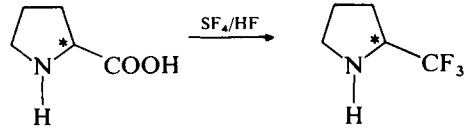
The vast majority of synthetic applications involves the use of sulfur tetrafluoride or diethylaminosulfur trifluoride (DAST) as fluorinating reagents. Other sulfuranes have been applied as reagents only in a very few cases. Two excellent reviews[318,319] cover very exhaustively up to 1986 the synthetic potential of the two sulfuranes mentioned above. Hence we will discuss here only the most recent reports on this topic and summarize in a comprehensive way various synthetic applications of the acyclic sulfurane **5** (Table 1).

Sulfur tetrafluoride, according to a patent[320], forms with 1-aminocyclopropanecarboxylate **696** the 1-trifluoromethylcyclopropylamine **697** (equation 332).



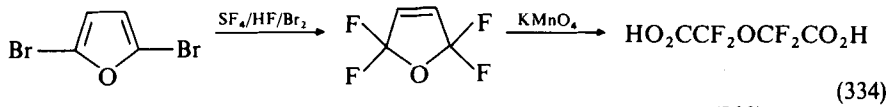
(696) (697) (332)

In a similar way, fluorodeoxygenation of (*S*)-proline **698** to (−)(*S*)-trifluoromethylpyrrolidine **699** was found to occur upon treatment of the amino acid with a $SF_4 - HF$ mixture (equation 333)[321].



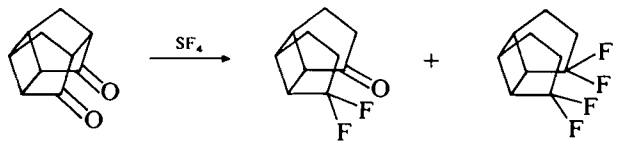
(698) (699) (333)

Fluorination of 2,5-dibromofuran **700** with a SF_4–HF–Br_2 system was found to give 90% of the tetrafluoro furan derivative **701**, which was subsequently oxidized by $KMnO_4$ to the dicarboxylic acid **702** (equation 334)[322].



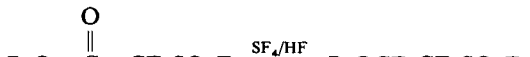
(700) (701) (702) (334)

Treatment of the diketone **703** with SF_4 afforded either difluoride **704** or tetrafluoride **705** in yields 72% and 91%, respectively, depending on the reaction conditions (equation 335)[323].



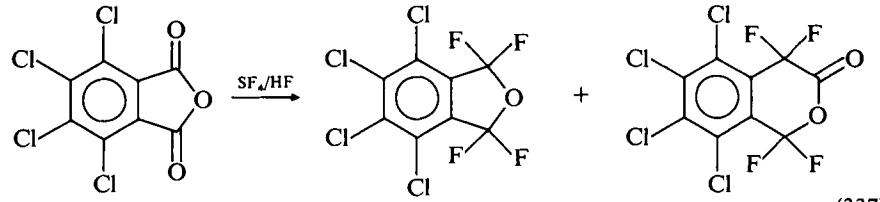
(703) (704) (705) (335)

Fluorination of (*O*)-perfluoroalkyl α-fluorosulfonyl difluoroacetate **706** with SF_4 in anhydrous HF afforded the corresponding perfluoroether **707** (equation 336)[324].



(706) (707) (336)

Under similar conditions tetrachlorophthalic anhydride **708** was converted into the cyclic perhalogenoether **709**. At a lower SF_4–HF ratio a mixture of perfluoroether **709** and perfluorolactone **710** was isolated (equation 337)[325].



(708) (709) (710) (337)

In the reaction of the iodo-bis-trifluoroacetate **711** with SF_4 in CH_2Cl_2 at −10 °C the corresponding difluoro derivative **712** was formed in 91% yield[326].

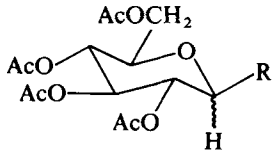
$$CF_3CH_2I(O_2CCF_3)_2 + SF_4 \longrightarrow CF_3CH_2IF_2$$

(711) (712)

More reports exist on the use of dialkylaminosulfur trifluorides as fluorinating reagents. In the majority of cases the *N*,*N*-diethyl derivative (DAST) is applied. However, it should be noted the DAST has a tendency to decompose violently when heated and presents a hazard if not properly handled. It has been shown[327] that its decomposition occurs in two steps. The first is a nonenergetic disproportionation to sulfur tetrafluoride and

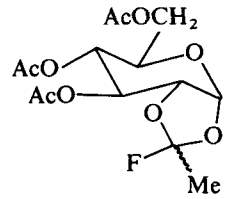
bis(diethylamino)sulfur difluoride. The latter is less stable and undergoes a vigorous exothermic decomposition, sometimes with detonation. The relative stability of several analogues of DAST was determined. Morpholinesulfur trifluoride was found to be most stable among the derivatives tested and its use in place of the less stable DAST was recommended. In spite of this warning, the use of DAST as a fluorinating agent has increased in recent years.

Treatment of glucopyranose **713a** with DAST in $CDCl_3$ gave the corresponding fluoride **713b**, exclusively. When THF-d_8 was used as a solvent, a mixture of the fluoroacetals **714** was formed[328].



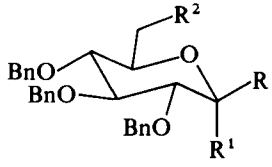
(713)

(**a**) R = OH
(**b**) R = F

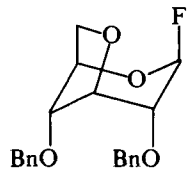


(714)

The reaction of 2,3,4-tri-*o*-benzyl-D-glucose **715a** with DAST afforded 3,6-anhydro-2,4-di-*o*-benzyl β-D-glucopyranosyl fluoride **716** as the major product (44%) by way of -3-benzyloxy group participation in the displacement of the intermediate 6-sulfoxy derivative[329]. The desired 6-deoxy-6-fluoro-2,3,4-*o*-benzyl-α- (**715b**) and β-D-glucopyranosyl-fluoride (**715c**) were formed in a combined yield of < 20%, but this yield could be increased threefold by carrying out the reaction in the presence of triethylamine[329].



	R	R^1	R^2
(**715a**)	H	OH	OH
(**715b**)	H	F	F
(**715c**)	F	H	F

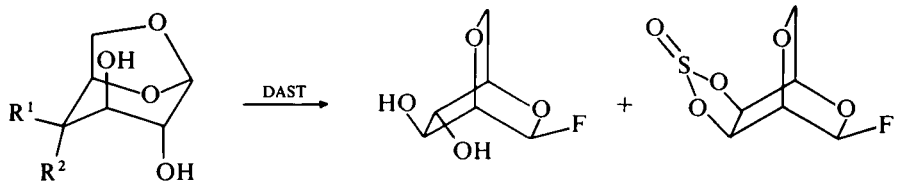


(716)

Fluorination of 1,6-anhydrohexapyranoses **717** with DAST in CH_2Cl_2 gave, after rearrangement, 2,6-anhydrohexapyranosyl fluorides **718** and **719** in 10% and 62% yield, respectively (equation 338).

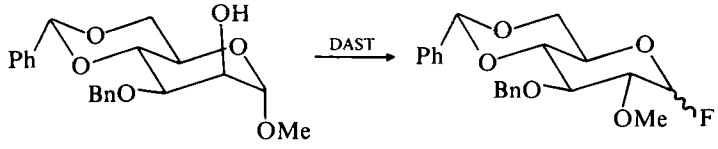
The monopyranoside **720** reacted with DAST in diglyme, giving a rearrangement to a mixture of α- and β-glucopyranosyl fluorides **721** in the combined yield of 75–80% (equation 339)[331].

An improved synthesis of 5-deoxy-2-fluoro-myoinositol **722** is based on the reaction of DAST with the 1,4,6-tri-*o*-benzyl-2,3-cyclohexylidene-myoinositol precursor **723**, followed by the appropriate deprotection reaction. With the keto analogue of **722** the *gem*-difluoro compound is formed[332].

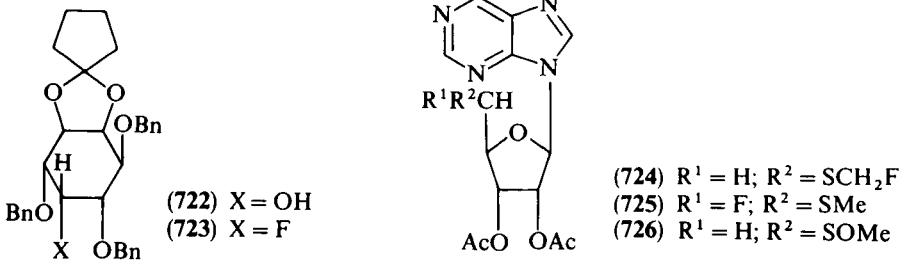


(717) (718) (719)

(a) $R^1 = OH$; $R^2 = H$
(b) $R^1 = H$; $R^2 = OH$ (338)



(720) (721) (339)

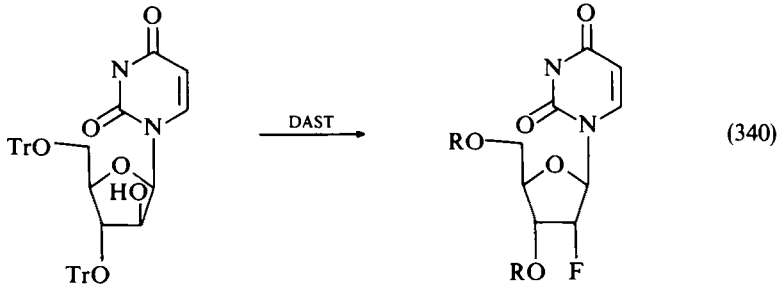


(722) X = OH
(723) X = F

(724) $R^1 = H$; $R^2 = SCH_2F$
(725) $R^1 = F$; $R^2 = SMe$
(726) $R^1 = H$; $R^2 = SOMe$

A recently reported[333] synthesis of fluorinated derivatives of 5′-deoxy-5′-(methylthio)-adenosine **724** and **725** was based on a Pummerer-type rearrangement of the corresponding sulfoxides **726** on treatment with DAST or its *N*,*N*-dimethyl analogue.

D-Deoxy-2-fluorouridine **727b** was obtained by reaction of the arabinofuranosyl nucleoside **728** with DAST followed by detritylation of **727a** (equation 340)[334].

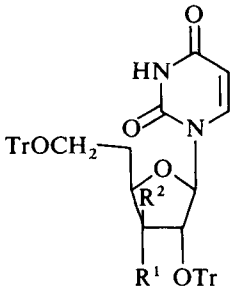


(728) (340)

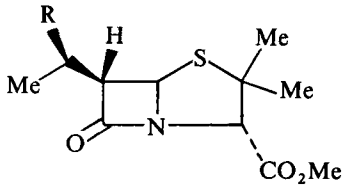
(727a) R = Tr
(727b) R = H

Displacement of a hydroxyl group in pyrimidine nucleosides **729a** having a vicinal diol system was achieved yielding **729b** in good yields using the same fluorinating agent[335].

DAST was also found to be effective for the conversion of the hydroxyl groups to fluorides in the presence of other highly reactive groups in β-lactams[336]. Thus, treatment of (hydroxyethyl)azathiabicycloheptanone **730a** with DAST at −78 °C and warming up to room temperature gave 50% of the fluoride **730b**.

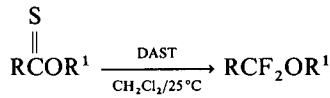


(**729a**) $R^1 = H$; $R^2 = OH$
(**729b**) $R^1 = F$; $R^2 = H$



(**730a**) R = OH
(**730b**) R = F

A recent mild, efficient and general procedure for the geminal fluorination of thionoesters **731** involves also their reaction with DAST[337]. Each of the thionoesters **731a–h** obtained from the carboxylic esters and the Lawesson reagent was smoothly converted to the corresponding α, α-difluoroethers **732** in dichloromethane at 25 °C (equation 341). The reactions were completed within 6 h, and no other volatile products were observed.

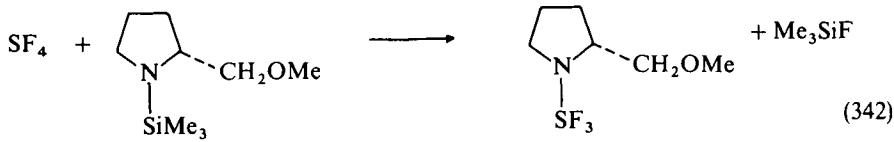


(**731**) (**732**) (341)

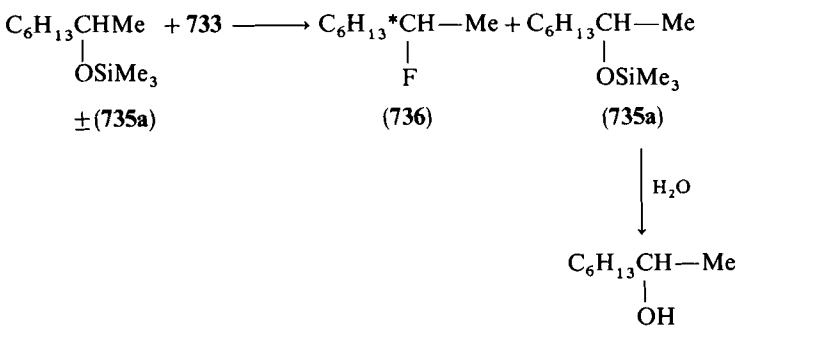
No	R	R^1	Yield (%)
a	n-C_7H_{15}	Me	77
b	c-C_6H_{11}	Me	81
c	Adamantyl	Me	68
d	Ph	Me	53
e	PhCH=CH	Et	53
f	Ph	CH_2SiMe_3	81
g	PhCH=CH	CH_2SiMe_3	74
h	1-Naphthyl	Me	72

(*S*)-2-(methoxymethyl)pyrrolidin-1-ylsulfur trifluoride **733**, prepared according to the above general methodology from sulfur tetrafluoride and the *N*-trimethylsilyl derivative of (*S*)-2-(methoxymethyl)pyrrolidine **734**, was found to be a very effective enantioselective fluorodehydroxylation reagent (equation 342)[338].

Thus, when recemic 2-(trimethylsilyloxy)octane **735a** was allowed to react with 0.5 equivalent of **733**, the examination of the alcohol **735b** derived from unreacted substrate indicated that only low kinetic resolution had been achieved (equation 343). Much better results were observed when this reagent was used for fluorination of racemic ethyl 2-(trimethylsilyloxy)propionate **737a**. The hydroxyester **738** derived from the unreacted starting material had 50% enantiomeric excess (equation 344)[338].

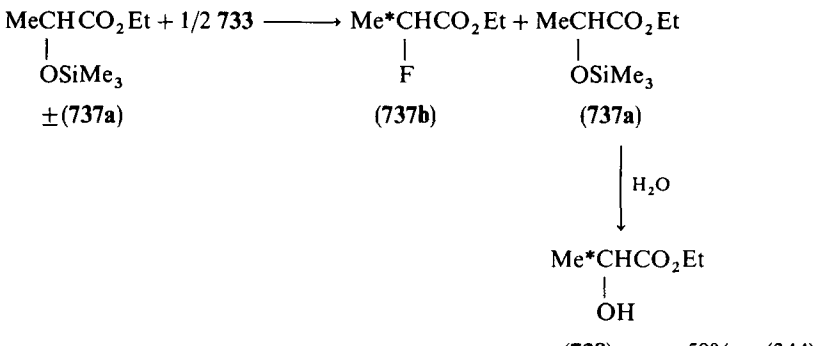


(734) (733) (342)

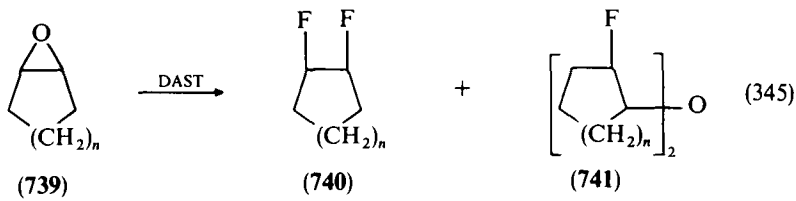


(735) ee = 8% (343)

DAST was found to react with epoxides to form geminal difluorides and bis-(2-fluoroalkyl)-ethers depending on the structure of the starting oxides[339]. Thus cyclopentene oxide **739a** and cyclohexene oxide **739b** oxides gave *cis/trans* mixtures of 1,2-difluorocycloalkanes **740a,b** and bis(2-fluoroalkyl)ethers **741a,b** (equation 345).



(738) ee = 50% (344)

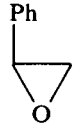


(345)

(739) (740) (741)

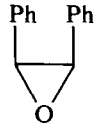
(a) $n = 1$
(b) $n = 2$

Styrene oxide afforded a mixture of difluoro compounds **742** and **743** (equation 346). *Cis* and *trans* stilbene oxides **744** on treatment with DAST gave a mixture of meso and racemic difluoro derivatives **745a** and **b** together with the unsymmetrical compound **746** (equation 347)[339]. Cyclooctene oxide and cyclohexene sulfide did not react appreciably under the same reaction conditions[339].



$$\xrightarrow{\text{DAST}} \quad HCF_2CH_2Ph + FCH_2CH_2Ph \qquad (346)$$

(742) **(743)**



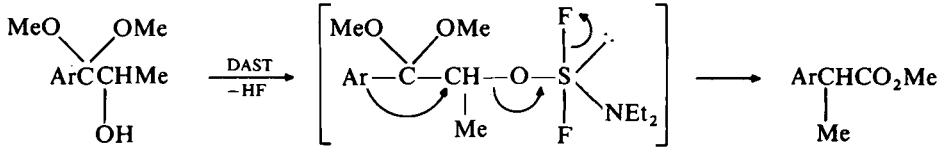
(744)

$$\xrightarrow{\text{DAST}} \quad PhCHFCHFPh + HCF_2CHPh_2 \qquad (347)$$

(745) **(746)**

(a) *meso*
(b) ±

Treatment of dimethyl acetals of aryl 1-hydroxyethyl ketones **747** with DAST affords smoothly methyl 2-arylpropanoates **748** in good yields as a result of the aryl group migration in the intermediate **749** (Scheme 73)[340].



(747) **(749)** **(748)**

No.	Ar	Yield of **748**(%)
a	Ph	74
b	PhC_6H_4	92
c	4-$Bu^tC_6H_4$	94
d	4-$MeOC_6H_4$	98
e	4-BrC_6H_4	74
f	6-$MeOC_{10}H_6$ – 2	84

SCHEME 73

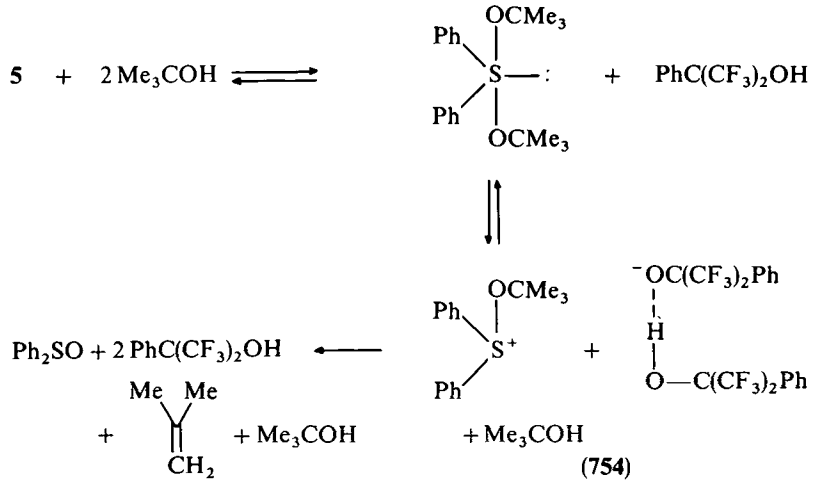
Regioselective fluorination of terminal acetylenic ketones **750** was observed when morpholinesulfur trifluoride (MST) was used as a fluorination agent (equation 348)[341].

$$\underset{\underset{\underset{\text{O}}{\|}}{\text{HC}\equiv\text{CCCH}_2\text{CH}_2\text{CO}_2\text{Me}}}{\textbf{(750)}} \xrightarrow{\text{MST}} \underset{\text{HC}\equiv\text{CCF}_2\text{CH}_2\text{CH}_2\text{CO}_2\text{Me}}{\textbf{(751)}} \qquad (348)$$

Under similar reaction conditions the acetylenic ketone **752** was converted into the corresponding difluoroacetylenic ether **753** (equation 349)[342].

$$\underset{\underset{\underset{\text{O}}{\|}}{n\text{—BuCC}\equiv\text{CCH}_2\text{OTHP}}}{\textbf{(752)}} + \text{MST} \longrightarrow \underset{n\text{—BuCF}_2\text{C}\equiv\text{CCH}_2\text{OTHP}}{\textbf{(753)}} \qquad (349)$$

Among other high-coordinated organosulfur species the acyclic sulfurane **5** (see Table 1) has a synthetic utility comparable with that of SF_4 or DAST. This reagent has been shown[343] to eliminate water from tertiary and secondary alcohols to form olefins and ethers. The experimental evidence is in favor of a dissociative mechanism pictured in Scheme 74 for the reaction of *t*-butyl alcohol.

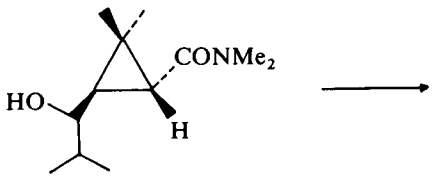


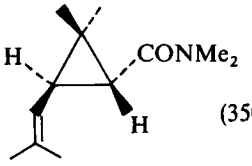
SCHEME 74

TABLE 8. Reactions of alcohols with **5** in $CDCl_3$ at room temperature[346]

Alcohol	Product	Yield (%)
t-Butyl alcohol	Isobutylene	100
t-Amyl alcohol	2-Methyl-2-butene	41
	2-Methyl-1-butene	59
1-Methylcyclohexanol	1-Methylcyclohexene	90
2-Cyclopropyl-2-propanol	2-Cyclopropylpropene	100
Cyclohexanol	Cyclohexene	100
trans-2-Methylcyclohexanol	3-Methylcyclohexene	100
3-Hydroxypropionitrile	Acrylonitrile	100
exo-2-Norborneol	Nortricyclene	100

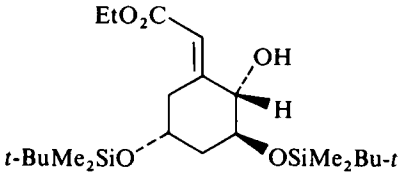
The use of this sulfurane as a dehydration agent is demonstrated in Table 8 and in equations 350–355 in which more complex alcohols were used as substrates.

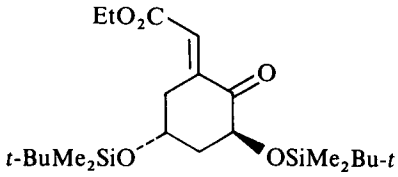




(350)[344]

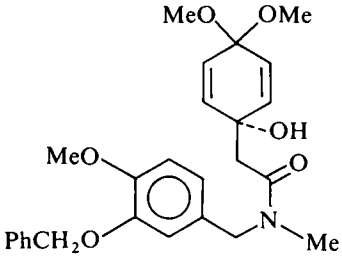
92%

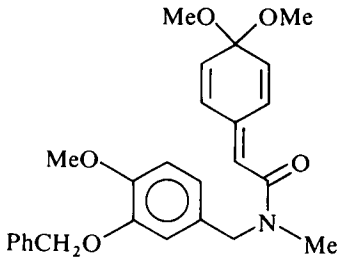




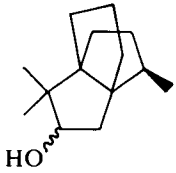
81%

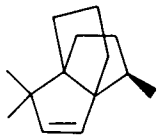
(351)[345]





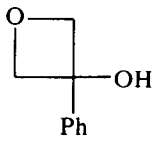
(352)[346]

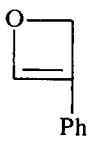




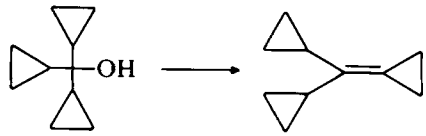
(353)[347]

66%



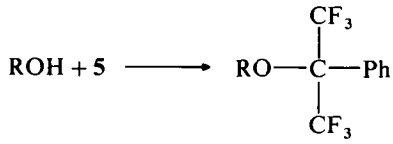


(354)[348]



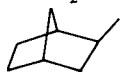
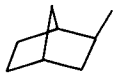
(355)[349]

It is of interest to note that primary alcohols react with **5** to form unsymmetrical ethers **755** especially in the absence of structural features increasing the acidity of the β protons (equation 356)[343b].

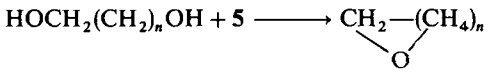


(356)

(755)

(a) R = Me (100%)
(b) R = Et (100%)
(c) R = $PhCH_2$ (44%)
(d) R =  (100%)
(e) R =  (100%)

A one-step synthesis of epoxides and other cyclic ethers **756** from diols and **5** has also been reported (equation 357)[350].



(357)

(756)

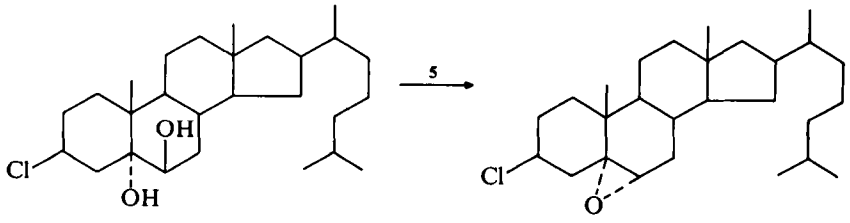
n	Yield (%)
1	60
3	72
4	39

However, the reaction of **5** with 1,6-hexanediol gave the corresponding bis-ether **757** in 97.5% yield (equation 358)[350]. Some other more complex cyclic ethers prepared by this procedure are presented in equations 359 and 360[351,352].

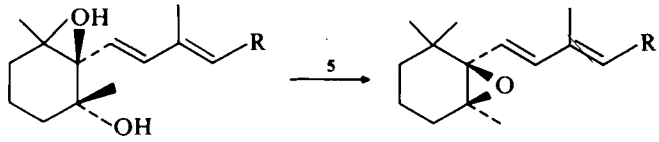
(358)

(757)

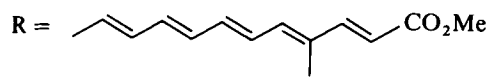
The reaction of secondary carboxylic amides with **5** follows two principal routes which are illustrated for the reaction of *N*-methylbenzamide (equation 361) and *N*-isopropylbenzamide (equation 362). For some amides, both modes of the reaction have been observed[353].

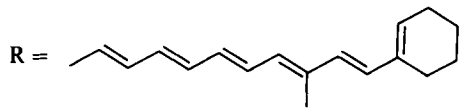


93% (359)[350]



(360)[351,352]



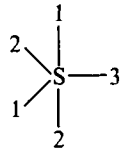


$$PhCONHMe + 5 \longrightarrow \underset{98\%}{PhCO_2C(CF_3)_2Ph} + MeN{=}SPh_2 \cdot \underset{98\%}{HOC(CF_3)_2Ph} \quad (361)$$

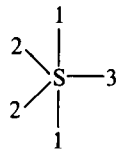
$$PhCONHPr\text{-}i + 5 \longrightarrow i\text{-}PrN{=}\underset{\displaystyle OC(CF_3)_2Ph}{\underset{|}{CPh}} \quad (362)$$

VI. STEREOCHEMICAL ASPECTS OF THE CHEMISTRY OF HIGH-COORDINATED SULFUR SPECIES

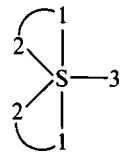
Compounds having either a trigonal bipyramidal or tetragonal bipyramidal geometry can exist in enantiomeric forms when the number of different ligands is high enough to create chirality in such structures. Thus, in the case of sulfuranes and their oxides, all structures containing at least three different ligands can be chiral. Moreover, considering the topological properties of such molecules it should be noted that, after incorporation of cyclic ligands into a trigonal bipyramidal structure, chirality may still appear in the more symmetrical spiro system.



chiral

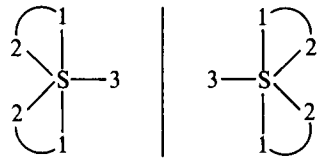


achiral



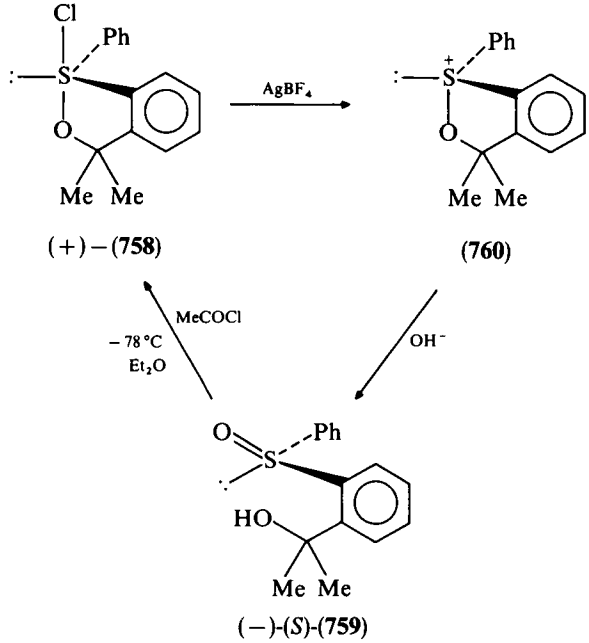
chiral

Enantiomeric forms of such a symmetrical spiro derivative with two pairs of equivalent ligands are pictured below.



For this reason, with the exception of (+)1-chloro-3,3-dimethyl-1-phenyl-[3*H*-2,1-benzooxathiole] **758**[182] all the sulfuranes and sulfurane oxides which have been till now prepared as optically active species belong to this category of spiro derivatives. They have been prepared by three different approaches: (a) stereoselective synthesis, (b) asymmetric synthesis and (c) nonclassical resolution of recemic sulfuranes.

The first example of an optically active sulfurane was the dextrorotatory chlorosulfurane **758** synthesized in 95% optical purity by treatment of (*S*)-2-(2-hydroxy-2-propyl)-1-phenylsulfinylbenzene **759** with acetyl chloride[182]. When this reaction was carried out at room temperature, a mixture of enantiomers of **758** in an approximate ratio 3:2 was formed. The absolute configuration of (+)**758** was suggested to be as shown in Scheme 75. The assignment was based on the results of its silver tetrafluoroborate induced conversion to the corresponding alkoxysulfonium salt **760** and hydrolysis of the latter to the starting sulfoxide **759** with retained configuration at sulfur. Because formation of the sulfonium salt **760** was considered to proceed with retention of configuration at sulfur and hydrolysis was assumed to involve inversion at sulfur, the stereochemical relationships between **758** and **759** and the absolute configuration of (+)**758** were established.

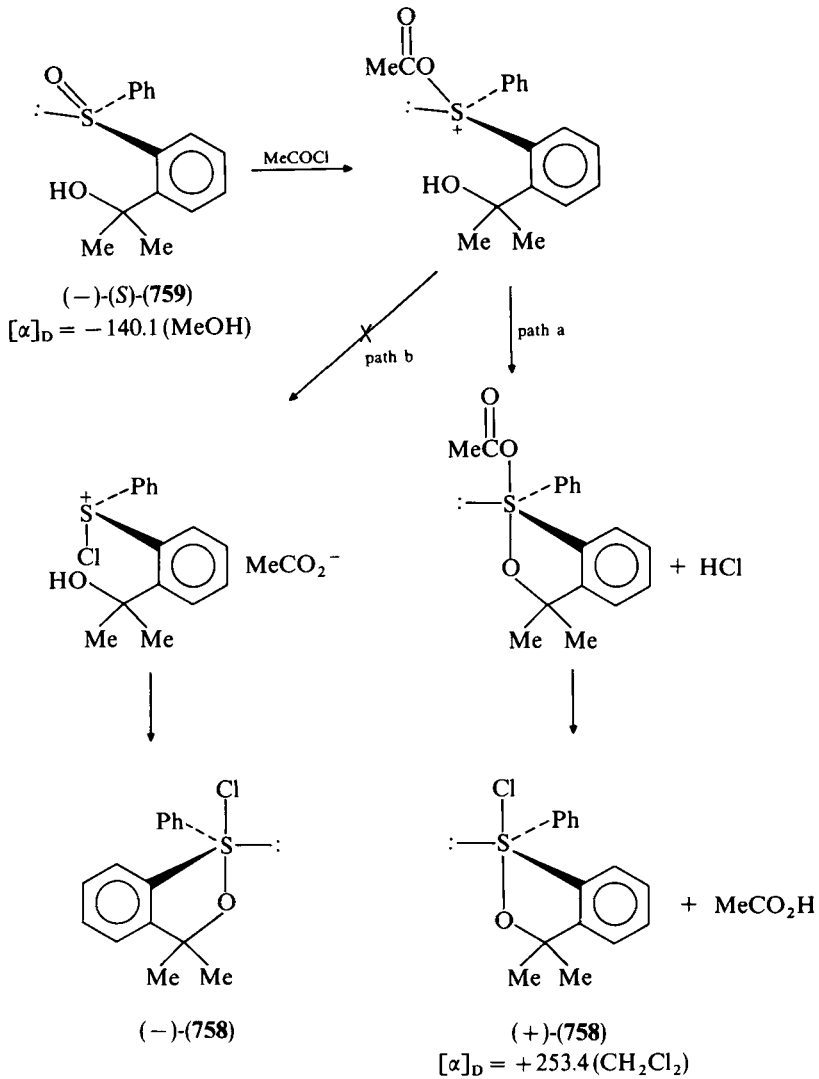


(+)−(**758**) (**760**)

(−)-(*S*)-(**759**)

SCHEME 75

This relationship strongly suggests that the low-temperature reaction of (−)−(*S*) − **759** with acetyl chloride follows path a (Scheme 76). At elevated temperatures, pathways leading to inverted product should become competitive (such as pathway b in Scheme 76).



(−)-(*S*)-(**759**)
$[\alpha]_D = -140.1$ (MeOH)

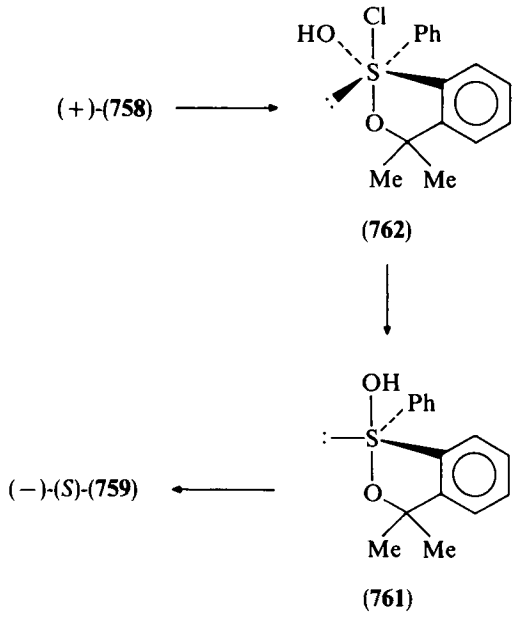
(−)-(**758**)

(+)-(**758**)
$[\alpha]_D = +253.4$ (CH_2Cl_2)

SCHEME 76

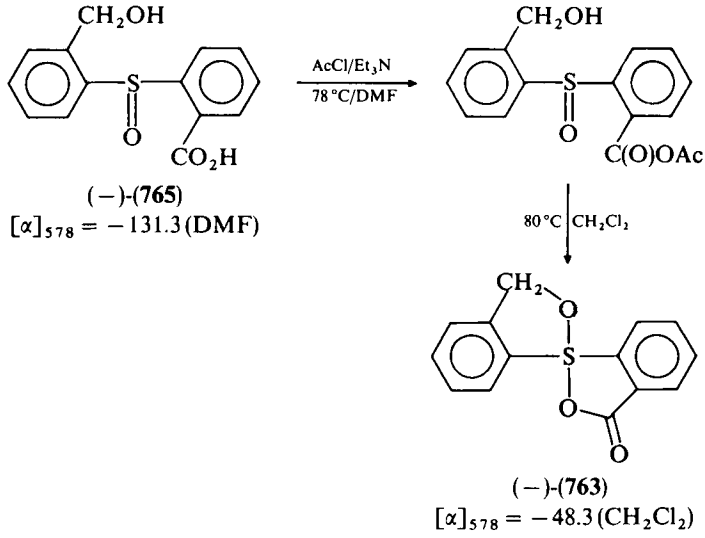
Reaction of the optically active sulfurane **758** with water in the presence of diisopropylamine or *N*,*N*-diethylaniline is rapid and gives the starting sulfoxide-alcohol **759** with retention of configuration at sulfur. An associative nucleophilic displacement at sulfur involving the formation of an octahedral sulfur intermediate **762** and hydroxy-

sulfurane **761** was proposed to explain the overall stereochemistry of hydrolysis (Scheme 77)[182].

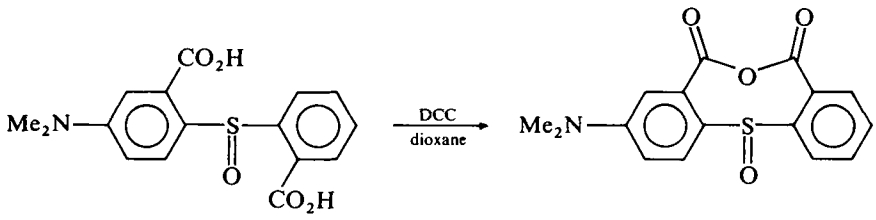


SCHEME 77

Two optically active spirosulfuranes **763** and **764** were obtained through the stereoselective dehydration of the corresponding optically active unsymmetrically substituted sulfoxides **765** and **766**, respectively (equation 363 and 364)[354].

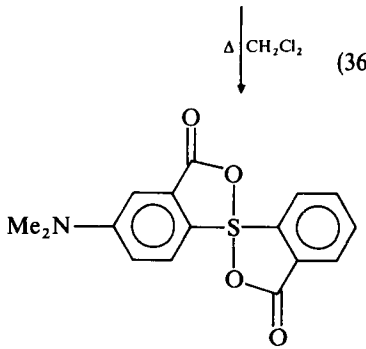


(363)



(+)-(**766**)
$[\alpha]_{546} = +72.0$(DMF)

(−)-(**767**)
$[\alpha]_{589} = -26.0(CH_2Cl_2)$

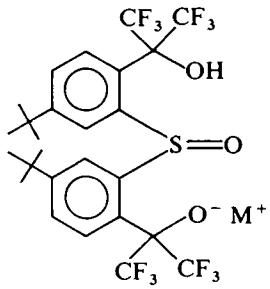


(364)

(−)-(**764**)
$[\alpha]_{589} = -29.3$(DMF)

Two other optically active spirosulfuranes, **263** and **6** (see Table 1) were prepared by an asymmetric dehydration of either the prochiral bis-hydroxysulfoxide **258** (equation 365) or the mono-tetra-*n*-butylammonium or the potassium salt of the bis-hydroxysulfoxide **768** (equation 366) in the presence of an optically active acid (HA*)[355].

258 $\xrightarrow{HA^*}$ (+)- or (−)-**263** (ee up to 75%) (365)

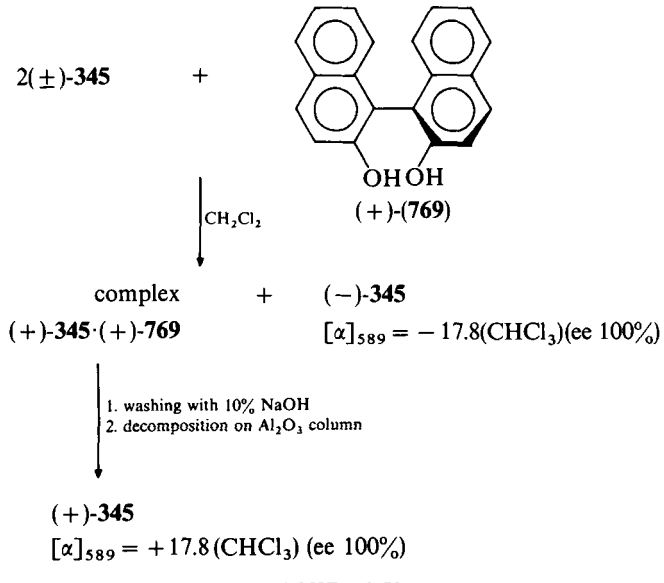


HA* → (+)- or (−)-**6**, $[\alpha]_{589}$ up to 13 (366)

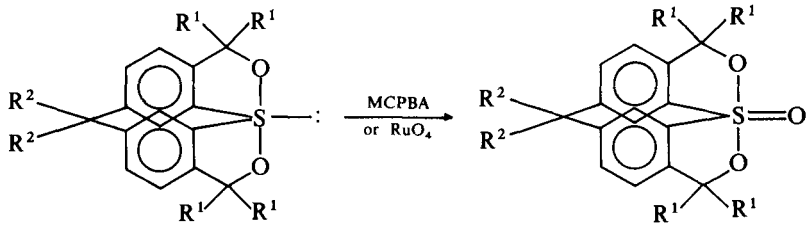
(**768**)
(**a**) M = *n*-Bu_4N
(**b**) M = K

It is interesting to note that a substantial increase in the optical purity of spirosulfuranes **263** and **6** was achieved either by their partial dissolution in pentane (for **263**) or by recrystallization from petroleum ether (for **6**)[355].

The first optically active spirosulfurane **345** (Table 1) containing a tridentate ligand was obtained by the nonclassical resolution of racemic **345** with optically active 2,2-dihydroxy-1,1-binaphthol **769** as a chiral solvating agent (Scheme 78)[356]. This is the first example of a kinetic resolution affording both pure enantiomers of the resolved compounds in a single operation (Scheme 78).



SCHEME 78



(**263**) or (**6**) (**403**) or (**7a**)

(**263**, **403**) $R^1 = Me, R^2 = H$
(**6**, **7a**) $R^1 = CF_3$, $R^2 = t\text{-Bu}$

263 $[\alpha]_{589} = +4.2$ $\xrightarrow{\text{MCPBA}}$ **403** $[\alpha]_{589} \cong -30$

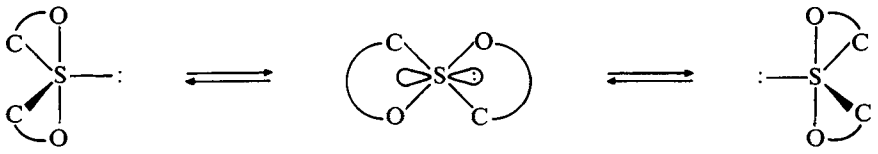
6 $[\alpha]_{589} = +216.5$ $\xrightarrow{RuO_4}$ **7a** $[\alpha]_{589} = +11.8$

SCHEME 79

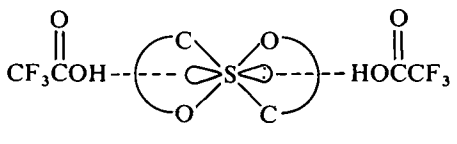
Quite recently, the first optically active spirosulfurane oxides **403** and **7a** have been prepared by the stereoselective oxidation of the corresponding optically active spirosulfuranes **263** and **6** (Scheme 79)[357].

The instantaneous oxidation of the dextrorotatory spirosulfurane **263** with *m*-chloroperbenzoic acid (MCPBA) gave the levorotatory spirosulfurane oxide **403** almost quantitatively. While oxidation of the sulfurane **6** with MCPBA is very slow, it can be very easily converted into the dextrorotatory oxide **7** upon treatment with ruthenium tetraoxide.

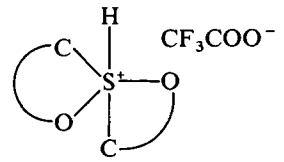
All isolated, optically active spirosulfuranes have been found to be optically stable indefinitely at room temperature. Detailed kinetic investigations of the thermal racemization of the spirosulfuranes **263** and **6** have shown that they lose their optical activity at temperatures above 80 °C. This process is slightly accelerated by protonic acids such as trifluoroacetic acid or trifluoromethanesulfonic acid. The uncatalyzed racemizations were found to have an energy barrier $\Delta H^* = 28.4$ kcal mol^{-1} for **263** and $\Delta H^* = 35.6$ kcal mol^{-1} for **6**. Drabowicz and Martin[355,357] have considered six mechanisms which could account for the uncatalyzed and catalyzed racemization of spirosulfuranes **263** and **6**. They include (a) hydrolysis to the corresponding symmetrical sulfoxide-diol, which could recombine to form the racemic sulfurane, (b) heterolytic oxygen–sulfur bond clevage to yield a sulfonium salt which could racemize by pyramidal inversion before recombination, (c) Berry pseudorotation processes involving intermediate structures with geometries near a trigonal bipyramid with an apical electron pair, (d) an inversion through a planar transition state (cuneal inversion) (Scheme 80), (e) acid catalysis which could involve the transition state **770** or (f) acid catalysis which could involve transition state **771**.



SCHEME 80



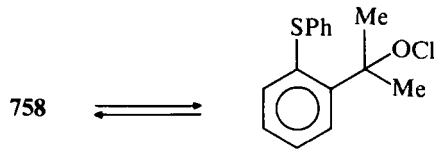
(770)



(771)

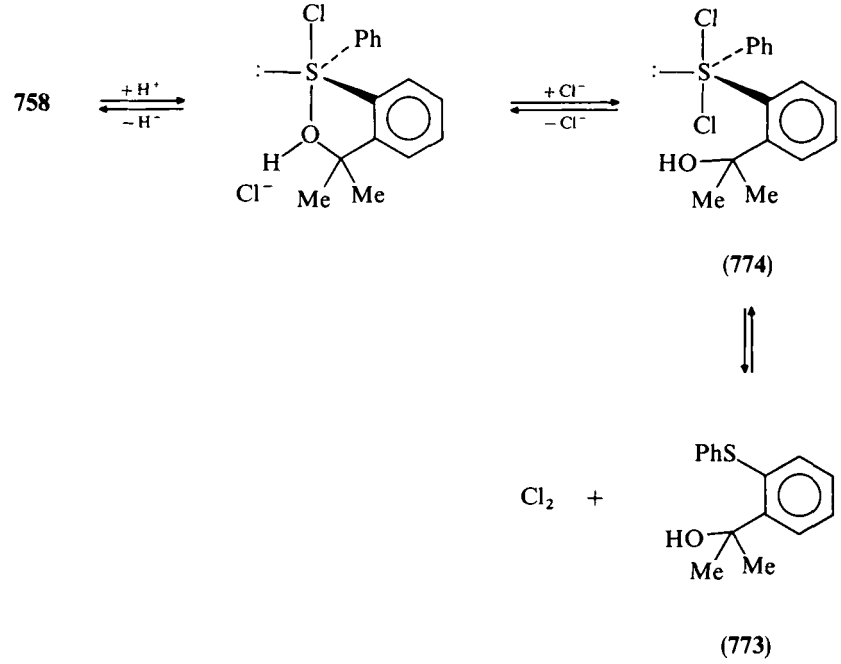
The experimented results are best rationalized by racemization processes which occur through a planar inversion transition state.

An initial rate constant of *ca* 10^{-6} s^{-1} was determined for the uncatalyzed recemization of (+)−**758** at ambient temperature. From this value a crude minimum value of $\Delta G^*_{23} = 25$ kcal mol^{-1} was calculated for this process, irrespective of whether it occurs by way of an equilibrium with hypochlorite **772** (equation 367), by pseudorotation or by inversion via a conformation involving a planar disposition of the four ligands about sulfur[182].



(772) (367)

On the other hand, this chlorosulfurane was found to recemize very rapidly on addition of HCl. The proposed pathway for this racemization involves initial protonation of the oxygen and equilibration with the achiral sulfide **773** or with the dichlorosulfurane **774** (Scheme 81)[182].



SCHEME 81

The thermal racemization of the optically active spirosulfurane oxide **7** can be conveniently followed by polarimetry at temperatures above 80°C. However, the isolated crude sulfurane oxide **403** was found to lose rapidly optical activity at room temperature upon dissolution in chloroform-d containing an excess of pyridine-d_5. Simultaneous recording of the ^{1}H-NMR spectra and measurement of optical rotation indicates that racemization of **403** is accompanied by its conversion into the corresponding sulfone-olefin **404** (equation 368) and that the latter reaction is much slower than racemization[357,358].

403 ⟶ **404** (368)

These results clearly indicate that different mechanisms are responsible for the recemizations of the spirosulfurane oxides **403** and **7**. The origin of these striking differences in the

optical stability of these closely related spirosulfurane oxides is not clear at present and requires further studies.

The stereochemical aspects of the chemistry of high-coordinated organosulfur species discussed above show that this topic is still in its infancy and further work is needed to explain the existing doubts and to develop more deeply this very interesting field of sulfur stereochemistry.

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CHAPTER **16**

Biological activity of sulfoxides and sulfones

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I. INTRODUCTION

Sulfoxides **2** and sulfones **3** are compounds having a sulfinyl (—SO—) or a sulfonyl ($—SO_2—$) group attached to two carbon atoms.

$$\underset{(1)}{R—S—R'} \quad \underset{(2)}{R—SO—R'} \quad \underset{(3)}{R—SO_2—R'}$$

These compounds have many chemical and industrial uses[1,2], and they have been thoroughly investigated because of their biological and pharmacological importance. In

Supplement S: The chemistry of sulphur-containing functional groups
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living organisms they may be generated from sulfides **1** by biological oxidation, e.g. as described for methionine[3].

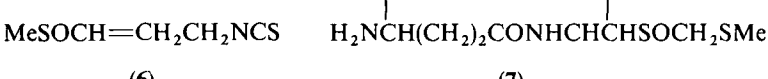
Compounds containing the sulfoxide group were reported to act as drugs, e.g. omeprazole **15** and others, that inhibit gastric acid secretion (antiulcer action)[4,5,47], insecticides[6] and potential radioprotectants[7].

As for sulfones—perhaps the most important drug is dapsone (4,4′-diaminodiphenyl sulfone) **42**, used for the treatment of leprosy[8], but active also against malaria, leishmaniasis and infections in patients with AIDS[9,10].

II. SULFOXIDES

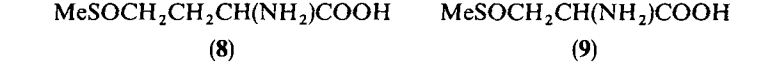
Sulfoxides have been found in small amounts in plants and animals. The simplest compound—dimethyl sulfoxide, DMSO (**2**, R,R′ = Me)—has been isolated from a variety of plants, e.g. corn, oats, onion, tomatoes, cucumbers and from milk[11]. It occurs in sea water, probably as a metabolic product from algae[12]. Its biological properties will be described later.

Allyl vinyl sulfoxide, (**2**, R = CH_2=$CHCH_2$, R′ = CH_2=CH) is a constituent of garlic oil[13]. Propanethial S-oxide, $CH_3CH_2CHS{=}O$ (**4**) is the lachrymatory factor of onion[14]. Derivatives of methylsulfinylisothiocyanates—$CH_3SO(CH_2)_nNCS$ (**5**)—have been found in mustard oils from Cruciferous plants[15], and the related sulforaphen **6** (first compound with optical activity due to an asymmetric sulfur atom) was isolated from radish seeds[16] and subsequently synthetized[17]. Various Basidiomyceteous mushrooms contain γ-glutamylmarasmine **7**[18].



(**6**) (**7**)

Esters of 2,2′-sulfinylbisethanol (**2**, R = R′ = $HOCH_2CH_2$—) were found in adrenal cortex[19]. Two amino acids with SO groups are known, namely methionine sulfoxide **8**[3] and 3-(methylsulfinyl)alanine **9**—an odor constituent in turnips which was also isolated from other plants such as cauliflowers, broccoli etc.[20].



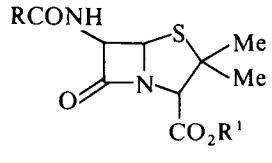
(**8**) (**9**)

A. Chemical and Biochemical Oxidation of Sulfides to Sulfoxides

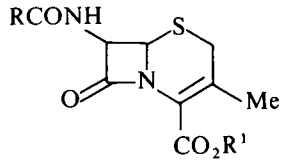
Methods for controlled oxidation of sulfides, that avoid overoxidation to sulfones, are listed by Johnson and Westrick[21]. They include: a solution of sodium metaperiodate in water or water–methanol at 0 °C (for details see Reference 22), *m*-chloroperbenzoic acid in dichloromethane at 0 °C or in ethyl acetate at −40 °C, *t*-butyl hypochlorite in methanol at −40 to −70 °C and hydrogen peroxide in acetone at 0 °C. The oxidation of methionine is described in Reference 3.

Penicillins **10** and cephalosporins **11** have been oxidized to sulfoxides in 90–98% yield by a safe and inexpensive procedure using a mixture of 35% hydrogen peroxide, formic acid and polyphosphoric acid. These compounds possess characteristic and marked antibacterial activity[23]. Changov and coworkers claimed to obtain good results in preparing sulfoxides of penicillanic acids (**10**, R^1 = H) with 30% hydrogen peroxide at 0 °C (55–90%, and purity more than 95%)[24].

The sulfoxidations of several organic sulfides were performed by using *t*-butyl hydroperoxide, hydrogen peroxide, *t*-cumyl hydroperoxide, diphenyl hydroperoxide etc.,



(10)



(11)

in the presence of chloroperoxidase or horseradish peroxidase. Stereospecificity of the product depends on the conditions of the reaction. *t*-Butyl hydroperoxide and chloroperoxidase at 4 °C yielded up to 92% excess of the *R* absolute configuration[25].

Alkyl *p*-tolyl sulfides (**1**, R = Me, Et, Pr and *i*-Pr, R′ = *p*-MeC_6H_4—) were oxidized by purified rabbit lung and mini-pig liver flavin-containing monooxygenase (FMO). The extent of enantioselective oxidation depended on the enzyme employed, the bulk of the alkyl substituent (e.g. lowest for R′ = *i*-Pr) and on pH. The analysis of product stereochemistry may be used as a method for the discrimination of catalytically distinct FMO isozymes[26]. Purified soybean lipoxygenase was found to oxidize thiobenzamide $PhC{=}S(O)_n(NH_2)$ (**12**, $n = 0$) to sulfoxide (**12**, $n = 1$) in the presence of linoleic acid. Inhibitors of lipoxygenase blocked the sulfoxidation[27].

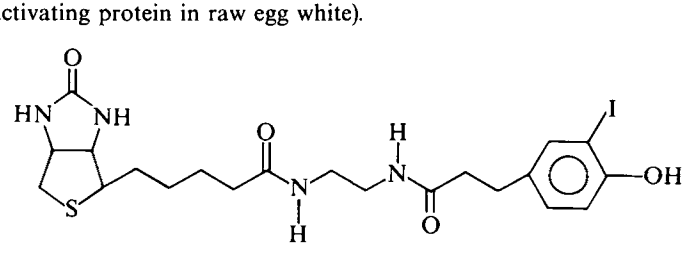
The specific case of biochemical sulfoxidation of the anti-ulcer drug cimetidine[28] by different species was studied by Schulz and Schmoldt[29]. Inhibition experiments with carbon monoxide and *n*-octylamine indicated that, with rat liver microsomes, this process is catalyzed by cytochrome(s) P-450, while with human material the cytochrome P-450 oxidation accounted for no more than 40% of the total[29].

The enhancing effect of methyl viologen (MV)[30] or flavin-adenine trinucleotide (FAD)[31] on the sulfoxide reduction, mediated by a combination of aldehyde oxidase (AO) from guinea pig, was investigated by Yoshihara and Tatsumi[32]. Anaerobic reduction of diphenyl sulfoxide (**2**, R, R′ = Ph) to the sulfide (**1**, R, R′ = Ph) was enhanced 6- and 100-fold by addition of FAD or MV. Thus they serve as electron carriers from the supplemented flavoenzymes to AO, a terminal reductase of sulfoxide.

Poor sulfoxidation of *S*-carboxymethylcysteine has been found in patients suffering from primary biliary cirrhosis, but not from several other liver diseases[33]. It has been found that individuals, who were good hydroxylators but poor sulfoxidizers, would be susceptible to chlorpromazine jaundice[34].

Rheumatoid arthritis patients, treated with penicillamine, were investigated for their ability to oxidize this compound. It has found that poor sulfoxidation status, compared with good sulfoxidation status, was associated with a 3.9 times higher incidence of toxicity[35].

The effect of sulfoxidation has been studied in binding of α- and β-sulfoxides of biotinylamidoethyl-3-(4-hydroxy-3-^{125}I/iodophenyl)propionamide **13** to avidin (a biotin-inactivating protein in raw egg white).



(13)

The 1:1 compound of avidin and the α-form of **13** has a dissociation half-life ($t_{1/2}$) of 25 days, which is about 1.6 times faster than that of the parent compound ($t_{1/2}$ 41 days), but the β-form dissociates 446 times faster ($t_{1/2}$ 0.092 day). The fact is apparently due to a steric effect. It is suggested that the α-form of **13** may be attractive as a tracer agent to facilitate studies and applications of the avidin–biotin system[36].

Sulfoxides (and other compounds) with increasingly longer hydrocarbon chains have been found to lower progressively the thermal denaturation temperature of proteins. This effect is explained by a hydrophobic interaction between the solute and nonpolar domains of the protein, and was studied by assessing the stability of phospholipid vesicles as reflected by solute-induced loss of vesicle contents. DMSO up to 3 M concentrations does not increase leakage rates. tetramethylene sulfoxide [**2**, R,R′ = —$(CH_2)_4$—] and diisopropyl sulfoxide (**2**, R,R′ = *i*-Pr) are much more active[37].

Inhibitors of collagen-induced aggregation of human platelets *in vitro* were isolated from crushed onion. These compounds may be formed by interaction of the aforementioned thiopropanal S-oxide **4** with alkane or alkenesulfenic acids produced in crushed onion[38].

From a series of sulfoxides tested, only the methyl phenyl (**2**, R = Me, R′ = Ph) and methyl *p*-chlorophenyl (**2**, R = Me, R′ = *p*-ClC_6H_4—) sulfoxides stimulated chondrogenesis at 10^{-2} and 10^{-3} M. Both compounds stimulate cartilage module formation, [^{35}S] sulfate incorporation and activity of the regulatory sequences of the collagen II gene[39].

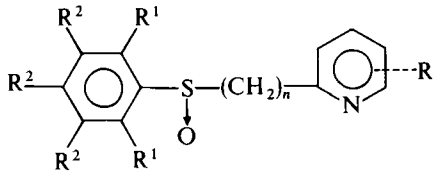
n-Decyl methyl sulfoxide (**2**, R = Me, R′ = $C_{10}H_{21}$) increased the permeability through hairless mouse skin of all amino acids and peptides tested[40].

The biological consequences of drug sulfoxidation and the effects on physicochemical properties and biological activity was reviewed by Mitchell[41].

B. Pharmacological Activity of Sulfoxides

Many compounds that contain the sulfoxide group elicit pharmacological activity. The simplest member, namely dimethyl sulfoxide DMSO, is a commercially important product, commonly used in chemical laboratories and in industry, particularly as an excellent solvent[1]. DMSO has been intensively studied for its biological activity, as it has many effects; e.g. it has been found to relieve symptoms of arthritis, secondary amyloidosis associated with rheumatoid arthritis[42], tendovaginitis, bursitis, myositis, skin induration and trophic ulcers[43]. It is used in veterinarian practice. DMSO is relatively safe—LD_{50} (in g/kg): orally, rats 20–28, monkeys, >4; i.v.: rats, 5.2–8.1, monkeys, 11. These and other details are summarized in a review[44] and in papers from a conference on the biological and pharmacological aspects of this agent[45].

Many sulfoxides are also pharmacologically effective. In recent years several agents attracted considerable attention as drugs useful for treating ulcers and gastric hypersecretion. A series of sulfoxides was patented several years ago[46]. The parent compound (**14**, R = R^1 = R^2 = H; *n* = 1) gave 60% inhibition in the stress-induced erosion test at 100 mg/kg.



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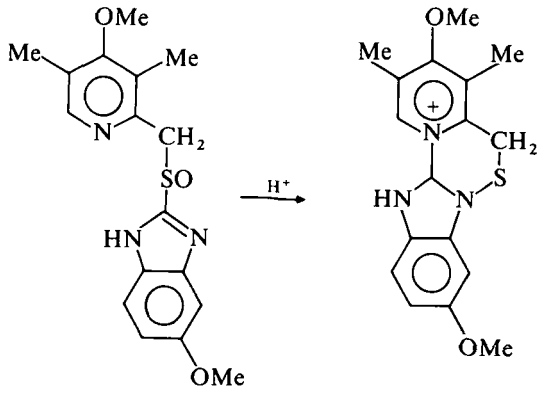


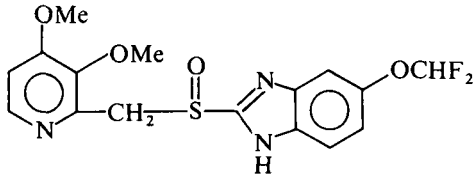
(15) (16)

A group of benzimidazole derivatives was developed later and the drug of choice in this area seems to be omeprazole (OM) **15**[4]. An extensive summary of up-to-date findings was presented recently in an excellent book, edited by Collen and Benjamin[47].

OM is now used in treating this and related diseases, e.g. the Zollinger–Ellison syndrome (ZES—recurrent peptic ulceration, a marked increase in gastric acid secretion and islet cell tumors[48]). It is an inhibitor of the H^+, K^+-ATPase. The ED_{50} for inhibiting both basal and stimulated acid secretion in man is about 27 mg[49]. A description of its mechanism of action may be summarized as follows: OM acts as a prodrug, it enters into the parietal cell and is converted in the secretory canaliculus to the sulfenamide **16** by acid. **16** reacts with two SH groups in the catalytic subunit of the H^+, K^+-ATPase[49,50]. OM inhibits also the K^+-stimulated *p*-nitrophenylphosphatase activity and the phosphoenzyme formation. Its binding to SH groups could be completely prevented by mercaptoethanol but not by cysteine or glutathione.[4]

The therapeutic value of OM may be emphasized by the finding that, by the dosage of 20–60 mg daily, 90–100% of duodenal ulcers were healed in 4 weeks. It is highly effective in healing ulcers, resistant to therapy with H^+ receptor antagonists[45] and successful in short-term treatment of reflux esophagitis[51].

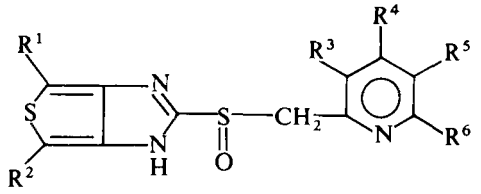
Recently a related bezimidazole derivative, BY 1023/SKF-96022 **17**, has been reported to act similarly to OM, but to show lesser interaction with cytochrome P-450[5].



(17)

The mechanism of its action was studied[52]. An automatic, high-performance liquid chromatography method was described for the determination of **17** and of its major metabolite (sulfone) in dog serum[53].

A series of 2[(2-pyridylmethyl)sulfinyl]-1*H*-thieno[3,4-*d*] imidazoles (**18**, **19**) has been prepared. The compounds act as potent inhibitors of gastric acid secretion. Their



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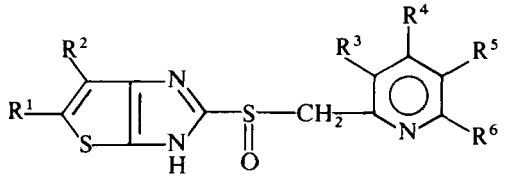


(19)

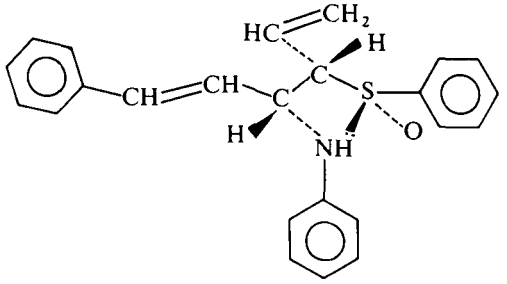
pharmacological profile is different from that of OM. The derivative **18**, R^1, R^2, R^4, R^5, $R^6 = H$; $R^3 = CF_3(CH_3)_2CH_2O$— was selected for clinical studies[54].

A number of organic sulfur compounds of the general formula **20** has been reported as potential antiradiation agents[7]. Among those were listed sulfoxides (Y = SO, Z = S and Y = Z = SO). Unfortunately no biological data were presented.

$$PhY(CH_2)_3SS(CH_2)_3ZPh$$

(20)

1-Phenyl-3-phenylamino-4-(*p*-toluenesulfinyl)-*trans*-1,5-hexadiene **21** has been prepared and found to have in vitro toxicity against P388 and L1210 murine leukemia cells in culture (LD_{50} 15 and 19 μg/ml, respectively). the compound compared favourably with the effect of doxorubicin[55]. It is suggested that it acts through inhibition of DNA and/or RNA synthesis[56].



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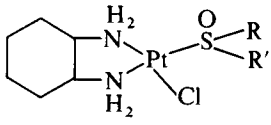
Platinum containing compounds of the general formula /PtCl(RR'SO)(diam)/NO_3, where diam is 1,2-diaminocyclohexane **22**, or 1,1-bis(aminomethylcyclohexane) **23**, and R,R' = Me, Ph, $PhCH_2$—, etc., were prepared and found active against L1210 leukemia



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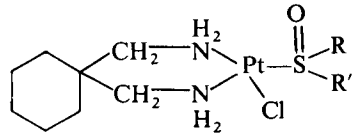
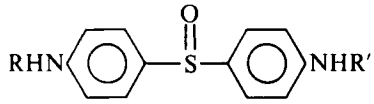


(23)

strain. The activity depends on the nature of the amine and the rest attached to SO. The 1,1-disubstituted compounds **23** were significantly more reactive than **22**[57].

Di(*p*-aminophenyl)sulfoxide **24**, an analog of the corresponding sulfone—dapsone **42**, is also an antibacterial (leprostatic) drug[58]. *cis*-5-Fluoro-2-methyl-1[*p*-(methylsulfinyl)-benzylidene] indene-3-acetic acid **25** (sulindac) is an antiinflammatory agent[59]. 2-[2-Methoxy-4-(methylsulfinyl)phenyl]-1*H*-imidazo-[4,5-*b*]pyridine **26** (sulmazole) is a cardiotonic, orally active nonglycoside, nonadrenergic inotropic compound[60,61].



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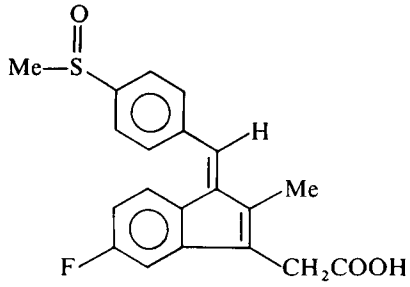

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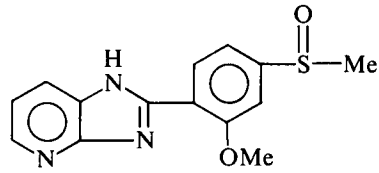
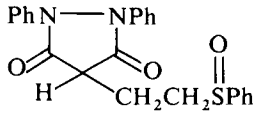


(26)

1,2-Diphenyl-4-[2-(phenylsulfinyl)ethyl]-3,5-pyrazolidinedione **27** (sulfinpyrazone, anturane) is an uricosuric drug[62]. Anturane was investigated by a special group as a drug that may prevent sudden death from heart attacks[63].

4-Hydroxy-α-{{[3-(4-methoxyphenyl)-1-methylpropyl]amino}methyl}-3-(methylsulfinyl)-benzenemethanol **28** (sulfinalol) is a β-adrenergic blocker and antihypertensive[64].



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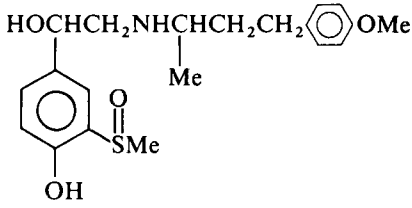
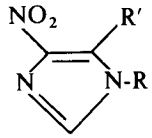


(28)

The earlier-mentioned lachrymatory factor of onion, thiopropanal S-oxide **4**, showed inhibitory activity against the spores of Aspergillus parasiticus[65].

A complex that contains ruthenium dichloride, a sulfoxide and 4-nitroimidazole, $RuCl_2(DMSO)_2(4\text{-}NO_2(Im)_2)$ where Im has the structure **29** was found to show better radiosensitizing properties and lower toxicity than those containing only the 4-nitroimidazole ligand.

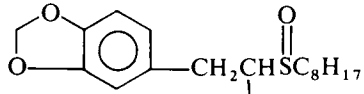


(**29**)

Substitution of DMSO by tetramethylene sulfoxide (TMSO) was also investigated. At 200 μM the complexes $RuCl_2(TMSO)_2(4\text{-}NO_2Im)_2$, where R,R′ = H or R = H, R′ = $CH_2CONHCH_2CH_2OH$, have promising sensitizing enhancement ratio values of 1.6 and 1.5[66].

Unpurified sulfoxides from petroleum have been found effective against *Psoroptes cuniculi* and *P. bovi* at about 0.5%. They were active against other parasitic insects[6].

1-Methyl-2-(3,4-methylenedioxyphenyl)ethyl octyl sulfoxide **30** is an insecticide and a synergist for pyrethrum, allethrin etc.[67].



(**30**)

III. SULFONES

There is scarce information on naturally occurring sulfones. Dimethyl sulfone (**3**, R,R′ = Me)[68] has been found in blood[69], in primitive plants such as *Equisetum arvensae* L., adrenal cortex of cattle[70] and urine of bobcats (*Lynx rufus*)[71].

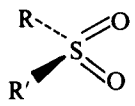
Hypotaurine **31** is oxidized by a hydroxyl radical to bis-aminoethyl-α-disulfone **32**, which is in turn oxidized to taurine **33** (TA). the disulfone was found in male sexual tissue[72,73].

$$H_2NCH_2CH_2SO_2H \longrightarrow (H_2NCH_2CH_2SO_2—)_2 \longrightarrow H_2NCH_2CH_2SO_3H$$

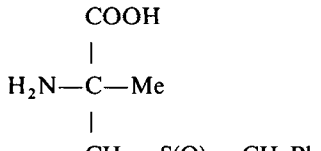
(**31**) (**32**) (**33**)

A. Biochemical Activity

The substituents on sulfur in sulfones **3** are arranged in a roughly tetrahedral pattern[21].



These are easily obtained from sulfides 1 and exhibit great chemical stability. A procedure for the preparation of *S*-benzyl-DL-α-methylcysteine sulfone (**34**, $n = 2$) from the corresponding sulfide (**34**, $n = 0$) by 30% hydrogen peroxide, in the presence of 70% perchloric acid and ammonium molybdate, has been reported by Griffith[74].



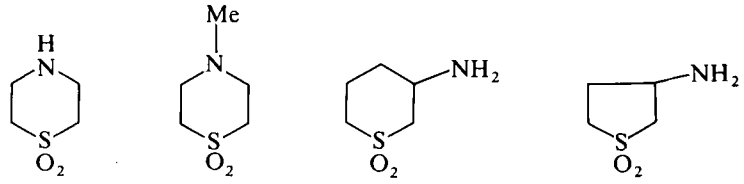
(**34**)

Methyl and ethyl vinyl sulfones (**3**, R = Me or Et, R′ = $CH{=}CH_2$) have a strong chemical affinity to functional groups of proteins: =NH, $-NH_2$, —SH, and they interact with these groups under mild conditions[75].

Divinyl sulfone (**3**, R,R′ = $CH{=}CH_2$) attached to agarose and coupled to monospecific antibodies has been used for purification of uteroglobin[76].

A method for immobilizing physiologically active substances on a carrier employs cross-linking agents of a general formula $X{-}SO_2L{-}SO_2X$ (**35**), where X, X′ = $CH{=}CH_2$, CH_2CH_2Y (Y is a nucleophile) and L is a divalent linking group. For example, thermolysin was immobilized on amberlite XAD-7 resin and retained 49% of activity[77].

Sulfone analogs of taurin (TA) have been found to act as modulators of calcium uptake and protein phosphorylation in rat retina.



(**36**) (**37**) (**38**) (**39**)

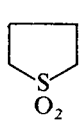
These compounds are equipotent inhibitors of phosphate incorporation (30–45%) into retinal proteins. Derivatives **38** and **39** were more potent stimulators of Ca^{2+} uptake than TA[78].

B. Pharmacological Activity

Many substituted sulfones possess pronounced physiological activity. Simple sulfones, such as the well-known solvent sulfolane **40**, are relatively safe. No overt toxic effects were noted in rats, guinea pigs and squirrel monkeys during inhalation exposure to **40** at 2.8–20 mg/m^3, LD_{50} *ca* 1.6–1.9 subcutaneously[79] and 1.9–5.0 g/kg orally[80] for various laboratory animals.

Derivatives that contain two sulfone groups—sulfonal, 2,2-bis(ethylsulfonyl)propane (**41**, R = H)[81] and its methyl homolog (**41**, R = Me)[82] were previously used in human and veterinarian practice. As possible habit-forming substances they are under control.

Diphenyl sulfones are very important drugs. The best known agent is the 4,4′-diamino derivative, dapsone (**42**, R, R^1, R^2 = H), used primarily for treatment of leprosy[8]. It is also mentioned as active against malaria, leishmaniasis, infections in patients with AIDS[9]



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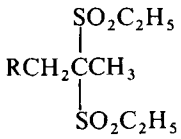
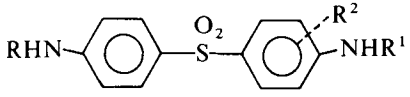


(41)

and discoid lupus erythematosus[83]. Dapsone is administered in doses of about 100 mg daily. Side effects such as hemolytic anemia, hepatitis and skin rashes have been observed[8].

The chemotherapy of leprosy, including the use of dapsone, spread of dapsone resistant strains and multidrug treatment has been reviewed[84].

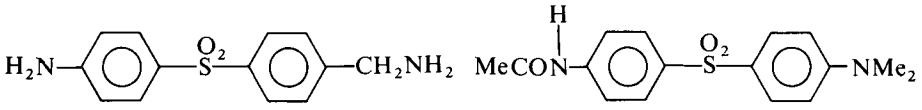


(42)

N, *N'*-Digalactoside of dapsone (**42**, R,$R^1 = C_6H_{11}O_5$, R^2 = H)[85], the *N*,*N'*-diglucoside disodium disulfonate, promin (**42**, R,R^1 = —CH(SO_3Na)CHOHCHOHCHOHCH$_2$OH; R^2 = H)[86], *N*,*N'*-disodium methanesulfinate (**42**, R,$R^1 = CH_2SO_2Na$; R^2 = H)[87] and ammonium salt of 4-sulfanilylsuccinanilic acid (**42**, R,R^2 = H; R' = $COCH_2CH_2COOH$)[88] are water-soluble compounds that elicit similar effects.

42 and several derivatives were identified as highly potent inhibitors of purified dihydropteroate synthase from Toxoplasma gondii (IC_{30} 1 μM). Toxoplasmosis is a life-threatening disease, particularly among patients with AIDS, so these sulfones may serve as important drugs. The most active were dapsone itself, as well as the 3'-chloro- etc. (**42**, R,R^1 = H; R'' = 3'-Cl) and N'-β-hydroxyethyl (**42**, R,R^2 = H, $R^1 = CH_2CH_2OH$) derivatives[10]. The last compound[89] and a homolog of dapsone, *p*-sulfanilylbenzylamine **43**[90], are antibacterial agents.

A series of related 4,4'-diaminosulfones was evaluated for their antimalarial activity against *Plasmodium berghei* infection in mice. Compounds where R,R^2 = H, R^1 = Me, Et and *n*-Bu, or R = H, R^1 = *n*-Pr, *n*-Bu and R^2 = 2-OMe, completely inhibited parasitaemia at 1 mg/kg for four days. Compound **44** was similarly active at 0.3 mg/kg[91].



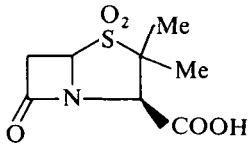
(43) (44)

The 2'-methyl-*N'*-propyl derivative (**42**, R = H, R^1 = Pr, R^2 = 2'-Me) is effective against malaria, when used together with 7,8-dihydrofolate reductase inhibitors[92].

Penicillanic acid sulfone **45** is an antibacterial used in combination with other β-lactam antibiotics[93].

2-(*p*-Aminosulfonylphenyl)1,2-thiazine sulfone **46** (sulthiame) is an anticonvulsant, that contains both the SO_2 and SO_2NH_2 groups[94].

N-[(1-Ethyl-2-pyrrolidinyl)methyl]-5-(ethylsulfonyl)-2-methoxybenzamide **47** (sultopride) and its hydrochloride are antidepressants[95].



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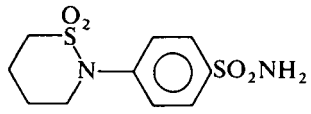
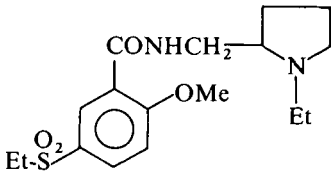
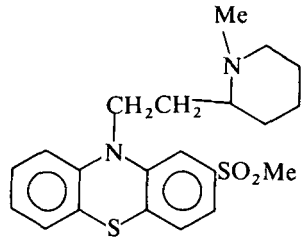


(46)



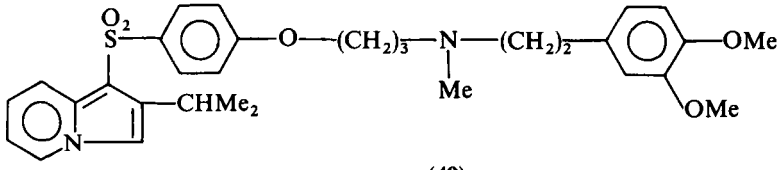
(47)



(48)

A phenothiazine derivative containing a sulfone group **48** (sulforidazine) is an antipsychotic and a dopamine receptor blocker[96].

Substituted indolizine sulfones like (2-isopropyl-1[(4-(3-*N*-methyl-*N*-(3,4-dimethoxy-*β*-phenethyl)amino)-propyloxy)benzenesulfonyl]indolizine **49** (SR 33557) represent a new class of inhibitors of L-type Ca^{2+} channels. The agent binds with high affinity to a single class of sites in a purified preparation of rat cardial sarcolemma membranes[97].



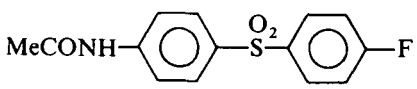
(49)

Aliphatic sulfones were prepared and tested as antitumor pharmaceuticals. The most active compound was **50** that at 20 μg/ml totally inhibited the growth of ulocarcinoma cells in cultures[98].

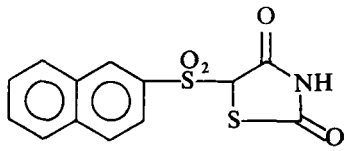
$$CH_2{=}CHCH_2SO_2CH_2CH_2CH{=}CHSSCH_2CH{=}CH_2$$

(50)

N-{4-[(*p*-Fluorophenyl)sulfonyl]phenyl}acetamide **51**[99] is an immunopotentiator, that when given to mice in a single dose of 100–600 mg/kg is capable of inducing a population of peritoneal microphages that inhibit the growth of tumor cells. It may be useful in treatment of neoplastic disease[100].



(51)

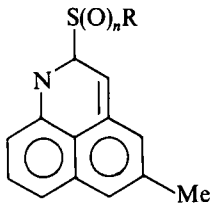


(52)

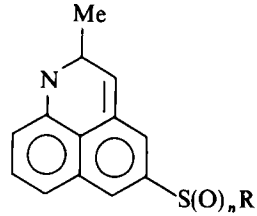
5-(Naphthalenesulfonyl)-2,4-thiazolidinedione **52** was equipotent to the antidiabetic drug ciglitazone in two animal models of noninsulin-dependent diabetes mellitus. Substituted derivatives were less potent[101].

Arylsulfonylnitromethanes $ArSO_2CH_2NO_2$ (**53**), where Ar is an aromatic group such as phenyl, naphthyl, etc., were prepared and found to act as aldose reductase inhibitors useful in treating diabetic complications[102].

(Arylsulfonyl)benzo[*h*]quinoline derivatives **54** and **55** (R = aryl) are effective microbicides at 200 μg/disc against Gram-positive cocci and Gram-negative bacilli. They were prepared by oxidation of the corresponding sulfides with potassium permanganate[103].



(**54**)



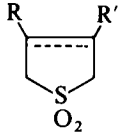
(**55**)

C. Agrochemicals

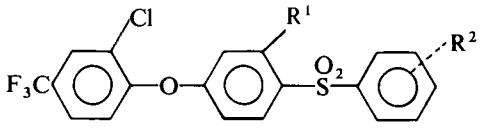
Many sulfones have been proposed and tested as agrochemicals for crop protection and as insecticides.

Five-membered cyclic sulfones, saturated and unsaturated, were prepared and found to retard the growth of plants. Particularly active was **56** (R = H, R′ = SO_2Ph)[104].

Phenoxyphenyl phenyl sulfones **57**, bearing various substituents (halo, alkyl, alkoxy etc.), have been found to act as herbicides. The compound (**57**, R^1 = OMe, R^2 = *p*-OMe) killed 100% of cocklebur (*Xanthium pensylvanicum*) at 1g/are and showed no toxicity to soybean[105].



(**56**)



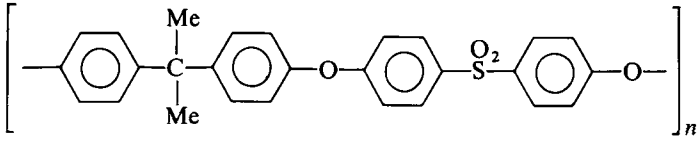
(**57**)

A series of thirty-six fluoroaliphatic sulfones were tested for their residual toxicity to the fire ant, *Selenopsis invicta* Buren. Several sulfones gave > 90% kill of the ants, exposed at 10 ppm for four days, and one compound (A13-10841) elicited appreciable mortality even at 1 ppm. They performed well at 10 ppm in soil, particularly during prolonged periods of time[106].

D. Sulfone-containing Polymers (Polysulfones)

Many organic polymers containing the sulfone group have found biomedical applications[107,108]. One of the most useful substances is the Udel polysulfone **58**.

These polymers, that could be produced in any desired color, are successful alternatives



(58)

to stainless steel and glass, as they are biologically inert, resistant to sterilization procedures and to common chemicals[109].

Polysulfones have found application also as ultrafiltration membranes. Several studies emphasized the advantage of polysulfone dialyzers during hemodialysis[110–112]. Purification of biological fluids, e.g. removal of interleukin-1 and tumor necrosis

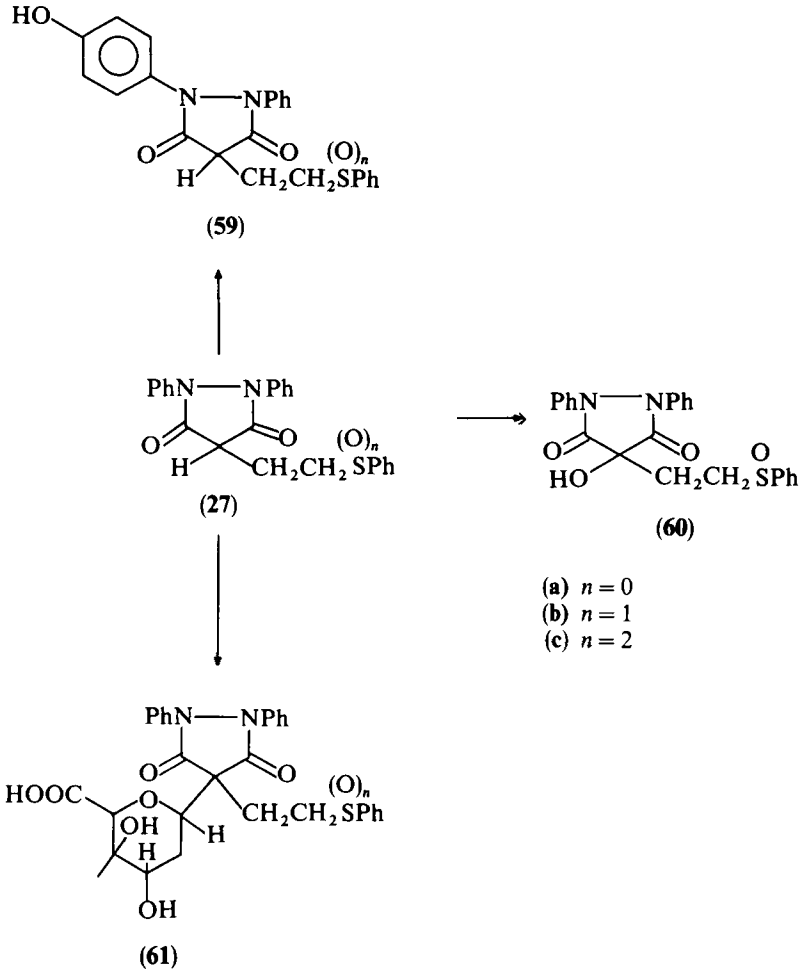


FIGURE 1. Metabolism of sulfinpyrazone **27b**

factor-inducing substances, has been successfully achieved by filtration through such membranes[113].

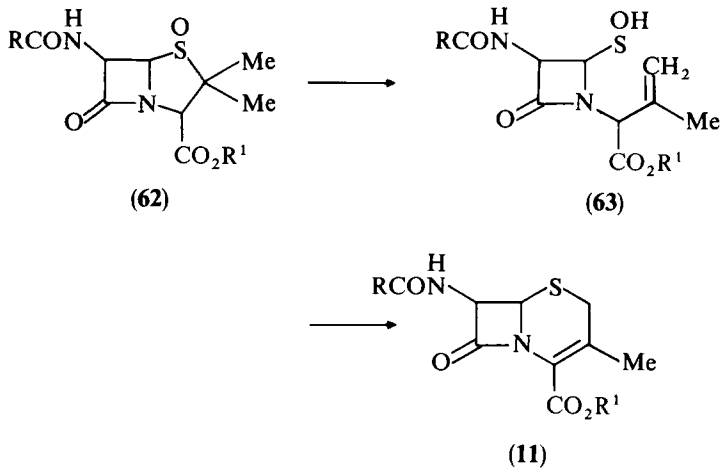
IV. METABOLISM OF SULFOXIDES AND SULFONES

Biotransformation of sulfoxides and sulfones involves changes in the carbon chain or ring attached to sulfur, the reduction–oxidation of sulfoxides and the occurrence of both processes. It should be noted that the oxidation to a sulfone is irreversible.

4,4′-Diaminodiphenyl sulfoxide (**24**, R = H) is converted to the *N*-glucuronide (**24**, R = $C_6H_9O_7$) and, in a very low amount, to the *N*-sulfamate (**24**, R = SO_3H)[114]. An example of the various metabolic pathways is provided by the fate of sulfinpyrazone **27b** (Figure 1)[115]. Reduction of **27b** gives the sulfide **27a**, while oxidation yields the sulfone **27c**. All three compounds are hydroxylated at the phenyl ring (**59a, b, c**). Hydroxylation occurs also at the C(4) position to give **60**, but only the isolation of **60b** in minute amounts has been reported, while the glucuronides of all three forms (**61a, b, c**) have been found. The appearance of the sulfide **27a** may be clinically important, since this metabolite shows a strong inhibitory effect on platelet aggregation in various experimental systems *in vitro*.

Similar conversion of the SO group to sulfide and sulfone has been observed for other compounds, such as sulindac **26**. Also, here it has been assumed that the sulfide metabolite is the active form of **26**[116].

The interrelation of some sulfoxides and sulfenic acids was examined recently in an extensive review on the biochemistry of sulfenic acids[117]. As an example, the metabolic pathway of penicillin sulfoxide **62** to cephalosporin **11** via the sulfenic acid **63** was described.



The biotransformation of omeprazole **15** and its conversion to the sulfide **16** has already been mentioned.

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CHAPTER 17

Organic sulfur in the geosphere: analysis, structures and chemical processes

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I. INTRODUCTION

Fossil fuels—petroleum and coal—have become in the last century mankind's main energy source, as well as a vast reservoir of petrochemicals. In the course of the search for fossil fuels, the relatively young interdiscipline of organic geochemistry tries to reveal the sources of fossil fuels and the processes that produce them. After some debate, the biological source for organic matter in the geosphere, in all its forms, was almost consensually accepted. The chemically controlled processes which so drastically change the structure of organic matter are complex and take place during very long periods of time. The reader who is unfamiliar with the subject is referred to the 'classic' book by Tissot and Welte[1].

Biosynthesized compounds have three main degradation pathways: chemical oxidation, biological recycling (including biological oxidation) and preservation. Preserved organic matter is deposited, in most cases in the bottom of water reservoirs such as the ocean floor, continental shelves, lagoons, deltaic areas, lakes, marshes and swamps. The preservation of organic matter is dependent both on the conditions in the deposition environment at the time of sedimentation and on the nature and structure of organic matter. Different biomolecules have completely different 'preservation potential'. Polypeptides and polycarbohydrates are considered as very labile, because they are easily hydrolyzed to water-soluble biologically recyclable amino acids and sugars. Lipidic compounds are usually considered as high preservation materials[1].

The first stage of the alternation of organic matter—*diagenesis*—is characterized by gradual loss of functional groups (indicated by the loss of H_2O, CO_2 and NH_3, or decrease in the O/C and N/C atomic ratios) accompanied by gradual condensation and polymerization. During this stage most of the preserved organic matter (more than 95%) polymerizes. These gradual, mostly thermal, changes are termed *maturation*. The organic matter at the end of the diagenetic stage is operationally classified into two fractions: *bitumen*, the fraction soluble in common organic solvents, and *kerogen*, the insoluble fraction in these solvents[2], namely geopolymers. Kerogens derived from high plants and usually deposited in fresh water are termed *coal* and undergo parallel, but in some aspects different geological processes than kerogens from marine origin. This review will concentrate more on marine-derived organic matter. Recently the classic ideas of kerogen formation via random repolymerization and polycondensation of lipids with sugars and amino acids was reappraised[3,4] and the concepts of resistant biomacromolecules and their selective preservation as a main pathway for kerogen formation were introduced.

After the formation and maturation of kerogen, along with minor amounts of bitumen, increasing thermal stress causes the commencement of the second stage of geological

transformation—*catagenesis*. This stage is characterized by thermal dissociation and disproportionation of the kerogen and bitumen into liquids (oil) or gaseous products (natural gas) and solid residues which gradually carbonize. Increasing thermal stress results in increasing formation of gas as a result of oil dissociation. (Coals usually release only gas.) The stage when liquid products are mainly produced is called 'the oil window'[1]. Figure 1 represents proposed pathways for diagenesis and catagenesis (which combine both 'classical' and recent concepts for kerogen formation)[1,3,4].

Sulfur is in many cases the third abundant element in the 'mature' organic matter in the geosphere following carbon and hydrogen. In some high sulfur samples most of the compounds contain sulfur; an example of such a case can be seen in Figure 2, which shows the results of a gas-chromatographic analysis of a bitumen from an organic-rich bituminous rock from Nebi Musa (Israel), where Figure 2a represents the FID response (carbon) and Figure 2b the FPD response (sulfur). Both detectors responded to most of the compounds, indicating the very high abundance of sulfur compounds in this sample.

The 'behavior' of sulfur during the diagenetic processes is dramatically different than that of any other element. Sulfur is present in the biomass mainly as part of amino acids, therefore processes similar to those controlling the removal of nitrogen would have been expected to gradually decrease the S/C ratio. However, in many cases a completely opposite trend is observed and the S/C ratio is significantly increased. It is now clear that this phenomenon is caused by chemical incorporation of inorganic sulfur into the preserved organic matter in the early stages of diagenesis[5-7].

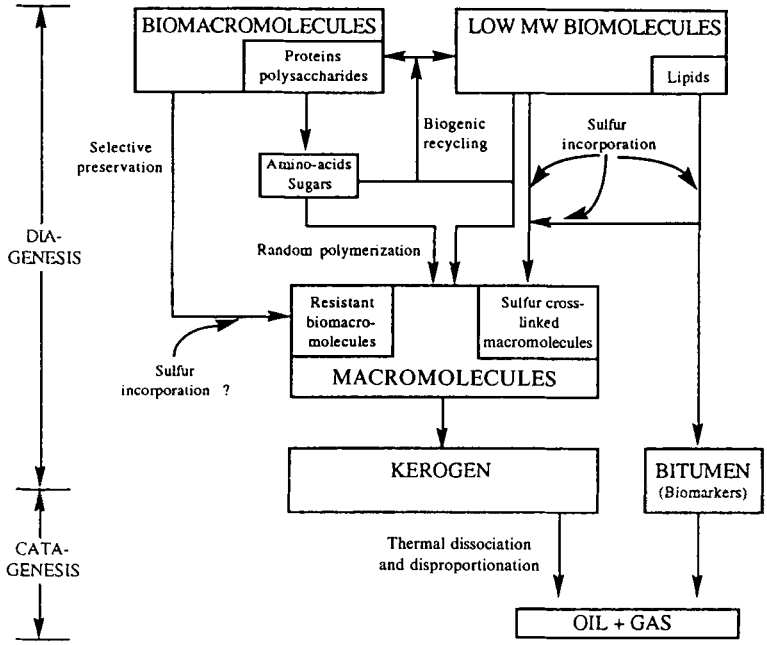


FIGURE 1. Proposed possible pathways for diagenetic preservation of organic matter in sediments. Based on a combination of the 'classic' pathway[1] and the recent theories on selective preservation of resistant biomacromolecules[3] and sulfur incorporation

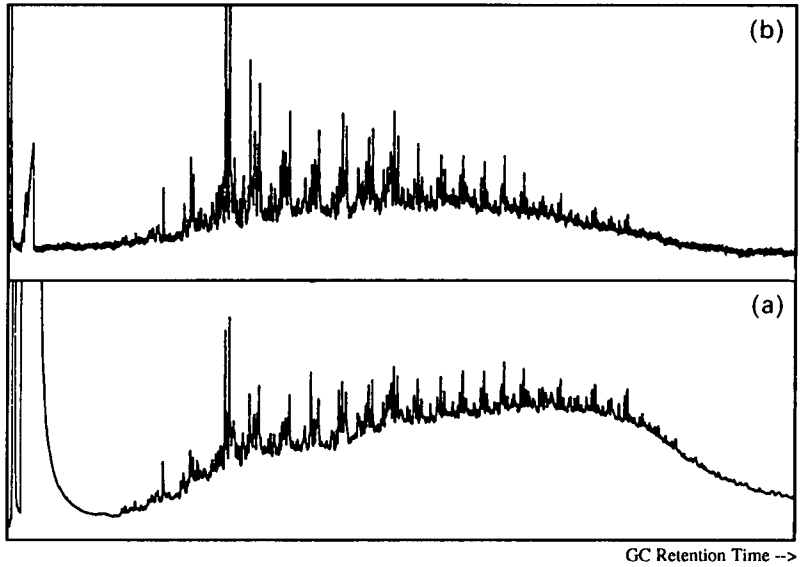


FIGURE 2. Gas chromatogram of the aromatic fraction of an extract of a bituminous rock from Nebi Musa (Israel): (a) FID response (carbon-containing compounds); (b) FPD response (sulfur-containing compounds)

The result of this process—high sulfur crude oils—is one of the biggest technical and environmental problems in the petroleum and coal industry and utilization. This review is aimed at the chemical structures, analytical techniques and chemical processes which are involved in the organic geochemistry of sulfur. Its first part concentrates on the structural information and analytical techniques used to identify these structures. The analytical methodologies and instrumentation are the rate-determining factors in the scientific progress in this field. Consequently, the main limitations of these methods are discussed in some detail in order to understand the current limits of our knowledge. On the other hand, improved analytical methods in the recent decade significantly increased our knowledge about structures of sulfur-containing compounds in oils and bitumens. Leading articles on this subject can be found in a book published in 1990[5], which also contains a historically oriented review[6].

The second part of this review concentrates on the chemical processes and proposed mechanisms of sulfur incorporation into organic matter in the geosphere and its transformations. The information on this subject, which is currently a focus of research, is very limited. Therefore some sections are somewhat more speculative and meant to provide the main hypotheses and ideas, rather than to bring only a limited number of facts.

This chapter is chemically oriented and therefore the more geological aspects of the subject, such as recognition of paleoenvironments, are not included. The reader is referred to a recent review article on the subject, which contains sections dealing with the geochemical significance of sulfur compounds[7], and to some additional articles[8-11].

II. ANALYTICAL METHODS

Sulfur compounds in the geosphere are present in all fractions of organic matter during all stages of geochemical processes. In most of the compounds and polymers divalent sulfur is

the most abundant form. Divalent sulfur compounds such as thiols, sulfides, thiophenes and polysulfides in very complex systems pose severe analytical problems. These problems had prevented the identification of complex sulfur compounds until a decade ago. The main reason for the problem is the similar behavior of sulfur and carbon in many analytical methods. For example, carbons and hydrogens adjacent to a sulfur atom do not have any special characteristics in NMR spectroscopy, or until recently there were no chromatographic methods for the selective separation of sulfur-containing compounds.

The main analytical tasks in organic sulfur analysis of geosphere origin are:

(1) The identification and quantification of sulfur content in organic matter (in the bulk or in specific compounds).

(2) The separation of sulfur compounds in complex systems, and the quantification of specific compounds or of groups of compounds (e.g. sulfides or thiophenes).

(3) The identification and assignment of the exact structure of the sulfur-containing functional group.

The following section will describe the major analytical methods and the limitations of each method. However, since every fraction of the organic matter in the geosphere has its own analytical problems and limitations, some of the more specific analytical problems will be discussed separately in the suitable sections.

Elemental analysis is the main method for the identification and quantification of sulfur in all fractions of organic matter. As will be discussed later this method has special importance in the analysis of solid samples (kerogens and coal), since the atomic S/C ratio is a tool for a rough estimation of the thermal behavior of these materials.

Separation techniques include several-column chromatography and TLC procedures which were developed for crude fractional separations. Most of these methods are conventional in organic chemistry except for some experimental differences and points of emphasis[7] and therefore will not be described here in detail. Ligand exchange chromatography (LEC) is quite useful for separation between different functional groups (i.e. sulfides, thiophenes and hydrocarbons) due to differences in formation constants of the complexes between the different compounds being separated and the metal ions impregnated in the stationary phase[12,13]. Silver ion (as $AgNO_3$) is most widely used[9,14,15], but other metal cations have also been examined and compared[13]. This method was recently used for the separation of apolar sulfur-containing oligomers[15].

Reversible chemical derivatization methods are also used to enhance polarity of a specific sulfur functional group. Selective separation of sulfides (or thiophenes) by their initial oxidation to the corresponding sulfoxides followed by chromatography and then reduction was successfully performed[15-17].

Temperature programmed gas chromatography is the main high-resolution separation technique in this research field[7]. The use of capillary columns is compulsory, however since only very small quantities of material can be analyzed, quantitative GC isolation of single compounds is almost impossible. Dual selective detectors for organic carbon (Flame Ionization Detector—FID) and for sulfur (Flame Photoionization Detector—FPD) are usually used to obtain general information about the composition of the analyzed sample and its sulfur compounds distribution. (An example is given in Figure 2.)

GC techniques limit the scope of compounds which are amenable for analysis only to the relatively low molecular weight and low boiling point compounds. This limitation is valid for all types of chemicals found in bitumens and mature crude oils, and has an effect on every research work and publication in the field. However, with sulfur compounds it is more important because around 40% of all sulfur compounds in crude oils (and in some cases much more)[1] have high molecular weight and are not GC amenable. In addition, because this heavy fraction has higher sulfur content than the lighter fractions this limitation is even more severe.

Thermal stability is another limitation that must be considered in the analysis of sulfur

compounds. For the analysis of mature crude oils GC techniques are most suitable because the majority of the compounds are formed by pyrolytic catagenetic processes and are therefore stable enough under GC conditions.

When immature samples are analyzed, the problem of low thermal stability of sulfur compounds becomes more severe because most of the compounds have been formed under mild conditions and have never been exposed to high thermal stress. This point is often neglected and never thoroughly examined. The experience of the writer with sulfur-containing synthetic model compounds formed at mild temperatures shows them to be thermally labile, and many of them were partly or even completely decomposed in the course of GC analysis under conditions identical with those used for natural sample studies. Recently this limitation has been demonstrated in GC analysis of an immature bitumen, rich with sulfide and polysulfide linkages[18]. High molecular weight compounds of this sample underwent thermal decomposition during heating of the capillary column, giving a wide unseparable peak termed by the authors 'S-rich hump'.

The upper-limit molecular weight for GC analysis was somewhat raised in the last few years when new GC capillary columns with stationary phases of high thermal stability were introduced[19]. These new columns enabled the final temperature of GC analysis to be raised to 450 °C, and the highest molecular weight (for hydrocarbons) which can be analyzed to about 800 daltons. This development enabled the identification of new dialkylthiophenes[20], but at the same time the problem of thermal instability had increased. It seems that this new technique is suitable only for thermally stable aromatic sulfur compounds.

High performance liquid chromatography (HPLC) has been also used[21], but not widely.

For identification methods, a computerized mass spectrometer coupled to a gas chromatograph is the most important analytical tool for the establishment of tentative structures. High-resolution MS often replaces elemental analysis and confirms the identification and existence of sulfur atom(s) in the molecule or in a fragment ion. Computerized MS is also an important tool to identify homologous series. This is performed either by computerized 'filtering' of compounds that contain the desired fragment and presenting a selective chromatogram of these compounds (traces chromatogram), or by using the mass spectrometer as a selective detector for desired high-resolution mass (single ion reconstruction—SIR or single ion monitoring—SIM mass fragmentograph)[22].

Figure 3 presents an example for the use of a SIR-GC/MS fragmentograph for the identification of sulfur compounds. Figure 3a presents the FID response for the sulfide fraction of Bellshil Lake petroleum[22]. Figures 3b, c and d present the SIR fragmentographs of selected fragments with m/z 115.06, 101.04 and 87.03, respectively. The fragmentation pattern leading to the formation of the selected fragments, and the structures of the identified sulfides, are indicated.

The molecular weight limitation also applies to most MS instruments which are capable of analyzing molecules of only up to about 800 mass units[6].

Another limitation of mass spectroscopy is the difficulty to distinguish between isomeric structures, such as anthracene and phenanthrene, or their derivatives. However, the information collected in the last decade on the mass spectroscopy of organic sulfur compounds enables a fairly reliable identification of known compounds when analyzing new samples[7]. Because of the limitation on definitive isomer identification, the elucidation of the structure of many sulfur-containing compounds has to be supported by additional chemical methods.

Synthesis of authentic reference compounds is the best method for definitive identification. Some general procedures for most abundant homologous series were developed and have been reviewed[22,23]. Unambiguous identification is accepted when both mass-spectral fragmentations and GC retention times on several columns of the unknown compound and the reference are identical. The isolation of single compounds and their

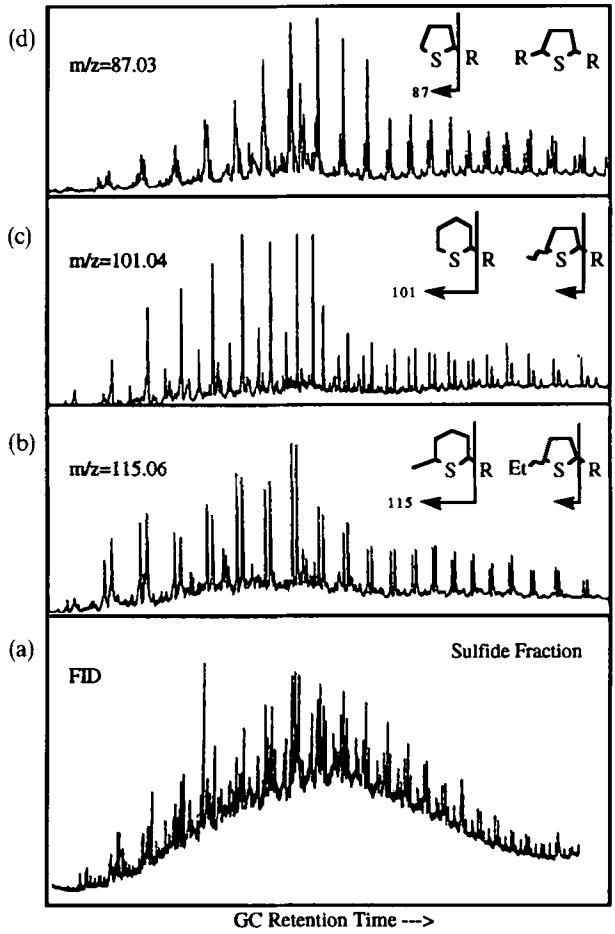


FIGURE 3. Gas chromatogram and SIR-GC/MS fragmentographs of the sulfidic fraction of Bellshil Lake petroleum[23]: (a) FID response; (b) *m/z* 115.06 ethylalkylthiolanes and methylalkylthianes; (c) *m/z* 101.04 methyl-alkylthiolanes and alkylthianes; (d) *m/z* 87.03 alkylthiolanes (and dialkylthiolanes). Reprinted with permission from *ACS Symposium Series*, Vol. 429. Copyright (1990) American Chemical Society

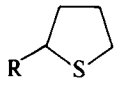
structure determination by spectroscopic techniques is not widely performed due to the complexity of the mixtures. The opinion of the writer is that, when thermal instability is suspected, such isolation is required.

In the last few years X-ray absorption techniques have been examined for the non-destructive identification and quantification of sulfur groups in oils and polymers. It has been found that X-ray absorption fine structure spectroscopy (EXAFS) and X-ray absorption near edge spectroscopy (mostly K-edge, but also L-edge) (XANES) are capable of determining the nature and structural forms of sulfur[24-31].

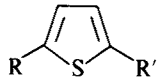
In K-edge XANES the energy scale—between the two extremes which are elemental sulfur and sodium sulfate—is 10 eV, from 2472.7 to 2482.6 eV[27], and the peak width is *ca* 1.5 eV. In this narrow range and in spite of the low resolution, a satisfactory quantitative resolution between different oxidation states of sulfur can be achieved. Therefore, quantitative analysis of sulfoxides in oxidized samples has been performed. With reduced sulfur groups, which are the main sulfur constituents in the geosphere, the situation is very problematic. The quantitative resolution between different model compounds is quite satisfactory even for closely related structures, if an appropriate statistical normalization and self-absorption corrections are performed. Oils and high molecular weight fractions are, however, very complex mixtures and, due to the low resolution, it appears to be impossible to distinguish between similar compounds. An effort is being made to use these methods to distinguish between sulfidic and thiophenic oils, in spite of the very small separation (*ca* 1 eV in K-edge XANES) and small structural differences between corresponding resonances. Waldo and coworkers[27,28] used this method to classify heavy high sulfur petroleums and asphaltenes into sulfidic, thiophenic and oxidized petroleums. The method is also used for coal[30,31] analysis in order to distinguish between organic and inorganic sulfur (pyrite, elemental sulfur and sulfates).

Chemical modification of the compounds is widely used to support MS identifications. Raney-Ni causes desulfurization by reductively cleaving C—S bonds and replacing the sulfur atoms by hydrogen atoms (equations 1–3).

$$R—S_x—R \xrightarrow{\text{Raney-Ni}} 2RH \tag{1}$$



$$\xrightarrow{\text{Raney-Ni}} RCH_2CH_2CH_2CH_3 \tag{2}$$

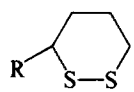


$$\xrightarrow{\text{Raney-Ni}} RCH_2CH_2CH_2CH_2R' \tag{3}$$

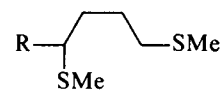
This method is used to determine the carbon skeleton of the analyzed compound by identifying the structure of the resulting hydrocarbon[20,21,32–34]. (For hydrocarbon analysis in complex mixtures, see Reference 19.) This method, when used on a whole sample or a whole fraction, provides the hydrocarbon 'fingerprint' of the oil[7,34], and it can be interpreted by conventional geological parameters[1]. Figure 4 shows an example of this method on the aliphatic sulfide fraction of Maruejols crude oil (France)[34]. This method is also being used as an analytical degradation method for high molecular weight compounds.

Kohnen and coworkers[18] developed recently a method, based on a reaction reported by Eliel and coworkers[35], to selectively transform di- or polysulfides into methyl sulfides by reaction with MeLi/MeI mixture (equations 4–6). This cleavage method was used mostly for high molecular weight compounds (see Section V.A).

$$R—S—S_x—S—R \xrightarrow{\text{MeLi/MeI}} 2RSMe \tag{4}$$



$$\xrightarrow{\text{MeLi/MeI}}$$



(5)

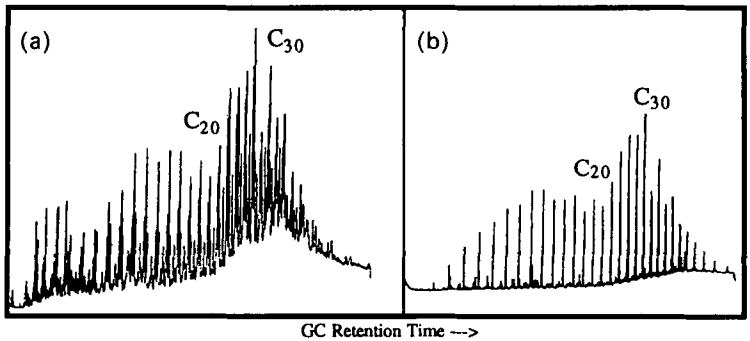
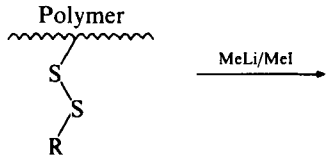


FIGURE 4. Gas chromatogram of the sulfide fraction of Maruejols crude oil (France)[34]: (a) FID response for the original fraction; (b) FID response for Raney- Ni desulfurization products. Reprinted with permission from *Nature*, **329**, 54. Copyright (1987) Macmillan Magazines Ltd



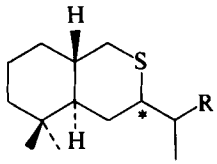
(6)

Monosulfides do not react, but thiols are methylated as well.

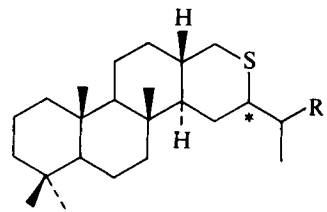
$LiAlH_4$ also cleaves di- or polysulfide linkages, forming two thiols. It was also used as a degradation method for high molecular weight fractions.

Additional information can be achieved by the oxidation of sulfides to sulfones or sulfoxides, which are chemically more active and have more characteristic spectroscopic features than the sulfides. The oxidized compounds are analyzed by IR, ^{13}C-NMR and ^{33}S-NMR spectroscopies (especially in coal extracts)[36]. However, these methods are rarely used due to their low resolution.

Deuterium labeling of hydrogens at an α position to a sulfoxide function was performed by Payzant and coworkers[32,37] to distinguish between possible isomers of compounds **1** and **2**. (For the meaning of the asterisk and for further discussion, see Section IV.E.)



$R = C_nH_{2n-1}$ ($n = 0$–14)
isoprenoid alkyl
(1)



$R = C_nH_{2n-1}$ ($n = 0$–17)
isoprenoid alkyl
(2)

Czogalla and Boberg[38] have reported the structures of a few hundred compounds in crude oils and proposed some rules for the identification of sulfur compounds. They regarded a structure as positively identified only if the compound was isolated (or isolated and oxidized to the corresponding sulfone) and compared with an authentic specimen, or if the structure was identified by Raney nickel desulfurization of an isolated compound, and the desulfurization product was compared to an authentic specimen or data from the literature. Structures suggested by comparison of data of isolated sulfur compounds with data from the literature or based on mass spectral data alone are regarded as 'probable or tentative'. It is important to note here that many of the high molecular weight structures which will be presented in the following sections belong to the latter category.

Some degradation techniques are used in the analysis of high molecular weight compounds, such as analytical pyrolysis and chemical degradation. These methods will be discussed in detail in Section V.A.

A very important analytical method involves measurement of stable isotope ratios. This is a method that can provide information on the chemical and physical 'history' of the compound rather than on its chemical structure. The most abundant stable isotopes of sulfur are ^{32}S and ^{34}S. Their average relative concentrations are 95.0% and 4.2%, respectively[39]. The exact ratio of isotopes can be altered during chemical and physical transformations as a result of kinetic and/or thermodynamic processes since the kinetic, rotational and vibrational energies of the molecules are mass-dependent[40]. The ratio change during such transformation is referred to as fractionation.

Isotope ratios are measured with specialized isotope ratio mass spectrometers, normalized to a standard. The standard used for sulfur isotopes is Canyon Diablo Meteoritic sulfur. The ratio is expressed according to equation 7, where the unit for $\delta\,^{34}S$ is per mil (‰).

$$\delta\,^{34}S = \left[\frac{(^{34}S/^{32}S)_{sample}}{(^{34}S/^{32}S)_{standard}} - 1\right]1000 \tag{7}$$

If the value of $\delta\,^{34}S$ is changed as a result of a chemical or physical transformation, the difference between the $\delta\,^{34}S$ value of the reactant and that of the product is referred to as isotopic discrimination[39]. The use of this method will be discussed in Sections VI and VIII.

III. SULFUR COMPOUNDS IN MATURE CRUDE OILS

Petroleum exploration is the driving force for most organic geochemical research, and therefore it is not surprising that, chronologically, the first sulfur-containing compounds in the geosphere were found in crude oils. Up to date most of the knowledge on organic sulfur compounds is derived from the analysis of thousands of samples collected all over the world in this century, mostly in the last four decades. The identification of several thousands of organic sulfur compounds was reported in the 1970s for most of the major oil fields in the 'noncommunist' world[1,41–43]. During the 1980s the information on oil fields in the former USSR was reviewed together with further information from the rest of the world[38,44,45].

A. Sulfur Content in Crude Oils

Crude oils are generally classified into two groups, based on the observation made by Tissot and Welte[1]. They based their observation on more than 9000 samples with an average sulfur content of 0.65% by weight. The distribution of the samples was found to be bimodal with a minimum at 1%. The two modes were therefore classified as 'low sulfur crude oils' for the mode containing less than 1% sulfur and 'high sulfur crude oils' for the

mode containing more than 1%. The majority of the samples belonged to the low sulfur crude oils, but this trend is strongly influenced by the fact that most of the samples were collected from explored and productive oil fields and does not reflect the actual distribution of worldwide reserves. Most of the world's known reserves are high sulfur oils and are probably as abundant, if not more, as low sulfur oils[1].

The content of sulfur in high sulfur oils varies from 1 to 14%[38,44]. Most of the sulfur is organically bound[6,41,44], but very minor amounts of elemental sulfur and dissolved hydrogen sulfide do exist in some crude oils[9].

The conditions in depositional environments, thermal history and mineral catalytic effects are probably the main factors controlling the content of sulfur in crude oils. Some fundamental correlations between sulfur content and reservoir environment were found and are well established, as described below.

Oils from carbonate deposits contain greater amounts of organic sulfur compounds than oils from clay-rich clastic deposits[1,44]. Although many of the clastic deposit oils are derived from nonmarine origins which are known to be sulfur-poor, oils from definite marine clastic deposits are still lower in sulfur relative to oils from carbonate deposits[1]. Several different explanations for this phenomenon were suggested. One explanation is that rapid formation of iron sulfides decreases the concentrations of reduced sulfur species available for organic reaction during the first stages of deposition. Clay muds contain higher amounts of iron relative to carbonate muds[1]. Another explanation is that clay minerals may possess catalytic desulfurization activity during the catagenetic processes[44].

Another correlation, which is not yet fully understood, is between the sulfur content and the relative amounts of nickel and vanadium in oils. Nickel highest-content values (*ca* 150 ppm) are found in low sulfur oils, while the highest vanadium amounts (up to about 1200 ppm) are found in high sulfur oils[1].

From the geochemical point of view one of the most important correlations is between the sulfur content and reservoir depth, namely with the oil's age and maturity. Statistical analysis of 2000 samples from different parts of the world[44] revealed that the sulfur content increases with depth until a maximum is reached at a depth of 1.5–2 km. With further depth increase the sulfur content is decreased. Rall and coworkers[43] also discuss this phenomenon, and reached a similar conclusion, but they also gave some examples contrary to this observation. This correlation is explained by the early diagenetic enrichment of the organic matter with sulfur, followed by catagenetic decomposition and desulfurization of sulfur-containing compounds during oil formation and maturaion. Desulfurization is accompanied by hydrogen sulfide evolution. This is supported by the higher hydrogen sulfide contents in natural gases at greater depth.

B. The Distribution of Sulfur Compounds in Crude Oils

The great majority of sulfur compounds identified in crude oils and in other geological organic sources contain divalent sulfur[1,6] (except for oxidized samples). The traditional classification of sulfur compounds was based on the distribution of the compounds between oil fractions, i.e. the compounds were classified by their boiling point.

Ho and coworkers[41] and others[44] classified the compounds by their chemical structure, and this classification will be used here. The quantification of each group of compounds is problematic, and estimations presented here must be regarded with caution. One major source of these problems is the large amounts of high molecular weight (MW) residues which are not amenable to the conventional analytical methods. It appears that this high MW residue contains a high percent of thiophenic condensed ring systems (see Sections III.F and V.B), and therefore any quantification of group-type analysis is biased.

C. Thiols

Thiols (mercaptans) comprise a minor component of sulfur compounds in crude oils. Thiol content in oils varies from zero to 0.12% weight in petroleum (or up to 7% weight of total sulfur compound content)[44].

Most of the identified thiols are aliphatic having low MW[1,42-44]. Figure 5 presents a few examples of identified thiols and their content in some specific oil fields. Secondary thiols are more abundant then tertiary and much more abundant than primary structures.

Aromatic thiols are less known. Rall and coworkers[43] reported the identification of 53 thiols in several oil fields but only one of them has been tentatively identified as benzenethiol (thiophenol).

High molecular weight thiols are most likely alkylthiophenols including polycyclic alkylthiophenols[44], but this assumption is not yet proven. Kaimai and Matsunaga[12] reported the possible occurrence of a group of alkylthiophenols which contain 10–15 carbon atoms in the side chain, but the complete structure was not established.

The relative abundances of thiols in sulfur compounds decrease with depth, and this is usually explained by their relatively low thermal stability[41-44]. an important observation that counters this general trend was noted by Ho and coworkers[41] and was also supported by Bolshakov[44], namely the occurrence of several mature oils which contain relatively high concentrations of thiols. This was explained by high-pressure and high-temperature reactions of hydrogen sulfide with reservoir oil (see further discussion in Section VIII.B).

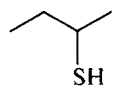
D. Sulfides

Sulfides are quantitatively high contributors to the sulfur content of many crude oils. Ho and coworkers found that the average content of aliphatic and alkylaryl sulfides reaches 45% in 78 crudes which they have investigated[41].

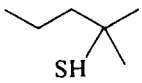
A variety of structures and molecular weights of sulfides are found in, and have been identified in, all the fractions of distilled oil. Figure 6 presents examples of sulfides according to common structural classifications.

MeSH
Methanethiol
2.40 (Wasson, Texas, USA)

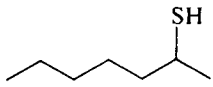
EtSH
Ethanethiol
5.30 (Wasson)



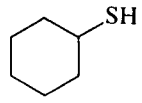
2-Butanethiol
3.86 (Wasson)



2-Methyl-2-pentanethiol
1.26 (Wasson)



2-Heptanethiol
1.048 mg/l Arabian



Cyclohexane thiol
1.20 (Wasson)

FIGURE 5. Examples of thiols found in petroleum and their content in the oil[44] (wt% × 10^3 unless otherwise indicated)

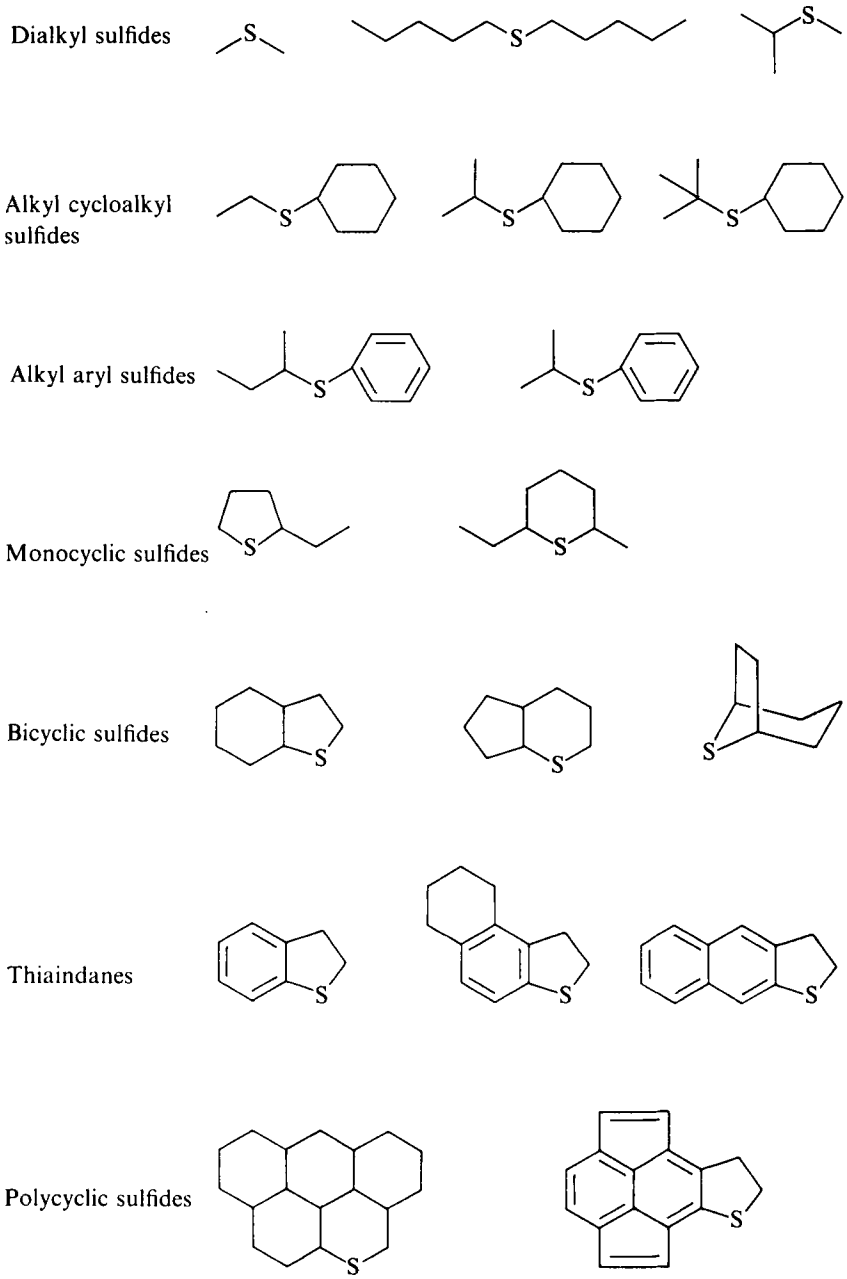


FIGURE 6. Examples of sulfides found in petroleum

Simple alkyl sulfides are more abundant in low molecular weight fractions of oils. These compounds are usually more abundant in oils that contain high concentrations of acyclic hydrocarbons[44].

In many oils, alkylated five-membered (thiolanes) and six-membered (thianes) sulfur-containing heterocycles constitute a major part of the sulfides. As a general rule the alkyl substituents are positioned α to the sulfur atom (i.e. 2,5-dialkylthiolanes and 2,6-dialkylthianes)[44,45]. They are usually relatively short normal or isoprenoidic alkyl groups which usually contain no more than ten carbon atoms[45].

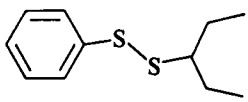
Many of the sulfur-containing condensed polycyclic hydrocarbons in high boiling fractions contain both aromatic and aliphatic structures, and as the number of condensed rings become more dominant[44], although their concentration in the whole bulk of sulfur compounds decreases as the number of fused rings increases.

As a rule, in most of the polycyclic compounds, the sulfur atom is located in a terminal ring. It is also noteworthy that in most of the bicyclic and higher structures the sulfur atom is at an α position to the next ring. This may indicate that these compounds are formed by cyclization of alkyl side chains of alkylated monocyclic compounds[44] (see Section VIII.E).

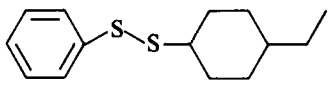
Many of the sulfur-containing condensed polycyclic hydrocarbons in high boiling fractions contain both aromatic and aliphatic structures, and as the number of condensed rings increases the number of aromatic rings and structures also increases[38,44]. Thiaindanes and thiatetralins are the lowest MW examples of such aromatic – cycloalkanic sulfur-containing compounds. They usually occur in fractions boiling above 230 °C, at concentration which usually do not exceed 10% of the total amount of the sulfides[44].

E. Disulfides

Disulfides belong to a very small group of sulfur compounds which have been identified in crude oils. During the period 1948–1966 the American Petroleum Institute (API) carried out a project (named project 48)[42,43] in which very thorough investigations were performed on several oil fields. In this project only three disulfides were tentatively identified: dimethyl disulfide, methyl ethyl disulfide and diethyl disulfide. More recently Nishioka[13] used ligand exchange chromatography (LEC) techniques to separate aromatic sulfur compounds other than condensed thiophenes from the Wilmington crude oil (1.28% sulfur[43]) and found 13 new aromatic disulfides according to MS determination alone. The most abundant were pentyl phenyl disulfide and C2-cyclohexyl phenyl disulfide **3** and **4** or their isomers.



(3)
40 mg/l



(4)
10 mg/l

F. Thiophene Derivatives

Thiols, sulfides and disulfides represent only a minor fraction of the total sulfur content of oils. The remaining sulfur is concentrated in the high molecular weight residual material. As previously mentioned, most of this sulfur is not amenable for direct analysis, so that the measurements of concentrations of other sulfur compounds becomes considerably less reliable. Some indirect analytical methods for the evaluation of sulfur functional-

TABLE 1. Distribution of sulfur compounds found in 78 crudes from worldwide selection of oil fields[41]

	Mean ± SD (%)	% Variation	No. of samples
Total sulfur	1.64 ± 1.97	119.8	78
Aliphatic sulfides	18.9 ± 9.2	48.7	25
Alkyl aryl sulfides and thiaindanes	25.8 ± 9.7	37.7	24
Thiophenes	3.3 ± 1.8	55.4	43
Benzothiophenes	5.8 ± 3.4	59.3	78
Dibenzothiophenes	9.0 ± 4.6	50.7	78
Benzonaphtothiophenes	5.9 ± 2.3	39.4	26
Sulfur not recovered	42.8 ± 13.6	31.7	78

ities in high MW substances, such as pyrolysis and X-ray absorption methods (see Section V.B), suggest that considerable amounts of the sulfur in these fractions are in thiophene derivatives[24-31].

Nevertheless, relatively light aromatic sulfur heterocycles are a major component of oils. Ho and coworkers[41] estimated the concentration of thiophenes and condensed thiophenes up to benzonaphtothiophenes to be between 12 and 36% of the total weight of sulfur compounds (see Table 1).

The parent thiophene is relatively rare, and in some instances is completely missing[43]. Alkylthiophenes are much more abundant than thiophene, but are still minor components in comparison with the condensed aromatic compounds. As with thiolanes, a distinguish-

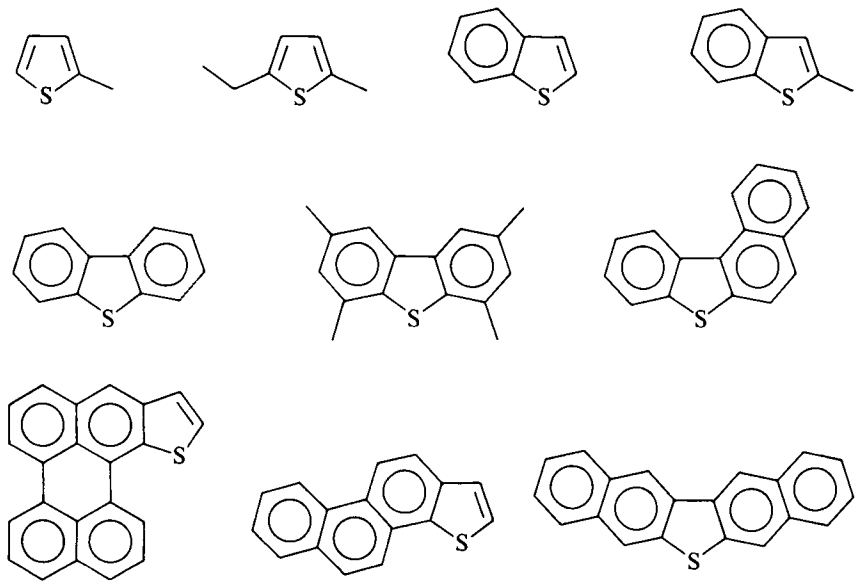


FIGURE 7. Examples of thiophenes and condensed thiophenes found in petroleum

able substitution pattern in the positions of the alkyl substituents is observed[44]. Monoalkylthiophenes are predominantly 2-alkylated in spite of the higher thermal stability of 3-alkylthiophenes. Dialkylthiophenes are usually 2, 5-disubstituted. In mature crude oils, the alkyl chains are usually short (C_1—C_3), and if one of the alkyl groups is longer the other one or two substituents are methyl groups[44].

Benzothiophenes and dibenzothiophenes have the widest distribution in crude oils. According to Ho and coworkers[41] Table 1 shows the concentration of the main groups of sulfur compounds, and these two groups are the only ones which have been found in all 78 major oil fields in the world, as indicated in the third column. As discussed above, the structures are not statistically distributed, and benzo- and dibenzothiophenes are no exception. The benzothiophenes are [*b*] fused as in 2-methylbenzo[*b*]thiophene. The rings of dibenzothiophenes (and higher homologs) are [*bd*] fused as in dibenzo[*bd*] thiophene. This phenomenon can be ascribed to the relative instability of benzo[*c*]thiophenes[44].

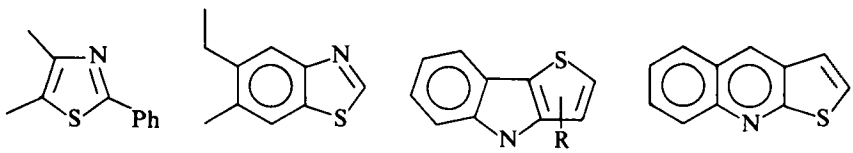
Substituent alkyl groups are usually attached to positions 2 and/or 4 of benzothiophenes, but the situation is less clear-cut than with lower heterocycles and many examples of alkyl- and polyalkyl-substituted benzothiophenes at any of the six possible positions are found[38]. (As will be discussed later, this phenomenon is much clearer in immature samples.)

As the number of condensed rings increases, the distribution of the isomers becomes more statistical, although detailed structural parameters have been poorly studied.

Examples of different thiophene-containing structures are presented in Figure 7.

G. Sulfur Compounds Containing Other Heteroatoms in Crude Oils

Nitrogen content in crude oils is usually much lower than that of sulfur; about 90% of the oils contain less than 0.2% of nitrogen[1]. Compounds containing both sulfur and nitrogen are found in numerous oils in low concentrations. Aromatic systems which contain both atoms in the same ring or in different rings have been identified[44]. Examples are:



Whereas structures containing only oxygen and sulfur are very rare in oils. Compounds of high molecular weight, in many crude oils, usually contain nitrogen and oxygen in addition to sulfur. These are referred to as high molecular weight NSO compounds[1]. Tissot and Welte attribute this observation to the high probability that two different heteroatoms will occur in a molecule with a mass above 700 daltons. These compounds are the major constituents of asphaltenes and resins and considered as the heavy ends of petroleum[1].

The functionality of the sulfur atoms in high molecular weight compounds and in solid polymers will be considered separately.

H. The Use of Structural Parameters for Geological Information

The need to gain geochemical information concerning the formation, origin and history of crude oils drove petrologists and organic geochemists to seek such information in the chemical structures and in the distribution of compounds in oils. The main parameters

which are being studied are thermal maturity of organic matter and correlation parameters such as oil – oil correlation and oil – source rock correlation.

Many structural parameters of hydrocarbons have been defined in order to determine the above factors. Most of these parameters are based on ratios between related structures, e.g. *n*-alkanes and isoprenoid chain length, naphthene ring numbers and aromatic substituent positions[1,46]. Very common examples, such as even-to-odd alkane chain length ratios and the phytane-to-pristane ratio, are used to assess biogenic source and environmental conditions during deposition, and as correlation parameters[1].

The use of sulfur-containing molecules as geological markers in oils is much more limited. Although aromatic sulfur compounds have been used together with hydrocarbons for correlation assessments, the use of sulfur compounds *per se* for such purposes has only recently started to be studied in detail.

The most frequently investigated molecules in this respect are benzothiophenes, dibenzothiophenes and their methylated derivatives[47-50]. Ho and coworkers[41] were the first to suggest a correlation between specific structural differences of sulfur compounds and the maturity of crude oils. By their use of group-type analysis methods they classified the 78 crude oils investigated by them into three categories: immature, mature and altered crudes. Immature crudes were characterized by higher amounts of nonthiophenic sulfides, which are relatively thermally unstable. (It should be noted that the term 'immature' used here is a relative term; there are other crudes which will be discussed later and which are even less mature.) Mature oils were characterized by higher abundance of more stable heteroaromatic compounds such as dibenzothiophenes. Oils with intermediate distributions were classified as altered crudes. They noticed that the benzothiophene-to-dibenzothiophene ratio (BDR) is quite different for the three classes of oils. BDR was found to be greater than 1.0 for immature, lower than 0.5 for mature and intermediate for altered crudes. On this basis several other ratio parameters have been suggested. The relative abundance of dibenzothiophene (DBT) and methyldibenzothiophene (MDBT) was found to vary with depth, Decrease in the ratio of 4-MDBT to DBT was the most noticeable in a basin containing type-III kerogen[47] (see Section V.A for kerogen-type definitions). Other related parameters were suggested[46,48,49], but the evaluation of maturity by these parameters must be carried out with caution since the effect of the type of the organic matter is substantial and not yet fully understood[48].

Some suggestions to use structural parameters of MDBT for source rock type evaluations (i.e. carbonate vs clastic) were published[47,50], but these also are not fully accepted and understood.

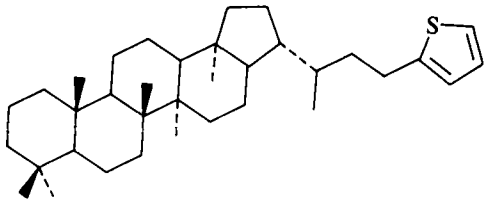
IV. SULFUR COMPOUNDS IN IMMATURE SEDIMENTS AND CRUDE OILS: BIOGENIC RELATED COMPOUNDS

During the last decade, as a result of improved analytical methods, a drastic and fundamental development changed and expanded our view and knowledge on organically bound sulfur in the geosphere. This change was even defined as a new era in the geochemistry of organic sulfur compounds. As described in the previous sections, the structures of the majority of compounds which have been identified in mature crude oils are noninformative as to their origin. This leads to great uncertainty concerning the first steps of inorganic sulfur incorporation into sedimentary organic matter. In the early 1980s several new sulfur compounds, with much more complicated structures than were known previously, were identified in immature bitumens. These compounds have carbon skeletons, which are distinctively related to a biogenic source, and in some cases a specific compound (or at least a series of compounds) of biological origin can be suggested as precursors.

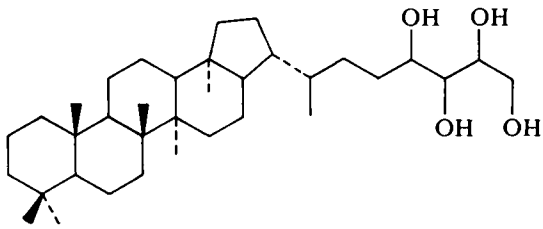
The first two homologous series were identified in 1983 in the Northern Alberta

(Canada) bitumens[32,37,51]. These are the bicyclic and tetracyclic isoprenoid sulfides **1** and **2** and their corresponding sulfoxides. No biogenic precursors were suggested for these compounds.

In 1984 a C_{35} hopanoid containing a thiophene ring (**5**) was identified in low-maturity organic-rich sediments[52]. Its structure has a very distinctive resemblance to the bacteriohopane tetrol **6**, which is a widespread membrane constituent of prokaryotes. Consequently **6** was suggested by the authors as the biochemical precursor of the substituted thiophene **5**[52].



(5)



(6)

These two discoveries were the starting point of a 'boom' of research and identifications of new compounds and novel homologous series. This enormous contribution was mainly a result of the work of three research groups: The Delft University of Technology group, The Netherlands (J.W. de Leeuw), the University of Alberta group, Canada (O.P. Strausz) and the Louis Pasteur University group, France (P. Albrecht).

The main achievements of this research effort during the 1980s were reviewed and interpreted in 1990[6,7].

A. Classification

Almost all divalent sulfur functionalities discussed in Sections III.A–G have also been identified in immature organic matter. As previously mentioned, these functionalities are incorporated into the carbon skeleton of biomarkers. Therefore, it is more informative to classify the compounds by their carbon skeleton rather than by the sulfur functionality. The most abundant sulfur groups are cyclic sulfides (thiolanes, thianes), cyclic di- and trisulfides (1,2-dithianes, 1,2,3-trithiepanes), thiophenes (and di- or trithiophenes) and benzo[*b*]thiophenes. In some instances sulfoxides (probably formed by oxidation of the corresponding sulfides in nature or during handling and storage) have also been identified. Thiols, acyclic sulfides and acyclic polysulfides were not identified unambiguously. However, the later series necessarily contains high molecular weight compounds, and there are good indications as to their existence in polar fractions, to be discussed in Section V.B. In the following sections a summary of all major groups of sulfur-containing

biomarkers identified to date is given. The main structural characteristics are emphasized and the principal references to detailed information indicated. More detailed structural and bibliographic data can be found in Reference 7. Di- and trisulfides are discussed separately, since their occurrence has special implications as to the origin of organic sulfur (see Section IV.I).

B. Normal Chain Carbon Skeletons[14,22,34,37,52,63]

Di-*n*-alkyl sulfur heterocycles are very common in immature sediments, bitumens and oils[22,34,54,55]. Usually they are found as homologous series, and in a wide variety of structural isomers. The heterocyclic ring can be located in every possible position along the chain. Nonterminal saturated heterocycles appear as *cis* and *trans* isomers, and therefore increase the complexity of the chromatogram (see Figures 3 and 4). One common characteristic for all structures is that the alkyl substituents are always positioned α to the sulfur as in 2, 5-dialkylthiolanes, 2, 5-dialkylthiophenes or 2, 6-dialkylthianes and as 2, 4-dialkylbenzo[*b*]thiophenes. Obviously, this is the reason why these compounds are classified under the category of normal chain carbon skeletons. Examples of most of the compounds have been identified by synthesis of authentic samples. The main homologous series (**7–11**) are presented in Figure 8.

Recently a related class of compounds has been identified—'mid-chain' 3, 4-dialkylthiophenes (structure **12** in Figure 8)[9,20]. The hydrocarbon skeleton of these compounds is a 1, 2-dimethylalkane of 34 to 52 carbon atoms and has a high even-to-odd carbon number ratio.

Another related subclass includes thiophenes with methylalkane carbon skeleton. Three

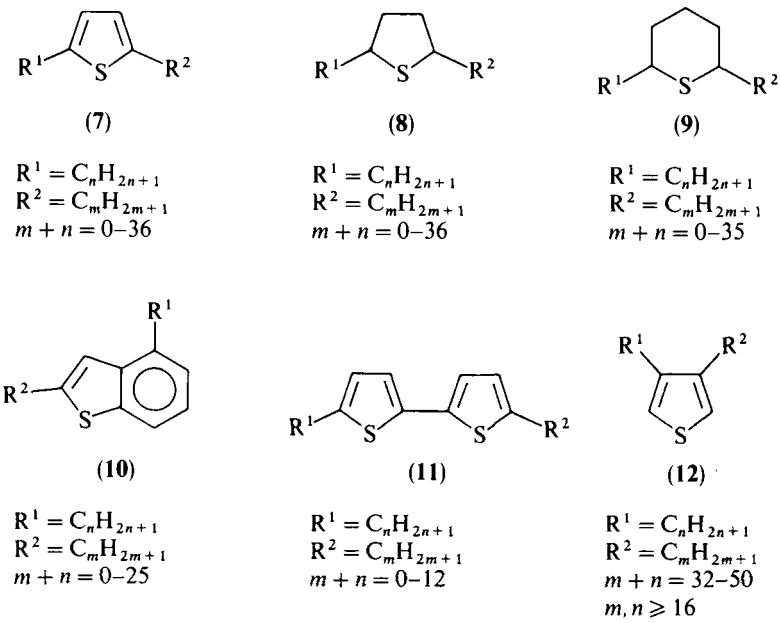
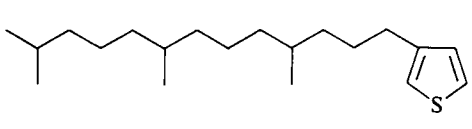


FIGURE 8. Sulfur heterocycles with linear carbon skeleton (or substituted with linear alkyl chains—**12**) identified in bitumens



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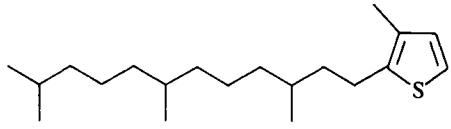

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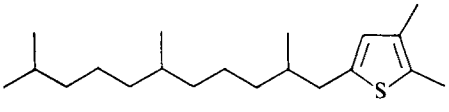

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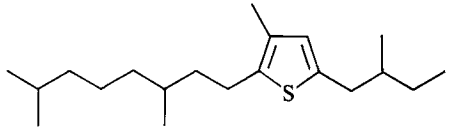

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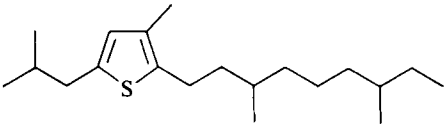

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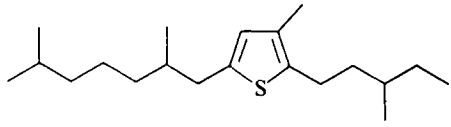

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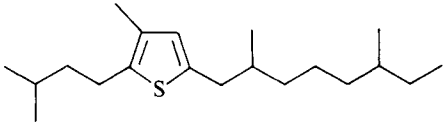

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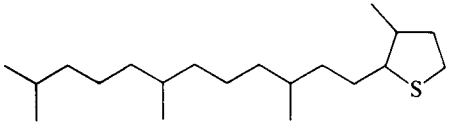

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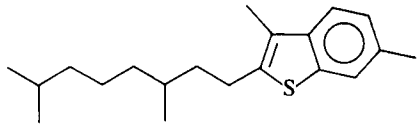

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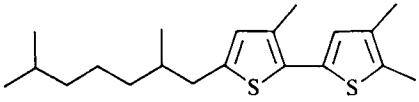

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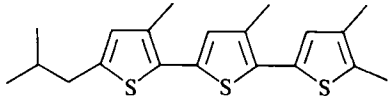


(23)

FIGURE 9. Sulfur heterocycles with isoprenoid carbon skeleton identified in bitumens

thiophene isomers with 9-methyloctadecane skeleton (and minor amounts of 2- or 3-methyl isomers) have been identified[56].

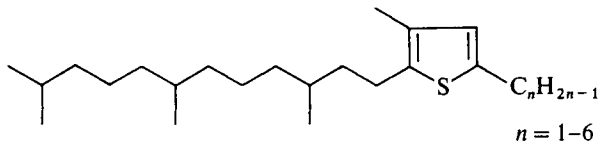
C. Acyclic Isoprenoid Carbon Skeletons[9,14,53,55,57–59]

Sulfur heterocycles with acyclic isoprenoid carbon skeleton are as widely occurring and as extensively studied as the linear carbon skeleton compounds. Compounds with 20 carbon atoms (C_{20}-isoprenoids) are most abundant and will therefore be considered separately. The most common heterocycles in this group are C_{20}-isoprenoid thiophenes. Of the many possible isomers, only seven have been found and identified (structures **13–19** in Figure 9). Two of them, i.e. **13** and **14**, are much more abundant than the others. The high distribution and specific location of the heterocyclic group in the molecule have been explained by the suggestion that the biochemical precursor of these two compounds (and possibly of **15** as well) is phytol, which is an omnipresent constituent of chlorophyll.

C_{20}-isoprenoid heterocyclic compounds other than monothiophenes are much less abundant, but have a wide variety of structures, i.e. thiolanes (**20**), benzothiophenes (**21**), bi- and trithiophenes[60] (**22, 23**) and cyclic di- and trisulfides. C_{20}-isoprenoid thianes have not yet been found.

A large variety of regular and irregular isoprenoid thiophenes with 15 to 40 carbon atoms have also been found. As with linear sulfur compounds all the isoprenoid heterocycles are substituted at the α position to the sulfur atom by at least one substituent. According to the isoprenoid rule, and depending on the position of the heterocyclic ring, an additional methyl group may also substitute non-α hydrogens.

A small subclass of compounds related to the last two major classes is a group of thiophenes having combined isoprenoid and short *n*-alkyl carbon skeleton. This subgroup contains two types of compounds with structures **24** and **25**[61].



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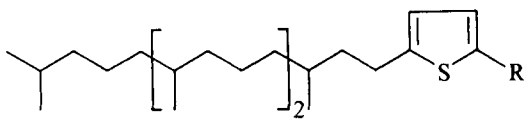


(25) R = H, Me, Et, *n*-Pr, *n*-Bu

The former is a C_{20}-isoprenoid thiophene substituted by an alkyl group from methyl to hexyl. The latter may be regarded as a thiophene substituted by a 2-C_{20}-isoprenoid and a short 5-alkyl group or a hydrogen.

D. Acyclic Highly-branched Isoprenoid Carbon Skeletons[14,21,59,62]

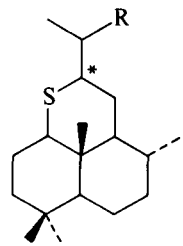
Three groups of sulfur-containing heterocycles with somewhat unusual carbon skeletons have been found to be quite abundant and in some cases they are even a dominant

component of the 'aromatic-thiophenic' fractions in bitumens from several locations. Figure 10 shows the three hydrocarbon skeletons and Figure 11 shows examples of sulfur heterocycles incorporating these structures. These heterocycles contain thiophene, thiolane, 1-oxothiolane and probably benzo[*b*]thiophene. Some of these compounds also contain 1–4 double bonds in the alkyl chains, which is a rare phenomenon in sulfur-containing hydrocarbons. Thiolanes and double bonds appear in relatively young sediments while thiophenes and benzothiophenes appear in relatively more mature samples (see Section VIII.C and E). The occurrence of the C_{20} group is more limited than the C_{25} and C_{30} groups.

Saturated and unsaturated hydrocarbons with the same skeleton have been found to be dominant in the hydrocarbon fraction of several immature sediments. The biogenic source of these structures is unknown since their occurrence in living organisms is quite limited[62].

E. Cyclic Terpenoid Carbon Skeletons[32,37,61]

As previously mentioned, the first sulfur compounds of the 'new era' in the organic geochemistry of sulfur that have been reported are cyclic terpenoid sulfides. Three subgroups have been identified: **1**, **2** and the tentative structure **26**.



(26)

$R = C_nH_{2n-1}$ isoprenoid alkyl ($n = 0$–14)

All three structures contain a thiane ring condensed with the aliphatic cyclic system. The sulfur atom is attached to the second carbon atom of the alkyl chain of the carbon skeleton (marked by an asterisk in the structure schemes). The sulfoxides of **1** and **2** have also been identified. All these compounds have been found only in Alberta crude oils except for **1** ($n = 0$), which was recently identified in a bitumen sample from Israel[63].

F. Steroid Carbon Skeleton[21,53,54]

Most of the sulfur heterocycles which are incorporated into a steroid skeleton have been investigated in the Rozel Point (Utah) seep oil (13.95% S)[43] by Schmid[54] and Sinninghe Damsté and their coworkers[21,53], although some of them had been found elsewhere too. As shown in Figure 12, both thiophenes and thiolanes have been identified. Two main groups can be noticed: thiophenes thiolanes (**27**, **30**) with a steroid side chain, and condensed ring thiophenes/thiolanes (**28**,**31**); a combination of the two is also known (**29**). Several stereoisomers and derivatives with additional alkyl substituents have been found.

One exception to these two groups is structure **32**, which has been tentatively identified in pyrolysis products[64].

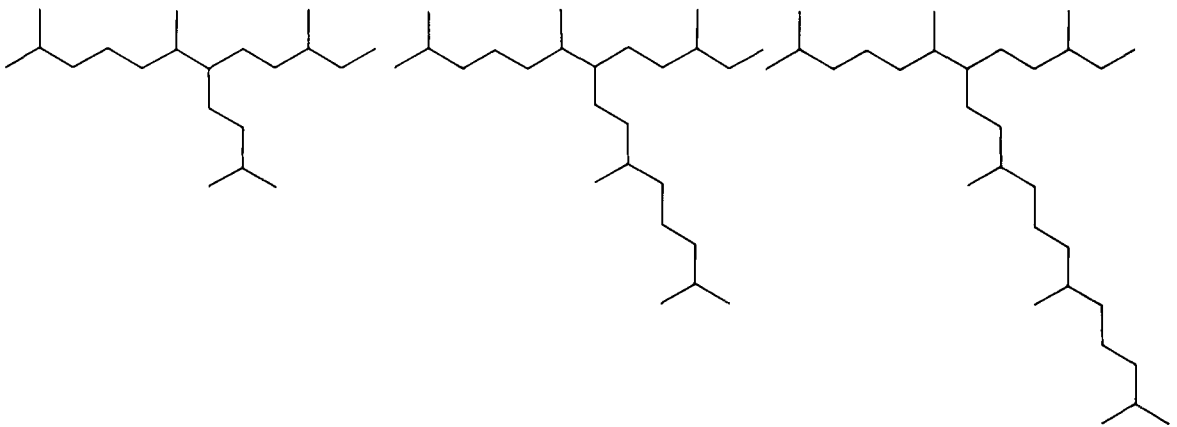


FIGURE 10. Carbon skeletons of 'highly branched' isoprenoid sulfur compounds which have been identified in bitumens

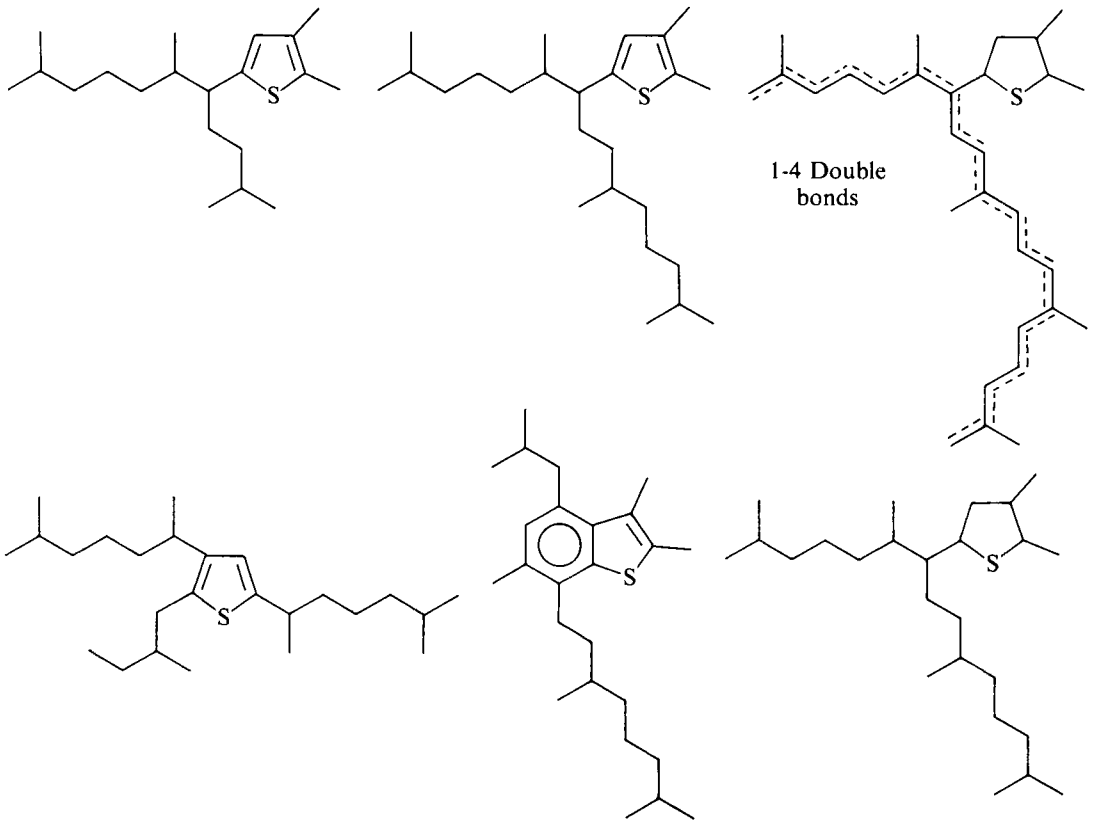


FIGURE 11. Examples of 'highly branched' isoprenoids sulfur compounds which have been identified in bitumens

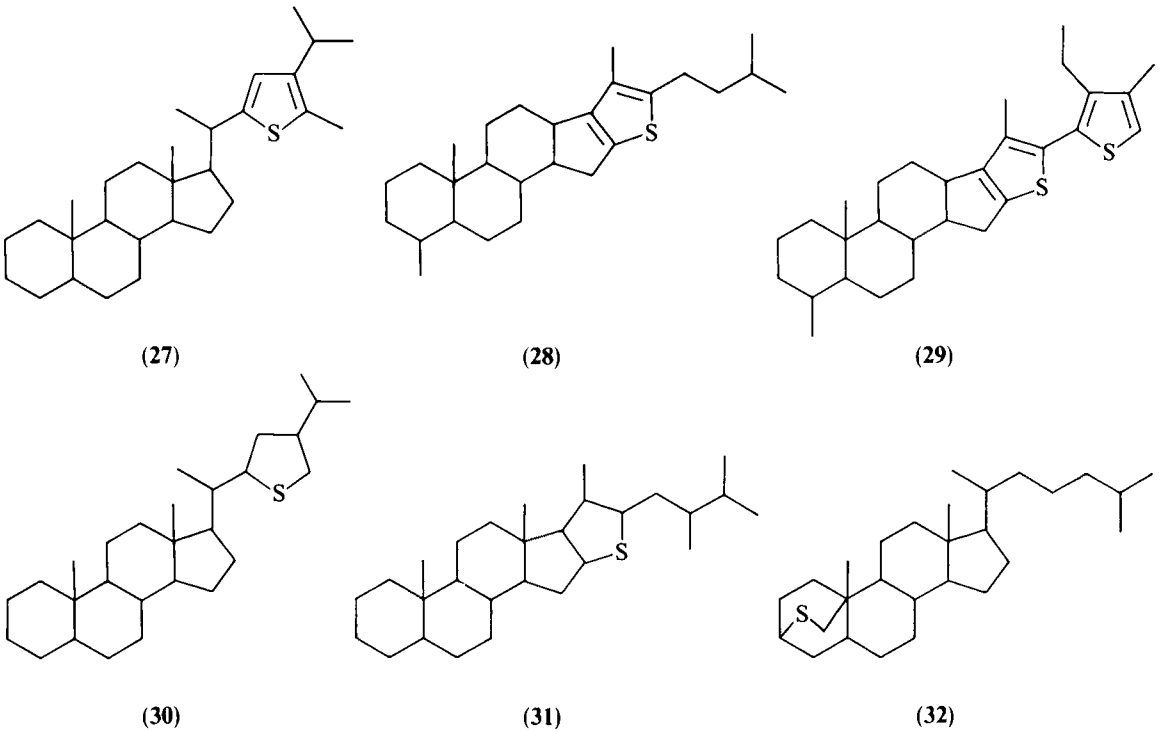


FIGURE 12. Examples of steroidic structures containing thiophene or thiolane rings which have been identified in bitumens

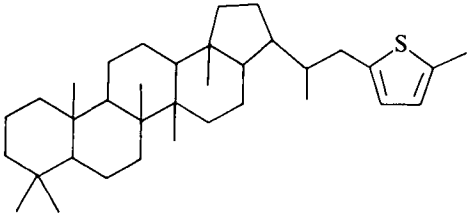
G. Hopanoid Carbon Skeletons[9,14,52,59]

The thiophene hopanoid **5** was one of the first biogenic related compounds reported and one of the first manifestations of the early incorporation of sulfur in organic matter. Other structurally related isomers of this thiophene were identified later (e.g. **33** in Figure 13). Most of the compounds are substituted by alkylthiophene as a side chain. Hopanoid sulfides have been found with a higher variety of structures, i.e. side-chain thiolanes (**34**), condensed thiolanes (**35**) and condensed thianes (**36**). Most of the hopanoid heterocycles contain 35 carbon atoms, but others such as the 3-methyl derivative of **5** and C_{30}—C_{35} series of **35** and **36** (substituted by short alkyl chains at the α position to the sulfur) have been also found.

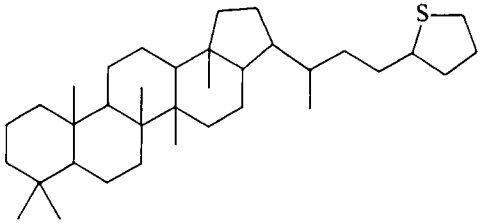
H. Triterpenoid Carbon Skeletons

Recently Adam and coworkers[65a] identified a novel type of organic sulfur compound. This is the triterpene **37** with the hitherto unknown feature of sulfur incorporation in positions 12 and 19 as a thiophene moiety.

The authors indicate the striking similarity of **37** to the high-plant triterpenoids of the Oleane series (e.g. **38**). This is therefore the first example of a distinctive high-plant derived precursor for an organic sulfur-containing compound. It is also noteworthy to mention the



(33)



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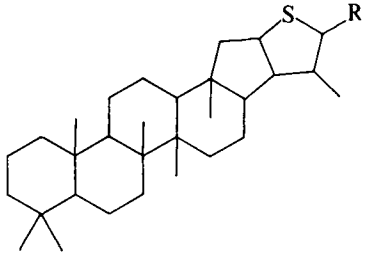
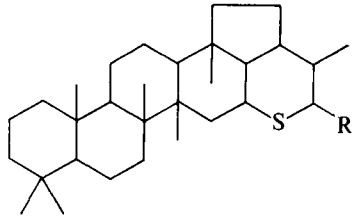


R = H, Me-Bu

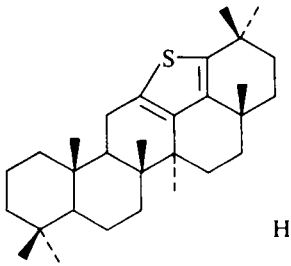
(35)



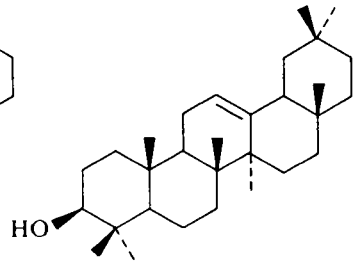
R = H, Me-Bu

(36)

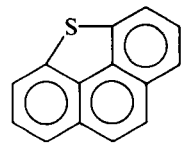
FIGURE 13. Examples of hopanoid structures containing thiophene, thiolane or thiane rings which have been identified in bitumens



(37)



(38)



(39)

resemblance between a substructure of **37** and the highly aromatic structure **39**, which is very common in coal[65b]—the geopolymer derived from high-plant organic matter[1].

I. DI- and Trisulfide Heterocyclic Compounds

Limited in distribution, but nevertheless geologically very important, are compounds containing di- or trisulfide heterocycles. Kohnen and coworkers have identified linear (**40**) and isoprenoid disulfides (**41** and **42**) and trisulfide (**43**) and hopanoid disulfide (**44**) in immature sediments in the Northern Appenines[66,67] (Figure 14). Disulfide steroids such as **45** have been tentatively identified in Rozel Point seep oil[54].

The detection of these compounds is considered as the first evidence at the molecular level for the incorporation of polysulfide anions into organic matter (see Sections VI and VII).

V. SULFUR IN HIGH MOLECULAR WEIGHT COMPOUNDS AND IN POLYMERS

As already discussed, due to analytical limitations most of the analytical work done so far was limited to low molecular weight compounds. Consequently, the study and understanding of the chemical structures of high molecular weight compounds in the geosphere is one of the most challenging goals of organic geochemistry.

As mentioned above, the definition of high molecular weight fractions is practically—rather than chemically—oriented. Three types of macromolecular fractions are usually considered[1,2,68]:

(a) Kerogen (and coal), including organic matter which is insoluble in common organic solvents.

(b) Asphaltenes, including organic matter which is soluble in polar organic solvents and insoluble in light hydrocarbon solvents.

(c) Resins, including organic matter which is soluble in organic solvents but is not amenable for GC analysis.

The solubility definitions reflect molecular weight differences, since kerogen is a geopolymer while asphaltenes and resins are smaller fragments with a chemical structure related to kerogen[1,6] from the same origin. The operational term—kerogen—is, however, a generalization covering a large variety of structures and compositions. Kerogen structures must reflect the history of the organic matter, i.e. its origin, depositional environments, preservation conditions, thermal alteration and other changes[1].

The term asphaltenes is also general; immature asphaltenes from bitumens are indeed structurally related to the soluble fractions (maltenes) and to kerogen. However, in mature oils where the composition in reservoirs changes due to migration, water washing or

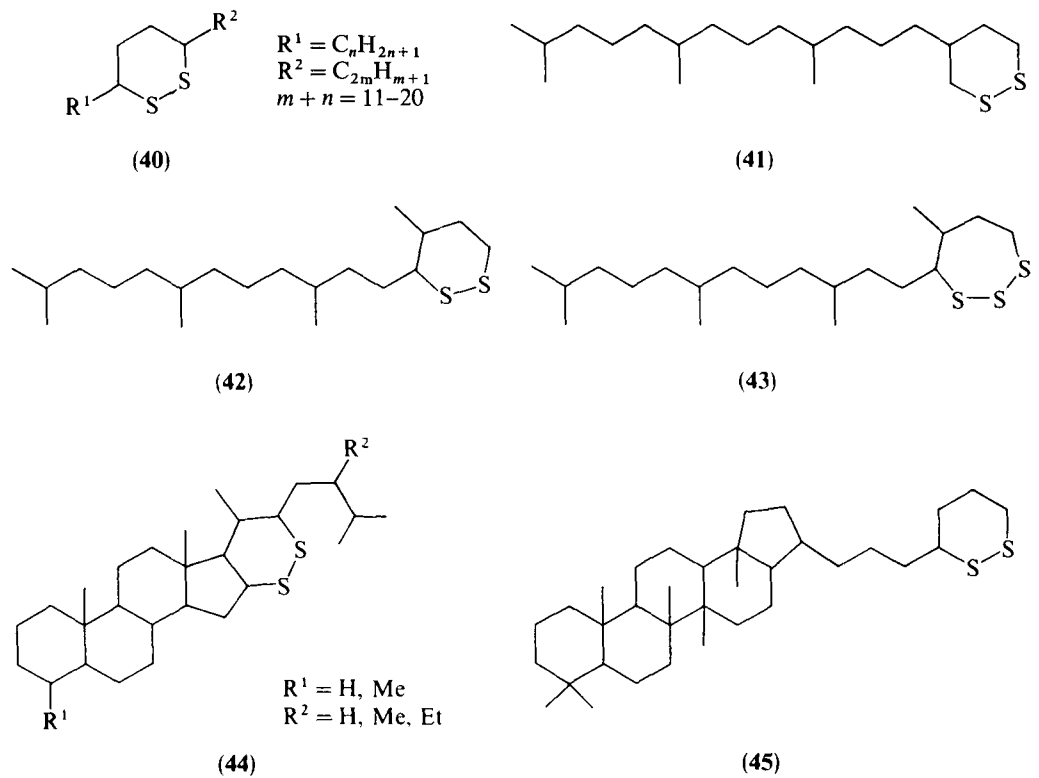


FIGURE 14. Cyclic disulfides (1,2-dithianes) and trisulfides (1,2,3-trithiepanes) which have been identified in bitumens

biodegradation, insoluble materials are formed and, by the above definition, they are also called asphaltenes, although structural relation to other fractions cannot be assumed.

In immature sediments, kerogen consists of more than 90% of the total organic matter[1,7]. The remaining extractable matter is defined as bitumen. Hence, our knowledge on the structures of sulfur compounds is limited only to a minor part of the organic matter in the geosphere.

Sulfur content in kerogen is similar to that in oils, and reaches up to 14% by weight in high sulfur kerogens[6].

A. Analytical Methods

Several general approaches have been developed for the elucidation of the chemical structure of macromolecules in geochemistry. Only those methods which have been used in order to assign the structure of sulfur moieties in macromolecules will be considered in the following sections.

(a) *Elemental analysis.* The most fundamental analytical method is elemental analysis and it is used extensively. Two of the parameters that can be derived from the elemental analysis, i.e. the H/C and O/C atomic ratios, are most useful in the classification of kerogens based on the plot first used by van Krevelen in 1961 for coals[1,69]. In this plot (the 'van Krevelen diagram') the atomic H/C ratio is plotted versus the O/C ratio of kerogens or coals (Figure 15). When atomic ratios from different kerogens and from different

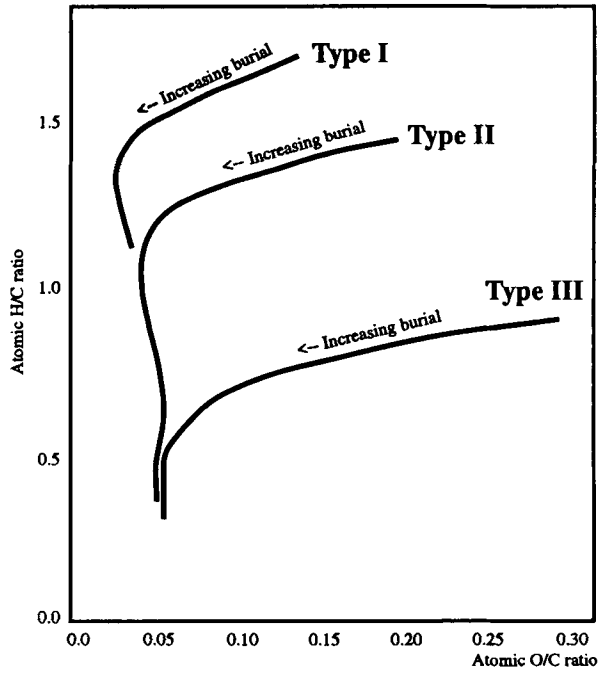


FIGURE 15. A schematic representation of the van Krevelen diagram

sources and depths are plotted on this diagram, they usually concentrate on three distinctive curves which are termed evolution paths[1]. These curves are taken to represent both the origin or the initial composition of a kerogen and its maturation level.

Kerogens of lacustrine algal origin are usually richer in aliphatic compounds, and therefore immature kerogens of this type have high H/C ratio and low O/C ratio, and are classified as Type-I kerogens. Type-III kerogens are usually derived from continental high plants having high concentrations of aromatic phenolic compounds. These kerogens have low H/C and high O/C ratios. Type-II kerogens are usually derived from marine phytoplankton, zooplankton and bacteria, and have intermediate H/C and O/C ratios. During maturation all three kerogen types condense, losing mostly water, carbon dioxide and methane, gradually decreasing in both H/C and O/C ratios while the kerogen approaches 100% carbon (graphite)[1]. This diagram can be used for rough evaluation of the type and quantities of the oil or gas that will be generated from an immature kerogen, and the degree of maturation required for this oil generation[1].

In sulfur-rich kerogens a new parameter, i.e. the S/C ratio, is used. Most of the sulfur high kerogens are classified by their H/C and O/C ratios as Type-II kerogens. However, as will be further discussed, due to the different thermal behavior of high sulfur kerogens they are defined as Type-II-S kerogens.

(b) *Spectroscopy.* It was mentioned above that IR and NMR spectroscopies find very limited use for the characterization of sulfur moieties in low molecular weight compounds and in polymers. The only spectroscopic methods that may prove useful are X-ray absorption methods, but even they are limited (*vide supra*).

(c) *Degradation techniques.* Since nondestructive methods fail to supply the necessary information for identification of sulfur functionalities, and elemental analysis can give only gross parameters, the main option left is to use degradation methods. Degradation is followed by analysis of the resulting fragments, from which the initial structure is reconstructed. Four kinds of information are needed for full structural reconstruction:

(i) Full analysis of the structure and the distribution of the fragmented structural units.

(ii) Quantification of the analyzed fragments in comparison to the initial macromolecule, i.e. how much of the macromolecule has decomposed and how much of the fragments were analyzed?

(iii) Definition of the structural similarities and differences between the fragments and the initial macromolecule. The questions here are: do the fragments represent the whole structure of the macromolecule and is their structure identical with subunits present in the macromolecule?

(iv) Establishment of the relations between the fragments, i.e. finding the connectivity of the fragments with each other within the macromolecules.

The following methods and techniques will be discussed according to these categories.

Analytical pyrolysis. There is no doubt that pyrolysis is the most widely used technique in organic geochemistry for studying the structure of macromolecules and polymers[70–74]. It is popular mostly because of its simplicity. In most cases, a small sample is heated, preferably as fast as possible to a desired temperature, and the fragments formed by the cleavage are removed by a stream of inert gas to an on-line analyzer, which usually consists of GC or GC/MS instruments. Some off-line methods are also used, enabling one to work with higher quantities of material[71,72]. Pyrolysis is a very useful technique for obtaining gross parameters and general information, which enable one to estimate the origin and maturation level of kerogens or even of whole rocks (Rock-Eval method)[1]. However, when the method is used for structure determination, examination in relation to the above four categories clearly indicates that it suffers from several inherent disadvantages.

First, pyrolysis is not a selective method and a range of products are formed. These include high molecular weight residues which have different structure than the starting material[68], resins and tars which are volatile enough at the pyrolysis temperature but

condense on the cooler parts of the system and cannot be analyzed, and a volatile fraction. Even this latter fraction is not completely analyzed because it consists of a complex mixture of chromatographically unresolved compounds[68]. In off-line methods, light and very volatile compounds can also be lost[7]. Consequently, full analysis is possible only for a part of the pyrolysis products which are clearly separated on GC columns.

Second, quantification is only partly possible. Off-line techniques enable one to quantify the residue and the collected products, but light products are lost. On-line techniques are very difficult to quantify. Quantitative information derived from the analyzed fraction possesses, however, structural importance[75,76].

Third, pyrolysis is a very drastic degradation technique which frequently involves the formation of highly reactive intermediates. The fragments (called pyrolysates) as well as the residue are analyzed after some sort of stabilization processes. Therefore, secondary reactions *must* take place. Even the formation of simple alkanes must take place by disproportionation of alkyl radicals by interactions with other compounds or with the (polymer) residues. This may lead to structural units which are not present as such in the starting material[68]. It should be emphasized that only the subunits of the polymer which are thermally stable at the temperature of the pyrolysis can conserve their structure. Hence, even if secondary reactions are minimized, only the thermally stable part of the polymer can be reconstructed. The secondary reactions may be minimized if the products are removed as fast as possible from the pyrolyzer and if the heating is very rapid, in the so-called flash pyrolysis techniques[7,68]. Secondary reactions are also reduced when the pyrolysis is performed at the lowest possible temperature[72].

Fourth, pyrolysis cannot give any information on the connections between the analyzed units because, in many cases (such as in sulfur-rich polymers), the connecting units are also the units which are lost (e.g. polysulfide cross-linkages). Circumstantial evidence must then be used in order to evaluate what are the linkages[64].

High sulfur macromolecules display additional difficulties, since there is a significant difference between the strength of S—S or C—S bonds and the strength of C—C bonds[64]. Alkyl sulfides are known to decompose at 400–800 °C to hydrogen sulfide and to the corresponding alkenes, and the C—S bond is the first bond to break[77]. Thermal decomposition of disulfides and polysulfides starts at temperatures which are 200 °C lower than those for analogous dialkyl sulfides[77]. It is therefore assumed that high sulfur kerogens lose most of the sulfidic and polysulfidic sulfur upon pyrolysis. This severe limitation caused most attention to be paid to the more thermally stable thiophene and benzothiophene moieties[64,70,75,76,78,79]. Thermal cyclization of sulfides to give sulfur heterocycles is also possible[77,80] and should be considered when pyrolysis results are analyzed.

Chemical degradation. If suitable reagents are available, chemical degradation methods are much more selective and can therefore be much more informative than thermal degradation. The use of chemical degradation methods is less widely spread and is restricted to academic research, since they are more tedious and time-consuming than pyrolysis.

The main disadvantage of chemical degradation methods is the low spatial accessibility of the reagents to the macromolecule. All the reagents for sulfur bond cleavage can be used only on soluble fractions (i.e. resins and asphaltenes) but not on geopolymers (kerogens or coal).

The three reagents usually used were already discussed in Section II:

(a) Raney nickel. If the high molecular weight fractions are cross-linked by (poly)sulfide bonds, they are transformed by this reagent into a mixture of hydrocarbons which are analyzed and quantified. Yields of resin and asphaltenes fractions are relatively low in comparison to lower alkyl sulfide fractions (1–20%)[18]. The composition of the residue of this reaction is unknown.

The complete desulfurization of the sample gives only the carbon skeletons of the 'building blocks' of the polymer. No information about the structures and positions of the linkages to sulfur of the sulfur-containing compounds can be derived. Deuterated Raney nickel was used to overcome this limitation[15,81] but it can lead to artifact labeling due to hydrogen exchange in the course of the reaction[68].

(b) MeLi/MeI. Reaction with these reagents has the advantages of Raney nickel desulfurization, i.e. full analysis of low molecular weight products and their quantification, although the yields are quite low (*ca* 10%). The method has some very significant advantages. Units that contain one sulfur atom, such as thiolanes and thiophenes, are intact and therefore this method enables one to distinguish between sulfidic and di- or polysulfidic linkages. The position of the di- or polysulfide linkage is clearly indicated and good reconstructions can be preformed. Thiols can be prelabeled using sodium ethoxide and CD_3I, and then they can be distinguished from disulfides by mass spectroscopy.

(c) $LiAlH_4$. Selective cleavage of di- or polysulfide linkages was also performed with $LiAlH_4$, which forms the corresponding thiols[15,82]. The main disadvantage of this method is the easy elimination of the thiol group as hydrogen sulfide during the electron ionization in the mass spectrometer. The clear identification of the position of the linkage becomes more difficult.

The analysis of organic sulfur in high molecular weight macromolecules and polymers is a challenge that requires more than one method. It seems that only a combination of all available methods and additional methods that, hopefully, will be developed in the future is necessary in order to solve the problem.

B. The Structure of the Sulfur-containing Moieties in Macromolecules and Polymers

From the structure of the sulfur-containing moieties described in the sections concerning crude oils and bitumens, one can reach a conclusion, based on simple extrapolation, that the same structures also dominate the high molecular weight fractions of organic matter, in the geosphere.

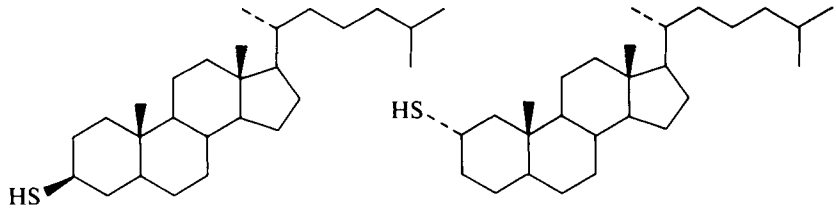
Elemental analysis and S/C ratios of high sulfur kerogens show that kerogens that contain above 7–8% sulfur (or an S/C ratio > 0.04) have one sulfur atom per < 25 carbon atoms. In very high sulfur kerogens (13–14% or an S/C ratio of 0.08–0.09) the ratio is 1:11–13 sulfur atoms to carbon[6]. This leads to the conclusion that sulfide or polysulfide cross-linkages must be present in the macromolecules[57]. As already mentioned, high S/C kerogens have different thermal behaviour than low sulfur kerogens from the same type. Orr[83] investigated high sulfur kerogens from Monterey (California) rock samples and found that these kerogens appear to generate (heavy, high sulfur) oil at significantly lower thermal exposures, and in lower maturity relative to 'ordinary' Type-II kerogens. He therefore suggested the term Type-II-S for kerogens having higher than 6% sulfur. Since essentially no information about the distribution of sulfur functional groups in kerogens or other macromolecules was available, except for elemental analysis, Orr suggested that this behaviour is caused by the low thermal stability of sulfide or disulfide cross-links, and that high sulfur kerogens are cross-linked by such groups. In light of our recent knowledge we may say that this suggestion seems indeed valid.

Recently there has been an increasing number of reports that confirm the polysulfide cross-linking theory, and a concept of 'natural vulcanization' is beginning to be accepted[3]. For example, X-ray absorption measurements show that heavy oils and asphaltenes[24–30] contain up to 40% sulfide/polysulfide moieties.

Schmid[84], Mycke[81], Adam[15] and their coworkers reported that, on column chromatography of high sulfur crude oils, such as Rozel Point seep oil, a reddish band elutes after the aromatic hydrocarbons. This fraction, which was defined as a hexane-soluble polymer (a

resin, by definition), consists of up to one-third of the petroleum weight and has high (> 10%) sulfur content. After Raney nickel desulfurization of this 'red band', about 30% was recovered as hydrocarbons. In the Rozel Point oil the latter were dominated by steranes and *n*-alkanes, which showed great similarities to the original alkane fraction of the oil. In the high sulfur polymers from other samples the resulting hydrocarbons were dominated by carotanes related to purple sulfur bacteria and acyclic isoprenoids of archaobacterial origin. These hydrocarbons are different from the hydrocarbons of the oils. Applying the same procedure on a high sulfur Monterey oil also yielded hydrocarbons of molecular weight distribution higher than the saturated hydrocarbon fraction[68].

Adam and coworkers[15,82] used $LiAlH_4$ for selective degradation of the Rozel Point crude oil, and conclusively identified cholestane-3β-thiol (**46**) and cholestane-2α-thiol (**47**) among the products.



(**46**) (**47**)

Kohnen and coworkers concentrated their efforts on an immature bituminous shale from the Vena del Gesso basin in the Northern Appenines (Italy)[18]. They used the MeLi/MeI and Raney nickel methods on several fractions and subfractions of the shale's extract after extensive column and thin layer chromatography. The Raney nickel desulfurization of the main sulfur-containing fractions resulted in the same hydrocarbons in all fractions and include *n*-alkanes, phytane, steranes, some hopanes and a diaromatic carotanoid. The heavier fractions (e.g. asphaltenes) have higher abundances of higher molecular weight hydrocarbons.

Figure 16 presents examples of the most abundant alkyl methyl sulfides obtained by MeLi/MeI treatment of the same sample. Three main groups of compounds were formed:

(a) *n-Alkanes.* Four different homologous series of monomethyl alkyl sulfides were identified, differing in the position of the methylthio group. 2-(Methylthio)alkanes comprise the major series while 1-, 3- and 4-(methylthio)alkanes comprise the minor series. Several mono(methylthio)alkanes with branched skeletons were also identified.

(b) *Phytanes.* Several methylthio substituted phytanes were identified. As with the *n*-alkanes, the substitution is in the four first carbons of the chain. 3-(Methylthio)phytane is by far the most abundant compound in this group. 1,3-Di(methylthio)phytane was also (tentatively) identified.

(c) *Steranes.* Several groups of (methylthio)steranes were identified. As shown in Figure 16, mono(methylthio)steranes are substituted at position 2 or 3. Di(methylthio)-steranes are probably substituted on the alkyl side chain as well (located at the C-22 position of the most abundant 24-ethylcholestane). There are also some indications that the asphaltene fraction contains tri(methylthio)-24-ethylcholestanes, where one methylthio group is located on C-22 of the alkyl side chain and the other two methylthio groups are located on the ring system.

The mono(methylthio) substituted hydrocarbons are suggested by the authors to be the end units of the macromolecule, connected to the rest of the molecule by one di- or polysulfide linkage. Di- or trisubstituted hydrocarbons are therefore considered as

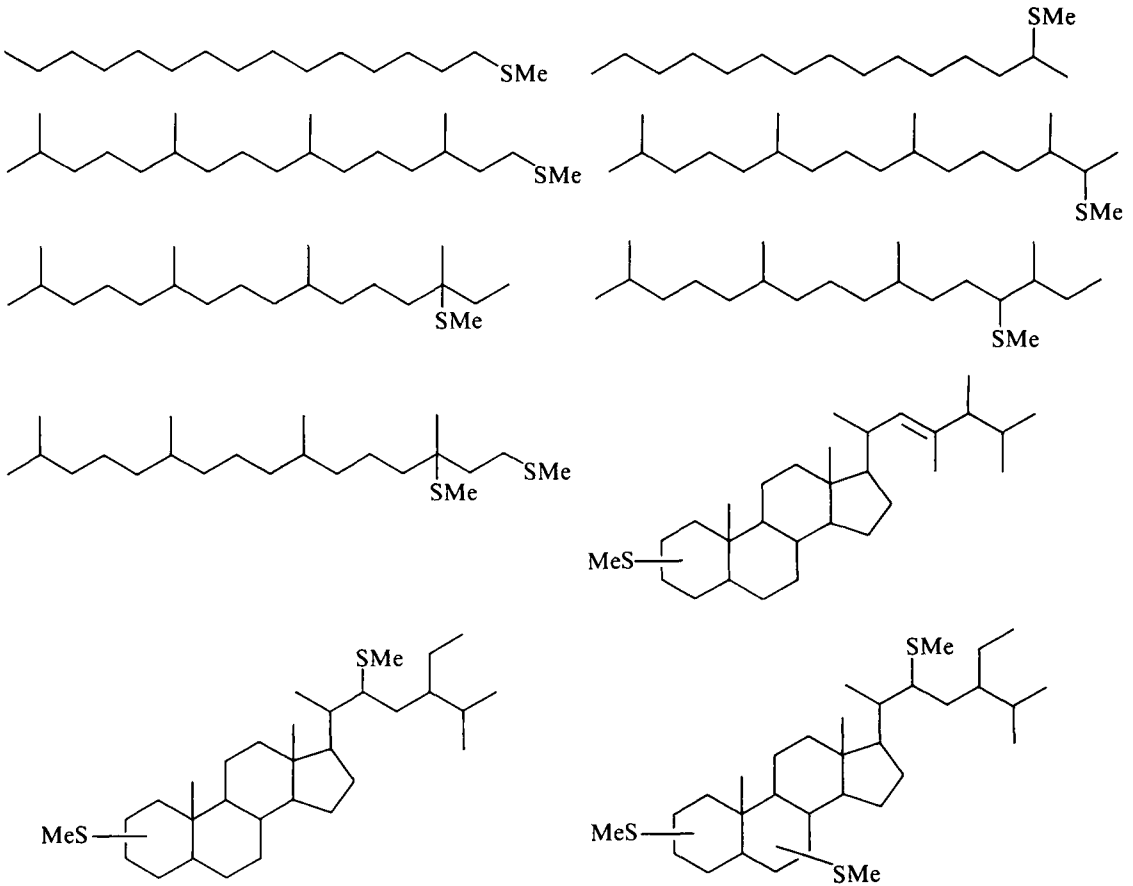


FIGURE 16. Examples of alkyl methyl sulfides identified after MeLi/MeI treatment of high molecular weight extract from Vena del Gesso bituminous shale[18]. MeS— directed to a center of a bond relates to a methylthio substituent on the steroidic A ring at an unspecified 2- or 3-position or a substituent at an unknown position on other rings

cross-links in the macromolecule. The sulfur-containing residue is suggested to be cross-linked by C—S sulfide linkages which do not cleave by MeLi.

The authors found qualitatively that the number of methylthio groups in the molecules increases from the light oligomers eluted with the 'apolar' fraction of the bitumen (the 'alkyl sulfide' subfraction) up to the asphaltenes fraction. The relative abundance of the 'cross-linked' units and the 'end-units' suggest that the 'alkyl sulfide' fraction contains dimers or trimers, the 'polar' resin fractions contain 3 to 5 unit oligomers and the asphaltenes contain 5 to 7 unit oligomers. This trend is in line with the molecular weight and solubility of the various fractions. Extrapolation of this observation suggests that immature sulfur-rich kerogens are similarly-built polymers.

These results support the model suggested by Schmid[84] for the structure of the 'red band' of Rozel Point crude oil. Figure 17 shows a modified model, which is also based on the Vena del Gesso bitumens.

In addition to the structures described here in detail, some other structures, which have been identified using Raney nickel desulfurization, may be attached in a similar manner to macromolecules. In resins and asphaltenes these structures contain both regular and irregular C_{25}–C_{27} isoprenoids, isoprenoids attached to short *n*-alkyl chains[64], C_{25} and C_{30} highly branched isoprenoids[74], C_{35} hopanoids[33,64] and β-carotane[64].

It seems reasonable that the Rozel Point oil and the Vena del Gesso bitumen are extreme examples of immature high sulfur structures, and that other macromolecules with lower sulfur content have less polysulfide and more monosulfide cross-linkages and sulfur

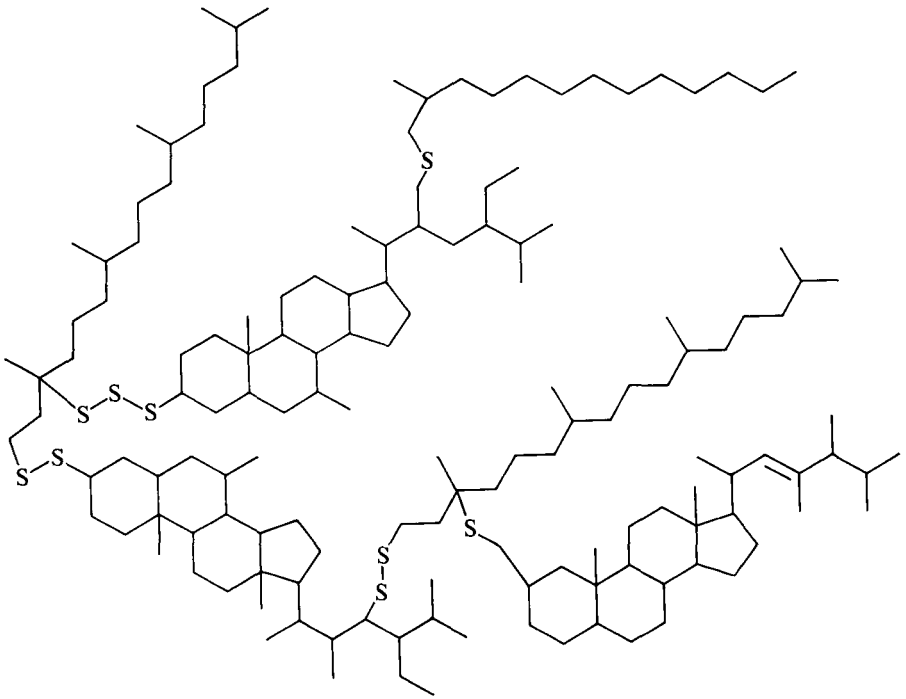


FIGURE 17. Molecular model of a sulfur cross-linked oligomer, probably found in high sulfur fractions and asphaltenes such as Rozel Point oil 'red band'[15,84] or the Vena del Gesso bitumen[18]

heterocycles. In the case of even lower sulfur-containing oils other cross-linkages may exist, but this is still to be proven.

As previously mentioned, all the recent discoveries using chemical degradation techniques are limited only to the soluble fractions of the high molecular weight compounds. For insoluble matter, namely kerogen and coal, analytical pyrolysis is still the most informative method[64,70,75,76,78,79,85].

Since pyrolysis can represent only the thermally stable moieties of the macromolecule, it is not surprising that the major part of the volatile, analyzable, organic sulfur pyrolysates of high sulfur kerogens (Type-II-S) are light alkyl thiophenes (C_4–C_{10})[64,75,78,79]. The thiophenes identified in pyrolysates represent only about 6% of the organically bound sulfur[86]. The rest of the sulfur is either released as inorganic gases (H_2S which is the major pyrolysis product, COS and SO_2) or remains in the residue[64,79]. H_2S is thought to be formed by thermal decomposition of sulfidic or polysulfidic cross-linkages[64,77].

Figure 18 shows an example of pyrolysis (400 °C) products from high sulfur kerogen isolated from a bituminous rock from Nebi Musa (Israel). The gas chromatogram of the aromatic fraction of the bitumen from the same rock is shown in Figure 2. The higher relative abundance of low molecular weight compounds in the pyrolysates, in comparison to the bitumen, is noteworthy.

X-ray absorption studies[24–31] show that it is very likely that thiophene moieties are a very abundant component of the macromolecular structure and their content is estimated to be 60% of the bound sulfur. This was mainly checked in heavy oils. The other components are (poly)sulfides and sulfoxide groups in oxidized samples. The relative content of the three components was used to classify heavy oils into three corresponding categories.

As with crude oils and bitumens, the number of isomers for each alkylthiophene which have been identified in pyrolysis products is limited in comparison to the theoretical number of possible isomers[64,75,79]. Careful analysis, using about 30, synthetically prepared, authentic samples showed that these light thiophenes can be classified into four

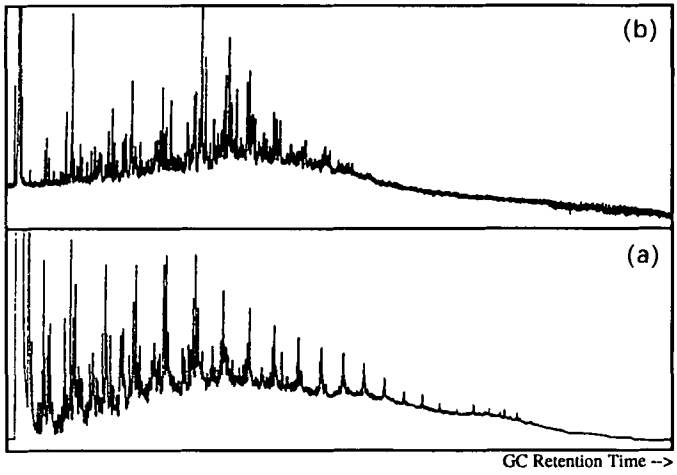


FIGURE 18. Gas chromatogram of the pyrolysis products (fluidized bed, 400 °C[71]) of a high sulfur kerogen isolated from a bituminous rock from Nebi Musa (Israel): (a) FID response; (b) FPD response

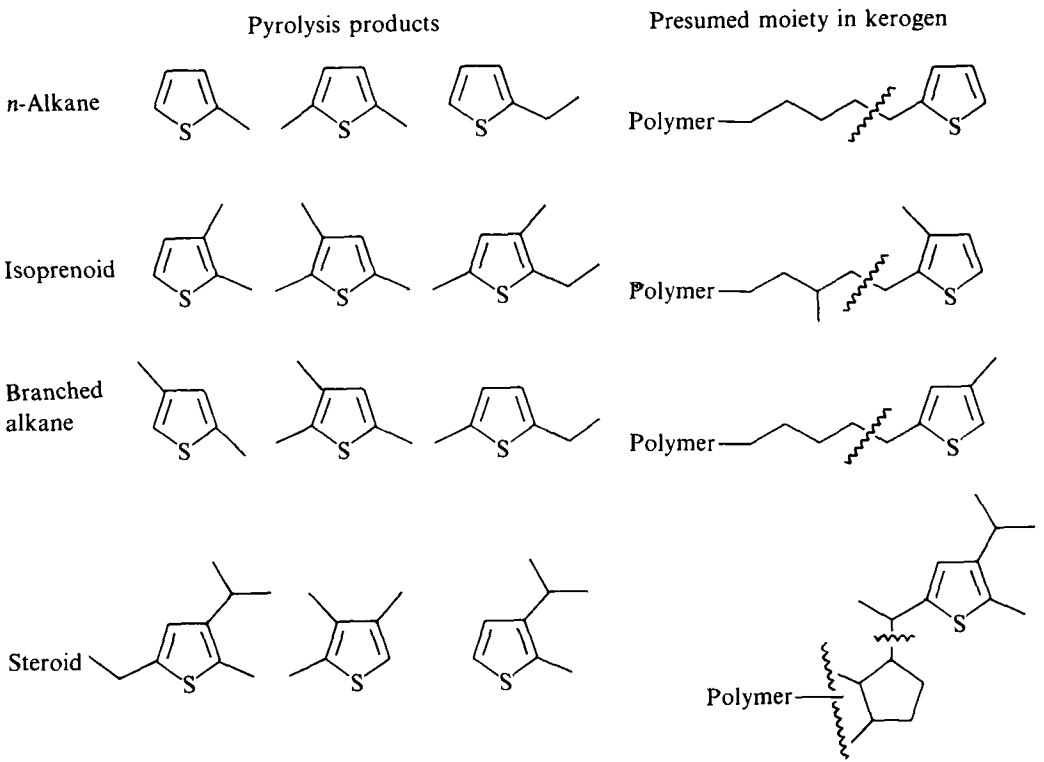


FIGURE 19. Examples for light alkylthiophenes which have been identified in flash pyrolysis products. Classification and presumed moieties in kerogens are those suggested in Reference 79

categories, which are shown in Figure 19 together with their correlation to the main carbon skeleton categories described above.

The first category is correlated to *n*-alkane carbon skeleton (examples are 2-methylthiophene or 2-ethyl-5-methylthiophene). This group also contains alkyl benzo[*b*]-thiophenes substituted with a single alkyl chain at either position 2 or 4, and benzo[*b*]-thiophenes substituted with an alkyl group at one of these two positions and a methyl group at a second position (e.g. 2-alkyl-4-methyl and 4-alkyl-2-methyl benzo[*b*]-thiophenes)[79].

The second category has been correlated to the long-chain isoprenoid thiophenes described earlier and can be regarded as the ruptured edges of these compounds[79]. An example is 5-alkyl-2,3-dimethylthiophene when the alkyl chain is isoprenoid.

The third category contains similar compounds with alkyl side chains which could not be classified in either of the two previous categories and were therefore classified as branched alkyl thiophenes. Three series have been identified in this category: (i) 2-alkyl-3,5-dimethylthiophenes and (ii) 5-alkyl-2,3-dimethylthiophenes when the alkyl is not an isoprenoid[79] (the latter group was correlated with the *anteiso* alkyl carbon skeletons) and (iii) 2-alkyl-4-methylthiophenes, suggested to represent *iso* alkyl carbon skeleton.

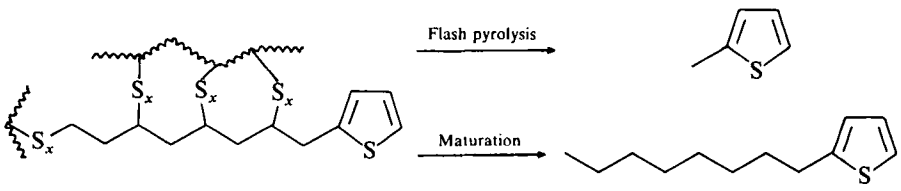
Alkyl thiophenes of a fourth category, related to a steroidic alkyl side chain, have been reported in tables and chromatograms of Reference 79 (see examples in Figure 19), but details on their identification were not given.

It should be noted that some of the lighter thiophenes can be classified in more than one category (Figure 19).

Thiolanes and thianes with *n*-alkyl carbon skeleton are minor components in pyrolysates of kerogens and asphaltenes[64,78,79]. This low abundance is explained by their low thermal stability. Monoalkyl heterocycles and 2-alkyl-5-methylthiolanes are the most abundant isomers[7].

Several investigations were carried out in order to find correlations and structural parameters of sulfur-containing pyrolysis products as a tool for geochemical information. Eglington and coworkers[76] have suggested using the relative abundances of three pyrolysis products: 2,3-dimethylthiophene, 1,2-dimethylbenzene and *n*-non-1-ene as a parameter to classify kerogens. High abundance of the thiophene was found to be an indication for Type-II-S kerogens, while high abundances of the second and third compounds indicated Type-III and Type-I kerogens, respectively. (Type-II kerogen had been found to be intermediate in abundance between the last two.) This parameter and some similar ratios were suggested also as maturity parameters. In a later work Eglington and coworkers[75] used the four categories of pyrolysis products which were discussed above to quantitatively classify 85 kerogen, coal, bitumen and asphaltenes samples using multivariate statistical techniques, and to correlate structural information and source kerogens.

The high abundance of light alkylthiophenes in pyrolysates has been ascribed to the relatively weak carbon–carbon bond β to the thiophene[64,75]. Sinninghe Damste and coworkers[64] indicated that alkythiophenes behave differently than analogous alkylbenzenes which are also present in kerogens. While alkylthiophenes produce light pyrolysates but long-chain alkylated products in the course of maturation[76], alkylbenzenes produce light products upon both pyrolysis and maturation. The authors suggested that this phenomenon is circumstantial evidence of the (poly)sulfide cross-linkages in kerogens. They based their model (and the above classification) on the assumption that in flash pyrolysis at the temperature used (usually 610 °C) the volatile products are formed by the rupture of only one chemical bond (equation 8). These facts and basic assumption lead to the model that alkylthiophenes are attached to the bulk of the kerogen by multiple (poly)sulfide linkages as in **48**[64].



(48) (8)

Sinninghe Damste and coworkers claimed that, during short and drastic flash pyrolysis, it is unlikely that multiple, relatively weak C—S bonds will break and release long-chain alkylthiophenes. Instead, the stronger, but single, C—C bond β to the thiophene breaks, with release of light alkyl thiophenes. At the mild temperatures and very long reaction times of natural maturation, multiple cleavages of weak C—S bonds are more likely than the cleavage of the single, stronger, C—C bond. This model can explain also the higher abundance of long alkylthiophenes upon flash pyrolysis of resins[64]. Since resins have lower molecular weight and lower degree of cross-linking it is reasonable that higher amounts of alkylthiophenes are attached only by one C—S bond to the rest of the molecule, therefore rupture of one weak bond releases these long alkylthiophenes.

The one-bond rupture assumption, on which this kinetic vs thermodynamic model is based, needs, however, further proof since even the release of the most simple volatile molecule in the system, i.e. hydrogen sulfide, requires cleavage of four bonds (two C—S and two C—H bonds).

Of special interest in this context is the comparison between the results of flash pyrolysis and of chemical degradation of high molecular weight fractions from two immature samples. The pyrolysis was preformed on a polar fraction of an extract of a Northern Appenines marl of Miocene strata in the Perticara basin (Italy)[64]. The chemical degradation (MeLi/MeI) results have been discussed above for several fractions of an extract from another Northern Appenines bituminous shale from the Upper Miocene basin of Vena del Gesso[18]. Both samples have also been desulfurized by Raney nickel, and the resulting hydrocarbons of the two high molecular weight samples are rather similar, containing *n*-alkanes, isoprenoids (dominated by phytane), steranes, a few C_{35} hopanes and a diaromatic carotanoid. The pyrolysates of the first sample contain large amounts of GC nonseparatable compounds. The separated compounds are dominated by Δ^2 and Δ^3 cholestenes, an unidentified C_{27} sulfur-containing steroid, C_{22} saturated and singly unsaturated linear thiolanes and thianes, and C_{20} isoprenoid thiolanes and thiophenes (containing singly unsaturated thiolanes). The unsaturation has been interpreted as indicative for (poly)sulfide linkages according to the above model.

If these structures are also found in the polymer, MeLi/MeI degradation should result in alkyl thianes, thiolanes and thiophenes with methylthio substituent(s) positioned on the alkyl side chain. Such compounds have not yet been identified in the Vena del Gesso sample. Moreover, methylthio substituents have been found to be positioned only on the four terminal carbons of the *n*-alkanes and C_{20} isoprenoids. This difference between the results of the two degradation methods should be further investigated.

Recently, pyrolysis of a high sulfur coal[75] resulted in low amounts of dimethyl disulfide, dimethyl trisulfide and higher amounts of dimethyl tetrasulfide. The origin of these compounds is unknown, but they may represent polysulfide linkages in this coal (defined as a first sample of Type-III-S kerogen).

To conclude with the presentation of data, it seems that very high sulfur immature kerogens and related macromolecules contain mainly (poly)sulfidic linkages. X-ray and pyrolysis results indicate that most of the kerogens consist of a combination of (poly)-

sulfidic cross-linkages between hydrocarbon moieties, and sulfur heterocycles (thiophenes, thiolanes, etc.) which are probably also connected to the polymer via (poly)sulfide linkages. The transformations, if any, from highly sulfidic kerogens to highly thiophenic kerogens have yet to be proven and studied.

VI. THE ORIGIN OF ORGANICALLY BOUND SULFUR IN SEDIMENTS: EARLY INCORPORATION OF SULFUR

It is well accepted that petroleum derives from preserved and diagenetically transformed biochemicals[1]. The content of oxygen and nitrogen in sedimentary organic matter is probably controlled by the biosynthetically bound heteroatom content in the biomass and by degradative pathways of the organic matter. Sulfur content, however, is not easily explained by such processes. The average sulfur content in living organism is about 1% of dry weight[87], whereas, as already discussed, the sulfur content in sediments is very often much higher. Since kerogen formation is a result of a very drastic selective preservation[3,4], it is tempting to consider selective preservation of sulfur-containing biochemicals as an explanation. This, however, is highly unlikely since most of the biosynthetically bound sulfur is in highly hydrolyzable and readily (bio)degradable polypeptides (in cysteine, methionine and cystine) or in less abundant sulfate esters in cell wall carbohydrates and sulfolipids[88,89]. These compounds therefore have very low 'preservation potential'[3]. Moreover, the large number of sulfur-containing molecules which have been identified in immature sediments show a distribution of structures that is completely different from that expected of compounds of biosynthetic origin. Most of the structures identified show that sulfur is usually positioned in specific locations in carbon skeletons which correspond to nonsulfur-containing lipidic precursors. This testifies to chemically controlled enrichment of functionalized immature organic matter.

Geological processes are very long, and long periods of time separate the formation of organic sediments (even those classified as immature) and their present-day research. This makes the study of the source and origin of geochemical phenomena quite difficult, which is the reason why most research in the field of sulfur enrichment as well as other related subjects is concentrated on recent sediments and extant microorganisms or in model systems.

Prior to molecular evidence concerning the chemical sulfur-enrichment processes, several studies on the bulk material suggested that sulfur incorporation is taking place in the very first stages of diagenesis. Gransch and Posthuma's[90] work in 1973 was one of the first publications to propose the formation of high sulfur crudes from high sulfur kerogens formed by early incorporation of sulfur in the form of H_2S or S^0.

Since then, several oceanographic studies on recent sediments showed a distinguishable increase of sulfur with increasing depth of the top layer of sediments. This phenomenon was found to occur in very different locations, under different conditions and with different compositions of the organic matter. Four examples will be given:

Aizenshtat and coworkers[91,92] studied in the early 1980s the sediments of Solar Lake, a tiny hypersaline stratified heliothermal heated pond located on the Sinai peninsula coast of the Gulf of Eilat (Egypt). They reported the continuous increase in the S/C ratio of protokerogen (a recently formed geopolymer from dead bacterial mats) from 0.011 on the upper layer to 0.075 at 80-cm-deep sediment.

Francois reported in 1987[93] a much more moderate but still continuous increase in the S/C ratio in humic acids extracted from a near-shore sediment core from Jervis Inlet on the coast of British Columbia. The increase was from 0.023 on the surface to 0.037 at a depth of 70 cm.

Kenig and Huc[71] reported in 1989 the analysis of living plants, surface and buried (proto)kerogens from the carbonate hypersaline lagoonal shores of Abu Dhabi. They

compared three different types of biological sources: algal mats from the upper intertidal zone, a mangrove community from the intertidal zone and lagoonal seaweeds. The S_{org}/C ratio of the three communities increased from 0–0.008 in living plants to 0.01–0.019 in surface mat and surface sediment and up to 0.019–0.037 in buried material.

Mossmann and coworkers[94] examined kerogens from sediment cores collected on the ocean floor of the Peru Margin. They report that S/C ratios range from about 0.03 to about 0.15, increasing steadily over the top 10 m of the sediment column before declining to values around 0.1.

The above examples clearly show that the sulfur enrichment of sediment in the very beginning of preservation is a fundamental and general natural process. This observation still doesn't prove that inorganic sulfur species react with organic matter in this process. In order to clarify this point it is necessary to survey the abundant sulfur species in natural waters (mainly oceans) and the processes that these species undergo.

Sulfate (SO_4^{2-}) is the most abundant sulfur ion in sea water (20–30 mmol l^{-1})[6,94] but it is much less abundant in fresh water. While this is the situation when oxygen is available and used by living organisms in respiration processes, the situation changes drastically in anoxic water, usually present in the lower layers of the water column and in interstitial waters. Under anaerobic conditions organisms must use other electron acceptors than oxygen for biooxidation processes, and a large number of organisms reduce sulfate to sulfide (in the form of HS^- in sea water, where the pH is around 8.1[95]) for this purpose[87]. This drastic change from an oxidizing sulfate-rich to a reducing sulfide-rich environment can occur within a very narrow O_2–H_2S interface of less than 1 mm[95]. This dissimilatory sulfate reduction is sometimes so intensive that sulfate is completely depleted in the interstitial waters[94]. This depletion point occurs close to the point where maximum sulfide concentrations are often observed[87,94,96].

The rate of sulfate reduction is highest in shallow water. For example, the rate in Solar Lake at 0.5-m water depth is five orders of magnitude higher than in the 2900-m-deep East Pacific continental slope. Consequently, 90% of the oceanic sulfate reduction occurs in less than 10% of the world's ocean area[97]. Quantitative estimates suggest that the production of sulfate-reducing bacteria could approach 10^{10} tons of sulfur a year (calculated as H_2S), much of which never leaves the anoxic soils and waters[98].

Iron is the main sedimentary chemical sink for reduced sulfur, forming ferric sulfide (FeS) and subsequently pyrite (FeS_2)[87,94,99]. The rate of sulfate reduction in many cases is higher than the rate at which it can be removed by reaction with iron[94,97]. The availability of iron thus becomes a fundamental factor in the concentration of sulfides in sedimentary environments. In turn, this factor has a very long-lasting influence on the sulfur content in petroleums formed millions of years after deposition (see Section III.A)[1,90]. This far-reaching correlation indeed serves as basic evidence for the role of reduced sulfur species in the enrichment of organic matter with sulfur.

Dissimilatory reduction of sulfate is, however, only one process which involves the reduction of sulfate, and it is restricted to anoxic environments only. Another process which is essential to all living organisms is the assimilatory sulfate reduction which utilizes sulfate for the biosynthesis of amino acids and other sulfur-containing biochemicals. This process involves different enzymatic pathways than dissimilatory sulfate reduction[100].

The fate of the residual sulfide which is not precipitated as iron sulfides is of major importance for the understanding of sulfur incorporation into organic matter. Two processes that compete for the consumption of sulfides are of relevance to this review. One is the reaction with organic matter, and will be discussed in detail later. The other is chemically and biochemically catalyzed oxidation[87,94,101].

Dissimilatory reductive pathways are relatively simple in the sense that H_2S (as HS^-) seems to be the only extracellular product of significant concentration whatever the species being reduced (sulfate, thiosulfate or elemental sulfur)[95]. In contrast, the oxidative

pathways are much more complex[95] in the sense that they produce a complex mixture of compounds having a wide range of oxidation states, such as polysulfides (S_x^{2-}), elemental sulfur (S_8), thiosulfate ($S_2O_3^{2-}$), polythionates ($S_xO_6^{2-}$) (in which tetrathionate $S_4O_6^{2-}$ is of metabolic significance) and sulfite (SO_3^{2-})[89,95,98]. The variety of different types of microorganisms leads to a large diversity of biochemical pathways that produce and use all these ions both as electron acceptors and as electron donors.

The most abundant sulfur species in anoxic waters are sulfides and elemental sulfur, which can be considered as a polysulfidic system. Elemental sulfur can accumulate by microorganisms in intracellular or extracellular globules[89]. Since elemental sulfur is practically insoluble in water, it seems that in order to be utilized it is enzymatically transformed into polysulfides[102]. Moreover, it was shown that sulfur globules of some species of bacteria contain only very small amounts of S_8 rings but more of long-chained polysulfides or polythionates[89].

It is obvious from this brief discussion that the lower layers of the water column and the interstitial waters are rich with a very complex mixture of sulfur-containing ions that can react with organic matter. The possible ways by which these ions can react with organic matter will be discussed, but first conclusive evidence that these ions, or some of them, are indeed reacting and incorporating into organic matter should be presented. Such evidence, that these reactions are the major source for most of the sulfur in geomolecules, was achieved by stable isotope fractionation studies (see Section II).

Biochemical processes show a wide variety of isotopic discrimination, depending on the specific enzymatic biogenic pathway. Ocean dissolved sulfate is the origin for essentially all the sulfur in anoxic marine organisms and sediments[94], and has $\delta^{34}S$ values of about + 20‰[103]. Assimilatory sulfate reduction has a relatively small discrimination of about − 2 to − 3‰[87]. Dissimilatory sulfate reduction has a very large isotopic discrimination ranging from − 20 to − 50‰[87,94], i.e. the resulting sulfides are lighter or have more negative $\delta^{34}S$ values than the precursor sulfate.

Dissimilatory produced sulfides in open systems therefore have typical light $\delta^{34}S$ values of about −24‰[87,94]. When the system closes, both sulfate and sulfide become heavier[87,94]. The term 'open' or 'closed' relate to the relative rates of incoming supply of sulfate to the system, and the rate of its reduction. 'Open' systems are systems where there is a rapid exchange of sulfate between the system and oceanic sulfate (e.g. upper sediment layers). Closed systems are systems where reduction of sulfate is faster than its exchange.

In contrast to biochemical sulfate reduction, only small isotopic fractionations occur when reduced sulfur species react (about − 5 to + 3‰)[94]. Since iron is the most efficient 'trap' for sulfides to form iron sulfides and subsequently pyrite, pyritic sulfur is usually the lightest in the system[94,96] (about 50‰ lighter than sea water sulfate)[96]. Pyrite is usually formed in the upper layer of the sediment, therefore buried pyrites represent the conditions (open vs closed system) at the time the sediment was deposited[94].

Organically bound sulfur in the upper layers is usually much lighter than sea water sulfate, but heavier than pyrite. Solar Lake upper-layer protokerogen sulfur has a $\delta^{34}S$ value of about − 13‰ in comparison to + 23.4‰ of interstitial sulfate[91]. Sulfur in kerogens from the upper layers of the Peru Margin has ^{34}S values of − 13.5 to −16.2‰ compared with − 29 to − 35‰ for pyritic sulfur[94]. These are two examples of this general phenomenon.

The enrichment of organically bound sulfur with ^{32}S is generally interpreted as evidence for secondary enrichment of organic matter by dissimilatory reduced sulfur species[104].

The more positive $\delta^{34}S$ values of organic sulfur in relation to coexisting lighter pyrite testified that some additional, heavy sulfur components are also present in the organic matter. One such component in the early stages of sulfur incorporation could be assimilatory sulfur, mainly in amino acids. If this is true, the organic sulfur in sediments should become lighter as these amino acids decompose and further enrichment of sulfidic

sulfur should take place. In Solar Lake[91] this trend is indeed observed, as $\delta^{34}S$ values decrease from about −13‰ to about −25‰ as the depth increased from the surface to 80 cm. In the Peru Margin samples the upper meter was much less sampled than in Solar Lake, but since the sample were collected from much deeper cores further investigations could be performed. These investigations show that organic sulfur continues to be heavier than pyritic sulfur all the way down the column, keeping a constant discrimination[94]. If there is no heavy sulfur contribution other than primary organic sulfur, this can only be explained by continuous rapid isotopic reequilibration between dissolved sulfur species (which become heavier) and the organic sulfur which has been incorporated during earlier stages. Mossmann and coworkers[94] find this unlikely, but the opinion of the writer of this review is that chemical equilibration which will cause isotopic exchange cannot be ruled out. An alternative explanation is that both heavy sulfate and light sulfide are incorporated into organic matter, but this is considered unlikely owing to the relatively low reactivity of sulfate ions in marine basic pH water, and the low stability of the resulting ester sulfates[6,94]. A third explanation offered by Mossmann and coworkers is that polysulfides are the heavy component. This is based on the observation that diffusing sulfides that cross the sediment–water interface are heavier than sulfides dissolved within the pore waters of surface sediments[94,96,105]. These sulfides can be subsequently oxidized to give heavy polysulfides which react with organic matter near the surface of the sediment. While, as will be discussed later, there is evidence that polysulfides are indeed a very important sulfurizing agent, the isotope effect discussed above should be further examined, especially because this model requires two isotopically distinct polysulfide types: a heavy type above the surface of the sediment which reacts with surface organic matter, and a light type in the upper sediment layers that reacts with iron minerals to give pyrite[94,96,106].

VII. MECHANISMS FOR SULFUR INCORPORATION

The exact mechanisms for the first steps of sulfur incorporation into organic matter, i.e. formation of the C—S bond and stabilization of the early formed sulfur-containing organic compounds, are as yet unknown. The mechanisms proposed until now are all controversial and the subject is under debate. The purpose of this section is to give details of the mechanisms suggested in the literature together with the reviewer's opinion. It is meant to be thought-provoking rather than a presentation of unequivocal facts and interpretations.

Any acceptable model should answer the following questions:

(1) What are the active sulfur species?

(2) What are the optimal conditions under which each of the species reacts?

(3) What are the organic active groups?

(4) Are the combined answers compatible with the conditions under which incorporation takes place in nature?

Based on both field observations and laboratory experiments, all the abundant sulfur species that have already been mentioned, i.e. sulfate[107], hydrogen sulfide[9,11,56,108–110], polysulfides[66,67,91,93,111–114] and elemental sulfur[115], have been suggested as sulfurizing agents.

Simulation experiments have shown sulfur enrichment of bulk natural materials using different sulfur reagents. Peat humic acids have been enriched by both elemental sulfur[115] and hydrogen sulfide[108], carbohydrates have been enriched with H_2S[109] and fatty acids gave sulfur compounds when heated with elemental sulfur[116].

Table 2 summarizes the chemical behavior of the major sulfur species under basic and acidic pH conditions. The table presents only reactions that seem possible at mild temperatures (< 100 °C) and in the presence of water. It does not present methods used in synthetic organic chemistry but suggests the main, kinetically active species that may be

TABLE 2. Reactivities of major natural inorganic sulfur species toward selected organic functional groups under aqueous conditions at basic and acidic pH[a]

	pH > 7				pH < 7		
	SO_4^{2-}	S_8	S_x^{2-}[b]	HS^-	H_2SO_4	S_8	H_2S
C=C double bond	–	–	–	–	+[119]	–	+[119–121]
Activated C=C double bond	–	–	+[112,114]	+[111,118]	+[119]	–	+[121,122]
Carbonyl group	–	–	+[123]	+[124]	+[119]	–	+[124,125]

[a] A positive sign indicates incorporation of the sulfur species.
[b] S_x^{2-} ions decompose under acidic conditions to H_2S and S_8.

important in nature. (For example, reactions such as those reported between elemental sulfur and ketones at gaseous ammonia atmosphere without an additional solvent[117] were not included.)

Sulfate esters which can be formed under acidic catalysis[119] are easily hydrolyzed to the corresponding alcohols under basic conditions. Therefore, sulfate can be incorporated into organic matter under acidic or neutral, but not basic, conditions. Such conditions occur mainly in peat-forming areas such as marshes and swamps. Casagrande and Siefert reported in 1977 the increase of sulfate ester concentration as well as total sulfur amounts in such areas (pH 4 – 7)[107]. They suggested that these esters are formed on phenolic-lignin groups and/or on carbohydrates. Under marine pH (*ca* 8.1) the significance of sulfate enrichment seems less likely.

Since elemental sulfur solubility in water is very poor, its activity at mild temperatures is very low. Casagrande and Ng[115] reported that sulfur reacted with humic acids in refluxing chloroform (62 °C) in which elemental sulfur was partly soluble. Thermal activation of S_8 rings requires temperatures of at least 110–130 °C to break the S—S bonds and to initiate free radical reactions[112,115,122,126]. However, such temperatures are not possible in most depositional environments.

The reduced sulfur species which are therefore acceptable as sulfurizing agents are hydrogen sulfide in acidic media and (bi)sulfide (HS^-, S^{2-}) and polysulfide anions in basic pH. Hydrogen sulfide and (poly)sulfide are both the only species for which some specific mechanisms were suggested for their incorporation into organic matter in sediments.

Hydrogen sulfide was suggested by Sinninghe Damste and coworkers as a 'quencher' of labile functionalized lipids[9,11,56]. They suggested the addition of H_2S to double bonds, especially in conjugated dienes as the direct mechanism for the formation of sulfur heterocycles (thiolanes, thianes and thiophenes) in nature. Based on this suggestion they proposed the corresponding dienes of almost all the sulfur-containing molecules in the geosphere as precursors[7]. Since many of these proposed precursors have not yet been found in nature, the authors raised the possibility that some of them may have once been produced by extinct organisms[7]. The addition of hydrogen sulfide to simple, unactivated double bonds, in the absence of initiators, occurs by an electrophilic mechanism, similar to that for the addition of water, and Markovnikov's rule follows. However, this reaction is usually very slow and it either does not take place or requires very severe conditions such as high pressure or temperature, unless an acid catalyst such as concentrated H_2SO_4 is present[119]. Under acidic conditions, this is also true for the reaction with other functional groups, since electrophilic protonation is the first step of the reactions[119–122,124,125].

As already mentioned, such conditions may exist in acidic marshes[107] or in the proximity to acidic sulfide-rich hot springs[110]. Therefore, the addition of H_2S to double

bonds can account for only a very small portion of sulfur enrichment, but it is not likely to explain it in most locations.

Under marine pH conditions, sulfides and polysulfides are the most abundant reduced sulfur species. Polysulfides are formed by nucleophilic reaction between sulfides and S_8 rings produced biogenically[122] by enzymatic processes[102], or as a result of sulfide oxidation[110].

In 1981 Aizenshtat and coworkers[92] proposed that the sulfur enrichment of recent sedimentary organic matter in Solar Lake (see Section VI) is mainly caused by polysulfide reactions with the organic matter. This proposal was based on the relatively very high concentrations of polysulfides (150 mmol l^{-1})[127] which have been measured in the interstitial waters of the lake.

Further evidence of the importance of polysulfides was provided by the report of Francois in 1987[93] that organic polysulfides were found associated with extracted humics from British Columbia. As discussed in the previous sections, in the last few years an increasing amount of molecular evidence for the incorporation of polysulfides was reported by Kohnen[18,66,67], Schmid[54], Adam[15,82] and their coworkers.

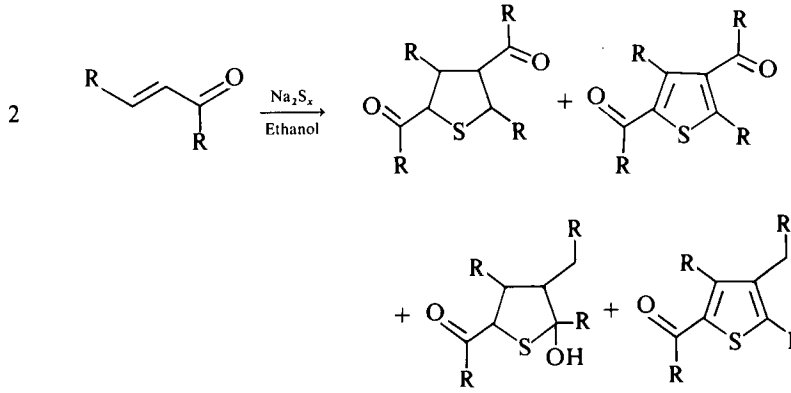
It seems that polysulfides play an important role, if not the major one, in the formation of high sulfur organic sediments. Consequently, the possible chemical mechanisms for their incorporation will be discussed in some detail. Sulfides and polysulfides are good nucleophiles and their reactions which create carbon–sulfur bonds are likely to involve electrophilic functional groups, either by addition to activated multiple bonds or by nucleophilic substitution of saturated compounds carying good leaving groups such as halide ions. However, organic halo compounds which are often used as precursors to sulfides in the laboratory[118] are not abundant in natural lipid products. Therefore, most attention was devoted to nucleophilic addition to activated double bonds, most often by a carbonyl group (Michael acceptors). Vairavamurthy and Mopper[111] reported the widespread occurrence of 3-mercaptopropionic acid in coastal marine sediments, and presented evidence for its formation from acrylic acid, probably by nucleophilic addition of bisulfide ion.

Although both sulfides and polysulfides can serve as nucleophiles, there are differences in their activities and in the sulfur-containing products they form. In their research Vairavamurthy and Mopper[111] compared the nucleophilic reactivities of bisulfides and polysulfides towards acrylic acid and acrylonitrile at different pH and ion strength conditions. They found that at equal concentrations of the nucleophiles the rate of polysulfide addition to both substrates was much higher. LaLonde and coworkers[112] used molecular frontier orbital theory (FMO) to explain these kinetic results and proposed that the reactivity increases with an increase in the number of sulfur atoms in the nucleophile and the degree of conjugation of the electrophile.

LaLonde and coworkers studied extensively the room temperature reaction between Michael acceptors and sodium polysulfides. They concentrated their effort on the reactions of chalcone (PhCH=CHCOPh) or some of its derivatives with saturated ethanolic solutions of alkali polysulfides at pH > 14[112]. The major products of these reactions were five-membered heterocycles (equation 9).

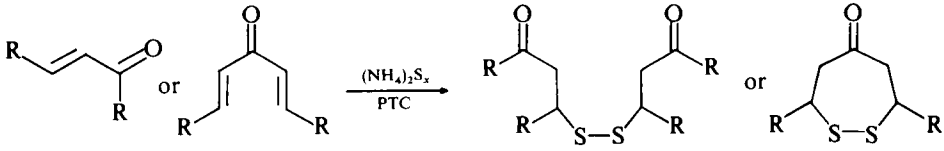
They proposed that such reactions could serve as model reactions to the geological origin of sulfur heterocycles such as thiolanes and thiophenes. LaLonde and coworkers also proposed some examples of electrophilic natural products which may react in this manner[112].

These model reactions may indeed explain some of the reactions and do provide an example for catalyzed C—S bond formation under basic conditions. However, the very harsh pH conditions which enable carbanionic dimerizations and cyclizations are not possible in most natural environments, except in some very unusual locations, and therefore such reactions are kinetically unfavourable.



(9)

In order to refine the above model and check whether under milder pH values some other reactions take place, additional reactions were studied by the writer in Jerusalem. These reactions, between α,β-unsaturated carbonyl compounds and polysulfides, were performed at room temperature under mild basic conditions at pH 8–9 or by using ammonium polysulfides. The reactions were performed in a two-phase system (aqueous and organic—with a phase transfer catalyst) which is much more comparable to natural environments than saturated ethanolic systems. The major products under these conditions were completely different from those described by LaLonde. These products contain disulfide dimers or, in some cases, cyclic disulfides[114] (equation 10).



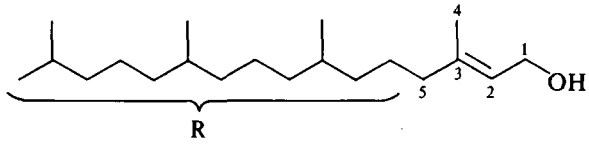
(10)

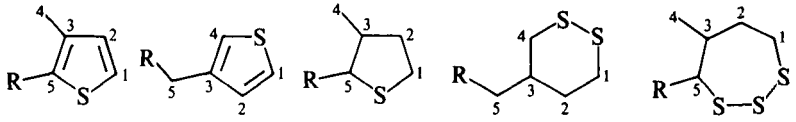
These reactions are therefore proposed as a model for the geological origin of polysulfide cross-linking or of cyclic polysulfides such as those observed by Kohnen and coworkers[18,67].

Both the 'acidic mechanism' and the nucleophilic addition mechanisms cannot account for all the organically bound sulfur structures which have been described in the previous sections. Some specific cases have been discussed in the organic geochemical literature. One of these cases, i.e. the transformation of phytol to C_{20}-isoprenoid thiophenes, will be presented here in detail.

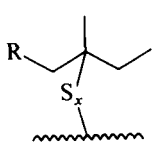
The very high relative abundance of C_{20}-isoprenoid thiophenes and related sulfur compounds, and the high specificity of the structural distribution of the isomers are generally interpreted as testifying that phytol is the precursor. The reductive and oxidative degradation pathways of phytol to phytane and pristane, respectively, are well documented and widely accepted as a paleoenvironment marker[1]. The degradation of phytol in (poly)sulfidic environment is as yet unknown, but C_{20}-isoprenoid thiophenes are found in recent and immature sediments[71,128]. In order to support a possible pathway some important structural features must be emphasized.

In the more abundant sulfur-containing C_{20}-isoprenoids the sulfur is bound to one of the first five carbons (C1–C5)[7,10,67] as shown opposite:

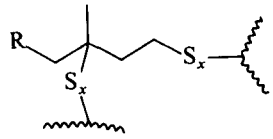




In polysulfide cross-linked polymeric fractions[18] the major phytanyl structural units are linked to the C_3 position (**49**). Phytanyl units which are linked to the macromolecular structure via two polysulfides linkages at C_3 and C_1 (**50**) are also present.

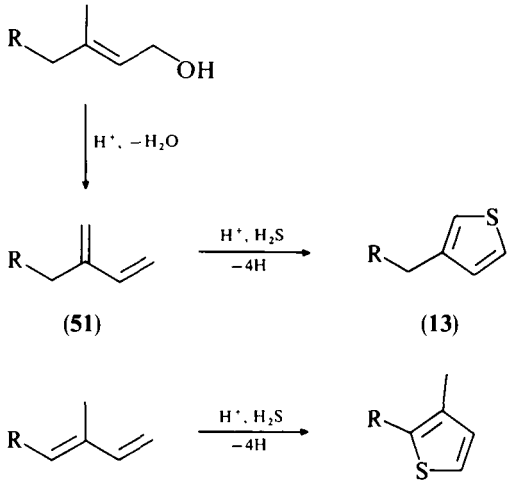


(**49**)



(**50**)

Phytadienes **51** and **52** formed after dehydration of phytol were suggested as precursors for C_{20}-isoprenoid thiophenes **13** and **14** by the mechanism shown in equation 11[8].



(11)

(**51**) (**13**)

(**52**) (**14**)

Simulation reactions of phytol and phytadienes in saturated H_2S solutions (pH 2.82–4.56) were carried out by Fukushima and coworkers[110], and indeed produced **13** and **14**. These thiophenes (along with a third minor isomer, **15**) were also found by this group in acidotropic fresh water lake sediments (Lake Usoriko, Japan). The lake water

shows pH below 4 due to the inflow of sulfide-rich hot spring water. Such pH values are unusual in marine water and hence this mechanism, which may be termed the acidic mechanism, can explain only partially the formation of C_{20}-isoprenoid thiophenes.

Polysulfide aqueous solutions are stable only at pH values higher than 6, and they reach high concentrations only at basic pH values[129,130]. Therefore, in natural marine sediments, which have such basic pH values, sulfides and polysulfides are most likely to form most of the C_{20}-isoprenoid sulfur-containing moieties. Kohnen and coworkers[18,67] suggested that the addition of polysulfides to phytadienes in a mechanism similar to the 'acidic' mechanism above accounts for the formation of cyclic di- and trisulfides, as well as for the polysulfide cross-linking in macromolecules. However, the addition of these strong nucleophiles to unactivated C=C double bonds seems unlikely.

The preferred polysulfide linkage to the C_3 position offers another clue to the mechanism. Kohnen and coworkers[18] interpreted this preference as a result of cationic mechanism, in which the addition of HS_x^- to phytadienes probably involves an intermediate carbocation. The most stable carbocation is the one with the charge on the most substituted C_3 carbon, and this position is therefore preferably substituted, giving products according to Markovnikov's rule. However, the problem with this explanation is that carbocation formation via acidic protonation is not likely to take place in the pH range of polysulfide stabilities, and of marine water. Moreover, it was shown[130] that protonated polysulfides (HS_x^-) do no occur in significant concentrations in alkaline polysulfide solutions. (Sulfanes H_2S_x which were also suggested as the reagents[11] are formed only in very acidic conditions like saturated hydrochloric acid[131] or under 'superacid' conditions[132] which are both impossible in natural marine sediments.) Very recently, a simulation reaction between sodium polysulfide and phytadienes in dimethylformamide (DMF) which produced a mixture of polysulfide cross-linked oligomers was reported[133]. Chemical degradation of these oligomers shows a preferred substitution on carbons 2 and 3, in accordance with Markovnikov's rule. The authors reported that this reaction also took place, with much lower yields, under PTC conditions. Phytol, in DMF, produced some cyclic di- and trisulfides in very low yields ($< 0.7\%$). These results were interpreted by the authors as giving support to the above mechanism and ruled out a possible radical reaction initiated by radical ions such as $S_3^{-\cdot}$ and $S_4^{-\cdot}$ which are present in DMF solutions.

An alternative 'basic' mechanism can be suggested. This mechanism involves a Michael-type addition of polysulfide to phytenal, a mild oxidative degradation product of phytol which has been found in nature[134,135]. Such addition will lead directly to a preferred polysulfide substituent at the C_3 position (β to the aldehyde). Another, second addition to the aldehyde function will then lead to substitution on both C_3 and C_1, as indeed found in sediments. It is difficult to explain this double addition by the 'acidic' mechanism[18].

Simulation reactions by the writer[63] show that phytenal readily reacts with ammonium polysulfide at room temperature to produce a red-orange oil. The ^{1}H-NMR spectrum of this oil show the disappearance of both vinylic and aldehydic protons of the phytenal, which is in accordance with the above suggestion. GC/MS analysis of this oil show that the mixture contains the two C_{20}-isoprenoid thiophenes (**13** and **14**) and elemental sulfur (Figure 20). These thiophenes are probably formed by thermal reaction of the labile product during GC analysis with the release of elemental sulfur. Although the exact course of this reaction is still under study, phytenal proved to be a 'polysulfide acceptor' and to yield sulfur-containing compounds.

Kenig and Huc reported recently[71] the analysis of recent sediments from the shores of Abu Dhabi (see Section VI). They presented the GC-FPD trace chromatogram of the extract fraction of a surface microbial mat which shows only two sulfur-containing organic compounds namely the thiophenes **13** and **14**. The authors report that all of the elemental sulfur from this fraction was removed before GC analysis. Nevertheless, the FPD chromatogram shows elemental sulfur, which is the same phenomenon observed in the

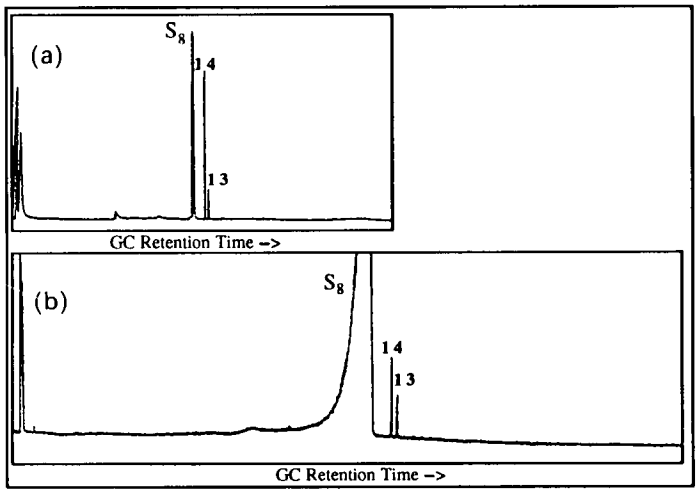


FIGURE 20. GC-FPD trace of: (a) fraction of an extract from surface microbial matt sediment from Abu Dhabi[71]; (b) the products of a simulation experiment between phytenal and ammonium polysulfides[135]. Both traces show the three sulfur-containing compounds in the mixtures: S_8, **13** and **14**. (a) reprinted with permission from *ACS Symposium Series*, Vol. 429. Copyright (1990) American Chemical Society

simulation reaction with phytenal. Figure 20 also shows this chromatogram. The great similarity between the two chromatograms may give support to the validity of the 'basic' phytenal mechanism, although it is still speculative. It also raises the question about the exact nature of the very early phytol–sulfur compounds.

There are several other examples for biomolecules which have been suggested as putative precursors for organic sulfur compounds. Almost all of their transformations to products can be explained theoretically by an acidic electrophilic or basic nucleophilic mechanism, with all the problems discussed above. The present reviewer prefers the nucleophilic mechanism.

C_{35}-Hopanoid thiophene (**5**) and its isomers were already mentioned as possible products of bacteriohopane tetrol (**6**)[8,52]. C_{35}-hopanes were also found to be incorporated via up to four intermolecular (poly)sulfide linkages to macromolecules[7]. Several mechanisms can be easily suggested for such transformations, but no experimental data have yet been available.

Steroidic moieties were reported to be linked to macromolecular structures by (poly)sulfide linkages to the carbons at position 2 or 3[15,18,82]. Sterane thiol was also identified in recent sediments. This was explained by 'acidic' addition of polysulfides to Δ^2-sterenes which are formed after dehydration of the 3-OH group of stanols[18]. Polysulfides are known to link cyclic ketones by replacing the carbonyl group[123] and therefore 3-stanones can be possible precursors for the alternative 'basic' nucleophilic addition.

Highly brached C_{25} and C_{30} isoprenoid sulfur compounds were suggested to originate from the corresponding unsaturated isoprenoids[56]. The co-occurrence in recent sediments (3000–6000 years) of highly branched isoprenoid polyenes and unsaturated similar thiolanes possessing two double bonds less than the corresponding polyenes was interpreted[62] as evidence for the formation of the thiolanes by a reaction of inorganic sulfur species with double bonds of the highly branched isoprenoid polyenes (the 'acidic'

mechanism). However, there is very little information about the possible biological source for both co-occurring compound types, and a common, as yet unknown, precursor may be involved in the formation of both. Moreover, the co-occurrence of polyenes and sulfur-incorporated similar compounds may also testify to the *low* reactivity of double bonds towards sulfur necleophiles.

C_{40}-carotanoids were found only after desulfurization of macromolecules[7,18]. This is in accordance with the FMO prediction of LaLonde and coworkers[112], who have suggested that conjugated polyenes are as active as Michael acceptors. According to them, a system with ten conjugated double bonds will have similar LUMO energy and reactivity to that of chalcone. It is also reasonable that such polyenes will polymerize rather than cyclize.

All the above examples clearly indicate that whatever the mechanism chosen, sulfides and (poly)sulfides can lead to both intramolecular cyclizations and intermolecular polymerization, thus explaining the formation of single compounds in bitumens and of high molecular weight macromolecules. However, these examples dealt only with single lipidic compounds as precursors. The recent reappraisal of kerogen formation[3] raised the importance of selective preservation of resistant biomacromolecules. The possible interaction between sulfur species and such biomacromolecules is unknown. The exact role of sulfur in this system should be considered. Do (poly)sulfides act only as polymerizing agents of low molecular weight molecules (a process termed 'natural vulcanization') or do they act to bind low molecular weight compounds to the biomacromolecules? Sulfur may also be incorporated into already existing polymers in a process which can be more suitable compared to industrial high-temperature vulcanization of rubber, and thus enhance their resistance to degradation processes.

Evidence of the last process may be found in the sulfur enrichment of protokerogen from Solar Lake[92]. Most of the degradative microbial mats organic matter consists of insoluble nonlipidic biomacromolecular matter. As discussed in Section VI, this material was considerably enriched with sulfur by polysulfides.

In coal geology the concept of selective preservation of biopolymers is well established[3]. Trunks of vascular high plants provide very resistent polymers (such as lignins), which even conserve the morphological structure of the plants and enable one to identify different macerals[1] by optical methods. The incorporation mechanism of sulfur into polymers such as lignins is completely unknown. Lignins are condensation products of 3-phenyl-3-propen-1-ol derivatives (coniferyl alcohol, sinapyl alcohol and *p*-coumaryl alcohol), which may be transformed into 3-phenyl-3-propenal moieties inside the polymer (see the proposed structure of lignin in Reference 1). Cinnamaldehyde (3-phenyl-3-propenal) reacts very readily with polysulfides[114] and therefore Michael-type nucleophilic addition may also play a role in the formation of high sulfur coals.

VIII. THE GEOLOGICAL TRANSFORMATIONS OF SULFUR COMPOUNDS

From the information given in the previous sections it is clear that there is a very large difference between immature high sulfur organic matter and mature high sulfur crude oils. The chemical processes which are involved in the transformation of polysulfidic, thermally unstable, immature kerogens and heterocycles with biogenic structure into condensed polyaromatic sulfur-containing and thermodynamically stable structures are only partly known. It is clear, from stable isotope investigations[136], that the sulfur found in crude oils indeed originates from incorporation processes during the early stages of deposition. This early incorporated sulfur becomes a cross-linking agent in high sulfur kerogens. The sulfur cross-linked kerogens produce, upon thermal exposure, high sulfur, usually heavy, oils. This was first suggested by Gransch and Posthuma[90], and later confirmed by Orr[104] and others[137]. Orr was the first to determine the unique thermal behavior of such kerogens (Section V.B). However, chemical details concerning those thermal reactions are still very unclear. In the following section we described some phenomena which may elucidate some

of the processes observed in the field or result from artificial thermal exposure of samples, in a somewhat oversimplified simulation of maturity processes (often termed 'artificial maturation'). Such experiments can hint at the possible trends of maturation, but the basic assumption that temperature can compensate for time must be viewed with caution.

A. Sulfur Elimination

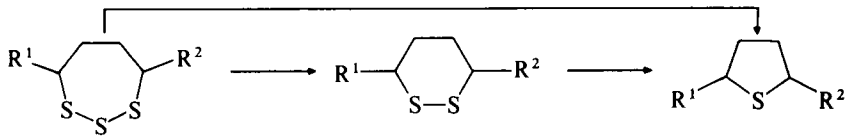
Sulfur incorporation into recent, functionalized matter is, as shown, a relatively fast process in terms of geological time scales. In the long term, sulfur contents gradually decrease. In some locations this is observed even in recent sediments, where sulfur content reaches its peak on the upper layers of the sediment column after which a slow decrease in the S/C ratio is observed. In the Peru Margin sediments[94], for example, the increase is observed over the top 10 m of the sediment, before decreasing to a constant S/C ratio. However, in other examples of immature sulfur sediments the organic sulfur content was found to be highly variable with depth[104]. This can be explained by the fact that depth correlations cannot be regarded as the only maturation parameter, because environmental changes during the time the layers were sedimented have a stronger influence than maturation alone.

Heating of protokerogen from Solar Lake to 175 °C results in a decrease in the sulfur content and in its elimination as elemental sulfur[91]. Stepwise pyrolysis of recent kerogens from Abu Dhabi also show release of elemental sulfur[71].

Upon further maturation the cleavage of polysulfidic linkages and the elimination of elemental sulfur and hydrogen sulfide is probably the most important maturation process[7]. Eglington and coworkers[75,76,86] found that the relative abundance of 2,3-dimethylthiophene in pyrolysates represent the organic sulfur content of kerogens (see Section V.B.). They found in both natural maturity sequences and in thermal experiments that this parameter decreases with maturation, thus indicating organic sulfur decrease. This finding confirmed the much earlier results given by Gransch and Posthuma[90] which indicate that organically bound sulfur is eliminated during the early stages of oil production. This sulfur elimination is probably the reason for early formation of heavy, high sulfur oil from Type-II-S kerogens, because the loss of sulfur cross-linking is accompanied by the release of smaller sulfur-containing molecules.

This gradual decrease in sulfur content is also described for crude oils[44,80], but it could be explained also as diluting effects.

Molecular level evidence as to the elimination of sulfur was suggested by Kohnen and coworkers[67]. They showed that less mature and less buried sediments (Peru upwelling area—Pliocene) contain cyclic trisulfides in concentrations relatively higher than those in more mature and deeper buried sediment (Vena del Gesso—Upper Miocene) which contain mainly cyclic disulfides. Many other sediments which are more mature contain only the monosulfide heterocycles, thiolanes and thianes, presumably formed as in equation 12.



(12)

B. Sulfur Incorporation

The fate of the sulfur released from organic matter is completely unknown. While its major part is 'lost', reincorporation cannot be dismissed. Thermal treating of organic

matter from sediments and elemental sulfur showed a remarkable sulfur enrichment. Heating protokerogen from Solar Lake with elemental sulfur[91] at 175 °C showed an enrichment of almost 100%. Schmid and coworkers[34] showed that elemental sulfur reacted with *n*-octadecane in a sealed glass tube between 200 and 250 °C and produced a complex mixture of C_{18}-alkylthiophenes. Similar results were also reported by Stoler[138]. These reactions, which are most likely radical chain reactions, cannot be acceptable as the main mechanism for early sulfur enrichment, but can contribute to sulfur compound content in kerogens and crude oils in reservoirs. Hydrogen sulfide is another possible source for reincorporation of sulfur in oils. Ho and coworkers[41] ascribed the occurrence of high thiol mature oils to H_2S incorporation. Orr[104] pointed out three sources of hydrogen sulfide in oil reservoirs: microbial sulfate reduction in low-temperature reservoirs (< 50 °C), thermal clevage from organic matter as described above and high-temperature nonmicrobial sulfate reduction. Orr also noted that thermal maturation of oil in the absence of sulfate may result in a continual decrease in sulfur content. Thermal maturation in the presence of sulfate in high-temperature reservoirs (> 80–120 °C) may result in competing sulfurization and desulfurization of oils, which can produce abnormally high thiol contents in oils. Such processes may be monitored by the increase in the S/N atomic ratio, because nitrogen continues to decrease and sulfur may be maintained at the same level. The $\delta^{34}S$ values of such oils (and related H_2S) will change towards the values of reservoir sulfate (because nonmicrobial sulfate reduction has low isotopic fractionation). H_2S release is therefore very different from the release of other light gas products such as methane and CO_2 since, unlike the latter relatively inert gases, H_2S can 'equilibrate' with organic sulfur. This point may have importance in the isotopic $\delta^{34}S$ values of the released H_2S.

A related process that may take place is the transformation of polysulfide cross-linkages to heterocyclic structures. This process is not yet documented for natural organic matter, but such pyrolytic processes do occur[77]. Cohen and Aizenshtat[80] showed that pyrolysates of preheated polyphenylene sulfide contain high relative abundances of aromatic sulfur compared to a nonheated sample, indicating thermal transformation from sulfidic to aromatic sulfur inside the polymer matrix.

C. Thiolane to Thiophene Transformation

The aromatization of thiolanes to the corresponding thiophenes (equation 13) was suggested by several authors[7,34,53,58]. Schmid and coworkers[34] reported that high amounts of thiolanes are present only in quite immature petroleums, and that these disappeared during thermal simulation experiments carried out on immature crude oils. Payzant and coworkers[22] also demonstrated the aromatization of linear alkylthiolanes and thianes to the corresponding alkylthiophenes upon heating to 350 °C in the presence of $CaCO_3$. Further evidence for this transformation was reported by Kohnen and coworkers[62] for highly branched isoprenoid sulfur compounds. These compounds have a very distinguishable carbon skeleton and can therefore be compared in different sediments and a maturity sequence can be suggested. The authors observed a decrease of thiolanes and an increase of the corresponding thiophenes when they compared sediments along such a maturation sequence. Pyrolysis results of immature high molecular weight fractions (from North Appenines)[64] in comparison to more mature kerogens (Jurf ed Darawish—Jordan) indicate that such transformations are probably occurring inside the polymeric matrix as well. Elemental sulfur is a known aromatization reagent[120] and it seems likely that it may

(13)

accelerate the transformation from thiolanes to thiophenes. The model reactions described by LaLonde and coworkers[112] showed that in some cases such aromatization occurs under very mild temperatures.

D. Conversion of Thianes to Thiolanes and Interconversion of Thiolanes

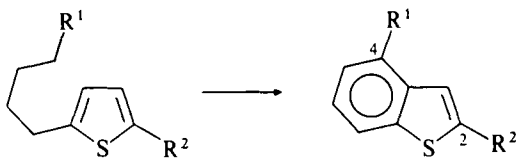
The simulation experiments performed by Payzant and coworkers[22] show that, besides aromatization, thianes are converted to the corresponding thiolanes (equation 14), thus indicating the higher thermodynamic stability of the five-membered heterocycles. Thiolanes were found in the same experiments to interconvert to new isomers (equation 15). The authors reported and suggested a mechanism for a three carbon atom 'hop' of the sulfur along the chain. For example, 2-dodecyl-5-methylthiolane was isomerized into 2-butyl-5-nonylthiolane. Monoalkyl thiolanes (sulfur atom at the end of the chain) proved to be more stable.

(14)

(15)

E. Cyclization and Aromatization of Alkyl Side Chains

The formation of alkyl benzo[*b*]thiophenes by cyclization reactions of the alkyl side chain of alkylthiophenes (equation 16) was suggested by several authors[7,34,58,64]. The main evidence for this proposed transformation is the unproportional high abundance of 2,4-dialkylbenzo[*b*]thiophenes relative to other isomers in sediments and oils[58]. The maturity sequence suggested for highly branched isoprenoid thiophenes[64] supports this pathway; only the most mature kerogens in this sequence (Jurf ed Darawish) contain highly branched isoprenoid benzo[*b*]thiophenes. Intermediate nonaromatic structures, which are expected if this pathway is correct, are not systematically documented (some of these structures, like thiatetralins, are found in crude oils; see Section III.D).



(16)

Pyrolysis experiments on kerogen (Kimmeridge, U.K.) after preheating at different temperatures for 72 h ('artificial maturation') show systematic decrease of alkylthiophenes and increase of alkylbenzothiophenes as the preheating temperature increased from 250 to 360 °C. This may suggest that such aromatization occurs inside the polymeric structure.

F. Alkyl Chain Cleavage

Most of the sulfur-containing molecules which have been described in mature crude oils are substituted by very short alkyl chains. The loss of such side chains was observed under

artificial thermal stress applied on linear alkyl heterocycles[22], and in natural maturity sequences for isoprenoids and cyclic terpenoids[37].

Other maturity changes, more relevant to crude oils, were discussed in Section III.H.

The use of isotopic fractionation to monitor the changes is a very powerful tool in ^{13}C isotope research[139,140]. Sulfur isotopes are also investigated[104,140,141], but since most particulars of the processes are not known in detail and the fractionation is very much influenced by external parameters, it is not yet possible to reach definite mechanistic conclusions from this information.

All the major transformations given above, as well as external influences such as oxidation (to sulfoxides), biodegradation and water washing[7,37], combine together to give the drastic change observed in the character of organic sulfur in the geosphere. This is also accompanied by the 'classical' maturation effects on other functional groups, such as decrease in the H/C, O/C and N/C ratios by loss of H_2O, CO_2, CH_4 and NH_3, and result in a gradual erasure of the biogenic character of organic matter in the geosphere[1].

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